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The Role of Pubertal Development in Adolescent Risky Decision-Making

By

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Abstract

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Adolescence is a period in development characterized by a greater tendency to engage in risky behaviors. The onset of adolescence is marked by puberty, which involves a dramatic rise in sex steroids. Existing neurobiological models have proposed that the rise in sex steroids during puberty influences the development of the adolescent brain, in particular the brain regions involved in the processing of socio-emotional information. According to these models, adolescents engage in more risk taking compared to children and adults because they process rewards differently and are more sensitive to their social environment. In a separate line of research, it has been hypothesized that changes in sleep during adolescence also contribute to the greater tendency to take risks. In this dissertation, we explored the role of pubertal hormones, social information, and sleep in adolescent risky decisions. To measure risk taking, we designed a child-friendly probabilistic decision-making game called the Jackpot task. In this task, participants could choose to take a risk or play it safe based on explicitly provided information about the risk level and stakes involved in their decision, and the type of cumulative performance feedback (social or monetary) they received. This task was administered in two independent samples of adolescents while they were lying in an MRI scanner, which allowed for examination of the reward-related brain processes associated with their risky choices. Pubertal hormone levels were measured based on saliva provided by the participants. Sleep was measured using a self-report questionnaire that was administered across five days. Participants also filled out various measures to capture individual differences in personality. While we did not find evidence for a peak in reward-related brain activation during adolescence, we did find large individual differences among adolescents in their behavior as well as their neural responses to rewards and social information. Reward-related brain responses associated with risk taking corresponded with higher levels of testosterone and stronger self-reported approach tendencies. The influence of social feedback, in the context of risky decisions, was stronger in girls with higher levels of estradiol and girls who reported greater susceptibility to peer influence. Adolescent girls with a preference for later bedtimes and with more irregular sleep patterns tended to make more risky decisions. These findings provide insight into some of the factors that contribute to adolescent risk taking and highlight the importance of using an interdisciplinary approach to investigate adolescent behavior.

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Other Co-authored Publications

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Moor, B. G., Op de Macks, Z. A., Güroğlu, B., Rombouts, S. A., Van der Molen, M. W., & Crone, E. A. (2012). Neurodevelopmental changes of reading the mind in the eyes. *Social Cognitive and Affective Neuroscience, 7*(1), 44–52. doi:10.1093/scan/nsr020

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Introduction

> *"The natural adolescent inclinations toward novelty, arousal, and excitement that emerge in association with puberty create an emotional tinderbox in which passions—both negative and positive—are ignited. This creates both a great deal of vulnerability among the young as well as a great opportunity to harness these emotions in the service of positive goals. And young people are often eager to face a great deal of risk to achieve the high-intensity feelings that can be so appealing in adolescence."*
>
> —Ronald E. Dahl, Annals of the New York Academy of Sciences (2004)

Adolescence is a critical time of change. During this developmental period between childhood and adulthood, adolescents undergo a complete physical, psychological, and social transformation. Adolescents experience a growth spurt, develop secondary sex characteristics, and become sexually mature. The adolescent brain continues to develop and even undergoes reorganization, resulting in the rapid accumulation of cognitive abilities and altered emotional experiences. Adolescents seek autonomy and become more in tune with their social environment; they spend less time with their parents and more time with their peers, the nature of their friendships changes, and they pursue romantic relationships. By the time they reach adulthood, adolescents have transformed from a dependent child into a self-sufficient individual.

These developmental changes allow for the appearance of adolescent-typical behaviors, such as the greater tendency to take risks. The engagement in risky behavior during adolescence causes morbidity and mortality rates to be relatively high despite a peak in physical health and cognitive abilities (Dahl, 2004). At the same time this critical stage of development is a period in which adolescents can gain valuable experiences by means of exploration. Hence, the tendency to engage in novel and sometimes also risky behaviors in adolescence might be adaptive (Peper and Dahl, 2013).

In the past decade, various neurobiological models have been proposed to explain the developmental increase in risk taking. According to the triadic model, adolescent risk taking results from (1) an overactive approach system, mediated by increased striatum activation in response to potential rewards, and (2) an underactive avoidance system, mediated by decreased amygdala activation in response to aversive aspects of a decision, in combination with (3) the reduced ability to regulate the overactive approach system due to the not-yet-fully-developed prefrontal cortex (Ernst, Pine, & Hardin, 2006; Ernst, Romeo, & Anderson, 2009; Ernst and Fudge, 2009; Ernst, 2014). Dual-systems models have proposed that risk taking results from a discrepancy in the development of different brain regions involved in risky decisions, which is particularly pronounced in adolescence. Specifically, these models suggest that limbic brain regions involved in the processing of emotions (e.g., nucleus accumbens) develop more rapidly than prefrontal brain regions involved in the regulation of these emotions. Consequently, adolescents are inclined to experience increased reward sensitivity and seek sensational experiences, which are pursued impulsively due to a lack of self-regulation (Casey, Jones, & Hare, 2008; Somerville, Jones, & Casey, 2010; Somerville and Casey, 2010; Casey, Jones, & Somerville, 2011; Steinberg, 2004, 2005, 2010). While there is evidence for a developmental mismatch in the structural development of subcortical and prefrontal brain

regions in adolescence (Mills et al., 2014), this discrepancy has not yet been related to self-reported risk and sensation-seeking tendencies.

Both the triadic and dual-systems models suggest that adolescents experience elevated positive emotions, as evidenced by hyper-activation of reward-related brain regions compared to children and adults that motivate them to engage in risk taking (Galvan, 2010). However, based on studies that demonstrated *hypo*-activation of reward-related brain regions in adolescents, it has also been suggested that adolescents engage in risk taking *to* elevate mood (Bjork et al., 2004, 2010; Bjork and Pardini, 2014). Furthermore, adolescents demonstrate individual differences in the engagement of risk taking (Galvan et al., 2007), and in the impact of those risky behaviors on mental health outcomes (Crone and Dahl, 2012). Thus, while there may be a biological basis for the inclination toward risk taking, other environmental factors play an important role as well.

The importance of social environment

Environmental factors that seem particularly influential in adolescence are of social nature. According to the social-information processing network (SIPN) model (Nelson et al., 2005), adolescents become more motivated by social goals, such as the attainment of high social status among peers, due to the development of brain regions that specialize in the processing of social information. Specifically, this model proposes that changes in adolescent motivations and behavior result from neurodevelopmental changes in brain regions involved in social cognition (i.e., the detection node), emotion processing (i.e., the affective node), and cognitive-regulation (i.e., the cognitive-regulation node).

Similarly, dual-systems models—proposed to explain why risk taking in adolescence often occurs in the presence of peers—suggest that adolescent brain development is characterized by changes in brain regions that process socio-emotional information on the one hand, and brain regions that regulate the motivation to engage in socially rewarding behavior on the other hand (Steinberg, 2008). As a consequence, the potential benefits of engaging in risky behavior are amplified by social factors and this motivational tendency is poorly regulated, particularly in the presence of peers. Another perspective, based on the belief that adolescents are capable of engaging in goal-directed behavior, is that adolescents are more attuned to socio-emotional information and regulate their behavior to accomplish social goals, such as engaging in risk taking to impress peers (Crone and Dahl, 2012).

Together, these models suggest that changes in the adolescent brain cause social cues to be particularly salient in adolescence, and social goals (e.g., to impress peers) strengthen the tendency to take risks.

The role of puberty

A common idea across most of the existing neurobiological models is that puberty, the biological process that marks the onset of adolescence (Dahl, 2004), plays an important role in adolescent brain development. Specifically, these models suggest that the rise in gonadal hormones (i.e., sex steroids) during puberty influences the development of brain regions involved in socio-emotional information processing, but not the brain regions involved in cognitive-regulation, which show a more protracted, age-related developmental trajectory (Nelson et al., 2005; Steinberg, 2008; Somerville, Jones, & Casey, 2010; Crone and Dahl, 2012). While the rise in sex steroids during

puberty is known to influence the physical changes needed for sexual reproduction, less is known about the influence of these hormones on adolescent neurodevelopment.

Originally it was thought that the brain was organized under the influence of sex steroids released during the first year of life. The neural networks established early in life were then activated by the sex steroids released during puberty. More recently however, animal research, particularly in rodents, demonstrated that sex steroids at puberty also play a role in establishing the neural networks, and not just activating them (Schulz and Sisk, 2006). Based on these findings, it has been hypothesized that puberty may be important for the reorganization of the human brain as well (Sisk and Zehr, 2005; Schulz, Molenda-Figueira, & Sisk, 2009).

The neuroendocrine changes associated with puberty are thought to influence the motivations of adolescents and determine which types of information are salient to them. The subsequent interaction of these endogenous changes with exogenous or environmental influences (e.g., social factors) is thought to shape adolescent behavior (Schulz, Molenda-Figueira, & Sisk, 2009). As such, the relatively transient biological event of puberty (~5 years) instigates a cycle of psychological and behavioral changes that occur throughout the 10 to 15 years that humans spend in adolescence, and can even have life-long consequences (Crone and Dahl, 2012). However, it should be noted that not all brain changes during adolescence are steroid-dependent (Spear, 2000; Sisk and Foster, 2004), indicating that puberty cannot account for all adolescent-typical behavior.

In accordance with the hypothesis that adolescence represents a (second) period in development of enhanced brain plasticity, an increasing number of studies have shown that pubertal hormones are indeed associated with structural brain changes during adolescence (Herting et al., 2014, 2015; Goddings et al., 2014; Menzies et al., 2015). Furthermore, pubertal hormones have been associated with behavior changes, such as the increase in risk taking, and associated changes in brain function (Peper and Dahl, 2013; Braams et al., in press). Again, it should be noted that not all brain changes are puberty-related; some developmental processes are age-related, or can be explained by an interaction between age and puberty (Goddings et al., 2014).

Together, these findings suggest that adolescence is a time of neural reorganization—influenced in part by pubertal hormones—and enhanced sensitivity to the social environment, which leads to altered psychological experiences and the engagement in adolescent-typical behaviors, such as increased risk taking.

Contributions of sleep

Sleep deprivation is thought to be another contributing factor of the increase in risk taking during adolescence (Shochat et al., 2014). Adolescents are particularly prone to sleep deprivation. While biological factors associated with puberty give rise to the inclination to go to sleep later at night, social factors also play a role (Carskadon, 1990; Carskadon et al., 1993). For example, earlier school start times impose earlier rise times, and the engagement in social activities at night—often involving melatonin-suppressing electronics—prevents adolescents from going to sleep (Owens, 2014). Together, these biological and social influences contribute to the adolescent-typical pattern of chronic sleep deprivation (McKnight-Eily et al., 2011), which is particularly prevalent in adolescent girls (Eaton et al., 2010; Vallido et al., 2009).

Previous studies have shown that sleep deprivation impacts behavior, including decision-making (Carskadon et al., 2004). Adolescents who reported more sleep problems (Thomas et al., 2015), or shorter sleep durations on weeknights (Meldrum and Restivo, 2014) tended to report more risky behaviors. For example, adolescents who received insufficient sleep (less than 8hrs), compared to adolescents who slept at least 8hrs, were more likely to exhibit health-risk behaviors, such as smoking cigarettes or marijuana, using alcohol, engaging in sexual activity, and consuming unhealthy beverages (McKnight-Eily et al., 2011). Aside from shorter sleep durations, inconsistency in the sleep patterns between week and weekend nights also contributed the engagement in risky behaviors, such as substance use and truancy (Pasch et al., 2010). Furthermore, adolescents who are evening types were more likely to report being sensation seeking compared to morning types (Muro et al., 2012). Lastly, later bedtimes and/or shorter sleep durations predicted the engagement in delinquent behavior (Peach and Gaultney, 2013) and the prevalence of violent behaviors at school (Hildenbrand et al., 2013). Together, these findings suggest that a lack of sleep and irregularities in sleep patterns across the week increase susceptibility to engage in risky behaviors in adolescence.

It has been hypothesized that sleep changes in adolescence contribute to increased risky behaviors through their influence on reward-related brain processes (Hasler and Clark, 2013; Hasler et al., 2014). Indeed, a neuroimaging study in a sample of early adolescents has shown that individual differences in sleep duration and reported sleep quality were associated with differences in the ventral striatum response to monetary rewards during a card guessing game (Holm et al., 2009). In another study, adolescents who reported poorer sleep quality demonstrated less cognitive regulation and enhanced reward-related brain processes, as well as reduced functional connectivity between the regions involved in cognitive regulation and reward processing, which in turn resulted in them taking more risks (Telzer et al., 2013). Furthermore, larger shifts in sleep midpoint (i.e., the number of minutes after midnight at which the midpoint of total sleep time falls) between week and weekend nights corresponded with reduced medial prefrontal cortex and striatum activation in response to monetary rewards (Hasler et al., 2012). Lastly, individual differences in the reward circuitry have been associated with particular circadian genes (Forbes et al., 2012). Together, these findings suggest that changes in sleep during adolescence impact the way they process information necessary to make decisions, which in turn may lead to increased risk taking, although there might be individual differences in the susceptibility to these changes.

Scope of the dissertation

The goal of this dissertation is to provide insight into why adolescents take risks. We explored the relation of adolescent risk taking (and associated brain processes) with puberty, social influences, and sleep. Furthermore, we aimed to gain insight into the complex interplay between these factors during adolescence. We used functional magnetic resonance imaging (fMRI) and designed a child-friendly decision-making task, which we administered in two independent samples of adolescents.

In Chapters 1–3, we explored the role of pubertal development in adolescent risk taking and associated brain processes. We focused on reward-related brain regions, such as the ventral striatum (VS) and more specifically the nucleus accumbens (NAc), based on a large body of research that suggests that changes in reward circuitry contribute to the

increase in risk taking during adolescence (for a review, see Galvan, 2010). In Chapter 1, we report the results of a cross-sectional study in a sample of Dutch adolescent boys and girls (aged 10–16yrs). In this study, we tested whether individual differences in the VS response to rewards during risk taking were associated with individual differences in sex steroids (testosterone and estradiol) associated with puberty, while controlling for age. In Chapter 2, we report the cross-sectional results based on the same sample of Dutch adolescents mentioned in Chapter 1 and an additional sample of young adults. The goal of this study was to identify contributing factors of individual differences in risk taking and associated reward-related brain processes by investigating their relations with age, self-reported pubertal maturation, and differences in self-reported approach tendencies. Furthermore, we report the longitudinal results based on the same adolescents, tested again two years later. This study focused on explaining the developmental changes in risk taking and associated reward-related brain processes. In Chapter 3, we set out to replicate the relation between testosterone and reward-related brain processes during risk taking (as reported in Chapter 1) in a separate sample of 11–13-year-old adolescent girls from the United States. In this cross-sectional study, we focused on differences in the NAc response to rewards during risk taking.

In the remaining chapters of the dissertation, we explored the role of other social factors in adolescent risk taking and associated brain processes based on the same sample reported in Chapter 3. In Chapter 4, we examined whether social information provided during decision-making modulated risk taking and reward-related brain processes. In Chapter 5, we investigated the relation between sleep in risk taking. Additionally, we tested whether pubertal development enhanced the influence of social information on risk taking, and the relation between sleep and risk taking.

Chapter 1. Testosterone levels correspond with increased ventral striatum activation in response to monetary rewards in adolescents

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Introduction

The onset of adolescence heralds a period of vulnerability—a time in development when natural tendencies to explore and take risks leads to a sharp increase in risky behaviors with a myriad of negative health consequences (Institute of Medicine and National Research Council, 2011). Yet, it is equally important to recognize that most youth navigate this developmental period quite well, and that a great deal of the exploration and risk-taking that occurs in adolescence is normative and can contribute to learning, discovery and positive development.

For these reasons there is growing interest in understanding at a deeper, more mechanistic level, normative developmental processes that underpin some of these maturational changes and may provide insights into the risks and vulnerabilities during adolescence. There has been particular interest in sensation seeking which appears to increase in association with pubertal maturation (Steinberg, 2008; Forbes and Dahl, 2010). Sensation seeking is regarded as a personality trait that is related to risk-taking behavior (Llewellyn, 2008). Sensation seeking not only peaks in adolescence, but also girls reach their peak at a younger age than boys (Romer and Hennessy, 2007), possibly due to sex differences in pubertal maturation. One study that replicated this developmental peak in risky behavior in an experimental setting showed that the preference for risk taking peaks at around age 14 (Burnett et al., 2010).

Developmental peak in reward sensitivity

The focus of a second line of research is on developmental changes in reward processing in adolescence, often assessed using risk-taking paradigms, and thought to be associated with risk-taking behavior (e.g., Van Leijenhorst et al., 2008, 2010a). The adult literature using such paradigms has shown that the striatum is sensitive to (monetary) rewards (Breiter et al., 2001; Delgado, 2007; McClure et al., 2004). Developmental studies have shown that in response to rewards, adolescents recruit similar brain regions (including the striatum) as children and adults. However, the extent to which these brain regions are recruited differs across age groups (Geier and Luna, 2009). Based on contradicting results in the field of developmental neuroimaging, two opposing models have been proposed to describe the nature of reward processing in typically developing adolescents; one model proposes that adolescents recruit reward-related brain regions, such as the striatum, to a lesser extent than children and adults (Bjork et al., 2004), the

other model proposes that adolescents recruit these brain regions to a greater extent (Ernst et al., 2005; Galvan et al., 2006; Geier et al., 2010; Van Leijenhorst et al., 2010a, 2010b). However, the convergence of evidence appears to support the model that specifically at the moment of receiving a reward, the striatum response is stronger in adolescents compared to children and adults (Galvan, 2010), suggesting that the adolescent inclination to take risks might be associated with increased sensitivity to rewards, as indicated by an adolescent-specific peak in activation of the striatum.

Pubertal maturation, gonadal hormones, and reward processing

According to Nelson et al. (2005) changes in affective processing during adolescence (e.g., reward processing and reorientation to peer social stimuli) may be associated with the increase of gonadal hormones at puberty that influence neural processing in the limbic brain regions, such as the striatum (see SIPN model: Nelson et al., 2005). This model suggests that changes in gonadal hormone levels (or different levels of puberty) are associated with changes in the magnitude and/or extent of the response to reward, specifically in the striatum. Thus, heightened sensitivity to rewards in adolescents could be related to structural and neurochemical changes that are unique to the adolescent brain. However, the exact nature of these changes, the relation with gonadal hormones, and how they affect motivational behavior in adolescents is not yet well understood (Doremus-Fitzwater et al., 2010). Therefore, our goal was to directly test the relationship between gonadal hormone concentrations and activity in the striatum in response to reward outcomes in adolescents across different stages of puberty.

Previous studies have shown in adults that the exogenous administration of testosterone increases the likelihood of disadvantageous or risky decision-making. More specifically, when performing the Iowa gambling task, higher testosterone levels lead participants to choose more often from card decks that resulted in large (as opposed to moderate) monetary rewards, despite a net monetary loss. This was interpreted as testosterone contributing to a shift to less punishment sensitivity and relatively greater reward sensitivity (Van Honk et al., 2004). Another study in adults that administered testosterone and focused on neural processing during reward anticipation showed that higher testosterone levels resulted in increased striatal activity (Hermans et al., 2010). Similar results were found in adolescents at different pubertal stages; the natural occurrence of higher testosterone levels corresponded with increased striatal activity during reward anticipation, but with decreased striatal activity during reward outcome processing (Forbes et al., 2010), suggesting that the relation between testosterone and striatal activity differs depending on the phase of risky decision making. Few studies have investigated the relation between estradiol, a pubertal hormone that is indicative of pubertal development in girls, and reward processing. However, it has been found that reward processing changes with menstrual cycle phase (Dreher et al., 2007).

Present study

In this fMRI study, we investigated the relation between reward processing and gonadal hormones in adolescent boys and girls. We used the Jackpot gambling task, in which participants could actively choose whether to take a (low or high) risk or not (i.e., skip the trial), and when they chose to take the risk participants received feedback indicating whether they had won or lost (10 Eurocents). This task design has several

advantages above passive gambling paradigms, as reward-related activity in the striatum is modulated by perceived control (Rao et al., 2008; Zink et al., 2004) and willingness of the participant to take a risk (Tricomi et al., 2004). Based on the previous findings showing that striatum activation peaks in mid-adolescence (e.g., Van Leijenhorst et al., 2010a), and that testosterone is associated with striatal activity during reward processing (Hermans et al., 2010; Forbes et al., 2010), we hypothesized that individual differences in gonadal hormone levels at different stages of puberty correlate with individual differences in reward-related activity in the striatum.

Material and Methods

Participants

In this study, 50 healthy, right-handed adolescents participated. All participants were aged between 10 and 16 years, 17 boys (*M* age = 13.5, SD = 2.3) and 33 girls (*M* age = 12.9, SD = 1.8). The sample of girls was doubled relative to the boys, because less variation in testosterone levels was expected. Prior to enrollment, participants were screened for psychiatric or neurological conditions, history of head trauma, and history of attention or learning disorders. Parents of the children filled out the Child Behavior Checklist (CBCL; Achenbach, 1991) to screen for psychiatric symptoms. All participants scored below clinical levels on all subscales of the CBCL.

All participants and their parents gave written informed consent, and participants were instructed and prepared for scanning in a quiet room with a mock scanner, which was used to explain the scanning procedure. The study was approved by the local Medical Ethical Committee.

Pubertal assessment

Participants were asked to complete two self-report measures of pubertal maturation, as well as to provide saliva samples to test for gonadal hormone levels. The self-report scales were (1) the picture-based interview about puberty (PBIP; Shirtcliff et al., 2009), and (2) the Pubertal Development Scale (PDS; Petersen et al., 1988). The PBIP consists of an interview with a research assistant about changes that happen when you grow up, with the assistance of a script and photographs. After this conversation, the research assistant leaves the room while participants report their assessment of their pubertal stage based on the presented photographs. Scores could range from 1 to 5, where "1" corresponds with no physical signs of puberty, and "5" corresponds with (seemingly) completed physical development. The PDS consists of five questions about physical development, where scores range from 1 (no physical changes) to 4 (development seems complete). Prior research has shown that the reliability of the PDS was high (α = .77 for boys, α = .81 for girls), and has demonstrated that the self-report data provide similar or even better indices of pubertal maturation than when the assessment was done by a nurse practitioner in the form of a physical examination, possibly because self-assessments are based on more continuous judgments as opposed to a one-visit decision (Shirtcliff et al., 2009).

Saliva was obtained by passive drool (Shirtcliff et al., 2001); each participant was requested to collect six saliva samples across two consecutive days, at fixed times in the evening (at 8, 8:30, and 9pm). These samples were collected at home, and stored in a fridge or freezer until participants brought them in on the day of the MRI scan. Collected

samples were immediately stored in a freezer at the university to prevent deterioration, and after collection was completed all samples were transported to an external institute where they were analyzed. For each participant, saliva was assayed for testosterone, estradiol, and dehydroepiandrosterone (DHEA), a precursor to the gonadal hormones. The mean hormone levels across the three samples that were collected each day correlated highly between the two days for both testosterone ($r = .93$, $p < .001$), estradiol ($r = .86$, $p < .001$), and DHEA ($r = .83$, $p < .001$), indicating that hormone levels were relatively stable across days, and hence a reliable indicator of the participant's basal hormone level. In the current study, the main focus was on testosterone, as this measure is most valid in both boys and girls (Shirtcliff et al., 2000). The self-report measures of pubertal status were used to validate the hormone measures (see also Shirtcliff et al., 2009).

Experimental task

While lying in the scanner, participants performed the Jackpot Gambling Task, an active gambling task in which participants could choose to take a (small or large) risk (i.e., to play) or not take a risk at all (i.e., to skip or reset the trial). On each trial, a slot machine was presented with two out of three slots showing two similar fruit types (e.g., 2 plums). In a yellow frame presented above the slot machine, three possible outcomes for the third slot were shown. In the low-risk condition, participants had a 67% (2/3) chance that the third slot would show a similar fruit type; in the high-risk condition, the chance was 33% (1/3). Based on this information, participants could choose to play (i.e., spin) or to skip the trial (i.e., reset). Upon selecting "spin", the outcome could be positive (i.e., monetary reward) or negative (i.e., monetary loss); upon "reset", the outcome was neutral (i.e., no monetary reward/loss; Fig. 1).

Participants were given 2 Euros to play; if participants won, 10 Eurocents were added, and if participants lost, 10 Eurocents were deducted. If participants chose to reset, no money was won or lost. Participants were told that they would be paid according to the final outcome at the end of the experiment.

Each trial started with a fixation cross, which was presented in the middle of the screen. Fixation was followed by the stimulus presentation (3000ms), during which the participant had to select a choice (spin or reset). After a choice was made (i.e., by button press), feedback was given (reward, loss, or reset) for 2000ms, before the next trial started (Fig. 1). If no response was given within the specified timeframe, the text "too slow!" was presented. Periods of fixation lasted between 1 and 6s, jittered in increments of 500 and 1000ms. In each condition, the choice to spin resulted in positive feedback in 50% of the trials, or negative feedback in 50% of the trials (independent of the presented risk). This was done to have a similar number of observations for reward and loss trials.

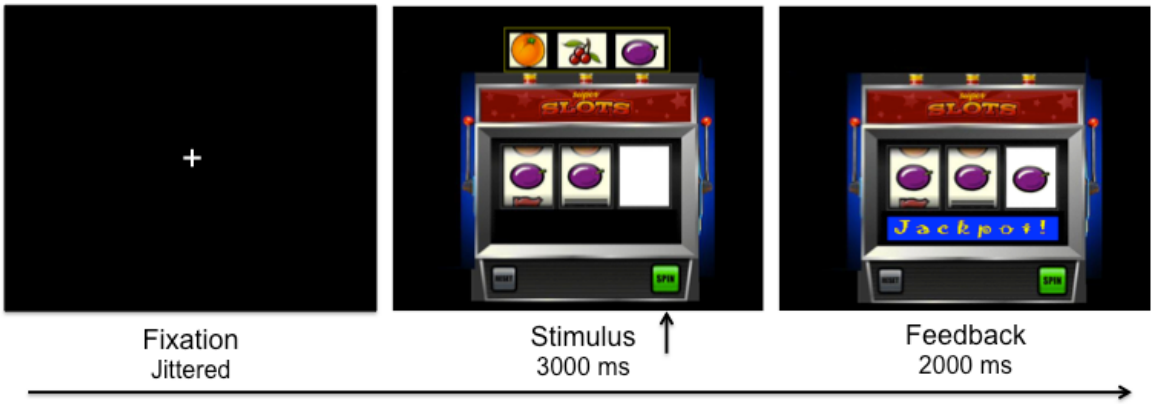

Fig. 1. The Jackpot gambling task. Example of a high-risk trial in which the participant chooses to spin (by a right button press) and wins (i.e., receives a monetary reward).

MRI data acquisition

Fifty trials (20 low-risk; 30 high-risk) were presented in total, over the course of one event-related scan that lasted approximately 5 minutes (1 run). The visual stimuli were projected onto a screen that participants could see via a mirror attached to the head coil. Scanning was performed using a standard whole-head coil on a 3 Tesla Philips scanner. Functional data were acquired using a T2*-weighted gradient-echo echo-planar pulse sequence (38 contiguous 2.75 mm oblique axial slices, using interleaved acquisition, TR = 2.2 s, TE = 30 ms, 2.75 x 2.75 mm in-plane resolution, 140 volumes per run). The first two volumes of each scan were discarded to allow for T1-equilibration effects. High-resolution T2*-weighed images and high resolution T1 anatomical images were collected at the end of the scan session. Head motion was restricted due to foam inserts that surrounded the head. Average head movement was .09 mm (SD = .05) for boys and .09 mm (SD = .05) for girls, and there were no significant sex differences in head motion ($p > .05$).

fMRI preprocessing and statistical analysis

Data preprocessing and analysis were conducted using SPM5 (Wellcome Department of Cognitive Neurology, London). Images were corrected for differences in timing of slice acquisition, followed by rigid body motion correction. Functional volumes were spatially normalized to echo planar imaging templates, respectively. The normalization algorithm used a 12-parameter affine transformation together with a nonlinear transformation involving cosine basis functions. During normalization the data was re-sampled to 3-mm cubic voxels. Templates were based on the MNI305 stereotaxic space (Cocosco et al., 1997). Functional volumes were smoothed with an 8-mm full-width at half maximum isotropic Gaussian kernel.

Statistical analyses were performed on individual subjects' data using the GLM in SPM5. In the whole-brain analysis, reward and loss outcomes were modeled as single events with zero duration at the onset of the presentation of the outcome. High risk and low risk outcomes were modeled separately, and collapsed in the analysis. Reset trials and trials on which the participant did not respond within the 3-sec time frame were modeled separately and were not included in the contrasts because on these trials participants did not receive feedback; they did not win or lose money after they had selected "reset" (i.e., chose *not* to play, or not to take a [low or high] risk), as opposed to

when they chose to play, and selected "spin". Only in the latter case did participants receive feedback indicating either monetary gain or loss.

Whole-brain analyses tested the contrast reward > loss which was computed across all participants, and for boys and girls separately. A two-sample t-test was performed to examine whether there were sex differences in neural activation to reward > loss. Because the time-course, physiology, hormones, and component physical changes of pubertal maturation differ markedly for boys and girls (Dorn et al., 2006), all analyses were performed separately for each sex, so that testosterone, estradiol, and DHEA levels were added as regressors to the reward > loss contrast for boys and girls separately. Task-related responses were considered significant if they consisted of at least 10 contiguous voxels that exceeded an uncorrected threshold of $p < .001$, unless otherwise specified.

To further describe patterns of activation, we used the MarsBaR toolbox for use with SPM5 to perform region of interest (ROI) analyses.

Results

Task performance

Performance (i.e., risk taking) was measured as the percentage of spinning trials, and compared across task conditions. As predicted, participants chose to play more often on low-risk trials (mean = 90.4%) than on high-risk trials (mean = 37.3%; $F(1, 49) = 162.95$, $p < .001$). No significant sex differences in choice selection were found; both boys and girls selected "spin" more often in the low-risk (LR) condition compared to the high-risk (HR) condition, and did so to the same extent (boy vs. girl for LR: 91.5 % vs. 89.8 %, for HR: 31.0 % vs. 40.6 %), $F(1, 48) = .99$, $p > .05$ (Fig. 2). Three boys and 3 girls never selected "spin" or selected "spin" only once or twice, after which they received only positive (reward) or negative (loss) feedback in the high-risk condition. For these participants the contrast reward > loss could not be calculated for the high-risk condition, and they were thus excluded from the analysis. This resulted in a sample of 14 boys (*M* age = 13.4, SD = .56) and 30 girls (*M* age = 12.9, SD = .38). There was no significant age difference between these groups, $F(1, 42) = .38$, $p > .05$.

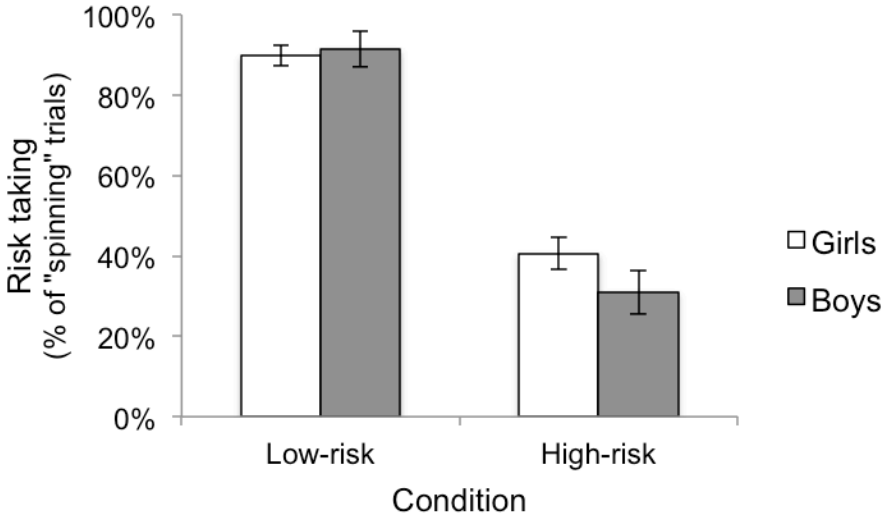

Fig. 2. Risk-taking behavior. Percentage of "spinning" trials in both low-risk (LR) and high-risk (HR) conditions, plotted for boys and girls separately.

Hormone results

Table 1 shows the average PDS and PBIP puberty scores, and overall mean levels of testosterone, estradiol, and DHEA for boys and girls separately.

Table 1. Puberty measures for boys and girls separately. Upper: Means (SD) for self-report and hormone measures. Lower: Bivariate correlations.

	Boys (n = 14)	Girls (n = 30)
Puberty measures:		
PDS	2.00 (.92)	2.46 (.81)
PBIP	2.96 (1.47)	3.10 (.97)
Testosterone*	26.11 (27.39)	14.48 (16.10)
Estradiol	4.79 (3.94)	5.30 (3.96)
DHEA	114.65 (69.35)	144.30 (96.93)
Bivariate correlations (Pearson *r*):		
PDS-PBIP	.886**	.718**
PDS-Testosterone	.786**	.385*
PDS-Estradiol	.801**	.508**
PDS-DHEA	.902**	.426*

* Significant at $p < .05$. ** Significant at $p < .01$.

Average PDS score did not differ significantly between boys (mean = 2.0) and girls (mean = 2.5, $p > .05$), and similarly average PBIP score demonstrated no significant differences between boys (mean = 3.0) and girls (mean = 3.1, $p > .05$; Table 1). Furthermore, because both measures (PDS and PBIP) correlated highly with each other for both boys ($r = .89$, $p < .01$) and girls ($r = .72$, $p < .01$; Table 1), only one measure (i.e., average PDS score) was selected and used for further analyses.

Next, we tested for sex differences in gonadal hormone levels. As predicted, testosterone levels were significantly higher in boys than in girls, $t(42) = 1.77$, $p = .04$. Estradiol levels and DHEA levels did not differ significantly between boys and girls (both p's > .05).

Correlations were computed between PDS scores and salivary hormone levels for boys and girls separately. These correlations were significant for testosterone, estradiol and DHEA (Table 1), indicating that the hormone levels assessed by saliva samples provided a sensitive index of puberty level. Given that testosterone level is the most reliable measure for both boys and girls, and previous studies had shown an impact of testosterone on neural systems of reward anticipation, analyses mainly focused on testosterone for testing for neural correlations in both groups. In addition, estradiol level was used to test for neural correlations in girls only (this measure has previously been found to be non-reliable for boys; Shirtcliff et al., 2009). Together, these relations set the stage for examining neural activation patterns in the Jackpot task, and how this activation is related to gonadal hormone levels.

Reward processing: main effects

First, we conducted a GLM analysis on the functional data modeled at the onset of the feedback presentation, and computed the voxelwise contrast of reward > loss averaged across high-risk and low-risk trials. The analysis was first performed across all participants, and then for boys and girls separately. The whole-brain analysis including all participants resulted in several areas of activation, particularly in reward-related brain regions including the dorsal and ventral striatum, and the medial orbitofrontal cortex (Fig. 3a). Whole-brain results for boys and girls separately resulted in bilateral activation in the striatum in both groups (Fig. 3a). A two-sample *t*-test did not result in different levels of activation in boys versus in girls. An overview of significant clusters and corresponding MNI coordinates are reported in supplementary Table S1.

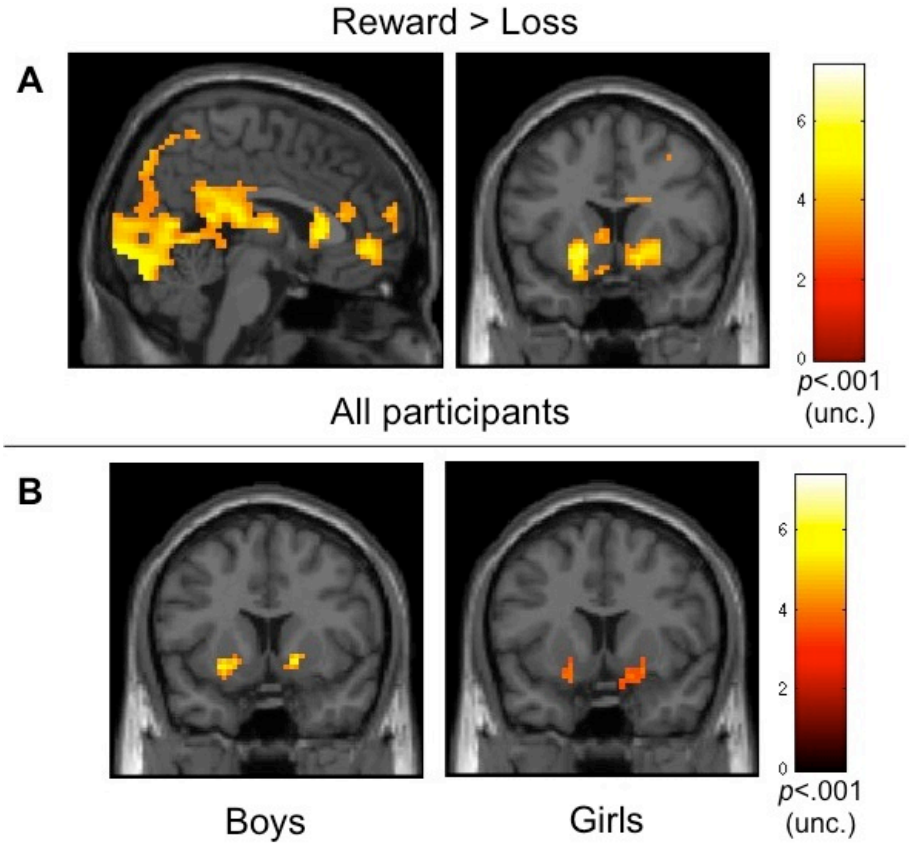

Fig. 3. Whole-brain results for the contrast reward > loss. (a) Regions of activation for all participants included the dorsal and ventral striatum, and the medial orbitofrontal cortex. (b) Regions of activation for boys and girls separately included the bilateral striatum in both groups.

Hormone level as predictor

A whole-brain regression analysis with testosterone level as predictor on the contrast reward > loss in boys (n = 14) showed that boys with higher testosterone levels had more activation in the bilateral ventral striatum (Fig. 4a, left panel). An overview of significant clusters and corresponding MNI coordinates is reported in supplementary Table S2. A similar whole-brain regression analysis with testosterone level as predictor on the reward > loss contrast was performed for girls (n = 30). This analysis did not result in activation at the threshold $p < .001$, but when the threshold was lowered to $p < .005$, activation was observed in the left ventral striatum at a similar location as in boys (Fig. 4a, right panel). An overview of significant clusters and corresponding MNI coordinates is reported in supplementary Table S2. Additionally, results of a whole-brain regression analysis with testosterone level as predictor on the reward > loss contrast including all participants (n = 44; 14 boys, 30 girls) also resulted in robust activation in the ventral striatum. These results are reported in supplementary Fig. S1.

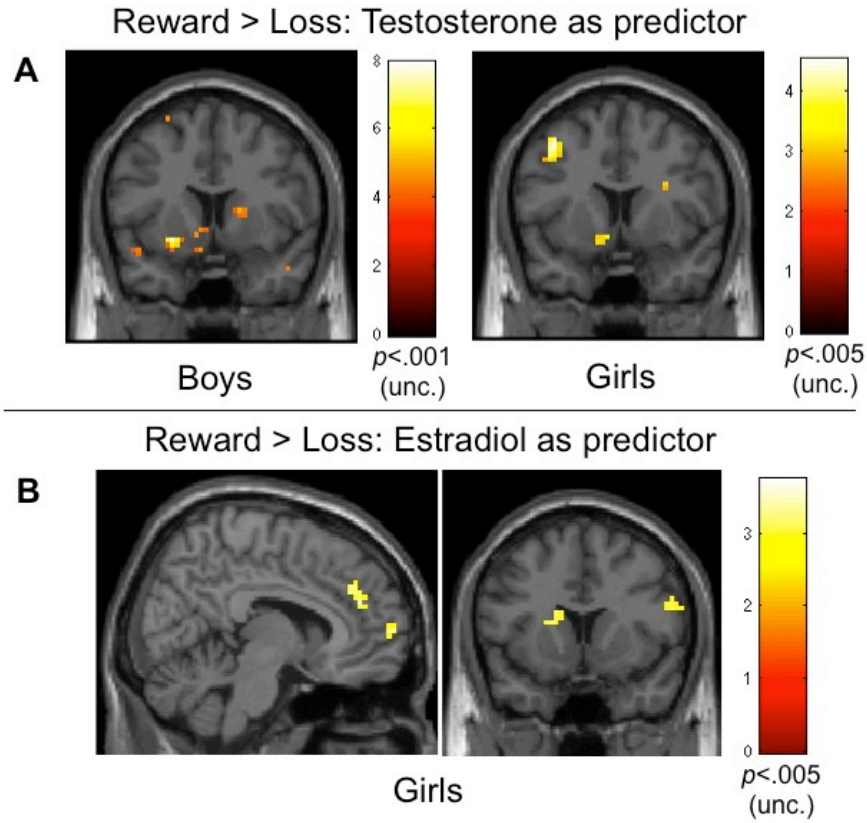

Fig. 4. Results for the regression analyses with gonadal hormones. (a) Regions of activation for reward > loss with testosterone as predictor included the bilateral ventral striatum in boys (left), and left ventral striatum in girls (right), at a threshold of $p < .005$. (b) Regions of activation for reward > loss with estradiol as predictor included dorsal striatum, DLPFC, and medial PFC in girls only, at a threshold of $p < .005$.

To further visualize patterns of activation sphere ROIs with a radius of 6 mm were created for boys and girls separately, based on the peak voxel of activation within the striatum that correlated positively with testosterone level in the specific groups (coordinates: $x = -24$, $y = 9$, $z = -9$ [boys]; $x = -12$, $y = 12$, $z = -12$ [girls]), and for both groups together, based on the point of overlap at $p < .005$ (coordinates: $x = -9$, $y = 9$, $z = -9$). As can be seen in Fig. 5, testosterone level predicted the extent of activation in these several areas of the ventral striatum, such that higher levels of testosterone corresponded with increased reward-related activation in both boys and girls.

Next, we chose to select an ROI in the left nucleus accumbens (coordinates, $x = -9$, $y = 6$, $z = 12$) that was based on a prior study by Van Leijenhorst et al. (2010a), with a radius of 6 mm. This region was chosen because this prior study also concerned a developmental study on risk taking using the same scanner and processing software, and it provides an ROI based on an independent sample. Similarly to our previous results testosterone level predicted the extent of activation in this area of the ventral striatum. Follow-up tests confirmed the whole-brain analyses and resulted in positive correlations for both groups (boys, $r = .75$, girls, $r = .34$, both p's $< .05$).

To test whether testosterone level, and not age, significantly explained individual differences in reward-related activation in the ventral striatum, we conducted a hierarchical regression analysis predicting striatal activation (i.e., parameter estimates from the independent ROI) based on age and testosterone level. Results of this analysis showed that age as a single predictor did not account for a significant proportion of the variance in activation of the ventral striatum in boys, $R^2 = .26$, $F(1,12) = 4.18$, $p = .06$, nor in girls, $R^2 = .00$, $F(1,28) = .00$, $p = .99$. When testosterone level was added to the regression, a significant contribution was made to explaining the variance in reward-related activation for boys, $\Delta R^2 = .31$, $p = .017$, and girls, $\Delta R^2 = .14$, $p = .044$. The model in which striatal activation was predicted by age and testosterone was significant in boys, $F(2,11) = 5.71$, $p = .01$, and tests of the individual regression coefficients showed that only testosterone level explained a significant proportion of the variance in activation in the ventral striatum, $b = .031$, $t(11) = 2.8$, $p = .017$. In girls, the model including both predictors was not significant, $F(2,27) = 2.24$, $p = .126$, however, there was a positive relation between testosterone and striatal activation, $b = .044$, $t(27) = 2.12$, $p = .044$. Despite a significant correlation between testosterone and age in both boys, $r = .58$, $p = .015$, and girls, $r = .41$, $p = .012$, there was no multicollinearity, as indicated by the variance inflation factor (i.e., $\sqrt{VIF} < 2.0$). These results suggest that individual differences in reward-related activation in the ventral striatum can be better explained by testosterone level as opposed to age.

Finally, a whole-brain regression analysis with estradiol level as predictor on the contrast reward > loss was performed in girls (n = 30). This analysis did not result in activation at the threshold $p < .001$, but when the threshold was lowered to $p < .005$, activation was found in the dorsal striatum, DLPFC, and medial PFC (Fig. 4b). An overview of significant clusters and corresponding MNI coordinates is reported in supplementary Table S3.

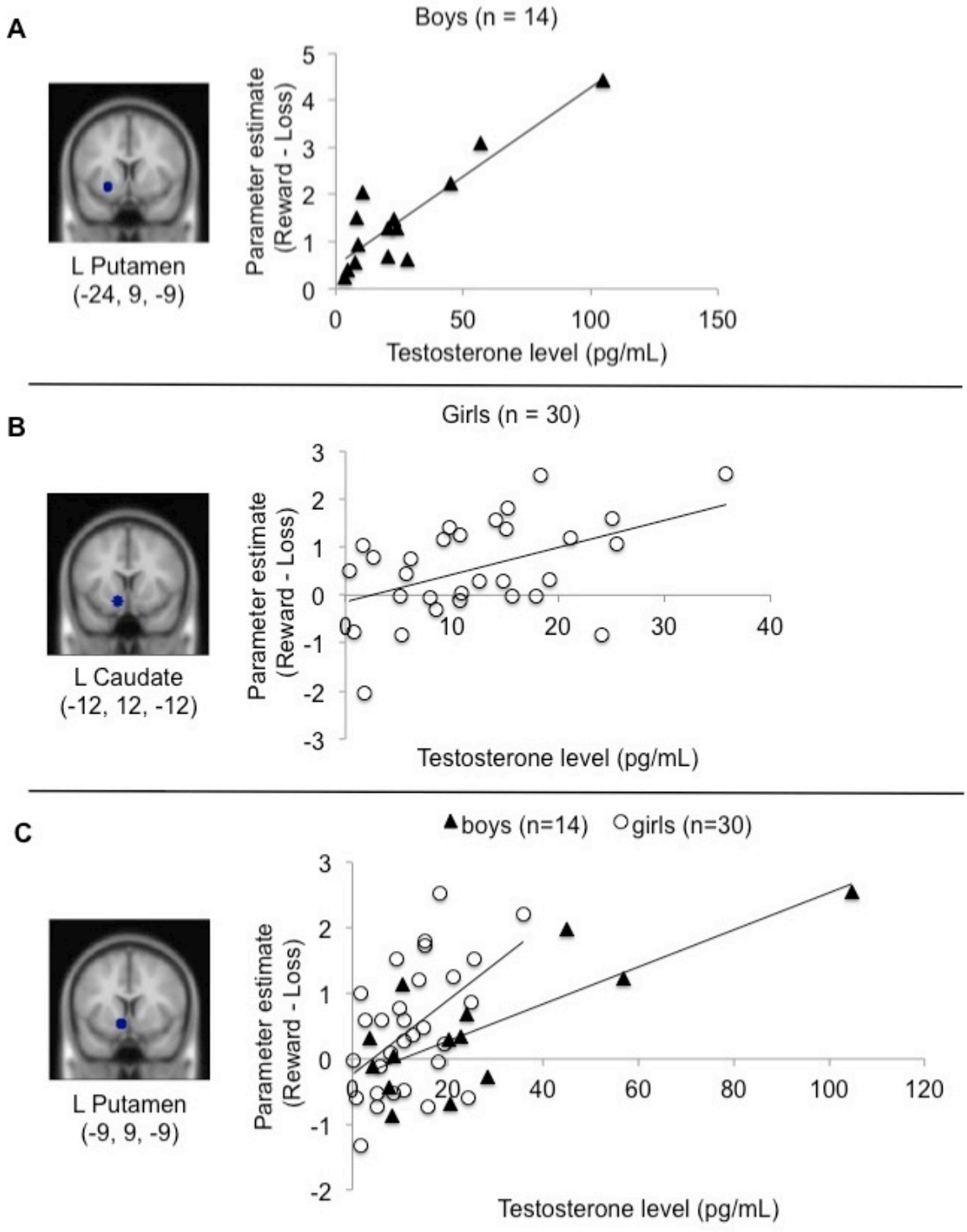

Fig. 5. Results of sphere ROIs (radius 6 mm) based on the peak voxel of reward-related activation that correlates positively with testosterone level for boys in (a) left putamen, for girls in (b) left caudate, and for boys and girls (i.e., overlap in activation) in (c) left putamen.

Discussion

The goal of this study was to investigate the relation between gonadal hormone levels and reward processing in adolescents. To test this, participants provided saliva samples and performed a simple gambling task while in the MRI scanner. During this task participants chose on each trial whether to take a (low or high) risk, or not (i.e., to skip the trial). When they had chosen to take the risk, participants either received or lost a monetary reward.

Girls and boys exhibit similar risk taking behavior

As predicted, participants showed increased risk taking on low-risk trials compared to high-risk trials, and this pattern of behavior was similar for boys and girls. In a prior behavioral study in which participants had to select between a response option with low probability of a high reward and high probability of a small reward (i.e., a forced gamble), boys were found to take more risks than girls. In this study, like the current study, the participants also played for small amounts of money (i.e., 10 Eurocents; Van Leijenhorst et al., 2008). Thus, it is unlikely that the absence of sex differences is related to small rewards per se, but rather, it is likely that the absence of a forced gamble results in different patterns of risk taking.

Girls and boys recruit similar brain areas in response to monetary reward

When participants chose to take a risk and won (i.e., received a monetary reward), they recruited brain areas including the dorsal and ventral striatum, and the medial orbitofrontal cortex (OFC). These brain areas play a key role in reward processing (Haber and Knutson, 2010). Whereas the ventral striatum has been associated with coding for subjective value of reward (Peters and Büchel, 2010), previous studies have shown that in the context of uncertainty (e.g., gambling task) also the dorsal striatum responds to valence (reward or loss) and magnitude of outcomes, showing strongest activation to large monetary rewards, and weakest activation to large monetary losses (Delgado et al., 2003). The medial OFC specifically responds to abstract rewards, such as monetary gain (Kringelbach and Rolls, 2004).

Adolescents showed no sex differences in reward processing; boys and girls displayed similar bilateral activation of the striatum. The absence of sex differences could be because divergence of the sexes in reward processing arises later in development, possibly influenced by puberty-related changes (Sisk and Zehr, 2005; Schulz et al., 2009). However, in this study we did not have enough power (i.e., observations per age group) to test this age by sex interaction. Most importantly, the task elicited strong and robust activation in the ventral striatum in both boys and girls, which sets the stage for the examination of hormone effects.

Gonadal hormone levels correspond with stronger reward-related activation

Results showed that testosterone levels were positively associated with activation in the ventral striatum in response to a monetary reward. Specifically, in the nucleus accumbens it was found that both in boys and girls higher testosterone levels predicted more reward-related activation. In girls this relation was only found at a less stringent threshold but was statistically confirmed using an independent sphere ROI analysis. These findings are in line with Nelson's social information processing network (SIPN)

model, which predicts that affective changes (e.g., changes in reward processing) are associated with changes in limbic brain regions, such as the nucleus accumbens, that are specifically influenced by gonadal hormones (Nelson et al., 2005). Furthermore, neuroanatomical studies have shown that gonadal hormones at puberty are associated with changes in both gray and white matter, with testosterone and estradiol showing differential effects in adolescent boys and girls (Peper et al., 2011). These findings suggest that both functional and structural changes in the brain are associated with individual differences in gonadal hormone levels at puberty.

These findings are also in line with previous literature showing that competition is associated with increased testosterone levels, and more importantly, winning as opposed to losing a monetary reward during a hypothetical competition is associated with a higher increase of testosterone levels (Archer, 2006). Furthermore, high basal levels of testosterone are associated with neurochemical and behavioral changes in response to winning as opposed to losing, whereas low basal levels of testosterone are not (Mehta et al., 2008), strengthening our conclusion that individual differences in testosterone levels at puberty may explain individual differences in the neural response to reward versus loss.

A previous study that also examined the relation between gonadal hormones and activation in reward-related brain regions, such as the striatum, resulted in opposite findings; not only did they find that striatal activity decreased with pubertal maturation, but also that testosterone level was negatively correlated with the neural response to reward (Forbes et al., 2010). A possible explanation for this discrepancy is the difference in experimental paradigms; in Forbes et al.'s study a card-guessing game was used in which participants guessed whether the next playing card would be lower or higher than the stimulus card presented. After participants selected a response, and were shown whether the trial was a possible gain or loss trial (anticipation phase), the next card was shown, followed by feedback that indicated whether they had won ($1), lost ($0.50), or nothing happened ($0; outcome phase). The neural response to reward was measured during the outcome phase, and was time-locked to feedback presentation, indicating gain, loss, or nothing. This occurred separate from, and after the outcome was presented (i.e., the next card). In the Jackpot task outcome (i.e., appearance of fruit in the third slot) and feedback (i.e., appearance of blue or red bar indicating gain or loss respectively) were presented simultaneously, and the neural response to reward was time-locked to this "combined" presentation. Thus, the neural response to reward may have represented different phases of reward processing in these two paradigms, possibly explaining the discrepancy in results. For future research it is important to disentangle the different phases of reward processing, as they also involve activation of different brain regions (Rademacher et al., 2010).

The relation between testosterone and reward-related activation was more robust in boys than in girls, possibly due to lower variability in testosterone level in girls than in boys. Results for estradiol, a more reliable measure of pubertal development in girls (Shirtcliff et al., 2009), also showed a positive relation with reward-related activation in the dorsal striatum, DLPFC, and medial PFC, although again at a less stringent threshold. Interestingly, the relation between reward-related activation with estradiol was in a different set of brain regions, namely those associated with cognitive control (Nelson et al., 2005). Indeed previous studies have shown that cognitive performance (e.g., working

memory) changes across the menstrual cycle (Jacobs and D'Esposito, 2011), suggesting that fluctuations in levels of estrogen (or estradiol) contribute to changes in prefrontal functioning. Also, estrogen-replacement therapy in postmenopausal women protects against cognitive decline across different domains of cognitive functioning, including attention, memory, and reasoning (Sherwin, 2002). These findings support the likelihood that individual differences in estradiol levels are associated with functional differences in brain regions that are involved in cognitive control. However, it is unclear which aspect of cognitive control is influenced by estrogen, and future research is needed to determine which brain regions are involved, and whether these overlap with the regions reported in this study.

Furthermore, these results should be interpreted with caution, because the analyses did not survive strict corrections for multiple comparisons, but provide interesting hypotheses for future research. A possible explanation for the absence of a robust relation between gonadal hormones and reward-related activation in girls, despite showing similar neural responses to reward compared to boys, might be that girls have less stable hormone levels due to the menstrual cycle, or possible measurement errors which are summarized below.

Limitations

One limitation of this study calls for cautious interpretation of the findings, namely that age was correlated with puberty score and testosterone level, possibly confounding the relation between testosterone and striatum activation. Reassuringly, hierarchical regression analyses showed that testosterone, not age, was the best predictor for neural activity in boys and girls. However, future studies should disentangle age and pubertal development by using a more narrow age range, matching girls and boys on age and comparing them across different levels of puberty (see also Forbes et al., 2010).

Future directions

The finding of neural differences in the context of risk taking in adolescents compared to children and adults, or across different stages of puberty is a first step towards understanding how neurodevelopment relates to changes in risk-taking behavior during adolescence. To fully comprehend the association between neural and behavioral changes (i.e., to know *when* neural differences become explicit behaviorally) it is important to note that adolescents make more risky choices for themselves than for others (Crone et al., 2008), that they are especially sensitive to social rewards (Doremus-Fitzwater et al., 2010), and (social) changes in the context of reward. For example, the presence of peers increases risk taking behavior, and the response of the striatum to reward (Chein et al., 2010). For future research, adding social context as factor in the risk-taking paradigm may provide insight into the relation between risk-taking behavior and neural processes.

Conclusion

Results of the present study showed that individual differences in gonadal hormone levels at different stages of puberty were positively associated with individual differences in the neural response to monetary reward, suggesting that the drastic rise of gonadal hormone levels at puberty may contribute to increased reward sensitivity (i.e.,

enhanced striatum response to reward) that is observed in adolescents. Despite that this finding was more robust in boys (for testosterone) than in girls (for testosterone and estradiol), these results provide insight into the underlying mechanism of reward processing, and further our understanding about the role of gonadal hormones in individual neural differences.

Supplementary Materials

Supplementary data associated with this chapter can be found in appendix A.

Chapter 2. A cross-sectional and longitudinal analysis of reward-related brain activation: Effects of age, pubertal stage, and reward sensitivity

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Introduction

Adolescence is characterized as a period of hormonal changes and pronounced changes in social-affective engagement such as increases in sensation seeking and risk taking. Neurobiological models of adolescent development have suggested that adolescents are more sensitive to rewards due to a relatively increased limbic response in combination with reduced down-regulation by the prefrontal cortex and other cortical areas (Ernst and Fudge, 2009; Nelson, Leibenluft, McClure, & Pine, 2005; Somerville, Jones, & Casey, 2010). Accordingly, these models suggest that such neurobiological changes may underlie adolescent-typical risky behaviors such as substance abuse, unsafe sexual behavior, and reckless driving (Dahl, 2004; Steinberg, 2008).

A typically found 'reward-network' in the brain includes dopamine-rich areas in the midbrain and their targets: striatum and medial prefrontal cortex (Blakemore and Robbins, 2012; Clark, Lawrence, Astley-Jones, & Gray, 2009; Tom, Fox, Trepel, & Poldrack, 2007). More specifically, ventral striatum (VS) has been implicated in anticipating and processing different types of rewards, as well as in producing learning signals known as prediction errors (Cohen et al., 2010; Delgado, 2007; Galvan et al., 2005; Knutson, Fong, Adams, Varner, & Hommer, 2001). Similarly, medial PFC–specifically the part that overlaps with the anterior cingulate cortex (ACC)–is also related to prediction-error coding (Van den Bos, Cohen, Kahnt, & Crone, 2012), but also to action-related reward associations (Kennerley and Walton, 2011; Rushworth et al., 2011), and detecting the need for increased control (Ridderinkhof et al., 2004). In contrast, a more ventral region of the medial prefrontal cortex, adjacent to medial orbital frontal cortex, has been implicated in coding rewards and is linked to representations of 'value' (Kuhnen and Knutson, 2005; McKell Carter, Meyer, & Huettel, 2010). Moreover, research indicates strong interconnections between the VS and several parts of the medial PFC. These so-called striatal-cortical loops may be important for regulating reward-related responses and subsequent goal-directed behavior (Haber and Knutson, 2010).

Together, these findings suggest that goal-directed behavior (e.g., risk taking) is driven by a reward-valuation system, in which VS encodes the more 'basic' aspects of reward and medial PFC integrates the different aspects of the reward to represent its subjective value and is important for selecting actions and controlling behavior.

Results of previous developmental functional MRI studies suggest that adolescent decision-making may be biased by a relatively hypersensitive VS response to rewards.

That is, research has indicated that adolescents (ages 13-17 years) show a larger VS response to rewards compared to children and adults (Galvan et al., 2006; Padmanabhan, Geier, Ordaz, Teslovich, & Luna, 2011; Van Leijenhorst et al., 2010a; 2010b). However, other studies have indicated striatal hypo-activation in adolescents during reward anticipation (Bjork et al., 2004; Bjork, Smith, Chen, & Hommer, 2010) or have shown little differences between adolescents and adults in VS response to rewards (May et al., 2004; Paulsen, McKell Carter, Platt, Huettel, & Brannon, 2012). Moreover, only some studies have found that the VS response to rewards correlates with risk-taking behavior in every-day life (Galvan, Hare, Voss, Glover, & Casey, 2007). Thus, several questions remain with respect to the specificity of the VS and medial PFC responses to rewards in adolescence and their relationship to risky behavior. For instance, it remains to be determined whether higher risk-taking in adolescence is associated with a higher VS response to rewards, a lower medial PFC response, or less functional connectivity between these areas (see also Cohen et al., 2012; Van den Bos et al., 2012). Mixed findings in adolescents‘ reward-related brain activation might have several causes, such as differences in task design and analyses (Galvan, 2010). In addition, prior contradictory findings may point toward individual differences in adolescence (Somerville et al., 2010). One important source of influences on subcortical and cortical responses could be pubertal development, which may serve as an important individual difference measure in adolescents' brain activation in response to rewards and appetitive cues. That is, gonadal hormone levels significantly increase during adolescence and have both organizational and activating effects on brain functioning (Blakemore, Burnett, & Dahl, 2010; Sisk and Zehr, 2005). For instance, higher testosterone levels have been associated with increased VS activation (Forbes et al., 2010; Op de Macks et al., 2011) and to adolescent typical risk behavior such as experimentation with alcohol (De Water, Braams, Crone, Peper, 2013).

Another possible source to explain individual differences in reward-related brain activation could be a persons' sensitivity to rewards. For instance, prior studies reported that activation in the VS correlated positively with self-reported (1) reward sensitivity, as measured by the behavioral approach system (BAS) scale (Beaver et al., 2006), (2) sensation seeking, as measured by the brief sensation-seeking scale (Bjork, Knutson, & Hommer, 2008), (3) impulsivity, as measured by the psychopathic personality inventory (Buckholtz et al., 2010), and (4) real-life risk taking (Galvan et al., 2007). Possibly, these personality differences in reward-related response tendencies may explain why some adolescents are more responsive to rewards than others.

In the current study we examined reward processing in adolescence in more detail. Specifically, we aimed to elucidate the relationship between reward-related brain activation, frontostriatal connectivity strength, and behavior. In addition, we focused on examining effects of age, pubertal development, and individual‘s self-reported reward sensitivity on reward-related brain activation. To these ends, we report two experiments using a risky decision task, in which participants could choose to take a gamble (and win or lose 10 Eurocents) or pass on this gamble (in which case nothing was gained or lost). We were specifically interested in the brain's response to rewards and losses as a result of an active gamble, since prior studies have shown that outcome monitoring is more salient when the outcomes are the result of an active choice (Rao, Korczykowski, Pluta, Hoang, & Detre, 2008; Tricomi, Delgado, & Fiez, 2004).

In the first experiment, we reanalyzed the adolescent sample (ages 10-16 years) previously reported by Op de Macks et al. (2011) and added a young-adult sample (18-25 years). The study by Op de Macks et al. (2011) primarily examined individual differences in the reward-related brain activation in relation to testosterone levels, but made no age comparisons. In the current study, we studied age, puberty, and individual differences in reward sensitivity in the same sample. The second experiment included a longitudinal extension of Experiment 1. That is, a subset of the adolescents from Experiment 1 was re-invited two years later, and completed the same risky decision task. This combined cross-sectional/longitudinal approach presents unique insights in the development of the reward system across adolescence and allows us to link changes in reward-related activation to individual's changes in behavior, age, pubertal development, and reward sensitivity.

Replicating prior studies, we expected to observe activation in VS and medial PFC when processing rewards. Second, we predicted that risk-taking propensity would be positively correlated with VS activation, negatively correlated with medial PFC activation and/or the strength of connectivity in this reward network. Third, based on prior findings we expected VS activation to change with age (quadratic or linear). Finally, we tested whether the VS response to rewards was related to pubertal development, or to self-reported reward sensitivity (as measured with the self-report BAS scale).

Methods Experiment 1

Participants

Seventy-eight right-handed participants (50 adolescents, 28 adults) were scanned while performing a risky decision task. All participants reported an absence of neurological or psychiatric impairments (on a brief screening module) and provided written informed consent for the study (parental consent and participant assent for minors). The cross-sectional adolescent data has been reported before in Op de Macks et al. (2011), but that study focused primarily on the association between individual differences in reward-related brain activation and testosterone levels in adolescents and did not examine age effects across adolescence. The goal of this study was to extend this (cross-sectional) dataset by including a sample of young adults. All procedures were approved by the local Medical Ethics Committee.

Three participants (ages 12, 15, and 16) showed head motion exceeding 3 mm during scanning and were therefore removed from further analyses. Accordingly, the final sample consisted of 75 participants (10-25 yrs, Mean = 15.9 years, SD = 4.1, 47 females). Mean head motion correlated with Age, $r = -.27$, $p = .02$, but was overall low, Mean = 0.85 mm, SD = .04. Pubertal development was measured for all adolescents (10-16-year-olds, $n = 47$, 32 females), using the Pubertal Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988)[1]. No PDS scores were obtained for the young adults, since we presume all of the adult subjects have completed puberty. PDS score was positively correlated with age in the adolescent group, $r = .62$, $p < .001$.

Participants completed two subscales (similarities and block design) of the Wechsler Intelligence Scale for Children or the Wechsler Intelligence Scale for Adults in

[1] The reason for choosing PDS as a puberty index instead of testosterone levels was because PDS measures were available for adolescents in both experiments (cross-sectional and longitudinal).

order to obtain an estimate of their intelligence quotient (Wechsler, 1991; 1997). Estimated IQ scores correlated negatively with Age, $r = -.4$, $p < .01$. Therefore IQ was included as a covariate of no-interest in further analyses.

Task

Participants performed the Jackpot task, a risky decision task that has been used to assess developmental changes in reward processing and risk-taking behavior (Op de Macks et al., 2011; see Fig. 1). In the Jackpot task, participants were presented with a slot machine with two of the three slots showing the same fruit. Participants were requested on each trial to choose between the risky option 'spin' (i.e., play), or the safe option 'reset' (i.e., pass trial). A play decision was indexed by a button press with the right index finger; a pass decision was indicated by a button press with the left index finger. The choice to play led to a monetary reward or loss (10/-10 Eurocents), whereas the choice to pass a trial led to no monetary reward or loss (0 Eurocents). The chance to win was indicated by pictures of the possible fruits for the third slot, which were visible to the participants. The chance to win varied between trials (67% versus 33%), although eventually rewards and losses occurred in 50% of the cases for both trials. Participants played 50 trials in total (30 high-risk trials and 20 low-risk trials) and for current analysis purposes all trials were averaged. In the prior study by Op de Macks et al. (2011) it was found that the reward-related brain activation did not differ between high and low-risk rewards. Therefore, averaging across these trials increased the power of the dependent measure. On average, there were 17 loss trials and 17 reward trials. Participants were given initial play money (2 Euros), and were instructed that they would be paid (in real money) according to the final outcome at the end of the experiment. We focused specifically on the outcome phase after play choices, since the design was not optimal to study the feedback and the decision phase separately. That is, 'pass' trials were followed by reset feedback and 'play' trials were followed by valence feedback. Given the short time window between choice and feedback, the choice trials were confounded by feedback type. For this reason, our analysis focused on the play trials, which were unpredictably followed by reward or loss.

Each trial started with a centrally presented fixation cross, followed by the stimulus presentation (3000ms). During this time participants had to select a choice (play or reset) by a button press. Subsequently, feedback was given (reward, loss or reset) for 2000ms. If no timely response was given, the text 'too slow!' was presented for 2000ms, followed by the next trial. This happened rarely, in less than .02% of the trials. Between trials a fixation cross was presented for 1-6 seconds, jittered in steps of 500 and 1000ms.

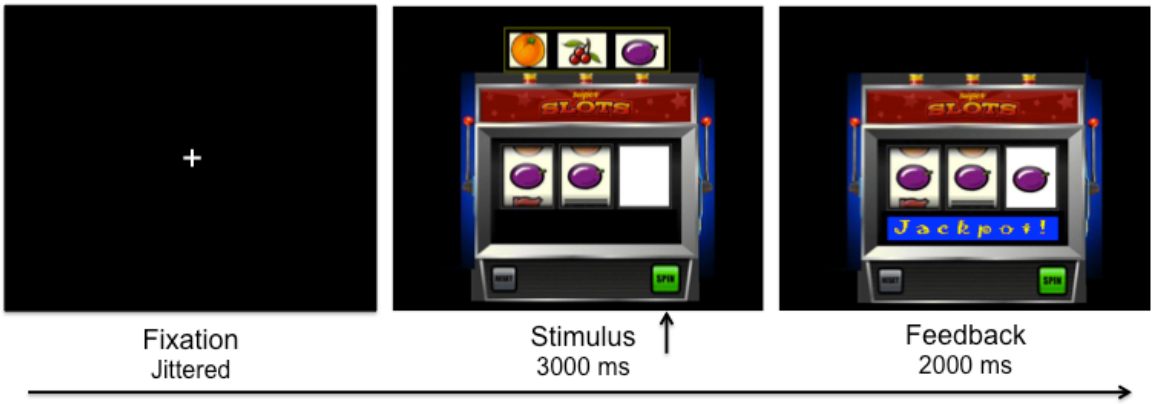

Fig. 1. The Jackpot task (Op de Macks, 2011). Example of a trial in which the participant is presented with a 1/3 chance of a reward (+10) and a 2/3 chance of a loss (-10). The participant decides to play by pressing the right button and which results in a reward (feedback screen). Reprinted from "Testosterone levels correspond with increased ventral striatum activation in response to monetary rewards in adolescents" by Z.A. Op de Macks, B. Gunther Moor, S. Overgaauw, B. Güroğlu, R.E. Dahl, & E.A Crone, Developmental Cognitive Neuroscience, 1, 506. Reprinted with permission.

Procedure

Before entering the scanner, participants received instructions and briefly practiced the task. All scanning procedures were explained using a mock scanner. The Jackpot task was acquired in a single run that lasted approximately 5 minutes. The task was one of a battery of four tasks and was presented first in the battery (for results of the other tasks, see Gunther Moor et al., 2012) lasting a total of approximately 50 minutes. Self-report measures were administered immediately after the scan in a separate room; for the adults, the BIS/BAS questionnaire was administered at home.

Reward sensitivity

Reward sensitivity was measured using the behavioral inhibition system/behavioral approach system scale (BIS/BAS; Carver and White, 1994). A recent study examined the psychometric characteristics of the Dutch version of Carver and White's (1994) BIS/BAS scales in two large independent samples of early and mid-adolescents; their findings confirmed that the scales are suitable for use in research settings (p. 500; Yu, Branje, Keijsers, Meeus, 2011). The BIS/BAS scales consist of 24 items across four scales: one BIS scale that measures punishment sensitivity and three BAS scales that measure reward sensitivity. Note that in the current study we were specifically interested in the BAS scales.

The BAS Drive scale measures the persistent pursuit of desired goals, the BAS Fun Seeking scale measures both desire for new rewards and willingness to approach potentially rewarding events on the spur of the moment, and the BAS Reward Responsiveness scale measures the positive response to (the anticipation of) rewards. Higher scores indicate greater reward sensitivity. Seventeen young adults (7 females) did not fill out the BIS/BAS scale, leaving a total of $n = 58$ who filled out the BIS/BAS scale.

MRI data acquisition

fMRI data were acquired with a standard whole-head coil using a 3-Tesla Philips Achieva scanner. T2*-weighted echoplanar images (EPIs) were obtained during one functional run, in which the first two volumes were discarded to allow for equilibration of T1 saturation effects. Volumes covered the whole brain (38 slices; 2.75mm slice thickness; interleaved acquisition) and were acquired every 2200ms (TE = 30ms). A high resolution T1 image was collected at the end of each scan session, together with a high-resolution T2-weighted anatomical scan with the same slice prescription as the EPIs. Visual stimuli were projected onto a screen that was visible for participants via a mirror attached to the head coil. Head motion was restricted due to foam inserts that surrounded the head.

fMRI preprocessing and statistical analysis

Data preprocessing and analysis were conducted using SPM8 (Wellcome Department of Cognitive Neurology, London). Images were corrected for differences in timing of slice acquisition, followed by rigid body motion correction. The T1 structural image was coregistered to the functional images and segmented according to gray matter, white matter, and cerebrospinal fluid. Functional images were then spatially normalized using the normalization parameters obtained from the segmentation procedure. For seven adolescents no T1 was obtained, due to time constraints or technical problems, in which case functional volumes were spatially normalized to EPI templates. The normalization algorithm used a 12-parameter affine transformation together with a nonlinear transformation involving cosine basis functions. During normalization the data was re-sampled to 3-mm cubic voxels. Templates were based on the MNI305 stereotaxic space (Cocosco et al., 1997). Functional volumes were smoothed with a 6-mm full-width at half maximum isotropic Gaussian kernel. Statistical analyses were performed on individual subjects' data using the General Linear Model (GLM) in SPM8. The fMRI time series data were modeled by a series of events convolved with a canonical hemodynamic response function. In a whole-brain analysis, reward and loss outcomes were modeled as single events with zero duration at the onset of the presentation of the outcome. This whole-brain analysis focused on the contrast [reward > loss]. Reset trials and trials on which the participant did not respond within the 3-s time frame were modeled separately, but were not included in contrasts. Task-related responses were considered significant if they consisted of at least 10 contiguous voxels that exceeded a family-wise error (FWE) or a false discovery (FDR) corrected threshold of $p < .05$ (see Results). For region of interest (ROI) analyses the MarsBaR toolbox in SPM8 was used (Brett, Anton, Valabregue, & Poline, 2002).

Psycho-physiological interaction

To study the interplay between VS and other brain regions during processing of rewards compared to losses, functional connectivity was assessed using psychophysiological interaction (PPI) analysis (Friston, 1997). In PPI, functional connectivity is defined as significantly correlated hemodynamic response patterns over time between brain regions as a function of the experimental task context, here reward versus loss processing. Note that this method does not imply directionality of connectivity between regions. The seed region in the PPI analysis was the right and left

VS mask based on the reward > loss whole-brain contrast. Since VS was bilaterally activated, two separate PPIs were conducted with the right and left VS mask. By means of a peak-detection algorithm, we detected a peak voxel of activation per participant within the (left and right) VS mask. Around this peak voxel a sphere of 7 mm was drawn to create a seed ROI. After the extraction of the time course from the VS mask and the psychological vector of interest (weighting rewards with 1 and losses with -1), their interaction term was computed. This interaction regressor indicated which brain regions are functionally correlated with the respective seed VS mask. In other words, the resulting estimates from this interaction regressor express the extent to which activity in each voxel correlates with the seed region more when processing a reward than when processing a loss.

Results and Discussion Experiment 1

Behavior

The average proportion of 'play' decisions was .67 (range = .28 – 1, SD = .14). A linear regression with proportion of plays as a dependent and Age as an independent variable showed no significant effect of Age (p values > .1). Similar analyses with PDS score, and the BAS scales (Drive, Fun-seeking, and Reward-responsiveness) as an independent variable, also showed no significant effects of PDS or BAS scores on proportion of plays (p values > .1). Together these results reveal that the tendency to make a risky decision was not related to age, pubertal development or individual's reported reward sensitivity. Note that this resulted in an approximately equal number of trials in the neuroimaging analyses across ages.

Whole-brain analyses

Results for the contrast [reward > loss; FWE corrected, $p < .05$, $k > 10$] across all participants revealed bilateral VS activation and a cluster of activation in the medial PFC (see Fig. 2). Reward-related activation was also found in the posterior cingulate cortex (PCC), and other frontal and parietal brain regions (see Table 1 for regions of activation and their coordinates). No significant results were found for the opposite contrast [loss > reward].

The first question we aimed to address was the relation between reward-related brain activation and proportion to play (i.e., gamble) in the Jackpot task. To detect brain regions in which reward-related activation correlated with behavior, proportion of plays was added as a regressor of interest in a whole-brain analysis [reward > loss], and IQ was included as a covariate. At an FWE corrected threshold, $p < .05$, $k > 10$, no regions were detected. At an FDR corrected threshold of $p < .05$, $k > 10$, proportion of plays showed a positive association with reward-related activation in VS, medial PFC, PCC, thalamus, and other frontal brain regions (see Fig. 2 and Table 1 for regions of activation and their coordinates). No significant results were found for a negative association with proportion of plays. Thus, VS and medial PFC were more active following rewards, for those individuals who more often played.

The next question we aimed to address was the relation between reward-related brain activation and individual differences in BAS scores (BAS Drive, BAS Fun-seeking, and BAS Reward-responsiveness). BAS subscales were added as regressors of interest in a whole-brain analysis [reward > loss, $n = 58$], and IQ was included as a covariate. At an

FWE corrected threshold ($p < .05$, $k > 10$), no regions were detected. At an FDR-corrected threshold of $p < .05$, $k > 10$, only the BAS Fun-seeking score showed a positive association with reward-related activation in VS, medial PFC, thalamus, and other frontal and parietal brain regions (see Fig. 2 and Table 1 for regions of activation and their coordinates).

Table 1. Coordinates for the brain regions showing activation for the Reward > Loss contrast and brain regions showing a positive correlation in the reward > loss contrast with proportion of plays and self-reported BAS Fun-seeking, peak voxels are reported at cluster level. PFC = prefrontal cortex, VS = ventral striatum, ACC = Anterior Cingulate Cortex, BA = Brodmann Area.

Anatomical Area		**MNI coordinates (mm)**			
	Cluster Size	*x*	*y*	*z*	Z-max value
Reward > Loss, FWE corrected p < .05, k > 10					
L VS	100	-15	15	-6	6.87
R VS	32	12	9	-9	6.23
R ACC (BA24)	38	6	0	33	5.46
L Posterior Cingulate Cortex	213	-6	-36	36	6.23
L Lateral PFC	88	-42	45	12	6.36
L Superior Frontal Gyrus	106	-21	33	45	6.76
L Superior Frontal Gyrus	99	-12	66	15	6.22
R Middle Frontal Gyrus	16	39	9	54	5.34
R Precentral Gyrus	58	21	-27	60	5.93
R Precentral Gyrus	12	42	-15	60	5.57
L Precentral Gyrus	23	-21	-30	60	5.71
R Putamen	11	30	-12	-12	6.10
L Thalamus	25	-6	-18	9	5.25
L Angular Gyrus	75	-39	-69	39	5.55
R Inferior Parietal Lobe	32	42	-42	57	5.31
R Superior Parietal Lobe	15	18	-54	66	5.00
L Middle Temporal Gyrus	10	-57	-45	6	5.09
L Occipital Lobe/Lingual Gyrus	1830	-12	-78	-15	7.82
Proportion of plays, FDR corrected, p < .05, k > 10					
R ACC/ (Para)cingulate Gyrus	887	3	45	18	4.43

R (Para)cingulate Gyrus	72	9	18	45	3.47
L ACC (BA24)	20	-3	12	24	2.98
R Lateral PFC	131	45	15	48	3.84
L Middle Frontal Gyrus	24	-27	9	54	3.38
R Middle Frontal Gyrus	11	30	12	57	3.11
R Superior Frontal Gyrus	20	18	42	39	3.35
L Inferior Frontal Gyrus	59	-39	24	-9	3.61
R Inferior Frontal Gyrus (BA9)	41	51	9	24	3.79
R Inferior Frontal Gyrus (BA47)	12	45	21	-6	2.85
L Precentral Gyrus	67	-45	-3	45	4.38
L Postcentral Gyrus	56	-51	-21	48	3.38
R Supplementary Motor Area	39	3	6	60	3.51
R Thalamus (including striatum)	339	9	-21	12	4.36
R Middle Temporal Gyrus	25	45	-54	6	3.15
L Posterior Cingulate Cortex	23	-3	-45	6	3.13
L Intracalcarine Cortex	191	-24	-66	9	4.28
L Precuneus / Occipital Lobe)	3047	-15	-54	39	5.26
BAS Fun-seeking scale, FDR corrected, $p < .05$, $k > 10$					
L ACC	135	-9	33	9	4.65
R ACC (BA24)	17	9	21	27	3.05
L Paracingulate Gyrus	16	-6	24	45	3.37
L VS (putamen)	235	-18	12	-9	4.08
R VS (putamen)	18	27	-3	-3	3.23
L Brainstem	103	-9	-21	-12	4.18
R Superior Frontal Gyrus	58	15	33	48	3.97
R Middle Frontal Gyrus	22	33	21	42	3.53
L Middle Frontal Gyrus	87	-33	27	45	3.46
R Inferior Frontal Gyrus	24	42	33	0	3.41
R Cingulate Gyrus	87	15	6	45	4.01
L Precentral Gyrus	14	-45	0	33	3.42
R Insula	38	27	24	9	3.82
R Insula	11	36	6	0	3.06

R Parietal Lobe (Precuneus)	77	15	-48	39	3.63
R Parietal Lobe (Angular Gyrus)	15	36	-51	39	3.32
L Parietal Lobe (Angular Gyrus)	13	-33	-60	39	2.98
R Superior Parietal Lobe	11	15	-51	69	3.22
L Intracalcarine Cortex	19	-3	-69	15	3.18
L Occipital Lobe / PCC	2261	-15	-45	-3	4.88
L Occipital Lobe (Cuneus)	34	-21	-72	18	3.45
L Lateral occipital cortex	14	-12	-84	36	3.26
L Lateral occipital cortex	11	-45	-63	21	2.89

No significant results were found for a negative association with BAS scores. Thus, VS and medial PFC were more active following rewards, for individuals who in every-day life are more willing to approach a potentially rewarding event on the spur of the moment, as measured by items such as "I'm always willing to try something new if I think it will be fun", and "I crave excitement and new sensations" (Carver and White, 1994).

Finally, we addressed the relation between reward-related brain activation and age, based on prior studies that reported a peak in adolescence in response to rewards (Ernst et al., 2005; Galvan et al., 2007; Van Leijenhorst et al., 2010a; 2010b). To detect brain regions in which reward-related activation correlated with linear and quadratic changes in age, Age and Age^2 were included as regressors of interest in a whole-brain analyses, with IQ included as a covariate. No results survived FWE or FDR correction. Lowering the threshold to an uncorrected $p < .001$ level, indicated a cluster of linearly increasing activity in left putamen ($x = -24$, $y = 6$, $z = 9$, $k = 33$), but no regions were found when testing for a linear decrease or a quadratic pattern. A similar whole-brain analyses to test the relation between reward-related brain activation and puberty ($n = 47$) also showed no significant cluster of activation, not even at an uncorrected threshold of $p < .001$.

Thus, in the current study, we found no evidence for a peak in the brain's response to rewards in mid-adolescence, and weak evidence for a monotonic age-related increase in reward-related activation. Instead, these results indicate that reward-related brain activation was predominantly related to propensity to play and self-reported individual differences in fun seeking across adolescence[2].

Functional connectivity

A final question was whether connectivity in a VS-medial PFC network was related to proportion of plays and other individual difference measures. For this purpose, two whole-brain PPI analyses with left VS and right VS masks from the whole-brain

[2] When including BAS-subscales (Drive, Fun seeking, and Reward responsiveness), proportion of plays, Age, and IQ as a covariate of no interest in one whole-brain analyses the reported effects generally remained. Only proportion of plays showed a weaker effect, in which an association with reward-related activity was observed specifically in medial PFC and at an uncorrected threshold of $p < .001$, $k > 10$.

analysis (see Fig. 2, upper panel) as seed regions showed that processing rewards compared to losses enhanced functional connectivity between VS and medial PFC (including ACC and dorsal medial PFC regions; FDR corrected, $p < .05$, $k > 10$). Analyses for left VS and right VS pointed to partly overlapping regions, including medial PFC, visual cortex, and other frontoparietal brain regions. However, functional connectivity with left VS showed an additional cluster in right anterior insula (see Fig. 3a and supplementary Tables 2 and 3 for functionally connected regions and their coordinates). We extracted the strength of functional connectivity between medial PFC and left VS, medial PFC and right VS, and right anterior insula and left VS for each participant. We tested whether the strength of these functional connections was correlated with individual's proportion of plays, age, pubertal development, and BAS scores. Results indicated no significant results for functional connectivity strength between medial PFC and (left and right) VS. However, functional connectivity between right anterior insula and left VS was related to proportion of plays in the task, in which larger connectivity was related to a lower number of plays, $r = -.30$, $p < .02$ (see Fig. 3b).

Summary Experiment 1

Taken together, whole-brain analyses revealed that rewards compared to losses activated a reward-related brain network, including VS and medial PFC. Whole-brain results indicated that reward-related activation in these regions was positively associated with proportion of plays and self-reported reward sensitivity (as measured by BAS Fun-seeking score). PPI analyses indicated increased functional connectivity after reward compared to losses between bilateral VS and (dorsal) medial PFC. Functional connectivity between left VS and right anterior insula also increased after rewards compared to losses, and this connectivity was associated with attenuated risky decision-making.

These cross-sectional results led to specific points of focus for the longitudinal analyses in Experiment 2. That is, in Experiment 2 we examined whether reward-related activation of VS and medial PFC [as defined by reward > loss activation] was related to changes in behavior, age and/or pubertal stage, and self-reported reward sensitivity over time.

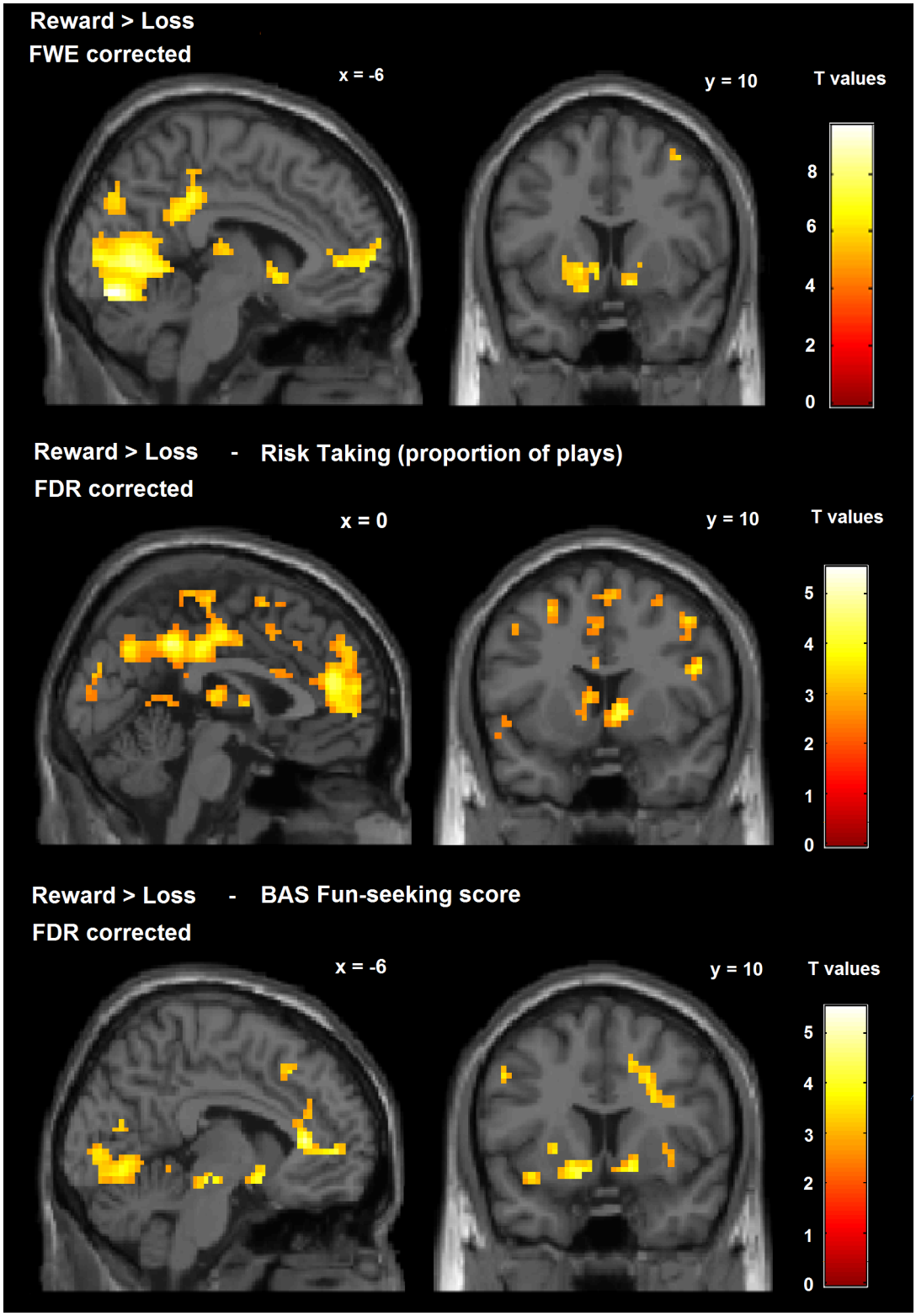

Fig. 2. Whole-brain results for the contrast [reward > loss] for all participants, at an FWE corrected threshold of $p < .05$, $k > 10$ (upper panel). Whole brain results for the contrast [reward > loss], displaying regions that showed increased activation with increased number of plays (middle panel) and displaying regions that showed increased activation with increasing BAS Fun-seeking score (lower panel). Both results are reported at an FDR corrected threshold of $p < .05$, $k > 10$.

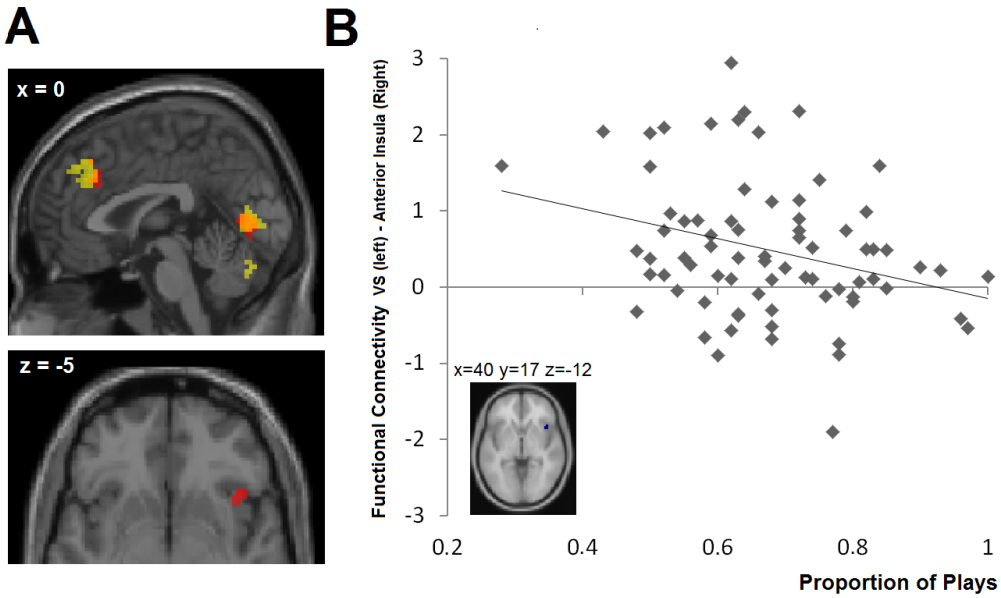

Fig. 3. (a) Whole-brain results for the psycho-physiological interaction regressor with a seed region in left VS (red) and right VS (yellow)—orange indicates overlap—at an FDRcorrected threshold of $p < .05$, $k > 10$. The interaction regressor shows regions that enhance functional connectivity with VS (left and right respectively) when processing rewards compared to losses. (b) Scatterplot depicting the positive association between functional connectivity between left VS–right anterior insula and proportion of plays.

Methods Experiment 2

Participants

A subset of the adolescents from Experiment 1 (n = 33) were scanned again approximately two years later, and were administered the same risky decision task. The goal of this study was to extend this dataset with a longitudinal sample. All participants signed informed consent (parental consent and participant assent for minors) and procedures were approved by the local Medical Ethical Committee.

Two participants showed head motion exceeding 3 mm during scanning at time point 2 (T2) and were therefore removed from further analyses. For longitudinal analyses, adolescents were included at time point 1 (T1) and T2 (T1: 10-16-years-old, Mean = 13.1 years, SD = 2.0; T2: 12-19-years-old, Mean = 15.3 years, SD = 2.1, 18 female). The average time difference between the first and second scan was 2.13 years (1.8 – 2.3 years, SD = .14).

The average head motion on T1 was significantly correlated with Age at T1, r = -.41, $p < .05$, however, head motion at T2 was not related to Age at T2, p = .2. Note that the mean head motion was low at both time points (T1: Mean = .1 mm, SD = .05; T2: Mean = .09 mm, SD = .04).

Similarly to T1, PDS scores at T2 were positively correlated with age at T2 (r = .39, $p < .05$). A repeated-measures ANOVA indicated an increase in pubertal development from T1 to T2, F (1, 30) = 32.8, p < .001, that did not differ significantly between boys (Mean PDS increase = .83) and girls (Mean PDS increase = .76), p = .8.

The task, procedure, and MRI acquisition in Experiment 2 were identical to those described in Experiment 1.

fMRI preprocessing and statistical analysis

Data preprocessing and analysis was conducted using SPM8 (Wellcome Department of Cognitive Neurology, London). Preprocessing steps in Experiment 2 were identical to those described in Experiment 1.

Two types of statistical analyses were performed on this longitudinal dataset. First, we used the ROIs defined based on the whole-brain analysis [reward > loss] in the cross-sectional study (left VS, right VS, and medial PFC) to examine longitudinal changes in neural activation related to changes in behavior, age, pubertal development, and individual's reward sensitivity. Second, we performed a whole-brain analysis on the longitudinal dataset within the GLM framework, with a 2 (reward, loss) × 2 (T1, T2) repeated measures ANOVA (flexible factorial design). The latter analysis allowed for a whole-brain inspection of a main effect of outcome [reward > loss], a main effect of time [T2 > T1], and an interaction between the contrast [reward > loss] × time.

Results and Discussion Experiment 2

Behavior

The proportion of plays in the adolescent longitudinal sample was .62 (SD = .13) for T1 and .63 (SD = .11) for T2. A correlational analysis between T1 and T2 showed that proportion of plays was significantly correlated across sessions (r = .41, p < .02), however, this correlation also indicates there was a fair amount of within-individual differences in choice behavior across time.

A set of linear regressions with proportion of plays at each time point as a dependent and Age (continuous) at each time point as an independent variable showed that Age did not significantly predict behavior on T1 and T2 (respectively) nor did Age on T1 predict the change in behavior from T1-T2. Similarly, BAS subscales and PDS scores at T1 and T2 did not predict proportion of plays on T1 and T2 (respectively) nor predicted scores on T1 the change in behavior from T1-T2 (all p values > .05). Thus, risk-taking propensity was generally stable across time and was not related to developmental factors and individual differences.

ROI analyses

We extracted individual activation values for the longitudinal dataset from the ROI masks used in the cross-sectional whole-brain analysis and focused on the contrast [reward > loss] in left VS (x = -16, y = 11, z = -5), right VS (x = 16, y = 11, z = -5), and medial PFC (x = -6, y = 55, z = 7). These ROIs were chosen to enable comparison with Experiment 1. A repeated measures ANOVA was performed for each ROI with reward-related activation at T1 and T2.

There was no effect of Time (i.e., Age) on brain activation in the VS and medial PFC. An additional correlational analysis for each ROI between reward-related activation at T1 and T2 showed no significant correlations over time within these ROIs.

We performed a linear regression [backward selection] with proportion of plays, PDS score, BAS scores, and IQ as independent and brain activation in an ROI [reward > loss] as a dependent variable. The same analysis was repeated with Age instead of PDS scores. These regression analyses were performed for behavioral scores and brain activation at T1, T2, and the change in behavioral scores and brain activation between T1 and T2.

The regression for medial PFC at T1 showed no significant results of any of these predictors. The regression analysis for left VS at T1 showed that BAS Fun-seeking score, $\beta = .51$, $p < .01$, and pubertal developmental score, $\beta = .32$, $p < .05$, were positively associated with left VS activation. A regression analysis for right VS at T1 showed that BAS Fun-seeking score was positively associated with right VS reward-related activation, $\beta = .51$, $p < .01$. A similar set of regressions for T2 showed no significant effects of Age, proportion of plays, PDS or BAS scores on reward-related brain activation at T2.

Crucially, regression analyses were performed with the change over time in reward-related activation in medial PFC, right VS, and left VS as dependent variables, and the change over time in proportion of plays, PDS score, and BAS scores as independent variables.

The regression for medial PFC showed no significant results of any of these predictors. A regression for left VS showed that the change in BAS Fun-seeking score was positively associated with the change in reward-related activation in left VS, $\beta = .38$, $p < .05$. A regression for right VS showed that the change in BAS Fun-seeking score was positively associated with the change in reward-related activation in right VS, $\beta = .36$, $p < .05$ (see Fig. 4).

These results suggest that an increased VS response to rewards is associated with increased self-reported fun seeking; this relationship is independent of developmental factors, such as age and pubertal development.

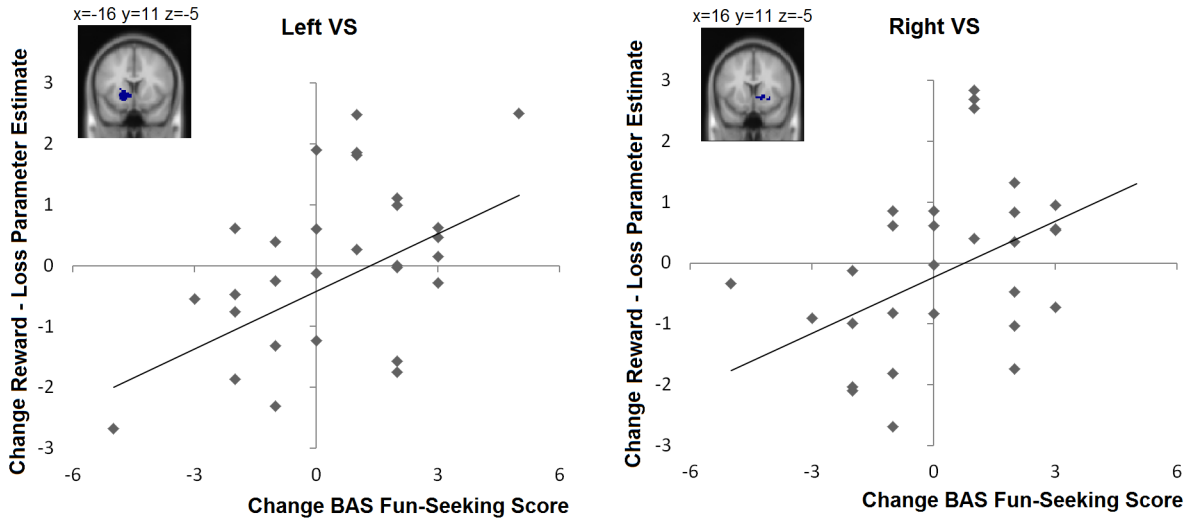

Fig 4. Scatterplots for the change in reward > loss activation (T1-T2) and the change in left and right Ventral Striatum (VS) and self-reported Fun-seeking.

Whole-brain analysis

To ensure that the pre-specified ROIs did not prevent us from observing brain regions that showed changes in activation over time when processing rewards compared to losses, we performed a whole-brain 2 (reward, loss) × 2 (T1, T2) repeated measures ANOVA (flexible factorial design) on the longitudinal dataset.

Results for the main effect of outcome [reward > loss] across all participants resulted in VS activation (right) and a cluster of activation in the medial PFC (see Fig. 5).

Reward-related activation was also found in the PCC and visual cortex (see supplementary Table 2 for regions of activation and their coordinates). No significant results were found for the opposite contrast [loss > reward]. The interaction term between reward-loss × time showed no significant results at FWE or more lenient corrected thresholds (FDR $p < .05$ and uncorrected $p < .001$).

Thus, even though correlations in ROI activation values indicate intra-individual variability in brain activation, there was a strong main effect of reward-related activation at the group level.

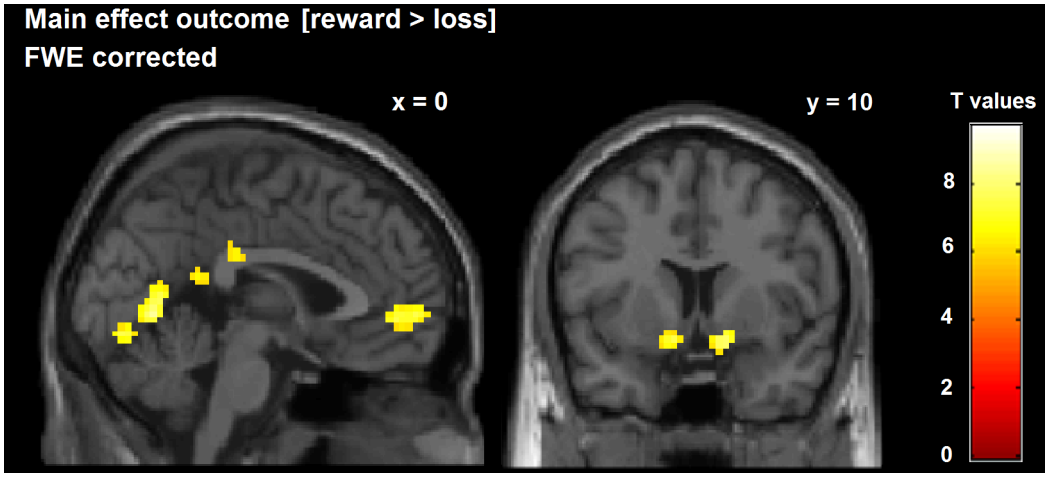

Fig. 5. Whole-brain results for the main effect of outcome [reward > loss] for all participants in T1 and T2 from a 2 x 2 flexible factorial ANOVA. Results are shown at an FWE-corrected threshold of $p < .05$, > 10 contiguous voxels.

General Discussion

The goal of this study was to examine stability, change, and individual differences in reward processing in adolescence. We first examined the relation between brain and behavior in the context of reward processing and risky decision-making. Second, we examined the effects of age, pubertal development, and reward sensitivity on reward-related brain activation in a cross-sectional and longitudinal comparison. To these ends, Experiment 1 utilized a risky decision task in a cross-sectional sample of adolescents and young adults. Experiment 2 was a longitudinal extension, in which an adolescent subset was re-studied using the same paradigm two years later.

For the current study, we used a task in which participants had the opportunity to play or pass. The advantage of this design is that rewards and losses are thought to be more meaningful when there is an active choice to play (Rao et al., 2008; Tricomi et al., 2004). Therefore, the analyses were focused on the brain responses to reward and loss following play trials. As expected, monetary rewards resulted in robust activation in the bilateral VS and medial PFC in the cross-sectional sample (Delgado, 2007; Knutson et al., 2001).

The longitudinal analysis confirmed these findings by revealing activation in a highly similar reward-related network including most predominantly VS and medial PFC. These activation patterns are in line with the functional roles of these regions, such as the coding of reward throughout various stages of decision-making for the VS (Liu et al.,

2007), and action regulation and control for the medial PFC (Ridderinkhof et al., 2004; Rushworth et al., 2012).

We, however, did not observe brain activation in the ventral medial PFC and the adjacent orbital frontal cortex. Given that these regions have been related to the representation and the comparison of value during risky choice (Kuhnen and Knutson, 2005; Rushworth et al., 2011), it may be that these regions are more readily activated in response to choice than outcome processing.

Interestingly, no results were found for the opposite contrast (i.e., loss > reward), suggesting that the brain regions involved in winning and losing overlap. This finding is supported by previous findings that also showed no results for the contrast no-gain versus gain in a similar design (e.g., Van Leijenhorst et al., 2010a). A possible explanation could be that in the current context negative feedback was not a learning signal and therefore there was no activation greater for loss than gain (Van Duijvenvoorde and Crone, 2013).

A whole-brain analysis showed that the propensity to play (i.e., to choose the risky option) was related to increased reward-related activation in both VS and medial PFC. That is, participants who generally played more often showed, as expected, increased activation in VS, but also increased activation in medial PFC after rewards compared to losses. Previous studies demonstrated that activation in medial PFC regions during decision-making was related to increased risk-taking tendencies (Van Leijenhorst et al., 2010a; Xue et al., 2009; but see Eshel, Nelson, Blair, Pine, & Ernst, 2007), which is consistent with its role in reward-related action tendencies (Rushworth et al., 2011; Rushworth et al., 2012). The current study extends previous findings by showing that medial PFC activation during outcome processing was positively related to the tendency to choose a risky option in a cross-sectional sample.

Developmental changes and individual differences

A current debate in the literature concerns the VS response to rewards in adolescence. Prior studies have reported both increases and decreases in mid-adolescence, although this may depend also on task demands (Bjork et al., 2010; Galvan, 2010; Richards, Plate, & Ernst, 2013). In a prior study by Op de Macks et al. (2011), which involved a subset of participants reported in this study, it was found that reward-related brain activation correlated positively with testosterone levels, in both boys and girls. This led us to hypothesize that reward-related activation would peak in mid-adolescence, as can be expected based on adolescent-typical changes in the dopamine system (Galvan, 2010; Luciana and Collins, 2012). However, a comparison with a sample of young adults (ages 18-25) did not show developmental differences related to age or puberty. Only at lower (uncorrected) thresholds, reward-related activation in left putamen increased linearly with age. Thus, these results report no direct evidence for a peak in adolescent VS activation and suggest that individual differences in adolescence may be more important.

Indeed, this study showed that reward responses in the VS were related to the extent to which participants reported to be fun seeking in everyday life. Previously, Galvan et al. (2007) reported that neural responses to rewards in adolescence could be partly explained by individual differences in risk-taking behavior in everyday life. It was previously reported in a large behavioral developmental study including 935 participants between ages 10 and 30 that self-reported sensation seeking peaks in mid-adolescence

(Steinberg et al., 2008). Possibly, findings in prior studies of heightened VS activation in adolescents compared to adults were driven especially by risk-seeking adolescents. The current study provided further evidence for this hypothesis by showing that within individuals, changes in fun seeking over time correlated positively with changes in reward-related VS activation. This longitudinal extension provides a strong case for the role of individual differences in reward-seeking behavior, which may bias some adolescents to respond more strongly to rewards than others. Further study is needed to study how hyperactivity in VS is related to individuals' learning and decision-making.

Functional connectivity

The next question concerned whether there was functional connectivity between VS and medial PFC. In the current study a functional connectivity analysis in the cross-sectional sample indicated increased connectivity between VS and medial PFC after processing rewards compared to losses. Contrary to expectations we did not find a relation between VS-medial PFC functional connectivity and task-related behavior (i.e., proportion of plays). Instead, increased functional connectivity was found between VS and insula after rewards compared to losses, and the strength of this functional connectivity was related to individuals' risky decision-making. That is, greater connectivity was associated with an attenuated tendency to play, suggesting a potentially regulatory role of the insula (see also Cho et al., 2012). Indeed, insula activation has been implicated in saliency detection (Menon and Uddin, 2010), harm avoidance (Paulus et al., 2003), and risk processing (Mohr et al., 2010). However, given the low number of trials in the current study, these results need to be interpreted carefully.

Previous work also indicated a relation between frontostriatal structural connections and choice behavior, in which higher integrity of frontostriatal white-matter tracts was associated with less impulsive choice behavior, suggesting that the PFC has a regulatory role over the VS (Peper et al., 2012). However, other findings demonstrated that more mature white-matter tracts in the frontal cortex (corpus callosum, connecting left and right prefrontal and orbital frontal cortex), is related to increased engagement in risky behaviors (Berns et al., 2009). These mixed findings indicate the need to further study how frontostriatal connections influence risk taking in adolescence.

Limitations

There are a couple of critical aspects to take into account when reporting and comparing studies on risk and reward processing (Galvan, 2010). First, studies may differ in the component of the decision-making process targeted (e.g., decision-making, cue/anticipation, and outcome). Due to its task design the current study focused specifically on outcome processing. However, future studies may profit from analyzing both decision-related and outcome-related responses (see also Barkley-Levenson, Van Leijenhorst, & Galvan, 2013; Paulsen et al., 2012; Van Leijenhorst et al., 2010a). Also, the current task was not aimed toward decomposing influences of risk, expected value, and reward that may drive individuals' decision-making. Combinations in future paradigms will be valuable to further disentangle these components of decision-making.

Second, it is important to consider the task contrast and/or baseline used across studies. That is, while this study used a typical contrast of reward vs. loss, future studies may benefit from a neutral baseline (e.g., including a neutral condition) to distinguish

whether differences in reward processing are due to differences in the brain responses to reward or responses to loss. Alternatively, parametric modulation of rewards and losses (e.g., Tom et al., 2007; Xue et al., 2009) may be a promising approach in distinguishing reward versus loss-related activation across development.

Third, even though the current longitudinal sample is an important starting point, the sample size is relatively small for detecting subtle developmental changes. We aimed to present these data as evidence that change scores are informative for understanding developmental patterns. In future studies, larger sample sizes will allow us to make stronger inferences about developmental trajectories. Related, the relative low number of trials for each contrast (i.e., on average, 17 reward and 17 loss trials) could hinder the detection of age-related changes. While previous fMRI studies reported developmental changes in reward processing based on similar numbers of trials per condition (i.e., 18 trials per condition; Bjork et al., 2004; Ernst et al., 2005), these studies included more than two conditions, suggesting the need for a larger number of trials in future studies.

Finally, task context may be driving age-related changes in risk-taking or brain activation. For instance, a recent study suggested that adolescents may be more ambiguity tolerant, instead of more risk-tolerant compared to adults, indicating they are more likely to take a risk under conditions of unknown probabilities (i.e., an 'ambiguous' decision-situation) compared to known probabilities (i.e., a 'risky' decision-situation) (Tymula et al., 2012). Future studies are important for disentangling adolescent sensitivities across different decision contexts, such as risky, ambiguous, or social decision contexts.

Conclusion

In the current study, we used a risky decision task to investigate neurodevelopmental changes (cross-sectional and longitudinal) in the processing of rewards and its relation to task-related behavior (i.e., the proportion of play choices), age, pubertal development, and individuals' reward sensitivity. Adolescence is characterized as a period of increased reward sensitivity and risk taking, but it remains unclear whether changes in reward-related brain activation drive the changes in risk-taking behavior. The results of the experiments reported here advance our understanding of the potential mechanisms underlying reward processing and risky decision-making in adolescence. Specifically, these results indicated that increased activation within a network of brain regions responsive to rewards—including VS and medial PFC—is related to an increased tendency to play and heightened self-reported fun seeking.

Longitudinal comparisons confirmed the association between VS activation and individual's fun seeking. Furthermore, we observed increased connectivity between VS and medial PFC after rewards versus losses, but only the increased functional connectivity between VS and insula was associated with attenuated risky decision-making. Future challenges lie in unraveling how localized brain activation and frontostriatal connections are related to changes in risk taking across adolescence and in creating paradigms that are sensitive to individual and developmental differences in risk-taking tendencies.

Supplementary Materials

Supplementary data associated with this chapter can be found in appendix B.

Chapter 3. Risky decision-making in adolescent girls: The role of testosterone and reward circuitry

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Introduction

Adolescence, the developmental period between childhood and adulthood, is a dynamic time of transition characterized by dramatic biological, cognitive, social, emotional, and behavioral changes. The onset of adolescence is marked by puberty (Dahl, 2004), a biological process that involves a substantial rise in sex steroids, such as testosterone and estradiol (Biro et al., 2014; Dorn et al., 2003, 2006; Shirtcliff et al, 2009). While the rise in sex steroids at puberty is known to lead to the physical and physiological changes necessary for sexual reproduction (e.g., the development of secondary sex characteristics), these hormones also influence the developing adolescent brain (Schulz et al., 2009; Schulz and Sisk, 2006; Sisk and Zehr, 2005). As such, the rise in hormones at puberty is thought to play an important role in activating the behavioral changes that characterize adolescents, such as increased risk taking (Forbes and Dahl, 2010; Peper and Dahl, 2013).

Indeed, adolescent risk taking has been associated with higher levels of testosterone (De Water et al., 2013; Vermeersch et al., 2008a), as well as estradiol (De Water et al., 2013; Vermeersch et al., 2008b); these findings were independent of age. Neurobiological models proposed to explain the adolescent increase in risk taking emphasize the role of sex steroids in the development of affective brain regions (Crone and Dahl, 2012; Ernst, 2014; Steinberg, 2010). Specifically, pubertal hormones are thought to increase the involvement of affective brain regions, such as the nucleus accumbens, resulting in enhanced valuation of rewards during adolescence, which in turn leads to increased risk taking (Blakemore and Robbins, 2012; Galvan, 2010; Somerville, Jones, & Casey, 2010; Spear, 2011; Steinberg, 2010). Consistent with these models, structural changes in subcortical brain regions involved in affective processing, such as the amygdala and caudate/nucleus accumbens, have indeed been related to pubertal stage (Goddings et al., 2014) and sex steroid levels (Herting et al., 2014; Peper et al., 2011), although another study failed to detect a relation between sex steroids and subcortical brain development in boys and girls (Koolschijn et al., 2014). Functional changes in reward-related brain regions have also been reported; there is evidence for enhancing effects of testosterone (Hermans et al., 2010; Van Honk et al., 2004) as well as estradiol (Dreher et al., 2007; Thomas et al., 2014) on reward processes associated with risk taking in adults. However, evidence for the role of these hormones during puberty in the functional (subcortical) changes of the adolescent brain is both limited and conflicting (Forbes et al., 2010; Op de Macks et al., 2011).

In a prior study, we used a version of the Jackpot task in which participants chose to play or pass based on information about the chance of winning 50 Eurocents; in the

low-risk condition the chance to win was 67%, and in the high-risk condition this chance was 33%. Among 33 girls and 17 boys (ages 10–16yrs), we demonstrated that increased levels of testosterone corresponded with increased ventral striatum activation when receiving a reward after making a risky decision (Op de Macks et al., 2011). This finding is in contrast with the *decreased* striatum response to rewards in the context of a card-guessing game, which was found among girls (ages 11–12yrs; $n = 39$) who reported more advanced pubertal maturation and had higher testosterone levels (Forbes et al., 2010). Given that these findings resulted from different experimental paradigms, direct comparison of the results is not possible. Furthermore, both studies focused on the relation between hormones and brain processes involved in risk taking, but did not establish the relation between hormones/brain processes and task behavior.

Thus, we designed a study to examine the relation between pubertal maturation and risk taking, as well as the reward-related brain processes involved in risk taking. We investigated this three-way relation by administering an updated, but similar version of the Jackpot task in a sample of young adolescents. This updated version of the task allowed us to study the influence of the *magnitude* of potential rewards, in addition to the *probability* of winning, on risk taking. We focused on individual differences during decision-making in the activation of nucleus accumbens (Haber and Knutson, 2010), a region known to be involved in reward anticipation/outcome processing and often reported to show increased activation in adolescents (compared to children and/or adults) in the context of risky decision-making (for a review, see Galvan, 2010).

The present study was conducted in girls only, for two reasons: First, pubertal maturation is very different in boys and girls; both the physical and hormonal changes associated with puberty, as well as the timeline along which these changes occur are different in boys and girls (Dorn et al., 2003, 2006; Shirtcliff et al., 2009). By focusing on one sex only, we optimized our power to investigate the relation between individual differences in pubertal maturation and differences in risk taking in this cross-sectional study. Second, girls provide us with the unique opportunity to study the association of both testosterone and estradiol with risk taking, as both sex steroids are released during the reactivation of the hypothalamic-pituitary-ovarian axis at puberty (i.e., gonadarche; Biro et al., 2014; Legro et al., 2000). Only one study to date has looked at the effect of manipulating both testosterone and estradiol on risk taking in a single sample (Goudriaan et al., 2010). However, this study was conducted in adult males. Another study that looked at risk taking (i.e., experimentation with alcohol) in a large sample of adolescents found a positive relation between individual differences in sex steroids and risk taking in boys, but not in girls (De Water et al., 2013). Given that both boys and girls show a developmental increase in risk taking after the onset of puberty (Shulman et al., 2014), it remains unclear what role sex steroids at puberty play in risk taking among girls.

For this study, we recruited the girls within a narrow age range around the onset of puberty (11–13yrs) to capture the developmental window during which the hormonal changes are occurring, while keeping age relatively constant (Dorn et al., 2003, 2006; Peper and Dahl, 2013). Given that the initial rise in estradiol and testosterone occurs 6 to 12 months *before* the appearance of the physical signs of puberty (i.e., breast development; Biro et al., 2014), we measured pubertal maturation based on self-reported physical changes, as well as saliva-based sex steroid levels.

We hypothesized that among 11–13 year-old girls those who were more advanced in pubertal maturation, as measured by more reported physical changes and higher testosterone and/or estradiol levels, would show increased (1) risk taking (Vermeersch et al., 2008a; 2008b), and (2) reward-related brain activation when making risky decisions (Op de Macks et al., 2011). To examine whether enhanced subjective valuation of rewards contributed to risk taking, we also looked at the relation of both risk taking and reward-related brain processes with self-reported experience of outcomes during risk taking.

Materials and Methods

Participants

The study reported here was part of a larger research project designed to examine the role of pubertal development in risk taking, future time perspective, and emotional decision-making. Seventy-eight healthy, adolescent girls (ages 11–13 years) were recruited through Berkeley Parents Network, word of mouth, and by re-contacting families that participated in prior studies in the lab. Participants were screened in a phone interview with their parent; they were included in the study if they were (1) right-handed, (2) native English speakers, (3) in school, (4) medically healthy (i.e., no history of neurological or psychiatric disorders and/or past or present use of neuropsychological medication), and (5) free from metal in or on their body (e.g., no braces) that would serve as a contraindication to fMRI. Before entering the study, written informed consent was obtained from the parent or legal guardian of the participant, and assent was obtained from the participant. All participants received compensation for their time and won additional money during some of the tasks, which was paid to them at the end of their visit via gift card. The University of California Berkeley Institutional Review Board approved all procedures.

Sixty-eight participants completed both lab visits, including an fMRI scan during the second visit (see below for a detailed description of the study procedure). Ten participants were excluded from analysis for the following reasons: (1) task-related imaging data were invalid due to technical problems[3] (n = 6) or movement (n = 3), and (2) response rate on the task was low (i.e., no response was recorded on 25% of the trials; n = 1). Thus, the results presented here are based on 58 participants: 23 11-year-olds, 19 12-year-olds, and 16 13-year-olds (M age = 12.4, SD = .92). Among the included participants 46.6% were Caucasian, 10.3% Asian, 5.2% Hispanic/Latin, 3.4% African-American, 24.1% were multi-racial, and 10.4% did not provide information about their race or ethnicity.

All participants scored within the normal range on the Child Behavior Checklist (CBCL; Achenbach, 1991), based on their total score. Furthermore, there were no age-related differences in cognitive functioning, as measured by their performance on the matrix-reasoning (MR) subtest of the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1991). See Table 1 for the means, standard deviations, and ranges for each age group.

[3] Only one run (instead of two) of task-related imaging data was collected (n = 2), the task did not work (n = 3), and the data was saved improperly leading to loss of the data (n = 1).

Table 1. Sample characteristics for cognitive functioning and behavioral problems: mean ± standard deviation (and range).

	11yrs (n = 23)	12yrs (n = 19)	13yrs (n = 16)	*Group diff*
WASI-MR				
Raw score	26.4 ± 3.6 (18–32)	26.8 ± 3.7 (19–31)	26.8 ± 3.8 (20–34)	$F(2, 55) = .09$, $p = .92$
Age-corrected score	56.9 ± 6.9 (42–68)	55.7 ± 7.3 (41–65)	52.8 ± 7.5 (39–67)	$F(2, 55) = 1.6$, $p = .22$
CBCL	(n = 21)			
Internalizing score	48 ± 7.3 (33–61)	50.8 ± 11.7 (33–70)	47.5 ± 9.5 (33–62)	$F(2, 53) = .65$, $p = .53$
Externalizing score	47.9 ± 11.9 (34–75)	47 ± 8.8 (34–62)	42.8 ± 8.4 (34–60)	$F(2, 53) = 1.3$, $p = .29$
Total score	45.9 ± 9.4 (29–62)	48.2 ± 11.6 (29–65)	43.6 ± 11.1 (24–61)	$F(2, 53) = .81$, $p = .45$

WASI-MR = Matrix Reasoning subtest of the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1991)
CBCL = Child Behavior Checklist, completed by the parent (Achenbach, 1991)

Study procedure

Each participant visited the lab on two separate occasions, which were spaced an average of 19 days apart (SD: 19 days, range: 0–125 days). Across the two lab visits, participants completed interviews, computer tasks, pen-and-pencil questionnaires, and an MRI scan. Saliva samples for hormone assessment were collected at home, during the time in between the two lab visits. The participants were instructed on how to conduct saliva donation (by passive drool) during the first lab visit, and they brought the samples to the lab on their second visit. Here we report the findings from the data collected during the second lab visit, except for the Pubertal Development Scale (PDS; Peterson et al., 1988), which was completed during the first visit (further described below). However, if there was a lag of more than 45 days between the two lab visits, the PDS was re-administered during the second visit to control for pubertal changes during this time. For the participants who filled out the PDS twice (n = 4), we used the average PDS score based on the second-time completion[4].

During the second lab visit, participants were scanned and filled out questionnaires that measured personality traits thought to be associated with risky behavior and social functioning (see supplementary Table S1 for a list of the measures). Before they entered the scanner, participants were instructed on how to play the fMRI task and they completed 12 practice trials. Then, the scanning procedure was explained and participants received a final screening for metal. Each participant completed five scans: a structural scan, followed by a resting-state scan, two task-related scans, and another resting-state scan. In between scans, we checked in with the participants to see how they were doing and whether they still wanted to continue. During these breaks, we also took the opportunity to remind them to keep their head still. Upon completion of the first structural scan, we visually inspected it for signs of excessive movement; if present, we collected an additional structural image at the end of the scanning procedure.

[4] Two 11-year-olds and two 12-year-olds were re-administered the PDS (interval range: 47 – 125 days). One 11-year-old returned after an interval of 53 days, but did not complete the PDS again. For this participant, we used the first-visit PDS score. We believe that the data for this participant is valid, since the two 11-year-olds who were re-administered the PDS after 50 and 125 days, only displayed a .2 and .0 score increase, respectively.

Participants were told about this possibility prior to scanning. In total, participants spent up to one hour in the scanner. The questionnaires were administered after the scan, in a separate room with an experimenter present.

All participants received a $55 gift card at the end of the first visit, and a $75 gift card at the end of the second visit. These amounts included compensation for their travel time, the time spent in the lab, and additional task winnings.

Self-reported pubertal development

All participants included in this study completed the Pubertal Development Scale (PDS; Peterson et al., 1988), a self-report measure of pubertal maturation. We used this measure based on previous research that demonstrated that this self-report measure has high reliability (α = .81 in girls) and can be compared to the scores derived from physical examination done by a nurse practitioner (Shirtcliff et al., 2009). The PDS consists of five questions about the physical changes associated with pubertal development that were scored from no physical changes (1) to development seems complete (4). The average of all five items (i.e., the total score) was calculated to provide an index of pubertal maturation (see Table 2 for the means of each age group). Note that PDS score increased with age (Table 2); post-hoc Tukey tests revealed that both 12- and 13-year-olds scored higher than 11-year-olds (p = .026 and p = .001, respectively), but did not differ from each other (p = .37).

Additional questions about height (in inches) and weight (in lbs) were also included in the questionnaire. Based on these measures, body-mass index (BMI) was calculated as a marker of physical growth during puberty (see Table 2). As reported in Table 2, there were no age-related differences in BMI.

Table 2. Sample characteristics for the developmental measures: mean ± standard deviation (and range).

	11yrs (n = 23)	12yrs (n = 19)	13yrs (n = 16)	*Group diff*
PDS				
Total score	2.2 ± .56[1,2] (1.2 – 3.2)	2.7 ± .68[1] (1.6 – 3.8)	3.0 ± .55[2] (2.2 – 3.8)	$F(2, 55) = 8.5$, ***p* = .001**
Hormones[a]		(n = 18)	(n = 15; n = 14)	
Testosterone	46.3 ± 14.1 (17.9 – 75.6)	53.4 ± 17.7 (32.2 – 93.9)	56.9 ± 20.6 (33.1 – 102.6)	$F(2, 53) = 1.9$, p = .156
Estradiol	1.2 ± .51[3] (.43 – 2.6)	1.6 ± .51 (.91 – 2.4)	1.8 ± .42[3] (1.1 – 2.7)	$F(2, 52) = 6.6$, ***p* = .003**
BMI	(n = 22) 18.8 ± 2.8 (14 – 25.1)	(n = 18) 19.2 ± 2.2 (15.6 – 24.3)	19.8 ± 3.4 (14.8 – 26.1)	$F(2, 53) = .66$, p = .52

[a] Hormones were measured in pg/mL. [1,2,3] Age groups that differ significantly from one another based on a post-hoc Tukey test ($p < .05$). PDS = Pubertal Development Scale (Peterson et al., 1988). BMI = Body Mass Index: weight (lb) / [height (inch)^2] * 703.

Hormone assessment

Testosterone and estradiol levels were measured based on two saliva samples provided by each participant. We used the passive drool method for saliva collection to minimize discomfort and maximize compliance (Shirtcliff et al., 2001). Participants were instructed to collect the two saliva samples on separate—preferably consecutive—mornings between 7:00 a.m. and 9:00 a.m. Participants were provided with 2 mL tubes, which they were instructed to fill up at least halfway, and straws, to aid saliva collection.

Before saliva collection, participants were asked to avoid (1) brushing their teeth or eating a major meal for at least 1 hour prior to collection, (2) eating anything acidic or high-sugar within 20 minutes before collection, and (3) taking something that stimulates the production of saliva. They were asked to rinse their mouth with water about 10 minutes prior to collection, and to store the samples in the freezer immediately upon collection. A form was provided for the participant to indicate the date and time of collection for the two samples[5].

Saliva samples brought into the lab were immediately stored in a freezer at -20 C. Testosterone (T) assays were conducted in the Kriegsfeld laboratory at UC Berkeley, using Salimetrics salivary testosterone enzyme immunoassay kits (http://www.salimetrics.com/). Assays were run in duplicate and were repeated for samples with *intra*-assay coefficients of variability (CVs) above 7%. Of these repeats, the assay results with the lowest intra-assay CV (i.e., highest reliability) were included for analysis (*M* intra-assay CV = 2.2%, SD = 1.9%, range: 0 – 9.4%). We ran all samples across 6 separate assays total with an *inter*-assay CV of 21.3%. Estradiol (E) assays were conducted at the University of New Orleans, Louisiana, under supervision of Dr. E. A. Shirtcliff (*M* intra-assay CV = 5.7%, SD = 5.3%, range: 0.08 – 28.8%).

Two participants were excluded from analysis; the samples from one 12-year-old were lost, and the samples of one 13-year-old were taken at the wrong time of the day (afternoon rather than morning). There were no significant differences between the two samples collected from each participant (T: $t(52) = .26$, $p = .80$; E: $t(51) = 1.7$, $p = .10$). Thus, hormone levels were calculated as the average across the two samples collected by each participant, unless one of the samples was excluded due to any of the following reasons: (1) collected more than 1 hour after the instructed time window (i.e., after 10:00 a.m.) ($n = 1$), (2) too dirty to be analyzed ($n = 1$), (3) collected more than 2 weeks later than the first sample ($n = 1$), (4) contained insufficient quantity of saliva ($n = 1$; estradiol only), or (5) had an intra-assay CV > 30% ($n = 2$; estradiol only); in these cases the value of the valid sample was used[6]. See Table 2 for the means, standard deviations, and ranges for each age group. Note that there were age-related differences in estradiol, but not in testosterone levels. Post-hoc Tukey tests revealed that 12- and 13-year-olds had (marginally) higher estradiol levels than 11-year-olds ($p = .057$ and $p = .003$, respectively), but did not differ from each other ($p = .44$).

See Table 3 for the correlations between all five developmental measures. As reported in Table 3, estradiol level corresponded with all other developmental measures (i.e., age, pubertal stage, testosterone level, and BMI; all r's $\geq .36$), whereas testosterone level only correlated with estradiol level.

[5] Forty-one participants completed the saliva collection form; however, four of them only provided information for one sample. For the 15 remaining participants who did not complete the saliva collection form, we were unable to verify compliance. We included both samples for these participants.

[6] This led to the exclusion of one additional 13-year-old for estradiol. Hence, results for testosterone are based on 56 participants, whereas for estradiol they are based on 55 participants.

Table 3. Pearson's correlations among the developmental measures.

Developmental measures	1	2	3	4
1. Age	—			
2. PDS	***r* = .47*** **	—		
	(*n* = 58)			
3. Testosterone	*r* = .25	*r* = .16	—	
	(*n* = 56)	(*n* = 56)		
4. Estradiol	***r* = .43****	***r* = .52*****	***r* = .36****	—
	(*n* = 55)	(*n* = 55)	(*n* = 55)	
5. BMI	*r* = .16	***r* = .41****	*r* = .21	***r* = .52*****
	(*n* = 56)	(*n* = 56)	(*n* = 55)	(*n* = 55)

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

The Jackpot task

All participants played a revised version of the Jackpot task (Op de Macks et al., 2011), a two-choice probabilistic decision-making game designed for use with children. In this task, the probability of winning or losing on a given trial is presented visually in a way that is intuitive to children. On each trial, a slot machine appeared with two out of three slots showing plums. The three possible outcomes for the third slot were shown in a yellow frame above the slot machine. To win, all three slots needed to show plums. In the low-risk condition, the chance to win was 67% (2/3); in the high-risk condition, the chance to win was 33% (1/3). Additionally, information about the reward at stake (1 or 3 points) was presented in a green frame above the slot machine. Thus, there were four types of trials: low-risk/low stakes (LR-1pt), low-risk/high stakes (LR-3pts), high-risk/low stakes (HR-1pt), and high-risk/high stakes (HR-3pts), which were presented in random order across the entire task.

Based on the information about risk level and stakes involved, the participant could choose to play (i.e., take the risk to win or lose 1 or 3 points), or pass (i.e., skip the trial), which was indicated by a button press with the right index or middle finger, respectively. The option to pass was added because prior studies demonstrated that outcome monitoring (or reward processing) is more salient when the outcome is the result of an *active* choice (Leotti and Delgado, 2014; Rao et al., 2008; Tricomi et al., 2004). Upon the button press (or after 2 seconds, in the absence of a response), the outcome was presented. When the participant chose to play, the outcome could be positive (gain) or negative (loss). Upon the choice to pass, the outcome was neutral (no gain or loss). If participants failed to respond, they lost 1 point. This was done to help maintain task engagement.

The task was administered across two runs of scans, separated by a self-paced break (during which we reminded participants to keep their head still). Participants completed a total of 96 trials across 4 blocks (i.e., 24 trials in each block); trials in each block were randomly selected from the four task conditions (i.e., LR-1pt, LR-3pts, HR-1pt, and HR-3pts). Each trial started with a 500ms fixation cross, which was jittered for an additional 0-8 seconds at 2-sec increments. Then, the stimulus was presented for a maximum of 2 seconds[7], during which the participant had to respond (or they would lose

[7] To ensure that each trial (stimulus, anticipation, and outcome phase) had the same duration, we added the leftover time from the stimulus phase (i.e., 2s minus the response time) to the end of the trial in the form of

1 point). Immediately following the button press came a 750ms anticipation phase. During this phase, the slot machine would spin (upon 'play'), or—to equate the visual experience of the anticipation phase across trial types—an "X" (for 'pass') or orange frame (for no response) would flicker in the third slot. The anticipation phase was followed by the outcome, which was presented for 2 seconds. When participants won, they saw three plums in a row and the words "you won". When participants lost, they saw a different fruit (orange or cherries) in the third slot accompanied by the words "try again". When participants passed or missed, the third slot showed an "X" or orange frame with the words "passed" or "too slow", respectively (Fig. 1).

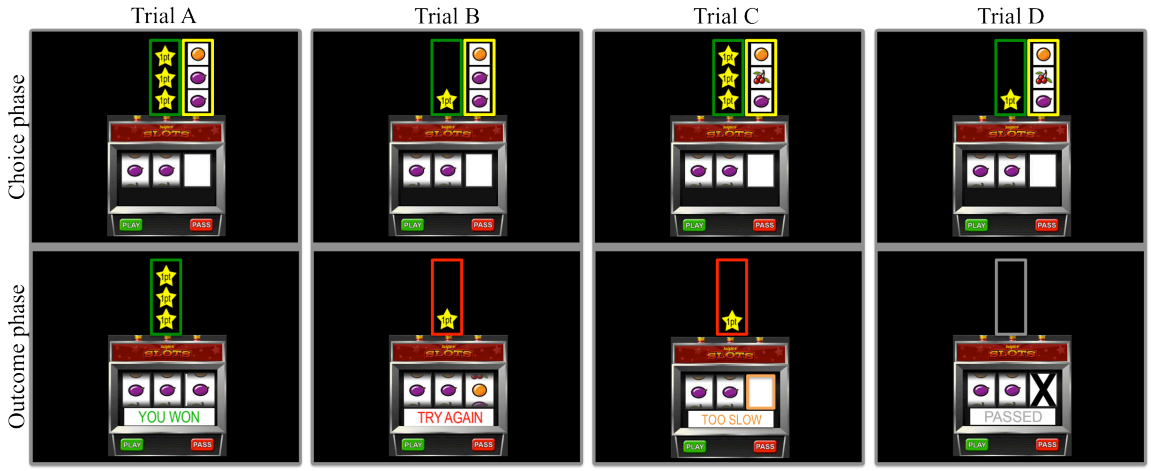

Fig. 1. Examples of trials in the Jackpot task, modified from (Op de Macks et al., 2011). There were four different stimuli conditions, which were presented in random order during the choice phase (top panel). During the outcome phase (bottom panel), participants were presented with four possible outcomes (depending on their choices). Trial A is an example of what the participant saw when the chance to win 3 points was 67%, chose to play, and won. Trial B: the chance to win 1pt was 67%, the participant chose to play, and lost. Trial C: the chance to win 3pts was 33%, the participant did not respond, and lost 1pt. Trial D: the chance to win 1 point was 33%, the participant chose to pass. Note that in actuality other combinations of choices and outcomes were possible, depending on participants' choices.

After every 6 trials, participants received feedback on their task performance. Hence, within each block (of 24 trials) there were 4 instances of performance feedback (i.e., feedback phases). These feedback phases lasted for 4s and were followed by 1s of fixation. There were two types of feedback, which were presented throughout an entire block. In the monetary feedback blocks, participants were shown how much money they had won; in the social rank feedback blocks, participants were shown how well they played compared to other girls who had played the task.[8] At the beginning of each run,

a fixation cross. In other words, we extended the time that the fixation cross was presented during the inter-trial-intervals by [2s – RT].

[8] We used a cover story in which we told participants that other girls who played the game were ranked based on their scores, and the participant's score would be compared to those other girls' performance. In actuality, we arbitrarily ranked the silhouettes of research assistants and participants from our pilot study—after obtaining written permission. During the first lab visit, a picture was taken of each participant's side profile. This picture was converted into a black-and-white silhouette, which was incorporated into the game, so that each participant would see herself traveling up and down the arrow during feedback presentation. The silhouettes of the "other girls" were consistent across participants, so that visual experience of feedback presentation was equal across participants (except for their own silhouette).

participants were instructed verbally (using the intercom) about which feedback type they would start with, and they received a written prompt that announced the switch of feedback type in between blocks. These transition phases lasted for 12 seconds and were followed by 2s of fixation. The order of feedback type was counterbalanced across participants. See Fig. 2 for a complete overview of the task design. For this paper, results were collapsed across feedback type, as there were no effects of feedback type on task behavior (see Behavioral Results).

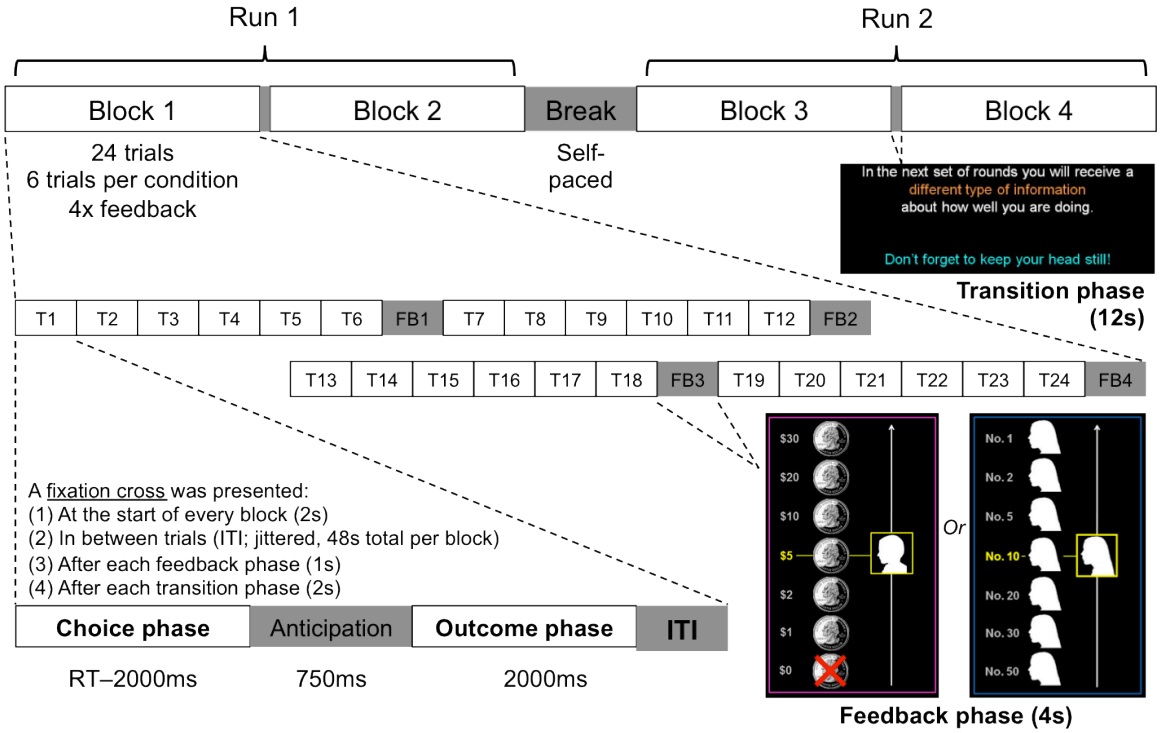

Fig. 2. Task design of the updated version of the Jackpot task. The task was administered across two runs of scans with a self-paced break in between. Each block consisted of 24 trials, 6 trials of each condition (presented in random order). Feedback phases occurred after every 6 trials (i.e., 4 times in each block). Throughout each block feedback type (Monetary or Social) was held constant and the order was counterbalanced between participants (MSMS or SMSM). Before each run started, participants were told which feedback type would be presented first; in between blocks (within the same run) they were visually prompted about the transition in feedback type (i.e., transition phase). Trials consisted of a choice phase, in which participants chose to play or pass based on information about risk level (33% or 67% chance to win) and stakes (1 or 3pts), and during the outcome phase, participants were shown whether they won or lost (or nothing changed).

Participants were instructed that they had $5 in play money and that they could increase this amount to an amount up to $30 if they chose to play. All participants were told that they would be paid according to their final score—in points—which was translated into a monetary amount at the end of the experiment. All participants won $10 because, in actuality, the choice to play resulted in positive feedback in 50% of the trials, regardless of the presented risk. This was done to have a similar number of observations for reward and loss trials upon a risky decision, to enable direct comparison of the brain response associated with gain and loss. The discrepancy between the presented probability of winning (i.e., 33% or 67%) and the experienced probability of winning

(i.e., 50%) did not affect choice behavior at the group level. Specifically, while the percentage of play choices differed between the four task conditions, $F(3, 55) = 83.0$, $p < .001$, there were no differences across the four task blocks (of 24 trials each), $F(3, 55) = .99$, $p = .41$. Furthermore, there was no interaction between conditions and blocks, $F(9, 49) = .74$, $p = .67$. These results indicate that participants adjusted their choices based on the information provided about risk level and stakes, but did not change their choice behavior over time (i.e., based on their task experience); the absence of a learning effect was similar across task conditions (see supplementary Fig. S1).

Self-reported task experience

After the scan, participants ($n = 56$) completed a questionnaire in which they were asked to rate their experience during the Jackpot task, using a 7-point Likert scale. Specifically, participants were asked to rate how happy (with 1 = very unhappy and 7 = very happy), satisfied (1 = very dissatisfied, 7 = very satisfied), excited (1 = very bored, 7 = very excited), proud (1 = very disappointed, 7 = very proud), and nervous (1 = very calm, 7 = very nervous) they felt during gain and loss outcomes following the choice to play. For example, participants were asked: "how did you feel when you played for money and won?" and "how did you feel when you played for rank and lost?".

For this study, we collapsed ratings across feedback types, and performed an exploratory factor analysis on the resulting scores. Using principal component analysis, three components were extracted (i.e., had eigenvalues > 1.0), which together explained 78.3% of the variance. While positive emotions (happy, satisfied, excited, and proud) loaded positively on the first component, nervousness loaded negatively on this component. The second component distinguished between winning and losing for all positive emotions, but not for nervousness. Nervousness loaded high on the third component. Based on these results, we reduced the data to a *Positivity* score (i.e., average across the positive emotions) and *Nervousness* score for each *Outcome* separately (i.e., gain and loss). See Table 4 for the group means. Note that there were age-related differences in reported positive emotions and nervousness experienced during gains, but not during losses. Post-hoc Tukey tests revealed that 11-year-olds reported having experienced more positive emotions during gains compared to 12-year-olds ($p = .014$; Table 4), whereas 13-year-olds did not differ from 11- or 12-year-olds ($p = .11$ and $p = .79$, respectively). Furthermore, both 12- and 13-year-olds reported having experienced more nervousness during gains compared to 11-year-olds ($p = .002$ and $p = .013$, respectively; Table 4), but their reports did not differ from each other ($p = .93$).

Table 4. Mean ratings of task experience for each age group separately.

	11yrs (n = 22)	12yrs (n = 19)	13yrs (n = 15)	*Group diff*
Gain				
Positivity	5.8 ± .68[1]	5.2 ± .60[1]	5.4 ± .61	$F(2, 53) = 4.6$, $\mathbf{p = .014}$
	(4.4 – 7.0)	(4.3 – 6.4)	(4.1 – 6.4)	
Nervousness	2.4 ± .84[2,3]	3.5 ± 1.1[2]	3.4 ± 1.2[3]	$F(2, 53) = 7.5$, $\mathbf{p = .001}$
	(1.0 – 4.5)	(2.0 – 5.5)	(1.0 – 5.5)	
Loss				
Positivity	3.6 ± .84	3.4 ± .29	3.4 ± .44	$F(2, 53) = 1.0$, $p = .37$
	(2.6 – 7.0)	(3.0 – 4.0)	(2.5 – 3.9)	
Nervousness	3.0 ± 1.3	3.7 ± 1.1	3.9 ± 1.3	$F(2, 53) = 2.9$, $p = .064$
	(1.0 – 5.5)	(2.0 – 5.5)	(1.0 – 6.0)	

[1,2,3] Age groups that differ significantly from one another based on a post-hoc Tukey test ($p < .05$).

MRI image acquisition

MRI scanning was conducted on a Siemens MAGNETOM Trio 3T MR Scanner using a 12-channel head coil at the Henry H. Wheeler, Jr., Brain Imaging Center at the University of California, Berkeley. During the structural scan, we collected one run (160 volumes) of anatomical images, which consisted of 160 slices acquired using a T1-weighted MP-RAGE protocol (TR = 2300 ms; TE = 2.98 ms; FOV = 240 x 256 mm; matrix size = 240 x 256 mm; voxel size = 1 mm^3; 160 volumes/run; 1 run). During the task-related scans, we collected two runs of functional images (285 volumes in 6.5 minutes for each run), which consisted of 24 axial slices acquired with an ascending interleaved gradient echoplanar imaging protocol (TR = 1370 ms; TE = 27 ms; FOV = 225 x 225 mm; matrix size = 96 x 96 mm; voxel size = 2.3 x 2.3 x 3.5 mm; inter-slice gap ~ 0.3mm). The fMRI task was programmed and presented using Visual Basic 6.0 software (http://microsoft-visual-basic.en.softonic.com/) and projected onto a frosted glass screen behind the head coil within the scanner bore. A mirror was placed on top of the head coil to allow the participant to see the display. Participants made their responses on an MRI-safe fiber optic response pad (Inline Model HH-1x4-L; http://www.crsltd.com). Head motion was restricted due to foam inserts that surrounded the head.

fMRI preprocessing

Functional images were converted from DICOM to 4D NIfTI format using MRIcron (http://www.mccauslandcenter.sc.edu). Preprocessing was performed using statistical parametric mapping, version 8 (SPM8; Wellcome Trust Center for Neuroimaging; http://www.fil.ion.ucl.ac.uk). Motion correction was performed using a two-pass procedure in which the images were first registered to the first image, after which they were registered to the resulting mean image. Images were corrected for slice-timing offsets using the first slice as a reference. Coregistration was performed with the mean image as a reference image, and the anatomical image as source image. Coregistered images were segmented using tissue probability maps (D'Agostino et al., 2004), and were warped using the International Consortium for Brain Mapping (ICBM) space template for European brains. Next, the images were smoothed with a 6 mm full-width half maximum (FWHM) Gaussian kernel. Finally, we used ArtRepair, a toolbox for SPM (Mazaika et al., 2009) to identify and remove volumes that showed movement greater than 0.5 mm. Participants were excluded from analysis if more than 20% of their volumes were removed (n = 3).

fMRI analyses

Statistical analyses were performed on individual subjects' data using the general linear model (GLM) in SPM8. Trials were modeled as separate zero-duration events starting at the onset of stimulus presentation. Note that while each trial consisted of a stimulus, anticipation, and outcome phase, these phases were not modeled separately due to the relatively short duration of the entire trial (i.e., max. 4.75s). Feedback phases (of 4s long) were also modeled as zero-duration events starting at the onset of feedback presentation. Transition phases were modeled as 12-sec events starting at the onset of the transition screen presentation. Here, we report the results of analyses collapsed across feedback type.

We created two separate subject-specific design matrices; one with three regressors of interest encoding for Play, Pass, and Miss (the *choice* model), and one with four regressors of interest encoding for Gain, Loss, Pass, and Miss (the *outcome* model). Note that the only difference between these two models is the further categorization of Play trials into (1) Play trials that resulted in Gains, and (2) Play trials that resulted in Losses, which allowed for comparison of Gain and Loss outcomes following the choice to play. For each of these first-level statistical models, regressors of no interest were added for the (1) feedback phases, (2) transition phases, and (3–8) the movement parameters (roll, pitch, yaw and displacement in superior, left and posterior directions).

To examine risk taking-related brain activation across the entire group, second-level statistical analyses were conducted to test the contrast Play vs. Pass trials. To examine reward-related brain activation across the group, we tested the contrast Gain vs. Loss trials (following the choice to play). Task-related responses were considered significant if they consisted of at least 10 contiguous voxels that exceeded a family-wise error (FWE) corrected threshold of $p < .05$.

To examine the relation between developmental measures (age, pubertal stage, hormone levels, and BMI) and brain processes associated with risky decisions, we applied the MarsBar toolbox for use with SPM8 (Brett et al., 2002) to extract parameter estimates from specific regions of interest (ROIs). We created our a-priori ROI by drawing a 4 mm-radius sphere around the coordinates for the bilateral nucleus accumbens ($x = \pm 10$, $y = 12$, $z = -3$; Haber and Knutson, 2010). We correlated the parameter estimates extracted for each participant with individual scores on each measure.

Behavioral Results

Task behavior across the group

Risk taking. A repeated-measures ANOVA with the percentage of trials on which the participant chose to play (i.e., risk taking) as the dependent variable and feedback type (social rank or monetary), risk level (low or high), and stakes (1 or 3 points to be gained or lost) as predictors showed main effects of both risk level, $F(1, 57) = 208.8$, $p < .001$, and stakes, $F(1, 57) = 5.0$, $p = .030$. Follow-up analyses revealed that girls chose to play more often in the low-risk (LR) condition ($M = 90.9\%$, $SD = .10\%$) compared to the high-risk (HR) condition ($M = 45.5\%$, $SD = .22\%$, $t(57) = 14.5$, $p < .001$), and when a large reward (3pts) was at stake ($M = 70.6\%$, $SD = .15\%$) compared to when a small reward (1pt) was at stake, ($M = 44.5\%$, $SD = .11\%$, $t(57) = 13.1$, $p < .001$) (Fig. 3a). There was no interaction between risk level and stakes, $F(1, 57) = 1.2$, $p = .27$, indicating that the effect of stakes was similar across risk levels.

Response times. Each participant's response time (RT) was measured as the average time in milliseconds between stimulus onset and the button press, excluding trials on which the participant failed to respond. Results of a repeated-measures ANOVA with RT as dependent variable and feedback type, risk level, and stakes as predictors showed a main effect of risk level, $F(1, 57) = 92.7$, $p < .001$, and an interaction between risk level and stakes, $F(1, 57) = 4.3$, $p = .043$. Follow-up analyses revealed that girls took longer to make their decisions in the HR condition ($M = 1001$ms, $SD = 144$ms) compared to the LR condition ($M = 869$ms, $SD = 167$ms, $t(57) = 9.6$, $p < .001$). Furthermore, girls were *faster* to decide when 3pts were at stake ($M = 862$ms, $SD = 139$ms) than when 1pt was at stake ($M = 876$ms, $SD = 168$ms) in the LR condition, whereas girls were *slower* to decide when 3pts were at stake ($M = 1011$ms, $SD = 179$ms) than when 1pt was at stake ($M = 992$ms, $SD = 171$ms) in the HR condition (see Fig. 3b). These results indicate that the girls were sensitive to the differences between the four task conditions, and most likely integrated both types of information to come to their decisions. Of note, while the interaction effect was significant, direct comparison of the means using paired-sample *t*-tests revealed non-significant differences for both contrasts: LR-1pt *vs.* LR-3pts, $t(57) = 1.04$, $p = .304$; HR-1pt *vs.* HR-3pts, $t(57) = 1.43$, $p = .158$.

No effects of feedback type were found for either risk taking or RT, indicating that in the aggregate the girls made similar choices across the four task conditions, regardless of whether they were receiving monetary or social rank feedback. Thus, we collapsed across the two feedback types for all remaining analyses.

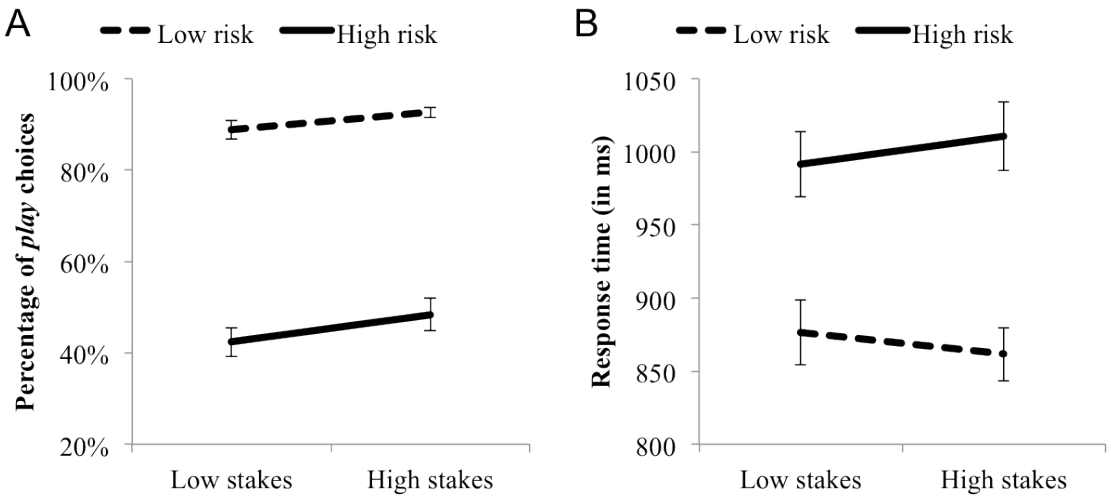

Fig. 3. (a) Risk taking plotted separately for small and large stakes in the low-risk (dashed line) and high-risk (solid line) condition; (b) response time plotted separately for the low-risk (dashed line) and high-risk (solid line) condition. Error bars represent the standard errors.

Individual differences in decision-making

Developmental measures. Correlational analyses showed that girls who engaged in more risk taking tended to have higher levels of testosterone (Table 5). Because the individual variance in risk taking in the LR condition was relatively small ($M = 90.9\%$, $SD = 10.1\%$, range: 54 – 100%) compared to the HR condition ($M = 45.5\%$, $SD = 22.4\%$, range: 0 – 88%; see supplementary Fig. S2a), we focused on risk taking in the HR condition only. Results showed that higher testosterone levels were associated with

increased risk taking when 1pt was at stake (r = .33, p = .014), but not when 3pts were at stake (r = .12, p = .366), indicating that girls with higher testosterone levels were more inclined to take risks when the expected value (i.e., probability * reward) was the lowest. According to Steiger's test (Steiger, 1980), these correlations were marginally different from one another (Steiger's z = 1.7, p = .084).

Furthermore, testosterone level was negatively associated with RT (Table 5), indicating that girls with higher testosterone levels tended to make decisions (to play or pass) more quickly. Because variance was similar between conditions for RT (LR condition: M = 869ms, SD = 144ms, range: 580 – 1160ms; HR condition: M = 1001ms, SD = 167ms, range: 627 – 1451ms) (see supplementary Fig. S2b), we explored the relations between testosterone level and RT for both the LR and HR conditions. Results showed that testosterone level was associated with RT in the LR condition (r = -.37, p = .005), but not in the HR condition (r = -.16, p = .231; Steiger's z = -2.4, p = .016), regardless of the stakes (LR-1pt: r = -.33, p = .012, LR-3pts: r = -.36, p = .006; HR-1pt: r = -.14, p = .295, HR-3pts: r = -.17, p = .215). These results indicate that girls with higher testosterone levels made up their minds more quickly when decisions were relatively "easy" (i.e., much less risky), but not when they were "harder" (i.e., more risky).

No associations were found with either risk taking or RT for age, PDS score, BMI, or estradiol level (see Table 5).

Table 5. Correlations between developmental measures and risk taking as well as response times across the entire task.

	Age (n = 58)	BMI (n = 56)	PDS (n = 58)	Testosterone (n = 56)	Estradiol (n = 55)
Risk taking (%)	r = -.03	r = .02	r = .02	***r* = .32**	r = -.07
	p =.827	p =.904	p =.902	***p* =.017**	p =.639
RT (ms)	r = -.09	r = -.03	r = -.09	***r* = -.27**	r = .17
	p =.501	p =.812	p =.488	***p* =.043**	p =.213

Self-reported experience. Correlational analyses showed that girls who, after playing the Jackpot task, reported feeling more nervous during outcomes (gains and losses) tended to be older and at a more advanced stage of pubertal development. See Table 6 for the correlations between self-reported experience and the developmental measures. Regression analyses further revealed that, when controlling for age, more advanced pubertal stage (i.e., higher PDS score) significantly predicted enhanced reported nervousness for gains (β = .35, p = .014; age: β = .21, p = .127), but not for losses (β = .11, p = .466; age: β = .28, p = .061). No associations were found between self-reported experience during gains and losses (i.e., positive emotions or nervousness about task outcomes) and the hormone levels. Although girls with higher estradiol levels (or higher BMI) tended to reported less positive feelings during gains (see Table 6).

No associations were found between self-reported experience and task behavior. However, there was a marginally negative association between risk taking and self-reported positive emotions during gains (Table 6), indicating that girls who rated gains as a more positive experience showed a tendency to choose to play *less* often. Further analysis revealed that this negative relation existed in the HR condition (r = -.30, p = .026), but not in the LR condition (r = .09, p = .517); these correlations were significantly different from one another (Steiger's z = 2.1, p = .035).

Table 6. Correlations between the self-reported experience of gains and losses during the Jackpot task and developmental as well as task behavior measures.

	Gains		Losses	
	Positivity	*Nervousness*	*Positivity*	*Nervousness*
Development				
Age (n = 56)	r = -.19, p =.16	**r = .38, p =.004**	r = -.19, p =.17	**r = .33, p =.012**
PDS (n = 56)	r = -.16, p =.23	**r = .45, p < .001**	r = -.06, p =.69	r = .24, p =.069
Testosterone (n = 54)	r = -.04, p =.77	r = .17, p = .22	r = -.07, p =.63	r = .07, p = .64
Estradiol (n = 53)	r = -.25, p =.067	r = .20, p = .15	r = -.05, p =.74	r = .05, p = .70
BMI (n = 55)	r = -.25, p =.063	r = .13, p = .34	r = -.22, p =.11	r = -.01, p = .93
Task behavior (n = 56)				
Risk taking (%)	r = -.23, p =.091	r = .01, p =.95	r = .02, p =.87	r = -.13, p =.36
Response time (ms)	r = .07, p =.62	r = .07, p =.60	r = -.05, p =.70	r = .20, p =.13

Imaging Results

Risk taking engages reward circuitry

Whole-brain results for Play *vs.* Pass trials across all participants revealed clusters of activation in bilateral striatum (caudate, putamen, pallidum, and nucleus accumbens), midbrain, and bilateral anterior insula (Fig. 4a). The opposite contrast, Pass *vs.* Play trials, did not reveal any clusters of activation. However, when we lowered the threshold to $p < .001$, uncorrected ($k > 10$ voxels), clusters of activation appeared in ventrolateral prefrontal cortex and inferior parietal lobe (see supplementary Fig. S3a). Whole-brain results for Gain *vs.* Loss trials revealed clusters of activation in bilateral ventral striatum and medial prefrontal cortex (Fig. 4b). We did not find any regions of activation for the opposite contrast (i.e., Loss *vs.* Gain trials). However, when we lowered the threshold to $p < .001$, uncorrected ($k > 10$ voxels), we found a cluster of activation in left thalamus (see supplementary Fig. S3b). See Table 7 for the MNI coordinates.

Results of our region-of-interest (ROI) analysis for the bilateral nucleus accumbens (NAc; Haber and Knutson, 2010)—which overlapped with the regions of activation that resulted from both the contrasts Play *vs.* Pass and Gain *vs.* Loss—revealed that across the group NAc activation increased with the decision to play, but not with the decision to pass. Furthermore, NAc activation during trials on which participants chose to play remained elevated when the choice to play resulted in gain, whereas NAc activation returned to baseline more rapidly for play choices that resulted in loss (Fig. 5a), indicating this region's involvement in reward-related processes. Of note, the NAc was differentially activated during the four task conditions, when collapsing across play and pass choices. Specifically, NAc was most active for the LR-3pts condition and least active for the HR-1pt condition, although activation in the latter condition was not significantly different from activation during the HR-3pts condition, $t(57) = 1.2$, $p = .22$. These results indicate that, regardless of the choices participants made, their NAc seemed to track the expected value associated with the trials (see supplementary Fig. S4).

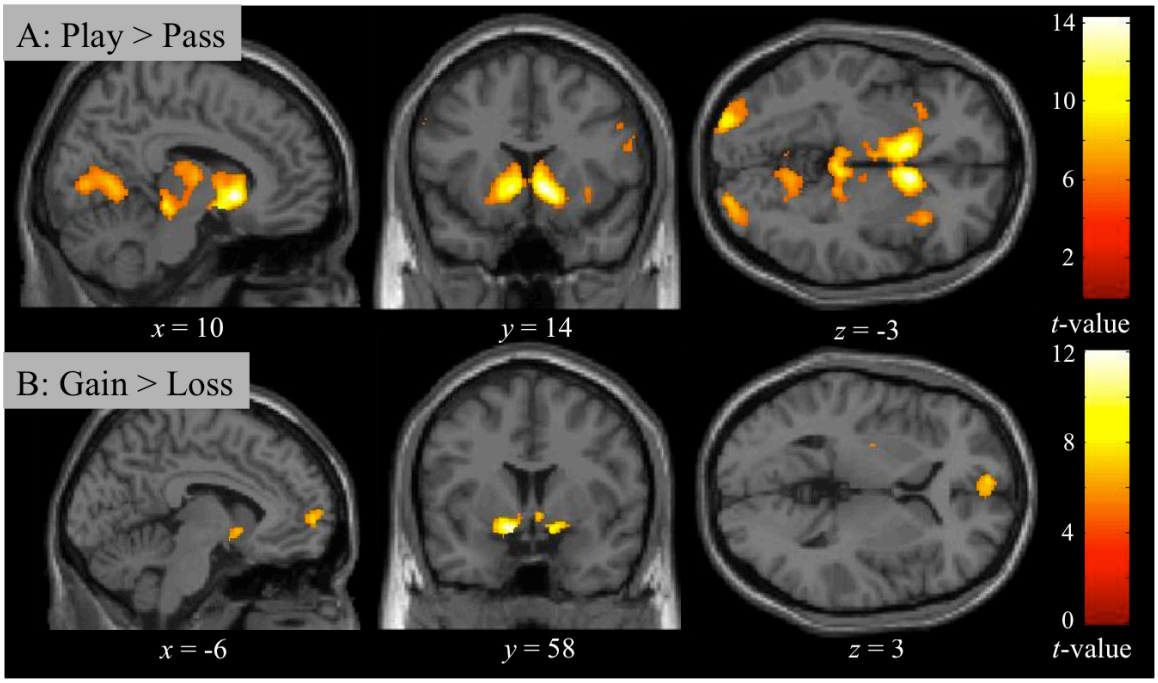

Fig. 4. Brain regions that showed increased activation for trials on which participants made (a) Play *vs.* Pass choices, and experienced (b) Gain *vs.* Loss outcomes (after the choice to play); both corrected for multiple comparisons (FWE) at $p < .05$, 10 voxels.

Table 7. Regions of activation associated with choice (Play vs. Pass trials) and outcome upon a risky choice (Gain vs. Loss trials) at a threshold of $p < .05$, FWE-corrected, $k > 10$ voxels, unless otherwise stated. All regions presented here survived correction for multiple comparisons (FWE) at the peak and/or cluster level.

	Peak-level			Cluster-level	
Contrast	MNI coordinates (x, y, z)	Brodmann area (BA)	FWE-corrected *p*-value	Volume	FWE-corrected *p*-value
Play – Pass					
Caudate head R	10, 14, -3		$p < .001$	7302	$p < .001$
Putamen L	-10, 9, -6		$p < .001$		
Putamen R	14, 6, -11		$p < .001$		
Occipital Inf Gyr L	-26, -96, -8	BA18	$p < .001$	1032	$p < .001$
	-40, -75, -11		$p = .002$		
Precentral / Frontal Inf Gyr R	51, 8, 30		$p < .001$	852	$p < .001$
Frontal Inf Oper Gyr R	57, 10, 19	BA45	$p < .001$		
Occipital Inf / Cuneus R	24, -96, -5		$p < .001$	403	$p < .001$
Occipital Inf Gyr R	36, -84, -8	BA18	$p = .001$		
Lingual Gyr R	8, -61, 1	BA18	$p < .001$	2637	$p < .001$
Lingual Gyr R	4, -72, 6	BA30	$p < .001$		
Lingual Gyr L	-10, -61, 3	BA18	$p = .001$		
Frontal Mid Gyr R	26, -3, 51	BA6	$p < .001$	417	$p < .001$
Supramarginal Gyr R	38, -39, 42	BA40	$p < .001$	312	$p < .001$
Parietal Sup Gyr / Precuneus R	22, -61, 51		$p = .001$		
Parietal Inf Gyr R	38, -43, 52	BA40	$p = .001$		
Parietal Inf / Inf Parietal Lobule L	-34, -48, 49		$p < .001$	609	$p < .001$
Parietal Sup Gyr L	-24, -58, 55		$p < .001$		
Parietal Sup Gyr / Precuneus L	-26, -51, 49		$p < .001$		
Precentral Gyr R	46, -3, 49	BA6	$p < .001$	90	$p < .001$
Precentral Gyr R	39, -7, 49		$p = .025$		
Insula / Inf Front Gyr R	34, 22, -3		$p < .001$	374	$p < .001$

Insula R	34, 10, -6		$p < .001$		
	28, 26, 4		$p = .007$		
Frontal Inf / Oper L	-48, 6, 28		$p < .001$	277	$p < .001$
Frontal Inf Oper L	-39, 3, 27		$p < .001$		
Anterior Cingulum L	-6, 39, 4		$p < .001$	73	$p < .001$
Occipital Sup L	-24, -73, 37	BA7	$p = .001$	84	$p < .001$
Frontal Mid Gyr L	-51, -6, 54	BA6	$p = .002$	122	$p < .001$
Postcentral Gyr L	-48, -13, 49	BA4	$p = .007$		
Precentral Gyr L	-58, 11, 34	BA9	$p = .002$	23	$p = .002$
Precentral / Frontal Mid Gyr L	-46, -1, 43		$p = .012$	35	$p = .001$
Anterior Cingulum R	3, 2, 28	BA24	$p = .014$	44	$p < .001$
Temporal Mid / Occipital Gyr R	45, -67, 1		$p = .023$	20	$p = .003$
Supramarginal / Postcentral Gyr R	54, -30, 48		$p = .024$	10	$p = .009$
Frontal Sup Gyr L	-22, 0, 52		$p = .026$	12	$p = .007$
Pass – Play (unc. $p < .001$, $k > 10$ voxels)					
Postcentral Gyr L	-45, -25, 54		$p = .004$	348	$p = .019$
Temporal Sup Gyr R	64, -52, 19	BA22	$p = .008$	158	$p = .260$
Frontal Inf Gyr L	-52, 29, 3		$p = .030$	902	$p < .001$
Temporal Sup / Mid Gyr R	56, -40, 4		$p = .061$	380	$p = .013$
Supramarginal Gyr L	-63, -46, 34		$p = .284$	631	$p = .001$
Gain – Loss					
Nucleus Accumbens L	-12, 4, -12		$p < .001$	504	$p < .001$
Putamen L	-28, -13, 1		$p = .007$	45	$p < .001$
Nucleus Accumbens R	14, 4, -12		$p < .001$	256	$p < .001$
Caudate R	6, 6, -6		$p < .001$		
Frontal Sup Med L	-6, 58, 3	BA10	$p < .001$	352	$p < .001$
Anterior Cingulum L	-9, 46, -2	BA32	$p = .005$	42	$p < .001$
Loss – Gain (unc. $p < .001$, $k > 10$ voxels)					
Thalamus R	4, -25, 4		$p = .049$	323	$p = .013$

Individual differences in reward circuitry

Correlational analyses showed that individual differences in NAc activation for Play *vs.* Pass were negatively associated with individual differences in risk taking ($r = -.28$, $p = .033$), indicating that girls who chose to play more often differentiated *less* between play and pass trials in terms of their NAc response. More specifically, girls who took more risks showed less NAc activation during trials on which they chose to play compared to baseline (i.e., fixation), but similar NAc activation during trials on which they chose to pass (compared to baseline). Moreover, the negative relation between behavior and NAc activation was significant for risk taking in the HR-1pt condition ($r = -.33$, $p = .011$; see Fig. 5b), but not for risk taking in the HR-3pts condition ($r = -.12$, $p = .39$; Steiger's $z = -1.7$, $p = .086$), or either of the LR conditions, for low stakes: $r = -.17$, $p = .22$ (Steiger's $z = -.99$, $p = .32$), and high stakes: $r = -.06$, $p = .65$ (Steiger's $z = -1.6$, $p = .012$). These results indicate that girls who showed less risk taking-related NAc activation took more risks, particularly in the condition with the lowest expected value.

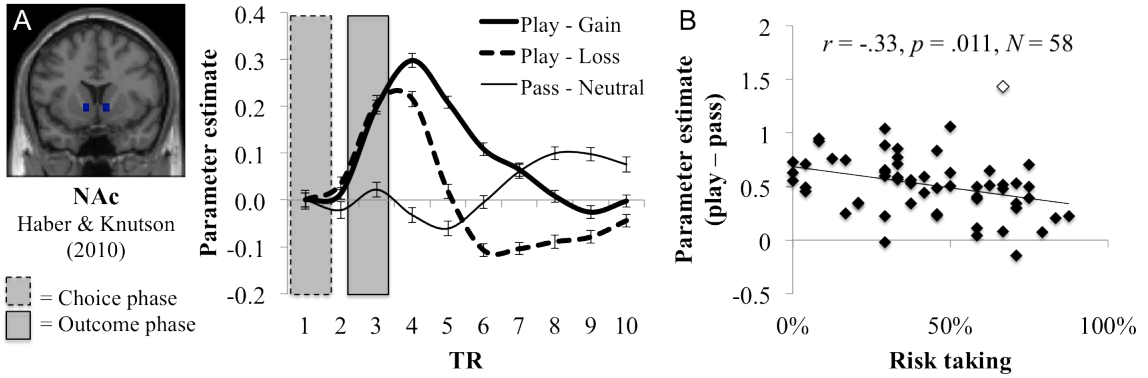

Fig. 5. (a) Nucleus accumbens (Haber & Knutson, 2010) activation across all participants (n = 58) for play (separately for gain and loss) and pass choices. Error bars represent standard errors. (b) Correlation between the percentage of play choices in the high-risk/low-stakes condition and risk taking-related nucleus accumbens activation. Exclusion of the extreme observation (β = 1.43; open dot) strengthened the relation between risk taking and NAc activation (r = -.43, p = .001, n = 57).

No correlations were found between NAc activation and RT (r = .21, p = .11, n = 58), self-reported experience of gains (r = .08, p = .58, n = 56), or any of the developmental measures: age (r = .02, p = .88, n = 58), pubertal stage (r = .18, p = .17, n = 58), BMI (r = -.10, p = .47, n = 56), testosterone level (r = -.17, p = .22, n = 56), although the relation with estradiol level was marginal (r = .26, p = .052, n = 55). Interestingly, a linear regression analysis including both hormones as predictors of NAc activation, and controlling for age, revealed that both testosterone (β = -.28, p = .047) and estradiol (β = .42, p = .006), but not age (β = -.14, p = .34), were significant predictors of NAc activation and together explained 16.2% of the variance in NAc activation, $F(3, 51) = 3.3$, p = .028. Of note, there was a positive correlation between testosterone and estradiol level (r = .36, p = .007, n = 55).

To examine whether there were any other regions besides NAc that correlated with risk taking, we performed an exploratory whole-brain analysis for Play *vs.* Pass with the percentage of play choices as a covariate of interest. No regions of activation survived correction for multiple comparisons. However, when we added the percentage of play choices in the HR-1pt condition only, we found a cluster of activation in right medial orbitofrontal cortex (mOFC; x = 9, y = 45, z = -14; peak-level FWE p = .039). Activation in this mOFC region showed a positive association with risk taking (Fig. 6a), indicating that girls who chose to play more often when the chance to win 1pt was 33% showed increased engagement of this region of their mOFC. More specifically, girls who took more risks activated their mOFC *less* during pass choices compared to baseline (r = -.27, p = .041), but showed no differences in their mOFC activation during play choices compared to baseline (r = .11, p = .40). No brain regions were found that showed a negative association with risk taking.

Additional correlational analyses showed that increased mOFC activation was associated with shorter RTs (r = -.26, p = .047) and less positive self-reported experiences of gains (r = -.30, p = .025), indicating that girls who were faster decision-makers and/or reported feeling less positive during beneficial outcomes following risky behavior showed increased mOFC activation for trials on which they chose to play as opposed to pass. No correlations were found between mOFC activation and the

developmental measures: age (r = -.03, p = .82), pubertal stage (r = .18, p = .18), BMI (r = .15, p = .26), and estradiol (r = .001, p = .99); except for testosterone level, which showed a positive association with mOFC activation (r = .33, p = .012; see Fig. 6b), indicating that girls with higher testosterone levels tended to show increased mOFC activation during trials on which they chose to play as opposed to pass. Finally, we conducted a linear regression analysis including the positivity rating of gains and testosterone level as predictors of mOFC activation; results showed that increased mOFC activation was predicted by both higher levels of testosterone (β = .33, p = .011) and less positive ratings of gains (β = -.30, p = .020), indicating that girls who have higher testosterone levels and/or rated gain outcomes as a less positive experience showed increased activation of mOFC during trials on which they chose to play compared to trials on which they chose to pass. Together, these variables explained 20.7% of the variance in mOFC activation, $F(2, 51) = 6.7$, p = .003.

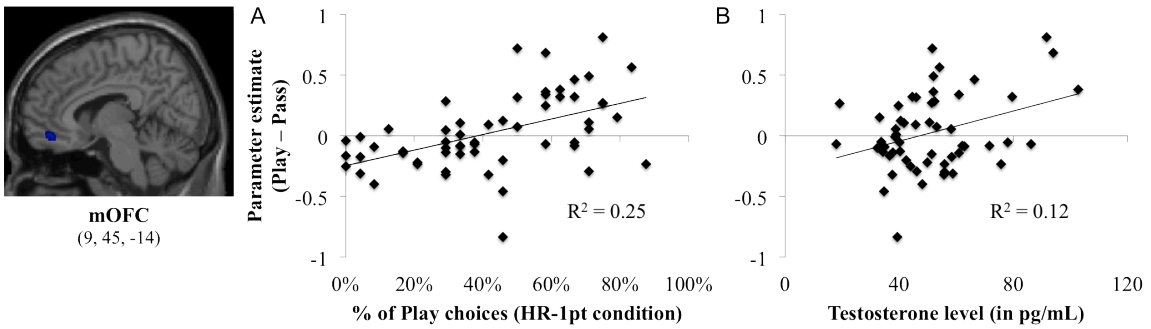

Fig. 6. Correlations between mOFC activation during Play *vs.* Pass trials and (a) risk taking (n = 58), as well as (b) testosterone level (n = 56).

Linking hormones, brain, and behavior

Given the correlations between testosterone level and risk taking (r = .33, p = .014), mOFC and risk taking (r = .49, p < .001), and testosterone level and mOFC activation (r = .33, p = .012), we conducted a mediation analysis to test whether the relation between testosterone and risk taking was mediated by activation in mOFC. Note that we could not test whether the relation between testosterone and risk taking was mediated by NAc activation, since there was no relation between testosterone and NAc activation (r = -.17, p = .22). Indeed, results of a Sobel test showed that mOFC activation mediated the relation between testosterone level and the percentage of play choices in the HR-1pt condition (Sobel's z = 2.4, p = .015), such that higher testosterone levels were associated with increased mOFC activation for Play vs. Pass choices, which in turn was associated with increased risk taking (Fig. 7a).

In sum, we found that in our sample of young adolescent girls, increased risk taking—particularly on trials in which the chance to win 1pt was 33% (i.e., in the HR-1pt condition)—was associated with a *less* positive experience of gains, *reduced* activation of NAc for Play vs. Pass trials, and *increased* activation of mOFC for Play vs. Pass trials, whereby enhanced mOFC activation mediated the relation between testosterone and risk taking. Results of a linear regression model including all four variables as predictors of risk taking (in the HR-1pt condition) showed that increased risk taking was predicted by increased mOFC activation (β = .40, p = .002), decreased NAc activation (β = -.30, p =

.010), and a less positive experience of gains (β = -.23, p = .054), but not by testosterone level (β = .12, p = .32). Together, individual differences in brain activation and self-reported experience of gains accounted for 41.6% of the variance in risk taking, $F(4, 49) = 8.7$, $p < .001$ (Model 1; Fig. 7b). However, this model did not provide significantly better fit compared to the model without self-reported experience (R^2 Change = 4.6%, $F(1, 49) = 3.9$, p = .054), which explained 37.0% of the variance in risk taking, $F(3, 50) = 9.8$, $p < .001$. Also depicted in Fig. 7b are the predictors of NAc and mOFC activation (Models 2 & 3).

Discussion

The goal of this study was to understand the relation between puberty, risk taking, and associated reward-related processes. We tested this relation in a sample of 11–13-year-old girls and found that risk taking (i.e., the percentage of play choices) was associated with *decreased* NAc activation and *increased* mOFC activation, which in turn mediated the positive association between testosterone level and risk taking.

Testosterone captures individual differences in risk taking

Based on previous literature (De Water et al., 2013; Vermeersch et al., 2008a, 2008b), we expected to find a positive association between risk taking and levels of both testosterone and estradiol. However, in our sample of girls, increased risk taking was associated with testosterone, but not with estradiol levels. The lack of a relation between estradiol and risk taking could be attributed to the cross-sectional nature of the present study and the narrow age range of our sample. While a cross-sectional study can be used to examine individual differences, a longitudinal study is needed to examine developmental *changes*. Given that estradiol serves as a better proxy for pubertal maturation in girls than testosterone (Biro et al., 2014), which is in accordance with our finding that estradiol (but not testosterone) concentrations increased with age, pubertal stage, and physical growth—as indexed by BMI (Table 3), it is possible that individual differences within our sample's narrow age range were not large enough for us to detect using a cross-sectional design. A longitudinal follow-up is needed to test whether *changes* in estradiol are related to *changes* in risk taking. The reason why we did find a relation between risk taking and testosterone using this cross-sectional design might be because testosterone in girls is a better indicator of individual differences in personality (Avgoustinaki et al., 2012), which may in turn impact decision strategies.

Another explanation could be that estradiol and testosterone target different neural mechanisms underlying risky decisions. While testosterone may target brain regions associated with approach behavior, as indicated by its association with striatum activation in the context of decision-making (Forbes et al., 2010, Hermans et al., 2010; Op de Macks et al., 2011), estradiol may target other brain regions, such as the prefrontal cortex (Jacobs and D'Esposito, 2011). This would be in line with findings showing a relationship between estradiol and frontal functioning in the context of risk taking (Dreher et al., 2007), but does not fit with findings showing that administration of estradiol during the early stages of menopause increases striatal, as well as ventromedial prefrontal, activation (Thomas et al., 2014). Further research is needed to study which brain regions are associated with estradiol functioning, particularly during adolescence (Van Wingen et al., 2011).

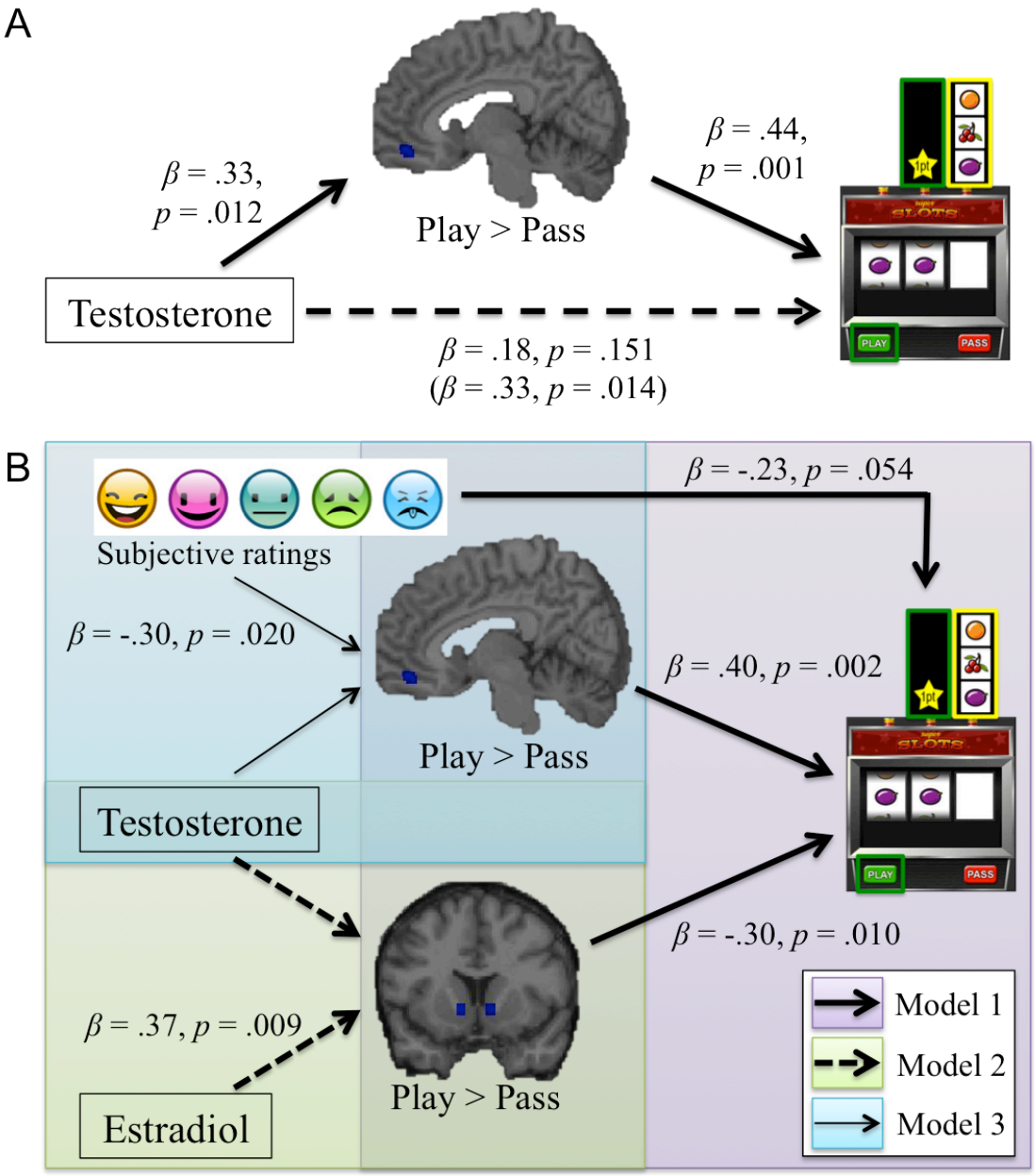

Fig. 7. (a) Mediation analysis results for the relation between testosterone level and risk taking, which is mediated by mOFC activation for Play vs. Pass choices. (b) A linear regression analysis including all variables that correlated with risk taking: The percentage of play choices when the chance to win 1pt is 33% is predicted by decreased NAc activation, less positive ratings for the experience of gains, and increased mOFC activation, whereby mOFC activation mediates the relation between testosterone level and risk taking (Model 1). Additional linear regression analyses showed that NAc activation was predicted by both hormones (Model 2); mOFC activation was predicted by self-reported positive experience of gains and testosterone level (Model 3).

Reduced NAc response is associated with risk taking

As expected, our study showed that risk taking (as opposed to opting out of a trial) was associated with increased activation in various reward-related regions, such as the striatum. It has been well established that the human striatum plays an important role in decision-making, and shows activation during both reward anticipation and reward evaluation processes (Delgado, 2007; Haber and Knutson, 2010), which corresponds with our finding that striatum activation remained elevated for risky decisions that resulted in gain, but not loss. While the dorsal striatum has been implicated in decision-making as a region involved in action selection (Balleine et al., 2007), the ventral striatum has been described as a region involved in reward processing (Haber and Knutson, 2010). This perspective is in line with our finding that both dorsal and ventral striatum were activated during the choice to play (i.e., approach behavior), but only ventral striatum was activated during gain (after the choice to play).

Here, we focused on the NAc, a brain region located within the ventral striatum and shown to be active during the anticipation of rewards (Haber and Knutson, 2010; Knutson and Greer, 2008). A common account for the increase in risk taking among adolescents is their increased sensitivity to rewards, evidenced by their elevated NAc/ventral striatum response to rewards, relative to children and/or adults, during risk taking paradigms (Blakemore and Robbins, 2012; Galvan, 2010; Galvan et al., 2006; Somerville, Jones, & Casey, 2010; Spear, 2011; Steinberg, 2010). However, there is also evidence for a reduced NAc response in adolescents relative to adults, particularly during reward anticipation (Bjork et al., 2004; 2010), which has been interpreted as a potential driving force for adolescent risk taking in order to increase activation of an otherwise blunted NAc. Our finding that girls who showed reduced NAc activation during trials on which they chose to play actually engaged in *more* risk taking seems to be in line with the latter interpretation. While it has been argued that the effects of reward-related hyperactivation in adolescents may be driven by a subgroup of neuro-*a*typical adolescents who suffer from behavioral disinhibition (Bjork and Pardini, 2014), another reason for the discrepancy between our results and that of other developmental studies can be the difference in study approach. The developmental studies that found NAc hyperactivation in adolescents based their results on group comparisons; they contrasted NAc activation in a group of adolescents with that of a group of children and/or adults, to make inferences about developmental changes. In contrast, the present study zoomed in on a narrow developmental window to look at individual differences in NAc activation associated with pubertal differences in girls around the same age (11-13yrs). Interestingly, another study that took a similar approach, relating individual differences in pubertal maturation within a narrow age range of 11-13yrs to differences in reward processing during risky decisions, resulted in comparable findings (Forbes et al., 2010). Specifically, they found that girls who were further along in their pubertal development showed *less* striatum activation in response to rewards.

Taken together, these findings suggest that while the girls who took more risks showed reduced NAc activation during the anticipation of rewards (i.e., during trials on which they decided to play), this does not rule out that adolescents, as a group, may still show a developmental increase in the NAc response to rewards, compared to children and/or adults. The best way to test this idea would be by conducting a longitudinal study (Crone and Elzinga, 2015). To date, a few longitudinal neuroimaging studies on risk

taking have been published, and report conflicting results. Two studies reported no change in reward-related NAc activation from mid-adolescence to early adulthood (Van Duijvenvoorde, Op de Macks, et al., 2014 [Chapter 2]; Lamm et al., 2014), whereas a third study based on a much larger sample reported a peak in NAc activation during adolescence (Braams et al., in press).

The role of mOFC in risk taking

Our exploratory analyses showed that girls who engaged in more risk taking showed *increased* mOFC activation during trials on which they chose to play, as opposed to trials on which they chose to pass. Specifically, girls who took more risks showed *decreased* mOFC activation for pass choices (compared to fixation). The OFC is known to play a key role in determining the subjective value of a potential reward by integrating sensory, affective, and motivational signals from sensory and subcortical brain regions (Wallis, 2007). Particularly when faced with complex decisions in which reward value is not straightforward, the OFC is thought to calculate reward value by performing a cost-benefit-analysis based on different aspects of a decision, such as how much energy is required, whether it fulfills the individual's need, and what alternatives are present (Wallis, 2007). This is in contrast with the NAc, which consistently responds to reward magnitude (and sometimes probability), but does not take into account features like delay in reward receipt and effort involved in obtaining the reward (Haber and Knutson, 2010). Furthermore, while the lateral OFC has connections with the sensory cortices and has been implicated in primary reward/punishment processing, medial OFC has connections with the limbic regions (including NAc) and is thought to be involved in determining subjective hedonic value for more abstract rewards, such as money (Peters and Büchel, 2010), especially the more anterior part of mOFC (Kringelbach and Rolls, 2004). Together, these findings suggest that reduced mOFC activation during trials on which the girls chose to pass reflects the lower subjective value of this decision for girls who chose to play more overall.

Given that the outcome is fixed for the choice to pass (i.e., nothing happens), but the uncertain for the choice to play (i.e., participants can win or lose points), it could be that these risk-taking girls are more sensation seeking and therefore value the decision to pass less highly. This hypothesis is supported not only by their increased engagement in risk taking, but also their faster decision-making (i.e., shorter RTs), which also correlated with mOFC activation. Interestingly, the girls who showed increased mOFC activation also reported experiencing less intense positive emotions during gains (but not losses) after the decision to play. It is possible that these girls engaged in more and faster risk taking to enhance their emotional experience during the task, particularly since they valued positive outcomes, like winning, as less pleasant. This finding is consistent with earlier work showing reduced self-reported excitement (but no differences in self-reported happiness) in adolescents compared to adults (Bjork et al., 2010), and more depressive symptoms with increased mPFC activation in adolescents (Forbes et al., 2010).

Medial OFC as a potential neural target of testosterone

Activation in mOFC for play vs. pass trials mediated the relation between testosterone level and risk taking, indicating that mOFC may be a potential target for

testosterone. This finding is consistent with results from a cross-sectional study conducted in a large sample of 8–25 year-old boys and girls, which showed that individual differences in mOFC structure mediated the relation between individual differences in testosterone level and risk taking on the balloon analogue risk-taking (BART) task (Peper, Koolschijn, & Crone, 2013). Specifically, this study found that girls with higher levels of testosterone tended to have a smaller surface area in mOFC, which in turn was associated with less risk taking. These results were interpreted as mOFC volume acting as a suppressor of risk taking by regulating behavior (Peper et al., 2013). Since the relation between brain structure and function remains unclear, it is unclear how our finding of increased mOFC activation mediating risk taking can be reconciled with these structural findings. Furthermore, the structural analyses were conducted across a much larger region of mOFC compared to where we found activation differences. Given the heterogeneity of the mOFC (Kringelbach and Rolls, 2004; Peters and Büchel, 2010; Sescousse et al., 2013), it remains to be tested in future studies whether functional and structural differences associated with increased risk taking occur in overlapping locations.

Differences in decision strategy

Among our sample of girls, individual differences in risk taking seemed to be best captured when there was a chance of 33% to win 1pt (as opposed to 3pts). A possible explanation is that the girls have different strategies for making these types of decisions; some girls may take a more deliberate or strategic approach, whereas other girls may take a more *feeling*-based or non-strategic approach. Furthermore, strategic and non-strategic decision-makers may behave more similarly when the potential reward is relatively high (3pts), but not when the potential reward is low (1pt). In other words, while strategic decision-makers may choose to pass, non-strategic decision-makers may choose to play in the condition where the choice to play is not very strategic (i.e., the expected value is the lowest). According to this idea, the girls with higher testosterone levels might be more likely to rely on a non-strategic approach, which could explain why they engaged in more risk taking when expected value was the lowest (and showed no differences when expected value was higher).

Another potential indicator that girls with higher testosterone levels applied different decision strategies is that girls with higher testosterone levels tended to score lower on the matrix-reasoning subtest of the WASI (r = -.26, p = .050, n = 56). This is consistent with animal studies in which testosterone was linked to the suppression of neural plasticity, resulting in impairment of hippocampal-dependent cognitive functioning (Atwi et al., 2014). To test whether discrepancies in cognitive functioning contributed to non-strategic decision-making, we conducted a linear regression analysis with both WASI-MR score and testosterone level predicting risk taking in the HR-1pt condition. Results showed that only testosterone was a significant predictor (β = .29, p = .032), not WASI-MR (β = -.12, p = .37), and the individual differences in testosterone level explained 12.0% of the individual variation in risk taking, $F(2, 53) = 3.62$, p = .034. These findings indicate that individual differences in cognitive functioning did not contribute to the differences in risk taking.

Limitations and future directions

The current Jackpot paradigm (revised based on the version used in Op de Macks et al., 2011) provided us with the opportunity to measure the effects of (1) stakes magnitude (i.e., the potential gain or loss of 1 *vs.* 3 points) and (2) feedback context (i.e., playing for money *vs.* social rank), in addition to (3) risk level (being presented with a 67% *vs.* 33% chance of winning), on both brain and behavior. Compared to the prior version, this task included almost twice the number of trials (96 instead of 50 trials) and was administered across 2 runs (instead of 1 run) of scans, each lasting about 6.5 minutes. In an effort to balance the acquisition of multiple scans (structural, functional, and resting-state) with the participant's task engagement, we obtained only two runs of the task. In the future, however, we might include an additional run, given the number of manipulations (i.e., eight task conditions). Fortunately, there was no effect of feedback context at the group level, so we could collapse across feedback contexts for the analyses reported in this paper.

In addition to including more trials, we might consider having a larger number of HR compared to LR trials, especially because we were interested in reward processes during risk taking (i.e., trials on which girls chose to play) and, as such, not all trials could be included in the analyses (trials on which girls chose to pass were excluded). While both risk level and stakes influenced choice behavior (and NAc activation), risk level had a larger effect, such that girls more often took risks in the LR condition. Having a higher proportion of HR trials would compensate for the decrease in risk taking when the probability of winning is smaller. That way, brain processes associated with both risk taking (play choices) and risk avoidance (pass choices) could be compared across the different conditions.

Another important limitation of this task is that it does not allow for distinction between choice and outcome-related brain processes. For example, it was not possible for us to distinguish anticipatory from consummatory reward processes within a trial. Consequently, we were unable to determine whether the activation differences in NAc and mOFC reflected differences in valuation processes *before* the decisions, or the outcome processes *after* the decisions (i.e., performance monitoring) that perhaps influenced subsequent decision-making (Crone, 2014). While NAc and mOFC activation have been implied in both valuation and monitoring processes, NAc is more consistently reported during reward anticipation (Haber and Knutson, 2010), whereas mOFC is reported more for reward consumption (Diekhof et al., 2012; Liu et al., 2011). These findings suggest that while both regions are involved in risk taking and process rewards, they may be contributing to different aspects of valuation. While other paradigms succeeded at disentangling the different reward processes associated with decision-making (Bjork et al., 2010; Forbes et al., 2010), these studies have not been able to capture its role in risk taking. Future research using pupillometry or electroencephalography (EEG), in addition to fMRI, might be a better method (i.e., has better temporal resolution) to capture individual differences in arousal associated with risk taking and outcome processing.

Lastly, due to the cross-sectional nature of the present study, we were unable to examine whether the individual differences in risk taking (and associated reward processes) were related to differences in pubertal maturation. To test whether the individual differences in testosterone level reflected developmental changes associated

with pubertal maturation, the use of a longitudinal design is strongly recommended for future studies.

Conclusion

These findings provide insight into the role of testosterone in risk taking and offer a potential neural mechanism (i.e., increased mOFC activation) to explain why some girls engage in more risk taking compared to others. The question whether developmental changes in hormone levels at puberty contribute to the developmental increase in risk taking that characterizes adolescents remains to be tested using a longitudinal design.

Supplementary Materials

Supplementary data associated with this chapter can be found in appendix C.

Chapter 4. The effect of social comparison on risk taking and associated brain processes in adolescent girls

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Introduction

Adolescence is characterized by increased risk taking. Neurobiological models that have been proposed to explain this developmental increase in risk taking include biological, cognitive, emotional, and social components (Crone and Dahl, 2012; Nelson et al., 2005; Steinberg, 2008). Yet, the social influences on risk taking have been greatly understudied. To date, studies have only focused on risk taking in the presence of peers; results showed that adolescents, as opposed to children and adults, make more risky decisions in the presence of peers (Chein et al., 2010; Gardner and Steinberg, 2005; Smith et al. 2014a), suggesting that adolescence is a time in development during which individuals are particularly sensitive to their social environment (Blakemore and Mills, 2014). Moreover, adolescents, but not children or adults, who engaged in more risk taking, showed increased reward-related activation, in both ventral striatum and orbitofrontal cortex, in the presence of peers compared to being alone (Chein et al., 2010). These findings suggest that rewards become more salient in the presence of peers, which may in turn increase risk taking. Another possible interpretation is that the presence of peers changes the intrinsic motivation of adolescents (Crone and Dahl, 2012), such that adolescents become more motivated to engage in risk taking to impress their peers, and achieve or maintain higher social status. Thus, the anticipation of gaining social status may be what increases reward-related brain activation during risk taking.

Social status, particularly among peers, becomes more important throughout childhood, and peaks in early adolescence (LaFontana and Cillessen, 2010). In an eye-tracking study in which fifth and sixth graders looked at pictures of their classmates, results showed that participants paid more attention to high-status (i.e., more popular) compared to low-status peers, particularly when they were popular themselves (Lansu et al., 2014). Another study tested the priorities of adolescents by presenting two hypothetical vignettes—one about increasing their social status and one about a conflicting goal—for them to choose from. Results of this study showed that by the time they are in high school, adolescents prioritize their social status among peers over academic achievement, adhering to social norms, and even over maintaining their friendships, as well as pursuing romantic relations (LaFontana and Cillessen, 2010). These findings suggest that adolescents are aware of their position within their social environment, and find it particularly important to attain high social status.

Previous studies have shown that risk-taking behavior in adolescence is influenced by social status. Using longitudinal designs, studies have shown that popularity in high school is predictive of risk behaviors throughout adolescence and well into early adulthood (Sandstrom and Cillessen, 2010). For example, popular high-school

students were more likely to use alcohol (Guyll et al., 2014) and engage in sexual activity (Mayeux et al., 2008) later on in adolescence. Interestingly, engaging in smoking behavior lead to increased social status (Mayeux et al., 2008), suggesting that adolescents engage in risk taking not only to maintain their status, but also to attain higher social status. In other words, risk taking can be seen as a form of status-seeking behavior.

While social status is known to influence thoughts and behavior, and becomes more important during adolescence (Koski et al., 2015), it is unclear whether puberty plays a role in enhancing sensitivity to status-relevant information. Puberty marks the onset of adolescence (Dahl, 2004), and is characterized by a substantial rise in sex steroids (Biro et al., 2014; Dorn et al., 2003, 2006; Shirtcliff et al., 2009). The rise in hormones during puberty is thought to reorganize the adolescent brain (Sisk and Zehr, 2005; Schulz et al., 2009), and shape reproductive behaviors (Sisk and Foster, 2004), but also impacting other (social) behaviors, such as risk taking (Peper and Dahl, 2013). While the role of puberty in status-seeking behavior has not yet been investigated, a study using a multi-player auction task in young adults showed that higher levels of testosterone corresponded with the willingness to incur monetary losses (by overbidding) for the sake of being the winner of the auction (Van den Bos et al., 2013). This finding suggests that the rise in hormones during puberty (e.g., testosterone) may play a role in enhancing status-relevant information, which in turn may enhance status-seeking behavior, even when faced with potential negative consequences, such as engaging in risky behaviors. This idea is consistent with existing neurobiological models proposed to explain the developmental increase in risk taking during adolescence, which argue that the hormonal changes during puberty influence the maturation of the brain regions involved in processing of socio-emotional information (Crone and Dahl, 2012; Forbes and Dahl, 2010; Nelson et al., 2005; Steinberg, 2008), such as information about one's social status.

In the present study, we set out to investigate the influence of status-relevant social information on risky decision-making, and associated reward-related brain processes. Specifically, we tested whether social rank performance feedback (e.g., you ranked no. 5) compared to monetary performance feedback (e.g., you won $5) differentially influenced risk taking as well as reward processing among adolescent girls. We predicted that the girls would show increased risk taking and enhanced reward-related brain activation in the context of receiving feedback about their relative performance (i.e., social rank) compared to their absolute performance (i.e., money) (Bhanji and Delgado, 2014).

Furthermore, we predicted that girls with higher testosterone levels would differentiate more between the feedback contexts with regards to their behavior and their reward-related brain responses (Van den Bos et al., 2013). We focused on activation in the nucleus accumbens (NAc; Haber and Knutson, 2010) based on prior work showing that the *anticipation* of both social and monetary rewards activate this region in the ventral striatum (Izuma et al., 2008; Rademacher et al., 2010; Spreckelmeyer et al., 2009), and the extent of activation is modulated by social context (Bhanji and Delgado, 2014; Engelmann and Hein, 2013). We also looked at differences in the medial prefrontal cortex (mPFC), given that the *receipt* of monetary rewards (Knutson et al., 2001, 2003) and social rewards (Izuma et al., 2008) has been associated with activation in this region. Moreover, activation in mPFC is sensitive to social context (Braams et al., 2014; Engelmann and Hein, 2013). Finally, the extent to which reward-related activation in

mPFC is modulated by social context has been associated with subsequent changes risk taking and competitive behavior (Bault et al., 2011).

Methods and Materials

Note. The same sample and experimental paradigm have been described elsewhere (Op de Macks et al., in prep; see Chapter 3]). Please refer to Chapter 3 (Methods and Materials) for a more detailed description of the sample and the study procedure. While the previous study focused on how manipulations of risk level and stakes (collapsing across feedback context) affected risk taking and reward processing (Op de Macks et al., in prep; see Chapter 3), the focus in this study is on the feedback context manipulation.

Participants

The results presented here are based on 58 participants: 23 11-year-olds, 19 12-year-olds, and 16 13-year-olds (*M* age = 12.4, *SD* = .92). Among the included participants 46.6% were Caucasian, 10.3% Asian, 5.2% Hispanic/Latin, 3.4% African-American, 24.1% were multi-racial, and 10.4% did not provide information about their race or ethnicity. All participants scored within the normal range on the Child Behavior Checklist (CBCL; Achenbach, 1991), based on their total score. Furthermore, there were no age-related differences in cognitive functioning, as measured by their performance on the matrix-reasoning (MR) subtest of the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1991). See Table 1 in Chapter 3 for the means, standard deviations, and ranges for each age group.

Pubertal development

Self-reported pubertal stage was assessed using the Pubertal Development Scale (PDS; Peterson et al., 1988). Both testosterone and estradiol were measured based on two saliva samples from each participant, collected at home across two (consecutive) mornings. Furthermore, we calculated body mass index (BMI) as a marker of physical growth during puberty. Please refer to Chapter 3 *Methods and Materials* for a more detailed description of these developmental measures; sample means of, and correlations between, these measures can also be found in Chapter 3, in Tables 2 and 3, respectively.

Jackpot task with feedback about performance

For this study, we used a version of the Jackpot task that included feedback phases, which were presented after every six trials and informed participants about their cumulative performance (see Chapter 3 *Methods and Materials* for a full description of the task). Cumulative performance was expressed either as the amount of *money* won (i.e., monetary feedback), or as the participant's *rank* compared to other same-aged girls who played the task (i.e., social rank feedback)[9]. The type of feedback presented during

[9] We used a cover story in which we told participants that other girls who played the game were ranked based on their scores, and the participant's score would be compared to those other girls' performance. In actuality, we arbitrarily ranked the silhouettes of research assistants and participants from our pilot study—after obtaining written permission. During the first lab visit, a picture was taken of each participant's side profile. This picture was converted into a black-and-white silhouette, which was incorporated into the game, so that each participant would see herself traveling up and down the arrow during feedback presentation. The silhouettes of the "other girls" were consistent across participants, so that visual experience of feedback presentation was equal across participants (except for their own silhouette).

the feedback phases was consistent across an entire block of 24 trials; there were 4 feedback phases—each with a duration of 4s followed by 1s of fixation—per block. In total, there were 96 trials across 4 blocks (two of each feedback type), which were administered across 2 runs of scans (with a self-paced break in between runs). At the beginning of each run, participants were instructed verbally (using the intercom) about which feedback type they would start with, and they received a written prompt that announced the switch of feedback type in between blocks; this transition phase had a duration of 12s followed by 2s of fixation. The order of feedback type was counterbalanced across participants, within each age group. An overview of the task design can be found in Fig. 2 of Chapter 3.

On each trial, participants decided to play or pass based on information about risk level (low or high) and stakes (1 or 3 pts) presented to them during the choice phase. Thus, there were four different task conditions: low-risk/low-stakes (LR-1pt), low-risk/high-stakes (LR-3pts), high-risk/low-stakes (HR-1pt), and high-risk/high-stakes (HR-3pts). Upon the button press to indicate their choice, participants received feedback about the outcome of their choice (i.e., the outcome phase). While outcomes of play choices could be gain or loss, outcomes of pass and miss choices were always neutral (no gain or loss) and loss (of 1pt), respectively (Fig. 1).

Here, we investigated whether choice behavior and/or reward-related brain processes *during the trials* differed as a function of the block, or feedback type (i.e., rank *vs.* money). Note that we did not analyze the feedback phases themselves, since there was no choice behavior during those phases and there were not enough instances of performance feedback presentation (i.e., eight for each feedback type) to reliably calculate and compare the brain responses during feedback presentation. For the remainder of this paper, we will refer to the trial-by-trial feedback provided during the outcome phase (i.e., gain, loss, or neutral) as *outcome*, whereas the performance feedback provided during the feedback phases—after every 6 trials—will be referred to as (social rank or monetary) *feedback*.

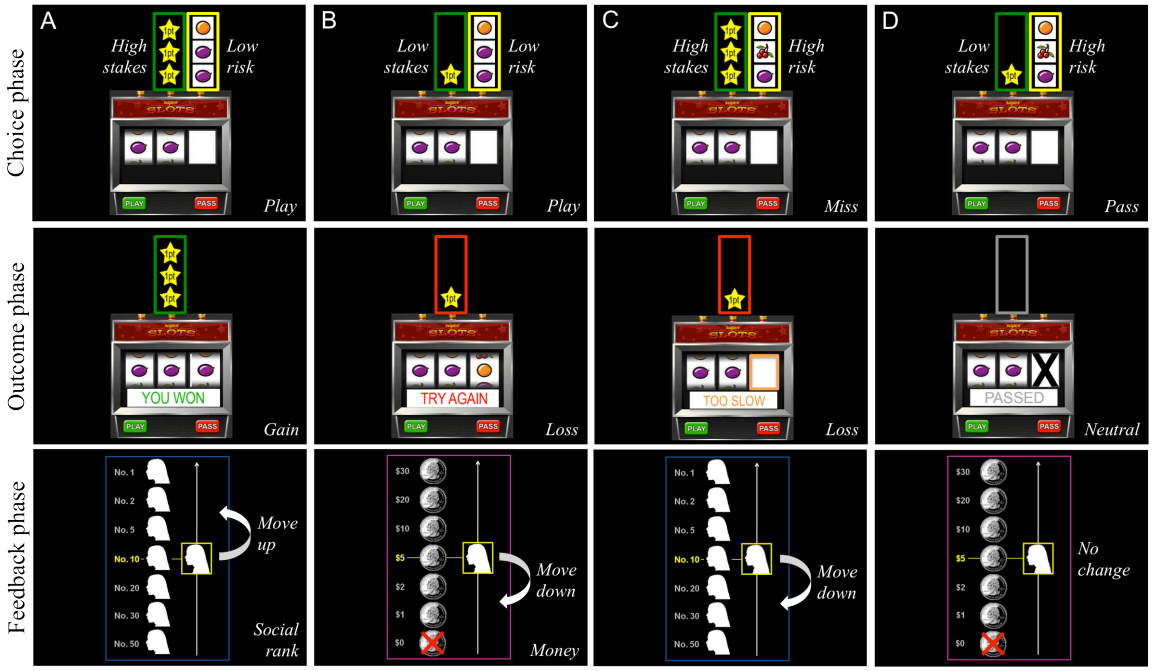

Fig. 1. Examples of trials (a–d) in the Jackpot task, modified from (Op de Macks et al., 2011). There are four different stimuli conditions, which are presented in random order during the choice phase (top panel). During the outcome phase (middle panel), participants are presented with 4 possible outcomes (depending on their choices). Trial A is an example of what the participant sees when the chance to win 3 points is 67%, chooses to play, and wins. Trial B is an example of a 67% chance to win 1 point, the participant chooses to play, and loses. Trial C: the chance to win 3 points is 33%, the participant does not respond, and loses 1 point. Trial D: the chance to win 1 point is 33% and the participant chooses to pass. Note that in actuality other combinations of choices and outcomes were possible, depending on participants' choices. After every 6 trials, either social rank or monetary feedback was provided (bottom panel), depending on the block (each participant was exposed to two blocks of each feedback type; the order was counterbalanced across participants). If the participant incurred a net gain, her picture (in the yellow box) moved up the arrow. If the participant incurred a net loss, her picture moved down. *Note.* Italicized labels are for clarification purposes and were not present in the actual task.

Resistance to peer influence

Participants (n = 57) completed the resistance to peer influence scale (RPI; Steinberg and Monahan, 2007). This questionnaire consists of 10 pairs of opposing statements; for example, *"some people go along with their friends just to keep their friends happy BUT other people refuse to go along with what their friends want to do, even though they know it will make their friends unhappy"*. The participant was instructed to choose one statement (of the two) and to report whether the chosen statement was "really true" or "sort of true" for them. The average across all 10 items (i.e., RPI score) serves as an index of how resistant the participant is to peer influence; the higher the RPI score, the more resistant the participant is. See Table 1 for the group means; there were no age-related differences in RPI score. Furthermore, RPI score did not correlate with any of the other developmental measures ($-.11 > r < .15$, $p > .27$; Table 2), indicating that individual differences in resistance to peer influence did not correspond with differences in pubertal maturation.

Table 1. Sample characteristics for the self-report measures: mean ± standard deviation (and range).

	11yrs (n = 23)	12yrs (n = 19)	13yrs (n = 16)	*Group diff*
RPI	(n = 22)			
Total score	3.0 ± .29	3.1 ± .45	2.9 ± .45	$F(2, 54) = .42$, $p = .66$
	(2.5 – 3.6)	(1.8 – 3.8)	(2.2 – 3.8)	

RPI = Resistance to peer influence

fMRI analyses

Image acquisition and preprocessing steps have been described in full detail in Chapter 3 *Methods and Materials*. In brief, statistical analyses were performed on individual subjects' data using the general linear model (GLM) in statistical parametric mapping, version 8 (SPM8; Wellcome Trust Center for Neuroimaging; http://www.fil.ion.ucl.ac.uk). Trials were modeled as separate zero-duration events starting at the onset of stimulus presentation. Feedback phases were also modeled as zero-duration events starting at the onset of feedback presentation. Transition phases were modeled as 12-sec events starting at the onset of the transition screen presentation.

We created subject-specific design matrices to look at risk taking and reward-related processes *during the trials*, separately for the social rank and monetary feedback context. For risk taking, we added four regressors of interest encoding choice (the *feedback-choice* model), separately for each feedback context: Social Play, Monetary Play, Social Pass, and Monetary Pass. For reward-related processes, we added six regressors of interest encoding outcome (the *feedback-outcome* model) for the Play conditions—Social Gain, Monetary Gain, Social Loss, and Monetary Loss—as well as for the Pass conditions—Social Pass and Monetary Pass. For each of these first-level statistical models, misses (trials on which participants failed to make a response within the allotted time) were modeled as a separate regressor. Additional regressors of no interest were included for (1) feedback phases, (2) transition phases, and (3–8) the movement parameters (roll, pitch, yaw and displacement in superior, left and posterior directions). The feedback phases themselves were not analyzed, since there were only eight instances of monetary and social rank feedback. More importantly, we were interested in the influence of social *context* on decisions, and reward processes during risk taking, not the influence of feedback per se.

To examine group-level differences in *risk taking*-related brain activation between the feedback types, second-level statistical analyses were conducted to test the contrasts Social vs. Monetary Play, and Social vs. Monetary Pass. To examine group-level differences in *reward*-related brain activation in the context of risk taking, we tested the contrasts Social vs. Monetary Gain, and Social vs. Monetary Loss (following the choice to play). Task-related responses were considered significant if they consisted of at least 10 contiguous voxels that exceeded a family-wise error (FWE) corrected threshold of $p < .05$.

Furthermore, we applied the MarsBar toolbox for use with SPM8 (Brett et al., 2002) to extract parameter estimates from specific regions of interest (ROIs). The NAc ROI was created by drawing 4mm-radius spheres around the coordinates for bilateral nucleus accumbens ($x = \pm 10$, $y = 12$, $z = -3$, as reported in Haber and Knutson, 2010); the mPFC ROI was based on one of the clusters of activation that resulted from the Gain *vs.* Loss contrast in the same sample of girls (Op de Macks et al., in press; see Chapter 3). Additional ROIs were created based on the whole-brain results by obtaining the region of

overlap between the functional and anatomical ROI available through the MarsBar anatomical automatic labeling (AAL) toolbox. We correlated the parameters extracted for each participant from the a-priori and masked ROIs with their age, pubertal stage (i.e., PDS score), body-mass index (BMI), as well as levels of testosterone and estradiol.

Results

Behavioral sensitivity to feedback context

Risk taking was measured as the percentage of play choices; response time (RT) was measured as the time between stimulus onset and the button press to indicate the participant's choice (in milliseconds). Despite the lack of a main effect of feedback type at the group level for risk taking, $F(1, 57) = .05$, $p = .82$ (Fig. 2a), and RT, $F(1, 57) = .01$, $p = .91$, there were *individual differences*—in both risk taking and RT—across the two feedback contexts. For example, some girls played more in the social rank feedback context, whereas other girls played more in the monetary feedback context (Fig. 2b). To index these individual differences, we calculated the *relative* difference (in percentages) between risk taking (or RT) in the social rank feedback context compared to the monetary feedback context (i.e., [rank – money]/money * 100). Hence, positive proportions represented more risk taking or longer RTs in the social rank feedback context, whereas negative proportions represented more risk taking or longer RTs in the monetary feedback context.

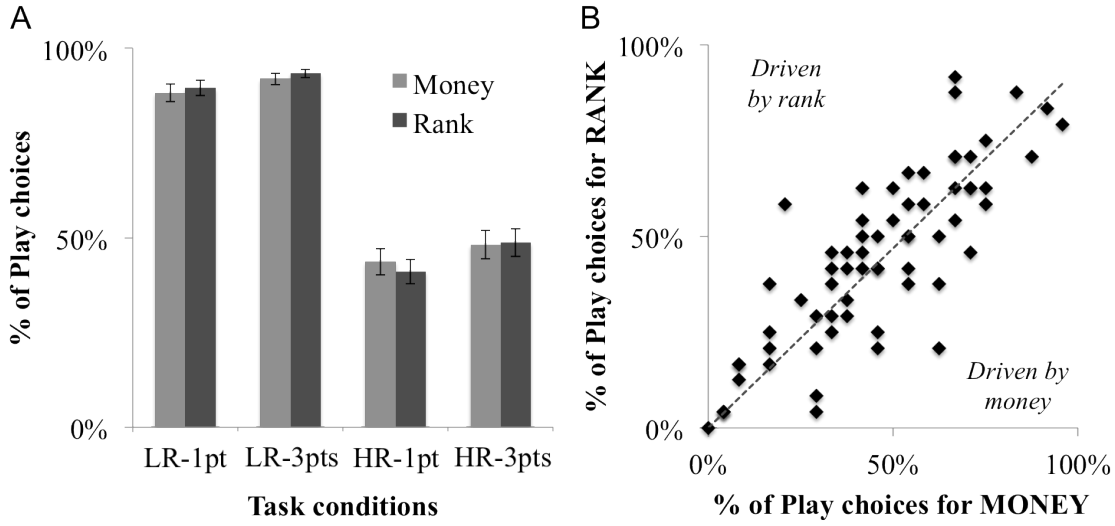

Fig. 2. (a) Risk taking in the 4 task conditions, plotted separately for the social rank and monetary feedback contexts. Error bars represent the standard errors. (b) Risk taking in the monetary feedback context plotted against risk taking in the social rank feedback context. Participants with greater perpendicular distance to the dotted line are more biased toward risk taking in a particular feedback context. Note that the dotted line does not represent the correlation.

None of the developmental measures were associated with the relative measures of risk taking or RT ($-.19 < r < .17$, $p > .15$; Table 2), indicating that differences in age, pubertal stage, BMI, or hormone levels did not explain the differences in task behavior between the social rank and monetary feedback contexts. Given that individual differences in the tendency to take risks were larger in the high-risk (HR) condition compared to the low-risk (LR) condition, we also looked at the relative measure of risk

taking for LR and HR conditions separately. However, in both the LR and HR condition, there was no relation between choice behavior and developmental differences.

Table 2. Correlations between developmental measures and self-reported resistance to peer influence, as well as the relative measures of risk taking and RT (in percentages).

	Developmental measures				
	Age	PDS	Testosterone	Estradiol	BMI
	(n = 57)	(n = 57)	(n = 55)	(n = 54)	(n = 56)
RPI score	r = -.06	r = -.07	r = -.01	r = .15	r = -.11
	p = .64	p = .59	p = .95	p = .28	p = .43
	(n = 58)	(n = 58)	(n = 56)	(n = 55)	(n = 56)
Risk taking	r = .01	r = .03	r = .17	r = .11	r = .12
(relative %)	p = .92	p = .85	p = .21	p = .45	p = .38
RT	r = -.19	r = .07	r = -.02	r = .01	r = .12
(relative %)	p = .15	p = .62	p = .89	p = .94	p = .40

RPI = resistance to peer influence; RT = response time; PDS = pubertal development stage; BMI = body-mass index

Furthermore, while self-reported resistance to peer influence (RPI score) was not associated with the relative differences in risk taking (r = -.03, p = .83, n = 57), there was a marginal negative association with the relative differences in RT (r = -.24, p = .076, n = 57). Specifically, in the HR condition, girls were relatively slower to decide (whether or not to play) in the social rank feedback context when they reported themselves as *less* resistant to peer influence (r = -.38, p = .004), whereas in the LR condition there was no such association (r = -.07, p = .61; Fig. 3); these correlations were significantly different from each other, Steiger's Z = 2.21, p = .027.

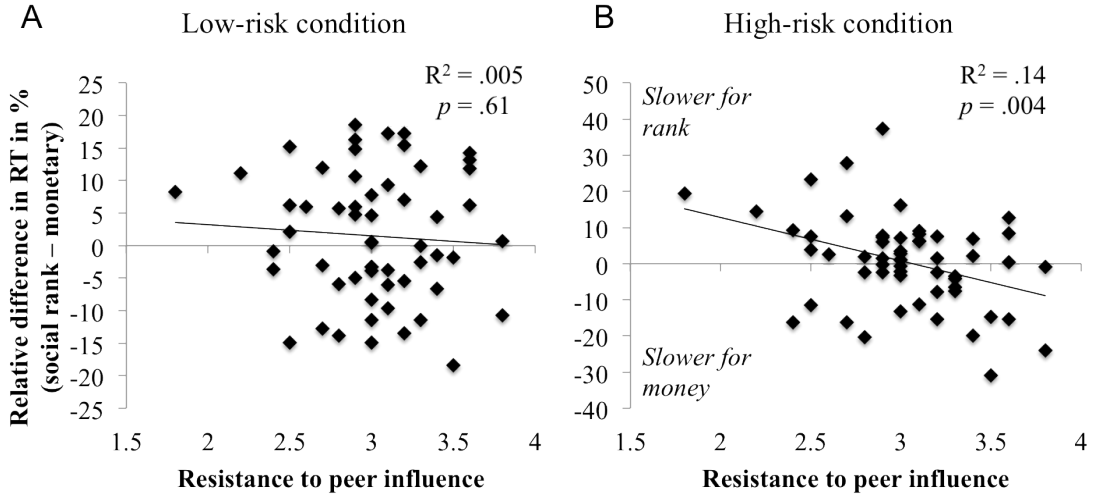

Fig. 3. Correlations between resistance to peer influence (i.e., RPI score) and the relative difference in response times (RT) for the social vs. monetary feedback context, plotted separately for decisions in the high-risk (a) and low-risk (b) condition.

Imaging results: main effects

Results of the whole-brain analysis across all participants (n = 58) for the contrast Social > Monetary Play revealed clusters of activation in bilateral insula, with the left peak at: x = -38, y = 17, z = -8 (cluster-level FWE corrected p = .004), and the right peak

at: x = 46, y = 22, z = -5 (cluster-level FWE corrected p = .002) (Fig. 4a). These results indicate that bilateral insula was more activated during trials on which participants chose to play in the social rank feedback context compared to trials on which participants chose to play in the monetary feedback context. Further examination of the patterns of brain activation in bilateral insula showed increased activation for Play choices—regardless of whether they resulted in Gain or Loss—compared to Pass choices for the social rank feedback context (Gain *vs.* Pass: $t(57) = 2.9$, $p = .005$; Loss *vs.* Pass: $t(57) = 2.5$, $p = .015$), but not for the monetary feedback context (Gain *vs.* Pass: $t(56) = .22$, $p = .83$; Loss *vs.* Pass: $t(56) = .78$, $p = .44$; Fig. 5a), indicating that bilateral insula distinguished between risk taking (Play) and playing it safe (Pass) when playing for rank, but not when playing for money. Additional clusters of activation were found in left fusiform (peak at: x = -30, y = -52, z = -14, cluster-level FWE corrected $p < .001$) and lingual gyrus (peak at: x = -12, y = -85, z = -3, cluster-level FWE corrected $p = .003$). No regions of activation survived correction for multiple comparisons (at either peak- or cluster-level) for the opposite contrast Monetary > Social Play, or for the contrasts Social > Monetary Pass, and Monetary > Social Pass.

Results of the whole-brain analysis across all participants (n = 58) for the contrast Social > Monetary Gain revealed clusters of activation in left fusiform gyrus (peak at: x = -32, y = -69, z = -11, cluster-level FWE corrected $p < .001$), and in right insula (peak at: x = 36, y = 16, z = -6, cluster-level FWE corrected $p < .001$) (Fig. 4b). No regions of activation survived correction for multiple comparisons (at either peak- or cluster-level) for the opposite contrast Monetary > Social Gain, or for the contrasts Social > Monetary Loss and Monetary > Social Loss. Although, at a lowered threshold of $p < .001$ uncorrected with $k > 10$ voxels, we found a cluster of activation in left insula (peak at: x = -38, y = 17, z = -9) for Social > Monetary Loss (see Fig. 4c). These results indicate that insula (and fusiform gyrus) was more strongly activated when playing for rank than money, regardless of the outcome (although insula activation was stronger on the right for gains, and on the left for losses). See supplementary Fig. S1 for the time-courses of the left and right insula, plotted for gain, loss, and pass trials, separately for social rank and monetary feedback.

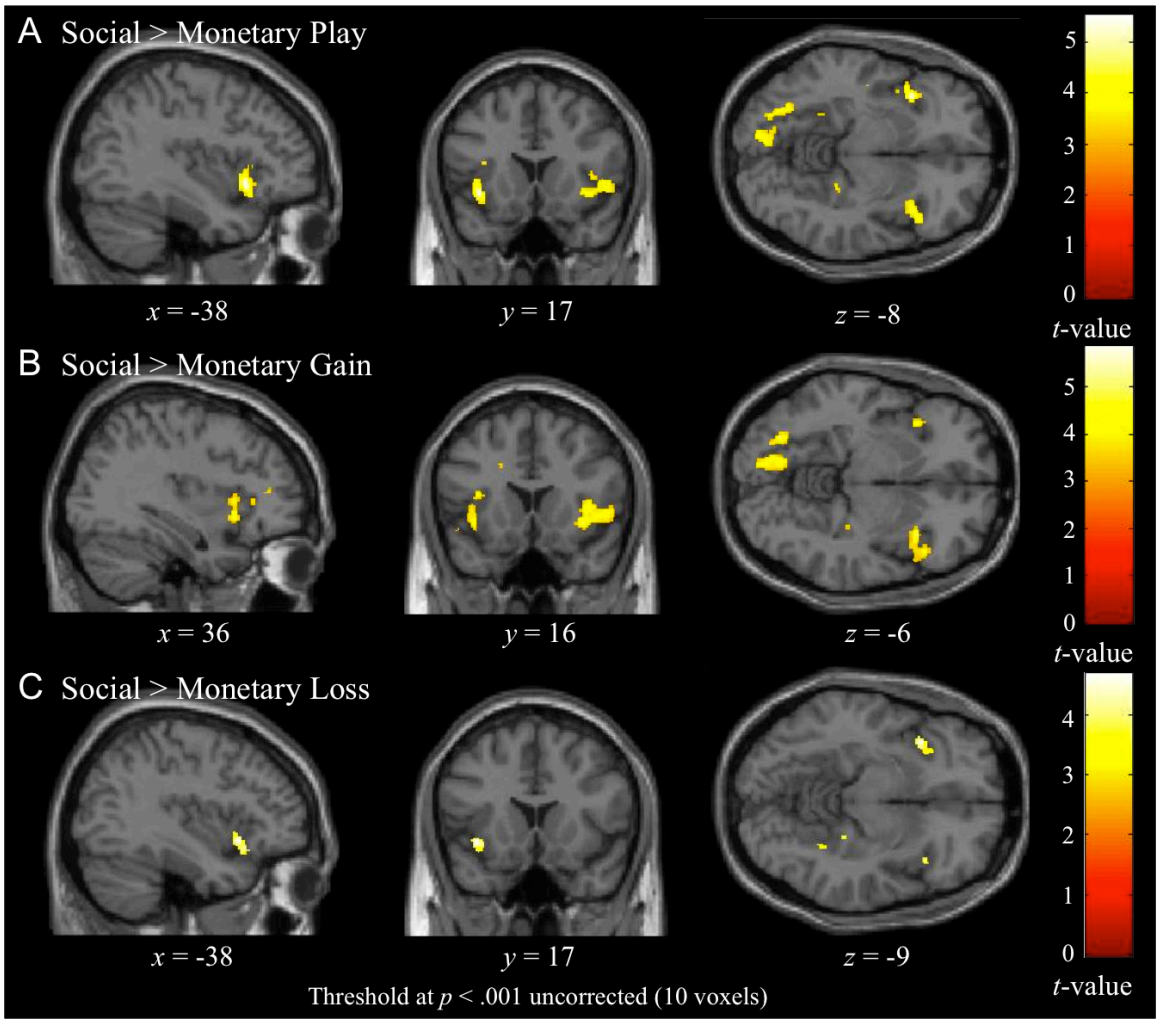

Fig. 4. Regions of activation for risk taking in the social rank vs. monetary feedback contexts (i.e., Social > Monetary Play; a), and for positive (i.e., Social > Monetary Gain; b) and negative (i.e., Social > Monetary Loss; c) outcome processing upon the choice to play, presented at $p < .001$ uncorrected, $k > 10$ voxels.

Individual differences in insula activation

We tested whether individual differences in insula activation were associated with any of the developmental measures. While testosterone level was not associated with differences in bilateral insula activation for Social > Monetary Play ($r = .18$, $p = .19$, $n = 56$), estradiol level was positively associated with activation differences ($r = .27$, $p = .048$, $n = 55$), indicating that girls with higher levels of estradiol showed increased activation of bilateral insula for risk taking in the social rank compared to monetary feedback context. Specifically, higher estradiol levels corresponded with increased risk taking-related insula activation in the social rank feedback context ($r = .40$, $p = .003$), but not in the monetary feedback context ($r = .22$, $p = .11$) (Fig. 5b); these correlations were marginally different, Steiger's $Z = 1.76$, $p = .078$. Even when controlling for age, which correlated with estradiol level ($r = .43$, $p = .001$, $n = 55$), risk taking-related insula activation in the social rank feedback context was predicted by estradiol level $\beta = .34$, $p = .018$, and not age ($\beta = .13$, $p = .38$). Individual differences in estradiol level—corrected for age—explained 16.9% of the variance in insula activation, $F(2, 52) = 5.3$, $p = .008$.

Furthermore, girls who engaged in relatively more risk taking in the social rank compared to the monetary feedback context showed decreased bilateral insula activation during risk taking in the social rank *vs.* monetary feedback context (r = -.27, p = .044, n = 58; Fig. 5c), indicating that girls who were biased toward the social context in their behavior, were similarly biased in their insula response.

There was no association between insula activation and response time (r = -.13, p = .32, n = 58), or resistance to peer influence (r = -.02, p = .90, n = 57).

Context effects on reward-related brain processes

We tested whether feedback context modulated activation in regions associated with reward anticipation (i.e., NAc; Haber and Knutson, 2010) and reward outcome processing (i.e., mPFC; see Chapter 3) during risk taking.

NAc. Results of a repeated-measures ANOVA predicting NAc activation based on feedback context (rank or money) and choice (play or pass) as within-subjects factors revealed a main effect of choice, $F(1, 57) = 188.1$, $p < .001$, but not feedback context, $F(1, 57) = 1.95$, $p = .17$. Specifically, NAc activation was increased for trials on which participants chose to play as opposed to pass, indicating its role in reward anticipation. There was no interaction between feedback context and outcome, $F(1, 57) = .23$, $p = .64$, indicating that NAc activation was similar across feedback contexts, for both choices (Fig. 6a).

No correlations were found between NAc activation for Social > Monetary Play and the developmental measures (age, pubertal stage, sex steroids, and BMI), or task behavior (risk taking and RT) (all p's > .05). Although, we found a marginal correlation between testosterone level and risk taking-related NAc activation in the social rank feedback context (r = -.25, p = .069, n = 56), but not in the monetary feedback context (r = -.18, p = .19); these correlations were not different from one another (Steiger's Z = -.72, p = .47). Also, age was marginally correlated with risk taking-related NAc activation in the monetary context (r = .23, p = .083, n = 58), but not in the social context (r = .17, p = .22); again, these correlations were not different from one another (Steiger's Z = -.69, p = .49).

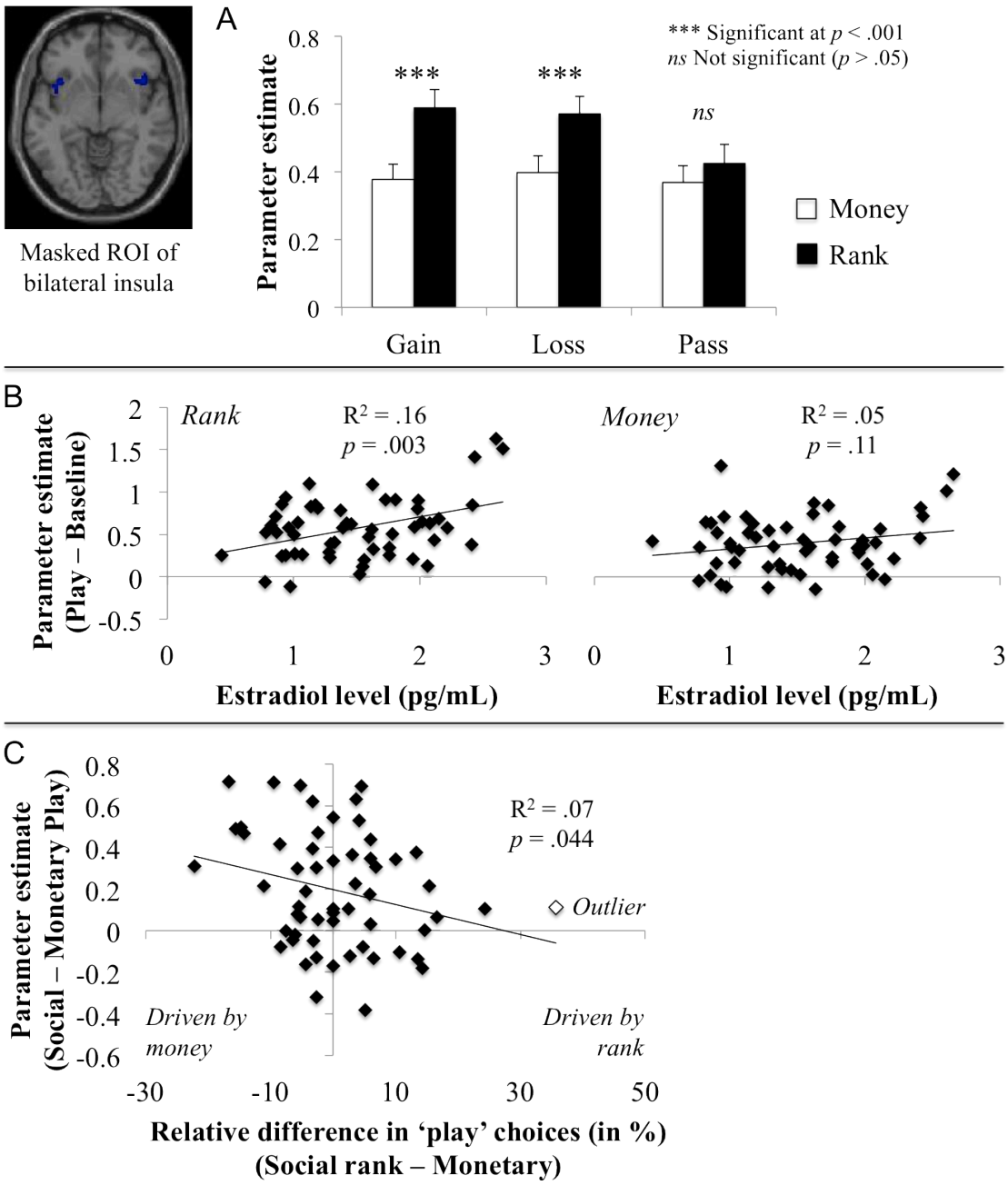

Fig. 5. (a) Average activation in bilateral insula for trials on which participants chose to play—plotted separately for gain and loss outcomes—or pass, plotted separately for the monetary (white bars) and social rank feedback context (black bars). Error bars represent standard errors. *** Significant at $p < .001$. *ns* Not significant ($p > .05$). (b) Scatterplots of estradiol level plotted against risk taking-related insula activation in the social rank (top) and monetary (bottom) feedback contexts. (c) Scatterplot of the difference in bilateral insula activation between the social rank and monetary feedback contexts against the relative difference in risk taking between the two feedback contexts (i.e., [social – monetary]/monetary). There was one extreme observation based on choice behavior (open dot); exclusion of this participant resulted in $r = -.28$, $p = .036$.

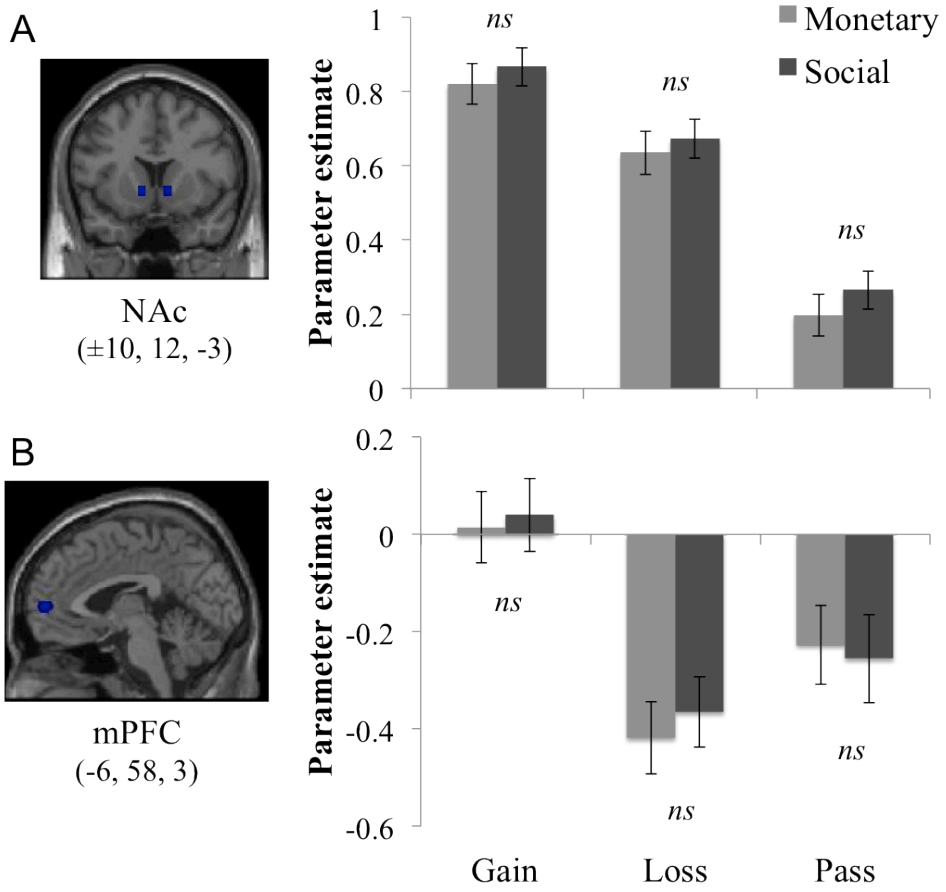

Fig. 6. (a) Average nucleus accumbens (NAc) activation plotted for trials on which participants chose to play (i.e., average of gains and losses) and trials on which they chose to pass, separately for the monetary (light gray bars) and social rank (dark gray bars) feedback context. (b) Average medial prefrontal cortex (mPFC) activation plotted for trials on which participants experienced a gain, loss, and neutral (i.e., pass) outcome, separately for the monetary (light gray bars) and social rank (dark gray bars) feedback context. Note that gain and loss outcomes followed the choice to play, whereas neutral outcomes followed the choice to pass. Error bars represent standard errors.

Interestingly, when we looked at individual differences in risk taking-related (i.e., Play > Pass) NAc activation for the feedback contexts separately (Fig. 7a), we found that both estradiol level (E) and pubertal stage (PDS) positively predicted NAc activation in the monetary feedback context (E: $r = .36$, $p = .008$, $n = 54$; PDS: $r = .34$, $p = .009$, $n = 57$), but not in the social rank feedback context (E: $r = .05$, $p = .69$, $n = 55$; PDS: $r = -.05$, $p = .70$, $n = 58$); these correlations were marginally different for estradiol (Steiger's $Z = 1.81$, $p = .070$) and significantly different for pubertal stage (Steiger's $Z = 2.39$, $p = .017$). Results of a linear regression analysis including E, as well as PDS as predictors of NAc (play > pass) activation in the monetary feedback context showed that, after controlling for age ($\beta = -.27$, $p = .071$), individual differences in both E ($\beta = .32$, $p = .042$) and PDS ($\beta = .31$, $p = .047$) explained 22.1% of the variance in NAc activation, $F(3, 50) = 4.72$, $p = .006$. These three predictors did not explain a significant portion of the variance in NAc activation in the social rank feedback context, $F(3, 51) = .46$, $p = .71$.

In contrast, testosterone negatively predicted risk taking-related NAc activation in the social rank feedback context ($r = -.26$, $p = .050$, $n = 56$), but not in the monetary

feedback context (r = .06, p = .68, n = 55); these correlations were marginally different from one another, Steiger's Z = 1.87, p = .060. No relations were found for age, BMI, or task behavior.

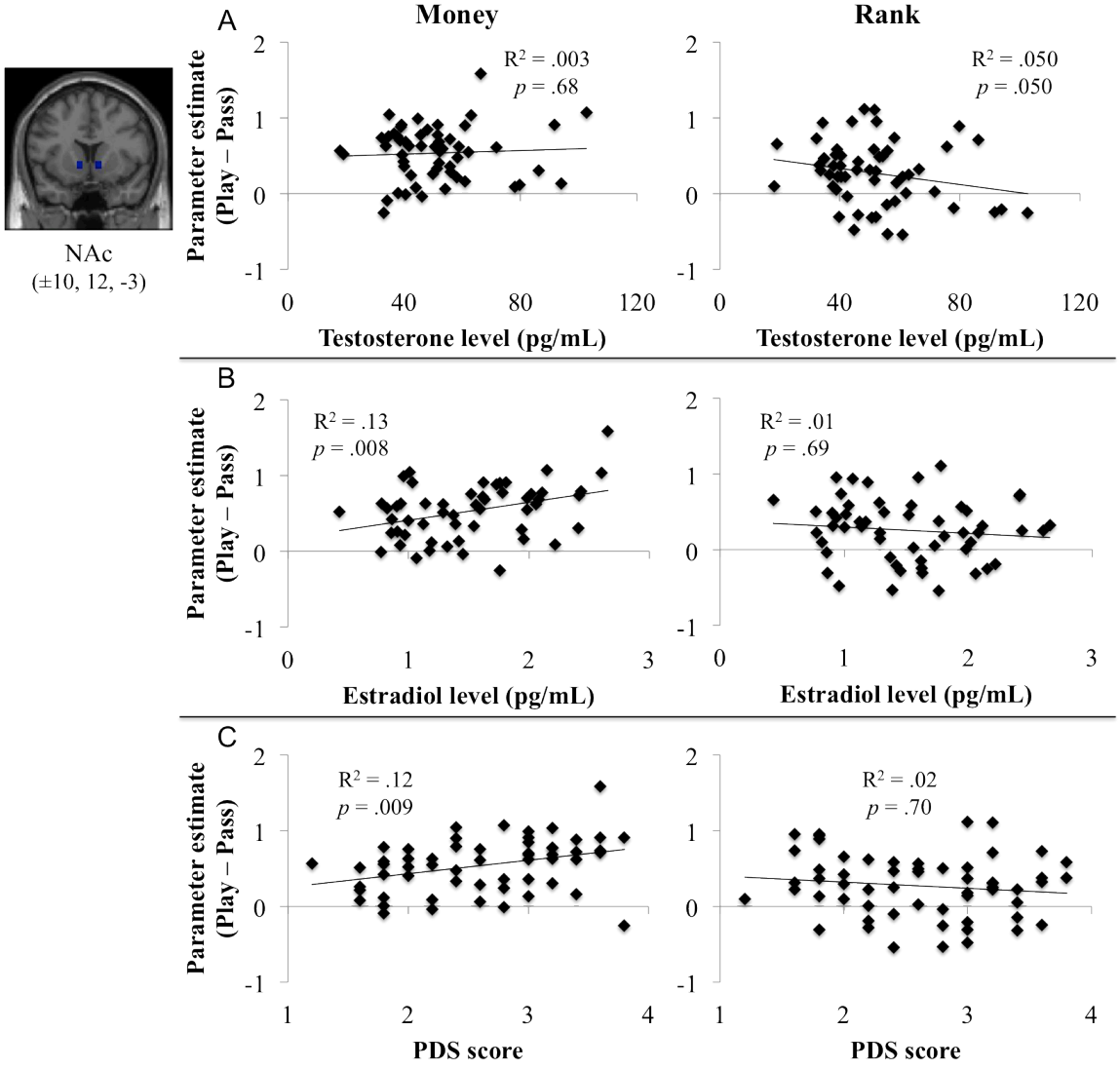

Fig. 7. Scatterplots depicting risk taking-related (i.e., Play > Pass) activation in nucleus accumbens (NAc) in the monetary (left) and social rank (right) feedback context plotted against (a) testosterone level, (b) estradiol level, and (c) pubertal stage (i.e., PDS score).

mPFC. Results of a repeated-measures ANOVA predicting mPFC activation based on feedback context (rank or money) and outcome after risk taking (gain or loss) as within-subjects factors revealed a main effect of outcome, $F(1, 57) = 57.5$, $p < .001$, but not feedback context, $F(1, 57) = .27$, $p = .61$. Specifically, mPFC activation was increased for trials on which participants chose to play and won as opposed to lost, indicating its role in reward outcome processing. There was no interaction between feedback context and outcome, $F(1, 57) = .11$, $p = .74$, indicating that mPFC activation

associated with risk taking was similar across feedback contexts, for both outcomes (Fig. 6b).

No correlations were found between mPFC activation for Social > Monetary Gain, or for Social > Monetary Loss and any of the developmental measures, or task behavior (all *p*'s > .05). However, for Social > Monetary Loss, there was a marginal negative correlation between mPFC activation and age (r = -.25, p = .064, n = 58). Further analysis revealed that loss-related activation in mPFC was associated with age in the monetary feedback context (r = .29, p = .029, n = 58), but not in the social rank feedback context (r = .01, p = .93, n = 58); these correlations were marginally different from one another, Steiger's Z = 1.85, p = .064 (Fig. 8a). Furthermore, when we looked at individual differences in reward outcome-related (i.e., Gain > Loss) mPFC activation for the feedback contexts separately (Fig. 8b), we found that age negatively predicted mPFC activation in the monetary feedback context (r = -.26, p = .045, n = 58), but not in the social rank feedback context (r = -.20, p = .14, n = 58); however, these correlations did not differ from one another (Steiger's Z = -.42, p = .67), indicating that the mPFC similarly differentiated between gain and loss outcomes in the monetary and social rank feedback contexts. No relations were found for pubertal stage, hormone levels, BMI, or task behavior.

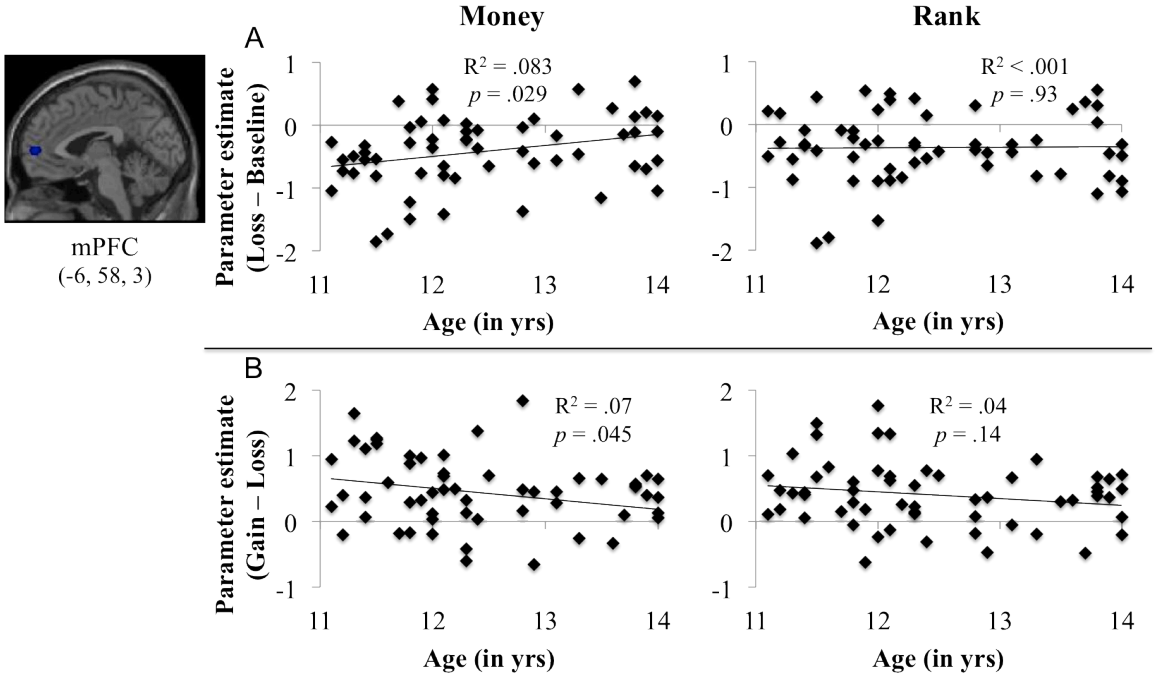

Fig. 8. Relations of age with brain activation in the monetary (left) and social rank (right) feedback context for (a) loss-related (i.e., Loss > Baseline) and (b) reward outcome-related (i.e., Gain > Loss) activation in medial prefrontal cortex (mPFC).

Discussion

In the present study, we examined whether receiving information about one's relative performance (i.e., social rank feedback) increased risk taking and associated reward-related brain processes compared to receiving information about one's absolute performance (i.e., monetary feedback). Results showed that across participants there were

no differences between the feedback contexts for task behavior, or anticipatory and consummatory reward processes (i.e., NAc and mPFC activation, respectively). These findings suggest that the presentation of status-relevant social information, as opposed to individual (monetary) performance feedback, did not influence risk taking or the way that these early adolescent girls processed rewards.

Previous studies have shown that among adolescents the presence of peers enhances risk taking and reward processes associated with risky decisions (Chein et al., 2010; Gardner and Steinberg, 2005; Smith et al., 2014a). While both the presence of peers and the presentation of rank information provide a social context, the psychological processes triggered by these two types of social contexts likely differ. For example, the presence of peers is more likely to induce brain processes associated with social evaluation. Previous research has shown that adolescents who believed that peers were watching them through a video camera showed a peak in mPFC activation compared to children and adults, and greater coupling between mPFC and the striatum (Somerville et al., 2013). These findings suggest that the thought or experience of being evaluated by peers influences reward-related processes that in turn could motivate adolescents to behave differently. Similarly, the presence of peers may induce brain processes associated with social conformity. Previous studies have shown that risk taking in the presence of a cautious peer (Cascio et al., 2015) or an expert (Engelmann et al., 2012) led to increased engagement of cognitive-regulatory brain regions, such as the dorsolateral PFC, and safer decisions. Together, these findings suggest that being ranked against peers may not trigger the psychological processes that influence risk taking or reward processing, and other (evaluative or conforming) processes may account for the influence of peer presence on brain and behavior. Future studies are needed to identify which psychological processes triggered by the presence of peers impact risk taking.

Another possible explanation is that the girls were less motivated to increase their social status because they were not familiar with the girls they were competing with. In other words, the current manipulation in which the girls were ranked against anonymous peers who also played the task may have been too subtle for inducing status-seeking behavior (i.e., increased risk taking). In future studies, this could be explored by testing whether being ranked against friends as opposed to disliked peers (Braams et al., 2014), instead of anonymous peers, enhances risk taking (and associated reward processes).

The role of the insula

Being ranked against peers, as opposed to receiving monetary feedback, altered neural processing during risk taking. Specifically, we found that anterior insula was more activated during risk taking when the girls were ranked against their peers, but not when they received monetary feedback. The insula, particularly the anterior part of the insula, has been implicated in the detection of salient events (Menon and Uddin, 2010), such as errors (Ullsperger et al., 2010). Besides its role in performance monitoring, the anterior insula has also been associated with task set maintenance (Nelson et al., 2010). While the posterior insula has been associated with interoception, the anterior insula has been implicated in subjective feelings (Craig, 2002). Because the anterior insula is consistently associated with a wide range of activities that involve the monitoring of both internal and external events, it has been hypothesized that anterior insula activation represents awareness of the self, others, and the environment (Craig, 2009). In the context of

decision-making, particularly under uncertainty (e.g., risk taking) and in the presence of social information, the anterior insula is thought to represent current (and predicted) emotional states of self (and others) and to integrate this internal information with external cues (from the social environment) to form a "subjective feeling state" that in turn guides behavior (Lamm and Singer, 2010). This role of anterior insula in adaptive decision-making was demonstrated in a study with young adults who were given the opportunity to adjust their decisions based on prior outcomes of their risky decisions (Xue et al., 2010). Results of this study showed that participants were more likely to take risks after playing it safe and this tendency was mediated by activation of anterior insula. The authors interpreted this finding as insula activation reflecting an "urge" (to take risks after playing it safe). The idea that anterior insula integrates information across social, emotional, and cognitive domains to influence behavior is further supported by the finding that different subdivisions within the anterior insula serve different functions (Chang et al., 2013), and by the finding that anterior insula communicates with a wide range of brain regions (Menon and Uddin, 2010).

Together, these findings suggest that when the girls were making risky decisions in the anticipation of being ranked against their peers, they reached a state of increased (self-) awareness compared to when they received monetary feedback. Furthermore, the receipt of social rank vs. monetary feedback may have been more salient and placed increased demands on task set maintenance, which is also supported by our finding of additional activation in left fusiform gyrus, a region involved in visual attention (Lim et al., 2013). Future studies using a network approach are needed to provide insight into the relation of anterior insula with reward-related or prefrontal brain processes associated with risk taking. Some tracks have already been made in a previous study based on an earlier version of the Jackpot task (Van Duijvenvoorde, Op de Macks, et al., 2014 [Chapter 2]). In this study, we demonstrated that individuals with stronger functional connectivity between the ventral striatum and anterior insula tended to play less often, suggesting that increased anterior insula activation in the presence of social (or other salient) information could influence reward-related processes during risk taking.

Another possibility is that the insula plays a role in keeping track of one's relative performance. This idea is supported by a study that used a multi-person decision task in which participants, who were part of a team, chose between two options (i.e., A or B) that produced arbitrary rewards (i.e., points). Each participant was exposed to four task conditions; the participant received either (1) no feedback, (2) feedback about what the other group members had chosen, (3) feedback about the rewards the other team members had received, or (4) both feedback about the choices and rewards of the other team members. Results showed that insula activation was parametrically modulated by the extent of group alignment; insula activation was highest when participants made choices and/or received feedback that differed from all their team members (Tomlin et al., 2013). While the parametric effect of rank on insula activation could not be tested using this paradigm (i.e., there were too few instances of the feedback phases to allow for direct comparison), these findings confirm the role of anterior insula in performance monitoring and suggest that the insula may be particularly engaged when feedback is social. Future research is needed to distinguish whether the social aspect or the relative aspect of the feedback enhanced insula engagement.

Individual differences in neural sensitivity to context

In contrast to our expectations, testosterone level was not associated with individual differences in the behavioral sensitivity to feedback context; girls with higher testosterone levels did not chose to play more often, or engage in faster decision-making when being ranked against their peers, as opposed to receiving monetary feedback. In fact, none of the developmental measures were associated with differences in behavioral sensitivity to context. Instead, differences in RT were associated with reported resistance to peer influence. Specifically, girls who reported being more susceptible (i.e., less resistant) to peer influence responded slower on high-risk trials in the social rank as opposed to monetary feedback context. These findings suggest that girls who reported being more concerned with their social environment took a more deliberate approach when making decisions in the social rank feedback context (relative to the monetary feedback context), especially when there was a relatively small chance to win. Thus, individual differences in sensitivity to feedback context may not be related to any developmental markers, but influenced by more trait-like factors, such as resistance to peer influence (RPI). However, this finding does not allow us to rule out developmental influences on context sensitivity, since the cross-sectional nature of the study prevents us from testing the relation between developmental changes and changes in behavior, as a function of context. Furthermore, it should be noted that RPI increases throughout adolescence, particularly between ages 14 and 18 years (Steinberg and Monahan, 2007), and therefore could serve as a developmental marker as well.

At the level of the brain, individual differences in (NAc, mPFC, and insula) activation between the two feedback contexts did not correspond with differences in testosterone level. Instead, girls with higher levels of estradiol activated insula more strongly for risk taking in the social rank, but not the monetary feedback context. This finding is consistent with studies that reported increased anterior insula involvement in adolescence (Smith et al., 2014b) and provides additional insight into the potential underlying mechanism (i.e., puberty-related changes) and context (i.e., social) in which these developmental processes are most salient. Although a longitudinal follow-up is needed to confirm whether changes in estradiol (reflective of pubertal maturation in girls) are indeed associated with increases in insula activation over time, this finding suggests that biological and social influences on brain processes associated with adolescent risk taking interact.

While social context seemed to be important for processes performed by the insula, monetary context seemed to affect processes performed by the NAc. Specifically, girls in a more advanced pubertal stages (as measured by the PDS) showed increased NAc activation for play vs. pass choices in the *monetary* feedback context, but not in the social feedback context. Further analyses showed that, after controlling for age, both estradiol and PDS score positively predicted NAc activation in the monetary feedback context, but not in the social rank feedback context. In other words, girls who were further along in their pubertal development showed increased reward-related activation during risk taking (as opposed to opting out) when they were playing for money, suggesting that the anticipation of money (but not of being ranked) became more rewarding with pubertal maturation. This finding is in line with a previous study that showed that the NAc was more sensitive to monetary than social rewards in young adults, while older adults showed the opposite pattern (Rademacher et al., 2014).

Taken together, these findings suggest that behavioral sensitivity to feedback context is mediated by personality traits, whereas neural sensitivity to feedback context depends on pubertal maturation. Future (longitudinal) studies are needed to investigate whether these pubertal influences on the brain lead to behavioral sensitivities to context later on in development.

Limitations and future directions

The greatest limitation of this study is its use of a cross-sectional design to investigate the relation between developmental measures and behavior, as well as the brain. While we corrected for age, a longitudinal design would be better suited to assess whether puberty-related (physical and hormonal) changes are associated with changes in risk taking and accompanied reward processes. More importantly, results from a longitudinal study could provide more insight into the impact of context on the developmental trajectories of reward processing and risk taking.

Another limitation of this study is the lack of a direct measure of social status among peers. For example, we did not ask the girls how they ranked themselves in their classroom, or how many friends they have, let alone how important social status is to them (LaFontana and Cillessen, 2010). These kinds of measures may have been better predictors of differences in risk taking between the two feedback contexts, and may have provided more insight into what psychological processes modulate reward-related brain responses in a social context.

Conclusion

The current study demonstrated that adolescent girls differ in their motivations to engage in risk taking; some girls took more risks when they were playing for money, whereas others took more risks when they were being ranked against peers. While behavioral differences between the social rank and monetary feedback contexts were associated with their self-reported resistance to peer influence, differences in brain function were related to puberty. While it remains to be tested—in a longitudinal follow-up—whether adolescent girls become *more* motivated during puberty to engage in risk taking to enhance social status, these cross-sectional findings provide evidence for the interaction between puberty and social influences in the context of risky decision-making.

Supplementary Materials

Supplementary data associated with this chapter can be found in appendix D.

Chapter 5. Risky decisions in adolescence: The role of sleep and pubertal development

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*Honors thesis by Orly Bell, completed under direct supervision of Zdeňa Op de Macks

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Introduction

Adolescence marks the transition from childhood to adulthood. This developmental period is characterized by a broad set of changes in appearance, intellectual abilities, and socio-emotional functioning. In this study, we focused on changes in decision-making, particularly in the context of risk, as risky decisions are more common among adolescents compared to children and adults. There are many factors that might contribute to the increase in risk taking in adolescence, including sleep and puberty. For my honors thesis, we looked at the relationship between risky behavior and sleep as well as pubertal development in young adolescent girls.

Increased risk taking in adolescence

Decision-making in the context of risk, or risk taking, is thought to involve both cognitive-regulatory and emotional (e.g., reward-related) processes (Casey, Jones & Hare, 2008; Steinberg, 2008). These psychological processes undergo substantial changes during adolescence and are thought to contribute to the transition from being a dependent child to a self-sufficient adult by enhancing exploratory behaviors, and as such creating learning opportunities. Indeed, compared to children and adults, adolescents engage in more sensation- and novelty seeking behaviors that often involve risk taking. Despite its adaptive function, risk taking can also lead to sub-optimal decisions and engagement in unfavorable or even dangerous behaviors, such as dropping out of school, illegal drug use and unprotected sexual intercourse, smoking cigarettes, and driving under the influence (Boyer, 2006; Eaton et al., 2011; Furby & Beyth-Marom, 1992). Consequently, adolescence is a time of increased vulnerability, which is evidenced by the two-fold increase in morbidity and mortality during adolescence compared to other times during the lifespan (Dahl, 2004).

Neural underpinnings. According to the *dual-process theory* (Casey, Jones & Hare, 2008), heightened risk taking among adolescents can be explained by a discrepancy between emotional and cognitive development. While emotional changes occur relatively early, cognitive abilities (e.g., self-control) develop gradually across adolescence and continue to mature into early adulthood. This temporal difference is thought to result in adolescence being a developmental period during which there is a tendency toward making more emotion-driven decisions. Evidence for this theory comes from neuroimaging studies that show relatively early functional changes in reward-related brain regions (with development peaking in mid-adolescence), whereas changes in the cognitive control regions—located predominantly in the prefrontal cortex—occur more gradually throughout adolescence and well into adulthood (Casey, Jones & Hare, 2008; Steinberg, 2008).

Another theory suggests that there are important changes in socio-emotional processing, which begin at the onset of puberty and might be crucial to understanding adolescent vulnerabilities (Crone & Dahl, 2012; Pfeifer & Allen, 2012). According to this

model, the rapid increase in hormone levels at puberty influence the development of brain regions involved in the processing of both social and emotional information. Simultaneously, cognitive prefrontal regions develop according to a more gradual, age-related trajectory and can be recruited in a flexible, context-dependent manner, since these regions demonstrate greater plasticity during adolescence. Together, these developmental changes are thought to underlie enhanced reward sensitivity and processing of social information during adolescence, which leads to increased sensation seeking and sensitivity to peer influence. Moreover, the enhanced socio-emotional processes are thought to interact with the more gradually developing cognitive-regulatory processes. Therefore, in this time of increased prefrontal plasticity, adolescents are able to flexibly adjust their behavior according to their socio-emotional context. As such, this model suggests that adolescents are more prone to risk taking in particular social environments (e.g., in the presence of their peers) (Chein, Albert, O'Brien, Uckert & Steinberg, 2011; Crone & Dahl, 2012).

Potential contributors. Sleep and pubertal development have both been linked to increases in risk taking, and may play a critical role in the increased risk-taking behavior observed in adolescence. Puberty serves as a biological marker for the onset of adolescence and is thought to contribute to the psychological and behavioral changes during adolescence (in addition to the physical changes associated with becoming reproductively mature). In particular, the marked rise in the concentration of gonadal hormones are thought to play a role in the adolescent-typical behavioral changes by sculpting neural circuits, thus influencing various brain processes (Sisk & Zehr, 2005). Additionally, these pubertal brain changes have been associated with changes in sleep patterns (Carskadon, 2011; Hagenauer, Perryman, Lee & Carskadon, 2009), which in turn have shown to affect risk-taking behavior (Dahl, 2008). Together, these findings suggest that adolescence is a period in development during which the biological changes associated with puberty influence behaviors such as sleep and decision-making, which also influence one another. This raises the question whether adolescents are more likely to go into a negative spiral of inadequate sleep and sub-optimal decision-making after puberty. To answer this question, this study tested the presence of a three-way relationship between puberty, sleep, and risk taking.

Puberty

Puberty and adolescence are not one and the same; puberty—with the rise in gonadal hormone concentrations as its hallmark feature—marks a time of reproductive maturation and associated changes in physical appearance, whereas adolescence denotes a time of social, emotional and cognitive maturation. The psychological changes in adolescence are thought to be caused by cortical remodeling of cognitive and limbic brain structures under the influence of pubertal hormones, and eventually lead to a mature adult brain (Peper & Dahl, 2013; Sisk & Zehr, 2005).

Hormonal changes during puberty. Pubertal maturation begins with a hormonal surge at the age of 9 to 10 years in girls, and 10 to 12 years in boys. The most dramatic change occurs during the first half of puberty, when transitioning from low levels in the pre-pubertal phase to very high levels of hormones during mid-puberty (Peper & Dahl, 2013). The rise in hormones is caused by a reactivation of the hypothalamus-pituitary-gonadal (HPG) axis, which is first active during pre-natal and early post-natal life,

quiescent throughout childhood, and active again at the start of puberty. The reactivation of the HPG axis stimulates the hypothalamus to release GnRH (gondatropin releasing hormone), which occurs during sleep. This hormone causes the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary, which in turn stimulates the release of gonadal hormones (i.e., testosterone and estradiol) from the gonads. The gonadal hormones (or sex steroids) drive the development of the secondary sex characteristics (Sisk & Zehr, 2005), which ultimately result in an individual's attainment of reproductive maturity.

Hormonal influences on the developing brain. The rise in gonadal hormones at puberty is also thought to be involved in the behavioral changes observed in adolescents. According to the *organizational-activational hypothesis* (Schulz, Moledna-Figueira & Sisk, 2009), the hormones that are initially involved in sexual differentiation during fetal- and early development (i.e., gonadal hormones) are re-activated during puberty and cause both organizational and activational effects on the developing brain. Activational effects are transient effects on the brain that are typically associated with the presence or absence of sex steroids, whereas organizational effects are long lasting as they sculpt the nervous system throughout development. Thus, the elevated concentration of gonadal hormones during puberty is thought to sculpt neural circuits during adolescence, affecting brain processes that might induce changes in behavior during this time period (Sisk & Zehr, 2005).

Evidence from MRI studies. Gray matter (i.e., tissue that consists mostly of neuron cell bodies and unmyelinated axons) develops according to an inverted U-shaped pattern over the course of one's lifetime. Moreover, gray matter development peaks at different ages across the different brain regions (Giedd et al., 1999). Discrepancies in the timing of these developmental peaks (at age 11.5 years for girls and at age 14.5 years for boys, which corresponds with the onset of puberty) have alluded to a potential role of gonadal hormones in structural brain development. Interestingly, Giedd et al. (2006) found that the dorsolateral prefrontal cortex (DLPFC), an area involved in controlling impulses (needed for decision making), takes longer than other brain regions to reach adult levels of cortical thickness. Due to the fact that the development of this region is not completed until adulthood, the ability to control impulses may not be fully developed during adolescence and may lead to making more risky decisions.

Another piece of evidence that puberty plays a role in structural brain development comes from MRI studies showing the emergence of sexual dimorphisms in particular brain regions at puberty. For example, amygdala volume was found to increase during puberty in males, whereas hippocampal volume was found to increase during puberty in females (Lenroot et al., 2007). These findings suggest that the rise in gonadal hormones at puberty influence structural brain changes in a sex-specific manner. More compelling evidence comes from studies showing that pubertal measures (i.e., hormone concentration and Tanner stage assessment) are associated with sex-specific brain changes. For example, Giedd et al. (1999) has shown that white matter increases linearly between childhood and adolescence, with the increase slowing and stabilizing as an individual enters adulthood. Conversely, gray matter decreases in the parietal cortex of boys, corresponding with the rise in testosterone at puberty (Neufang et al., 2009). In addition, some evidence points to the involvement of ovarian hormones in female brain organization (e.g., Neufang et al., 2009; Schulz, Molenda-Figueira & Sisk, 2009), though

less is known about the specific effects of estradiol. These findings suggest that pubertal development is associated with structural remodeling of the brain and point to the need of studying boys and girls separately since pubertal development differs across the sexes both in terms of its physical consequences and the hormones that are driving it (for a review, see Blakemore, Burnett & Dahl, 2010).

Puberty and risk taking. While previous research has shown that adolescence is a time of increased risk taking (Steinberg, 2008), little is known about to the role of pubertal hormones. One study found that testosterone in adolescent boys was correlated with self-reported risk-taking behaviors, whereas estradiol was correlated with risk taking in adolescent girls (Vermeersch, T'Sjoen, Kaufman & Vinke, 2008a; 2008b). These findings suggest an association between sex-specific pubertal hormones and risk taking during adolescence. Other studies looked at the relationship between pubertal hormones and reward processing in the context of risk taking. Forbes et al. (2010) reported that higher testosterone levels in boys corresponded with increased activation in reward-related brain areas during the anticipation phase of a card guessing game. In contrast, higher testosterone levels—in both boys and girls—corresponded with decreased activity in these brain areas during the outcome phase. These findings suggest that the relationship between testosterone and brain activation may differ depending on the phase of decision-making. In a more recent study, Op de Macks et al. (2011) found that both girls and boys with higher testosterone levels showed increased activation in reward-related brain areas while receiving a monetary reward on a simple gambling task. Furthermore, higher estradiol levels in girls were associated with stronger activity within reward-related brain areas, but these results were not as robust as the testosterone finding. Together these findings suggest that pubertal hormones are associated with activation in brain areas associated with risk-taking behavior, and these hormones may have sex-specific effects. However, more research is needed to tease out these sex differences.

Sleep

Sleep is an essential part of our daily lives. Human beings sleep for approximately one-third of their lifetime. In an infamous study on sleep deprivation, Everson, Bergmann and Rechtschaffen (1989) found that in rats sleep deprivation for more than 11-32 days is fatal. Furthermore, many studies in adults have shown that total or selective sleep deprivation greatly impairs daily functioning by causing attentional difficulties, problems with memory and immune system functioning, emotional instability, psychosis and other mental health problems (Bryant, Trinder & Curtis, 2004; Trenell, Marshall, & Rogers, 2007; Walker, 2009). The evidence on sleep deprivation clearly points to the importance of adequate sleep and its necessity to survive.

Sleep stages. Sleep is characterized by several stages: rapid eye-movement (REM) sleep and stages 1-4 of non-rapid eye movement (NREM) sleep. The most common way to study the sleep stages is by using polysomnography (PSG), a multi-parametric measure that consists of electroencephalography (EEG), electromyography (EMG) and electro-oculography (EOG). These measures provide information about brain activation, muscle tone, and eye movements, respectively. Using this technique has not only lead to the discovery of the sleep stages, but has also helped us to characterize the stages and understand the differences between them. During stages 1 and 2 of NREM sleep, people show low frequency brain waves that are synchronized and high in

amplitude. During stages 3 and 4 of NREM sleep, also known as "Slow Wave Sleep (SWS)," the brain waves are even lower in frequency, very high in amplitude and synchronized. During all stages of NREM sleep the individual experiences lowered muscle tone and relatively little eye movement. In contrast, during REM sleep the eyes make horizontal movements and there is no muscle tone (i.e., atonia). In addition, the brain waves are very high in frequency, low in amplitude, and desynchronized; characteristics that are similar to those of brain activity seen when the individual is awake. REM sleep is associated with dreaming and occurs in a cycle, with periods of NREM sleep in between, of approximately 90 minutes throughout the night. Each sleep stage is crucial, and missing out on one of the stages can impair daily functioning. For example, previous research has shown that selective REM sleep deprivation is associated with the onset or maintenance of mood disturbances (e.g., depression or post traumatic stress disorder), indicating the importance of REM sleep in regulating emotion (Walker, 2009; Walker & Van der Helm, 2009).

Sleep regulation. According to the *two-process model* proposed by Borbely & Acherman, Trachsel & Tobler (1989) sleep is regulated on a day-by-day basis through two interacting rhythms. The first process is the daily *circadian rhythm*, an endogenous oscillating cycle of approximately 24 hours. The circadian rhythm originates in and is controlled by the suprachiasmatic nucleus (SCN), which is located in the hypothalamus. The SCN is sensitive to light, which is how it regulates the sleep-wake cycle. The second process is the homeostatic rhythm, also known as "sleep pressure." The *homeostatic rhythm* continuously rises throughout the day and dissipates during sleep. Through their interaction, these two processes regulate sleep.

Chronotype and social jetlag. Chronotype refers to the tendency to prefer being awake either in the morning or in the evening. Individuals can range from being a morning type (lark like; wakes up at an early hour and goes to sleep early) to being an evening type (owl like; likes to stay up late and wake up later in the day) (Horne & Ostberg, 1976). Changes in social schedules (i.e., school and work) interfere with the preference for a later sleep schedule. A common way to quantify the day-to-day variations in sleep onset, offset and duration is by calculating the midpoint of sleep, which is defined as the moment in time halfway through total sleep duration. The discrepancy that results between the midpoint of sleep on weeknights (when individuals have school or work) and weekend nights can be referred to as *social jetlag* (Wittmann, Dinich, Merrow, & Roenneberg, 2006). The jetlag that people undergo when they travel across time zones is comparable to the shift that people undergo in their sleep from weeknights to weekends. However, social jetlag is chronic and affects the individual a lot more than the jetlag one experiences when they travel to a different time zone. Social jetlag is more pronounced in individuals that are more evening type because they have to readjust their schedule to a greater extent during the week due to social demands (Wittmann et al., 2006).

Changes in sleep across the lifespan. Sleep architecture, total time asleep, and the preference for the timing of sleep (i.e., chronotype) change across development. A recent meta-analysis of PSG studies identified four sleep parameters that showed age-related changes across the lifespan: Total sleep time (TST)—particularly the time spent in REM sleep, sleep efficiency (SE), and the amount of slow wave sleep (SWS) all decrease with age, whereas wake after sleep onset (WASO) increases with age. This increase in

WASO becomes most pronounced in early adulthood (around age 30 years) after which it worsens exponentially at a rate of approximately 10 minutes per decade of age (Ohayon, Carskadon, Guilleminault & Vitiello, 2004).

An individual's chronotype, the tendency to exhibit a preference for being awake in the morning or evening, also changes across development (Roenneberg, et al. 2007). In particular, during adolescence (approximately around the age of 13) there seems to be a developmental shift towards preferring later bed times and evening activities, causing the individual to change into more of an evening type than they previously were. As the individual matures there is a gradual shift back to more of a morning preference; this shift is thought to be a marker of the end of adolescence (Colrain & Baker, 2011).

The uniqueness of sleep during adolescence. Adolescence is a period of dramatic biological and social changes that can affect sleep (Colrain & Baker, 2011). Adolescents not only show decreased sleep duration (Carskadon, Acebo & Jenni, 2001; Hagenauer et al., 2009), but they also show a shift to later bed times. During the week adolescents tend to accumulate sleep debt (Colrain & Baker, 2011). While this is a normal part of development, previous research has shown that an increase in sleepiness as well as a decrease in total time asleep is associated with poorer achievement in school, more illnesses, poorer self-esteem, difficulty initiating behaviors that are related to long-term rewards, increased irritability and anger (Dahl, 1999; Drake et al., 2003). These findings indicate the importance of sleep for an individual's well being and serves as a potential target to prevent an individual from going down a negative spiral of harmful behaviors, particularly in adolescence.

Many studies have hypothesized that developmental changes during adolescence may alter the circadian system, which in turn changes the timing of sleep, and the architecture of sleep (Carskadon, 2011; Dahl & Lewin, 2002; Peper & Dahl, 2013). Although the exact cause is unknown, it is speculated that later melatonin release might contribute to a shift in the circadian rhythm (Carskadon, Acebo, Richardson, Tate & Seifer, 1997). In addition to the circadian shift, evidence suggests that there is also a slower rise in homeostatic sleep pressure (Jenni, Achermann, & Carskadon, 2005). Both the circadian and the homeostatic changes are thought to contribute to the shift in sleep preference during adolescence.

In addition to changes in sleep regulation, there is accumulating evidence that gonadal hormones play a crucial role in restructuring sleep during adolescence (Hagenauer et al., 2009). For example, pubertal development has been associated with an increase in reported sleep problems (Knutson, 2005). Research in other mammals (e.g., rhesus macaque, rats, as well as other mammals) help support the hypothesis that the sleep changes are intrinsic biological processes that occur during pubertal maturation (Hagenauer et al., 2009). These biological changes in adolescence are critical for the individual to become a fully functioning adult, yet in our world today (a world that is continuously on the go) these changes are amplified. Later sleep onset in adolescents is stimulated both biologically and by the environment (i.e., from the lights of our computers, TVs, etc.). Consequently, there is an increased likelihood of individuals not receiving sufficient sleep due to the lights from our appliances, which influences circadian timing (Carskadon, 2011). These findings suggest that as an adolescent continues to mature, there is an intrinsic biological process that delays their sleep phase, as well as an extrinsic desire to stay up later.

Sleep and risk taking. Research has shown that sleep deprivation leads to increased risk taking in adults (Frings, 2012; McKenna, Dickinson, Orff, & Drummond, 2007). One possible explanation is that people become more emotionally driven after receiving less sleep, as evidenced by studies that showed poorer emotion regulation after being deprived of sleep. After just one night of sleep deprivation participants rated negative visual stimuli more negative and showed more amygdala activation than their well-rested counterparts (Yoo et al., 2007). In another study, Tempesta and colleagues (2010) showed that sleep-deprived subjects had a negative bias towards neutral pictures while the ratings for pleasant and unpleasant pictures were similar to the control group. While these findings suggest that sleep deprivation biases emotions to be more negative, there is also evidence for a bias towards more positive emotions (Gujar, Yoo, Hu & Walker, 2011). These findings suggest that decreased sleep impacts regulation of both positive and negative emotions, which in turn might influence how an individual sees and interacts with the surrounding world. Adolescence is a sensitive period for socio-emotional development and may be a particularly vulnerable time for the impact of sleep on social and emotional functioning, potentially affecting decision-making under emotional circumstances including risk.

Another explanation for the phenomena of increased risk taking behavior in sleep deprived adults is that decreased amounts of sleep, as well as fatigue, can influence cognitive processes involved in decision-making, such as risk perception. In a recent study, Frings (2012) found that adult gamblers who were fatigued were more likely to place higher bets and were not able to differentiate between higher and lower risk bets, compared to well-rested gamblers who found higher risk bets less attractive than lower risk bets. These findings support that decision-making, especially in the context of risk, is influenced by sleep or the lack of it. If these sleep effects are found in adults, it is plausible to think that we would see similar effects in adolescents, particularly as adolescence is a time of cognitive change.

Indeed, studies have shown that in adolescents chronotype and social jetlag are associated with risk-taking behavior (Hasler et al., 2012; Killgore, 2007; O'Brien & Mindell, 2010; Telzer, Fuligni, Lieberman, & Galvan, 2013). Specifically, Killgore (2007) found that adolescents who reported being more evening type, as indicated by lower scores on the Morningness/Eveningness Questionnaire (MEQ; Horne & Osteberg, 1976), also reported more impulsiveness and risk taking. According to O'Brien & Mindell (2005) there was a significant difference in self-reported risk taking between adolescent groups with a larger social jetlag compared to those with a small social jetlag. Specifically, they found that individuals who were in the group that exhibited a large social jetlag also reported higher levels of increased risk-taking. This suggests that adolescents who do not get enough sleep, either because of social constraints (i.e., school) or because of their chronotype, are more prone to engage in risk-taking behaviors.

Neuroimaging studies have also shown that activation in reward-related processes associated with risk taking increase with sleep loss and social jetlag (Hasler et al., 2012). Telzer et al. (2013) found that participants who reported poorer sleep quality also reported that they were more likely to engage in risky behaviors outside the laboratory setting and they reported a greater perception of positive consequences for engaging in these behaviors. Together, these findings suggest that there is an increase in reward

sensitivity during adolescence that potentially leads to increased motivation to seek behaviors that are rewarding in nature. Sleep loss may therefore contribute to a negative spiral of behaviors (e.g., substance abuse, driving in a car without a seatbelt, and engaging in unsafe sexual behaviors) during this sensitive time period.

Current Study

In this study, we aimed to gain a better understanding of the interactions between sleep, pubertal development, and risky decision-making. A better understanding of the three-way relationship between sleep, puberty and risk taking is essential for designing treatment and prevention programs for youth who are at risk for developing psychopathology associated with risk taking (e.g., drug abuse). The literature suggests that there is an association between both pubertal development and sleep, and sleep and risk taking, but more research is needed to understand the relationship between puberty and risk taking. However, there is evidence for an association between puberty and the brain processes involved in risk taking (i.e., reward processing).

We explored the possibility that the relationship between puberty and risk taking is mediated or moderated by sleep using multiple measures of sleep, self-reported pubertal stage, and risk-taking behavior on a gambling task. To our knowledge, only one study has investigated this three-way relationship. Results of this study showed that less sleep was related to pubertal differences, as well as differences in reward-related brain activation during a card guessing game (Holm et al., 2009). These results suggest that changes in sleep (related to pubertal maturation) are associated with changes in reward processing, which may underlie increased risk-taking in adolescence.

However, Holm et al. (2009) did not report on the risk-taking *behavior* (i.e., they focused only on the brain processes that may underlie it) and they focused on sleep during the weekend only, preventing them from measuring social jetlag. Social jetlag is not only a common phenomenon in adolescence, but has also been shown to be associated with risk taking. To address these limitations, we assessed risk taking using a gambling task and collected self-report data on reward- and sensation-seeking behaviors outside the laboratory. In addition, we collected sleep measures across five days including 3 weeknights and 2 weekend nights, enabling us to examine the effect of social jetlag on risky behavior.

Hypotheses. Based on previous findings, we predicted that adolescents who are in a more advanced pubertal stage would report shorter sleep duration, worse sleep quality, and/or greater social jetlag than adolescents who are in a less advanced pubertal stage (Hagenauer et al., 2009; Hasler et al., 2012; Holm et al., 2009). We also predicted that adolescents who are in a more advanced pubertal stage would take more risks than adolescents who are in a less advanced pubertal stage (Vermeersch et al., 2008a; 2008b). In addition, we predicted that adolescents who report sleeping less, worse or more irregularly (i.e., have greater social jetlag) would show increased risk taking (O'Brien & Mindell, 2005). Finally, we were interested in testing the three-way interaction between sleep, puberty, and risk taking. While we did not have any specific predictions about the nature of this relationship, we examined the possibility of both a mediating and moderating effect of sleep on pubertal development and risk-taking behavior.

Method

Participants

Seventy-five healthy, adolescent volunteers participated in the study. Analyses were based on 49 participants who completed both the task and the sleep logs. We specifically excluded girls who completed their sleep logs during school vacations (i.e., summer and winter vacation). We recruited females aged 11 to 13 years (11-year-olds: n = 18; 12-year-olds: n = 18; 13-year-olds: n = 13; mean age = 12.4, SD = .9 yrs) through Berkeley Parents Network as well as word of mouth. We conducted this study in girls due to the fact that the emergence of puberty is different in girls and boys (Giedd et al., 2006, Peper & Dahl, 2013) and these differences might account for variations in behavior.

Exclusion criteria were left-handedness and the presence of braces or a permanent retainer because part of the study was conducted in an fMRI scanner. In addition, participants were screened for the presence of behavioral problems, as measured by parent-ratings on the Child Behavioral Checklist (Achenbach, 1991), past or present use of neuropsychological medication and/or neurological or psychological disorders, and whether the participants' first language was English. Before entering the study, written informed consent was obtained from both the participant and the parent or legal guardian of the participant. All participants received compensation for their time, and could additionally win up to 15 dollars by playing the computer tasks. The University of California Berkeley Institutional Review Board approved all procedures.

Study procedure

Each participant completed two lab sessions at the UC Berkeley campus. The first session involved the administration of questionnaires, computer tasks, and an interview. The second session involved an fMRI scan. The study reported here is part of a larger research project that examined the role of pubertal development in decision-making, future time perspective, and emotions. My honors thesis focuses on the data collected during the second lab visit, except for the Pubertal Development Scale (PDS; Peterson, Crockett, Richards & Boxer, 1988), which was completed during the first session. However, if there was a lag of more than one month between the sessions, the PDS was re-administered during the second session to control for pubertal changes during this time. On average, the two sessions were spaced apart by about 3 weeks, during which the participant was instructed to collect two saliva samples and complete a sleep diary for 5 consecutive nights, which they brought in on their second lab visit. Prior to the scan, each participant was screened for the presence of metal using an fMRI contraindication form. Parents were asked to complete the Sensitivity to Punishment and Sensitivity to Reward Questionnaire for Children (SPSRQ-C; Colder & O'Connor, 2004) while the participant completed the Morningness/Eveningess Questionnaire (MEQ; Horne & Ostberg, 1976).

The participant was then taken by the research assistant to a separate testing room where she was instructed on how to play the task in the scanner. Each participant completed a practice round on the testing-room computer to ensure understanding of the task before entering the scanner. The participant was then taken into the scanner room where she received a final screening for metal and the scanning procedure was explained to her. Each participant completed five scans; a structural scan, 2 resting-state scans, and 2 task-related scans. The results of the imaging data will not be a part of my honors thesis. However, I will focus on the behavior on the task that was completed inside the

scanner. Another set of questionnaires was administered after the scan. Each participant was compensated for her time and won an additional $10 for playing the task.

Pubertal development

All participants completed the Pubertal Development Scale (PDS; Peterson et al., 1988), a self-report measure of pubertal maturation. The PDS consists of five questions about the physical changes associated with pubertal development that were scored from no physical changes (1) to development seems complete (4). The average of all five items (i.e., PDS score) is calculated to provide an index of pubertal maturation. Previous research demonstrated that this self-report measure has high reliability (α = .77 for boys, α = .81 for girls) and can be compared to the scores derived from physical examination done by a nurse practitioner (Shirtcliff, Dahl & Pollak, 2009). See Table 3 for sample range, mean and standard deviation.

Sleep measures

Participants completed two sleep measures: (1) The Morningness/Eveningness Questionnaire (MEQ; Horne & Ostberg, 1976) and (2) a five-day sleep diary that includes mood ratings (Gregory et al., 2011). The MEQ is a 10-item measure for chronotype, the tendency to exhibit either a preference for the morning or evening. Higher scores indicate an inclination towards morningness (i.e., the tendency to prefer an earlier rise and earlier bed times, and to function most effectively earlier in the day), while lower scores indicate an inclination towards eveningness (i.e., the tendency to prefer a later rise and bedtime, and to function more effectively later in the day). See Table 3 for mean, and standard deviation of our sample.

Sleep diaries were completed at home and collected on the second day of testing. To capture both weeknights (3) and weekend nights (2), participants were requested to complete the sleep diaries for five consecutive nights starting on a Thursday night. Every morning upon awakening, participants reported on their sleep during the night before by indicating the time they went to bed, how long it took them to fall asleep, the time they woke up in the morning, the number of times and duration they were awake during the night, the quality of their sleep, how easy it was to wake up in the morning, and the method by which they awoke (i.e., alarm clock, parent, etc.). In addition, mood (ranging from neutral to happy) and anxiety (ranging from neutral to anxious) at bedtime were measured. Based on these measures, we calculated the averages of each of the following measures across all 5 nights: sleep onset latency, total sleep time, wake after sleep onset, sleep efficiency, midpoint and the difference between the midpoint on weekend versus week nights (i.e., social jet-lag; Wittmann et al., 2006) to include in our analyses (see Table 1 for operationalization). To calculate the midpoint of sleep, we determined at which time the midpoint of the total sleep duration (i.e., total sleep time) fell, and used the number of minutes after midnight to quantify this measure (e.g., if the midpoint of sleep is at 1:30AM, it is reported as 90 minutes). See Table 2 for the mean, standard deviation and range for the sleep measures, separately for pre/early and mid/late pubertal girls.

Table 1

Sleep measures that were calculated based on the sleep diary data

Measure	Operationalization
Sleep onset latency	The number of minutes it took to fall asleep after having gone to bed
Total sleep time	The number of minutes between the time they went to bed and the time they woke up in the morning, subtracted by the number of minutes it took to fall asleep and the number of minutes awake during the night
Wake after sleep onset	The number of minutes spent awake after sleep onset, based on the total number and duration of awakening(s)
Sleep efficiency	= (Time asleep / time in bed) * 100%
Midpoint	The number of minutes after midnight that the midpoint of the time asleep falls (time fallen asleep[1] to the time of waking)
Social jetlag	The average midpoint on weekend nights minus the average midpoint on week nights

[1]Time fallen asleep was calculated based on reported time that participants went to bed and how long it took them to fall asleep.

Table 2

Descriptives of the Sleep Measures[1]

Sleep Scales	Pre/Early Pubertal Girls (n = 25)				Mid/Late Pubertal Girls (n = 24)			
	Mean (SD)		Sample Range		Mean (SD)		Sample Range	
	Week	*Weekend*	*Week*	*Weekend*	*Week*	*Weekend*	*Week*	*Weekend*
Total Sleep Time (in minutes)	525 (44.8)	550 (78.1)	436 - 592	407 - 747	523 (39.8)	550 (54.0)	425 - 611	432 - 657
Wake After Sleep Onset (in minutes)	35 (21.7)	35 (31.6)	8 - 91	6 - 120	33 (22.4)	26 (17.0)	2 - 95	0 - 64
Sleep Quality (scores range from 1-100)	72.6 (14.7)	71.7 (21.7)	40 - 97.3	25 - 99	74.6 (15.5)	78.3 (14.5)	36 - 100	51 - 99.5
Ease of Waking (scores range from 1-100)	55.5 (23.4)	71.2 (22.0)	16.7 - 95	27.5 - 99.5	61.0 (21.5)	72.5 (22.2)	14.7 - 99.3	33.5 - 100
Mood (scores range from 0-10)	**7.3 (2.2)***	**7.7 (2.0)***	2.3 - 10	2 - 10	**5.7 (2.2)***	**6.1 (2.8)***	1 - 10	.5 - 10
Anxiety (scores range from 0-10)	2.5 (2.1)	**2.4 (2.3)~**	0 - 7.67	0 - 8.5	1.9 (1.7)	**1.3 (1.3)~**	0 - 6.67	0 - 5
Sleep Latency (in minutes)	32 (20.9)	25 (21.0)	8 - 91	5 - 82	29 (22.7)	22 (16.7)	2 - 95	0 - 64
Sleep Efficiency (%)	93.6 (3.8)	93.8 (5.6)	84.1 - 98.3	78.4 - 98.8	94.1 (3.8)	95.3 (2.8)	85.5 - 99.5	89.8 - 100
Midpoint (in minutes)	154 (35.0)	**208 (51.9)~**	82 - 257	104 - 315	161 (34.2)	**235 (50.5)~**	98.7 - 208	140 - 331
Social Jetlag (in minutes)[2]	- 54 (57.8)		-233 - 36		-75 (59.5)		-213 - 2	

[1] (Marginally) significant findings are in bold: ~ $p < .10$, * $p < .05$

[2] Social Jetlag is the difference between week and weekend means of midpoint

Individual-difference measures

Sensation seeking scale for children (SSS-C). This 26-item forced-choice questionnaire was administered to assess participants' inclination towards sensation seeking (Zuckerman, Eysenck, & Eysenck, 1978). Each item consists of a sensation-seeking option and a non-sensation-seeking option. Participants were instructed to select the option most relevant to them. The SSS-C has three subscales: thrill and adventure seeking (TAS), drug and alcohol seeking (DAS), and social disinhibition (SD). An example of items on the TAS subscale is: "I'd never do anything that's dangerous" versus "Sometimes I like to do things that are a little scary," while the DAS subscale includes items like: "I think it it's too dangerous for people to take drugs" versus "I sometimes wonder what it would feel like to be high on drugs, even though I know it would be dangerous." An example of items on the SD subscale is: "I don't like being around kids who act wild and crazy" versus "I enjoy being around kids who sometimes act wild and crazy." See Table 3 for sample mean and standard deviation.

Behavioral inhibition system – behavioral activation system (BIS-BAS). This 20-item questionnaire uses a Likert-type response scale ranging from "very true for me" (1) to "very false for me" (4) to measure the inclination to approach or avoid situations across four subscales: behavioral inhibition (BIS), behavioral activation system-drive (BAS-Dr), fun seeking (BAS-FS), and reward responsiveness (BAS-RR) (Carver & White, 1994). An example of the items on the BIS subscale is: "I worry about making mistakes," while the BAS subscales include items such as: "I go out of my way to get things that I want" (BAS-Dr), "I crave excitement and new sensations" (BAS-FS), and "When good things happen to me, it affects me strongly" (BAS-RR). See Table 3 for sample mean and standard deviation.

Barratt impulsiveness scale (BIS-11). This 30-item questionnaire uses a Likert-type response scale ranging from "rarely/never" (1) to "almost always/always" (4) to assess the inclination of an individual towards impulsive behavior (Patton, Stanford & Barratt, 1995). For our analyses, we included only the first-level subscales: attentional impulsivity (AI), motor impulsivity (MI), and non-planning impulsivity (NPI). An example of items on the AI subscale is: "I 'squirm' at plays or lectures," while the MI subscale includes items such as: "I act on the spur of the moment," and the NPI subscale includes items such as; "I say things without thinking." See Table 3 for sample mean, and standard deviation.

Sensitivity to punishment and sensitivity to reward questionnaire for children (SPSRQ-C). This 33-item questionnaire measured the participant's sensitivity to reward and to punishment based on parent report. This questionnaire uses a Likert-type response scale ranging from "strongly disagree" (1) to "strongly agree" (5). The total score is comprised of four subscales: sensitivity to punishment (SP), sensitivity to reward-impulsivity/fun seeking (SR-I/FS), drive (SR-Dr), and reward responsiveness (SR-RR). An example of the items on the SP subscale is: "Whenever possible, your child avoids demonstrating their skills for fear of being embarrassed," while the SR subscales include items such as: "The possibility of obtaining social status moves your child to action, even if this involves not playing fair" (SR-I/FS), "Your child likes competitive activities" (SR-Dr), and "Your child often does things to be praised" (SR-RR) (Colder & O'Connor, 2004). See Table 3 for sample mean and standard deviation.

Table 3

Descriptives of the Individual Difference Measures [1]

Questionnaire Scales	Score Range	**Pre/Early Pubertal Girls (n = 25)** Mean (SD)	**Mid/Late Pubertal Girls (n = 24)** Mean (SD)
Pubertal Development Scale (PDS)	1 - 4	2.0 (.31)	3.1 (.32)
Morningness/Eveningness Questionnaire	10 - 43	29.8 (3.61)	30.2 (4.19)
Sensation Seeking Scale for Children (SSSC)			
Total Score	0 - 26	**10.7 (3.47)** ~	**12.7 (3.88)** ~
Thrill and Adventure Seeking (TAS)	0 - 12	7.2 (2.33)	7.6 (2.48)
Drug and Alcohol Seeking (DAS)	0 - 7	.6 (.98)	.9 (1.37)
Social Disinhibtion (SD)	0 - 7	**3.0 (1.63)***	**4.1 (1.66)***
Behavioral Inhibtion System (BIS)	7 - 28	19.7 (3.06)	20.5 (3.57)
Behavioral Activation System (BAS)			
Fun Seeking (BAS-FS)	4 - 15	11.1 (1.90)	12.2 (2.48)
Drive (BAS-Dr)	4 - 16	**8.6 (1.83)***	**10.3 (2.49)***
Reward Responsiveness (BAS-RR)	5 - 20	17.0 (1.77)	17.0 (1.98)
Barratt Impulsiveness Scale (BIS-11)			
Total Score	30 - 120	62.2 (8.54)	66.2 (8.93)
Attentional Impulsivity (AI)	8 - 32	14.8 (2.96)	15.9 (3.59)
Motor Impulsivity (MI)	11 - 44	21.9 (3.44)	23.8 (4.39)
Non-Planning Impulsivity (NPI)	11 - 44	25.4 (4.41)	26.7 (4.73)
Sensitivity to Punishment (SP)	15 - 75	38.9 (8.93)	40.6 (9.67)
Sensitivity to Reward (SR)			
Impulsivity/Fun Seeking (SR-I/FS)	7 - 35	14.8 (3.84)	14.9 (4.69)
Drive (SR-Dr)	4 - 20	12.5 (3.23)	11.8 (4.36)
Reward Responsiveness (SR-RR)	7 - 35	24.2 (3.85)	24.4 (4.36)

[1] (Marginally) significant findings are in bold: ~ $p < .10$, * $p < .05$

Experimental task

Each participant played a revised version of the Jackpot task (Op de Macks et al., 2011). On each trial, a slot machine was presented with two out of three slots showing two similar fruits. The three possible outcomes for the third slot were shown in a yellow frame above the slot machine. In the low-risk condition, participants had a 66.7% (2/3) chance that the third slot would show the same fruit type; in the high-risk condition, the chance was 33.3% (1/3). Additionally, information about the reward at stake (1 or 3 points) was presented. Based on this information, the participant could choose to play (and take the risk to win or lose 1 or 3 points), or to pass (and skip the trial). The participant indicated their decision by pressing a button with their index or middle finger of their right hand, for play or pass respectively. Upon this button press (or after 2 seconds in the absence of a response), the outcome was presented. When the participant chose to play, the outcome could be positive (gain) or negative (loss). When the participant chose to pass, the outcome was neutral (no gain or loss). If participants failed to respond, they lost 1 point. This was done to stimulate task engagement.

After every 6 trials, participants were shown performance feedback. For half of the trials participants were shown how much money they had won and for the other half of the trials participants were shown how well they played compared to others girls who had played the task. The order of the feedback type was counterbalanced across participants. At the start of the game, participants were given 5 dollars play money; if they chose to play, they could increase their winnings up to 30 dollars. If participants chose to pass, no money was won or lost. All participants were told that they would be paid according to their final score—in points—which was translated into a monetary amount at the end of the experiment.

Each trial started with a fixation cross, which was "jittered" with a minimum of 500 milliseconds. Then, the stimulus was presented for 2 seconds and the participant had to respond within that time window (they would lose 1 point if they missed). Stimulus presentation was followed by the anticipation phase, which lasted 750 milliseconds. If the participant decided to play, the slot machine would spin. To equate the visual experience of the anticipation phase across trial types, an "X" or an orange frame would flicker in the third slot upon the decision to pass or the failure to respond, respectively. The anticipation phase was immediately followed by the outcome, which was presented for 2 seconds. When participants won, they would see three of the same fruits in a row and the words "you won" were presented. When participants lost, they saw a different fruit in the third slot and the words "try again" were presented. When participants passed or missed, the third slot showed an "X" or orange frame accompanied with the words "passed" or "too slow", respectively. See Figure 1 for two example trials in which the participant chose to play. Across the task, the choice to play resulted in positive feedback in 50% of the trials, independent of the presented risk, resulting in an equivalent number of observations for reward and loss trials.

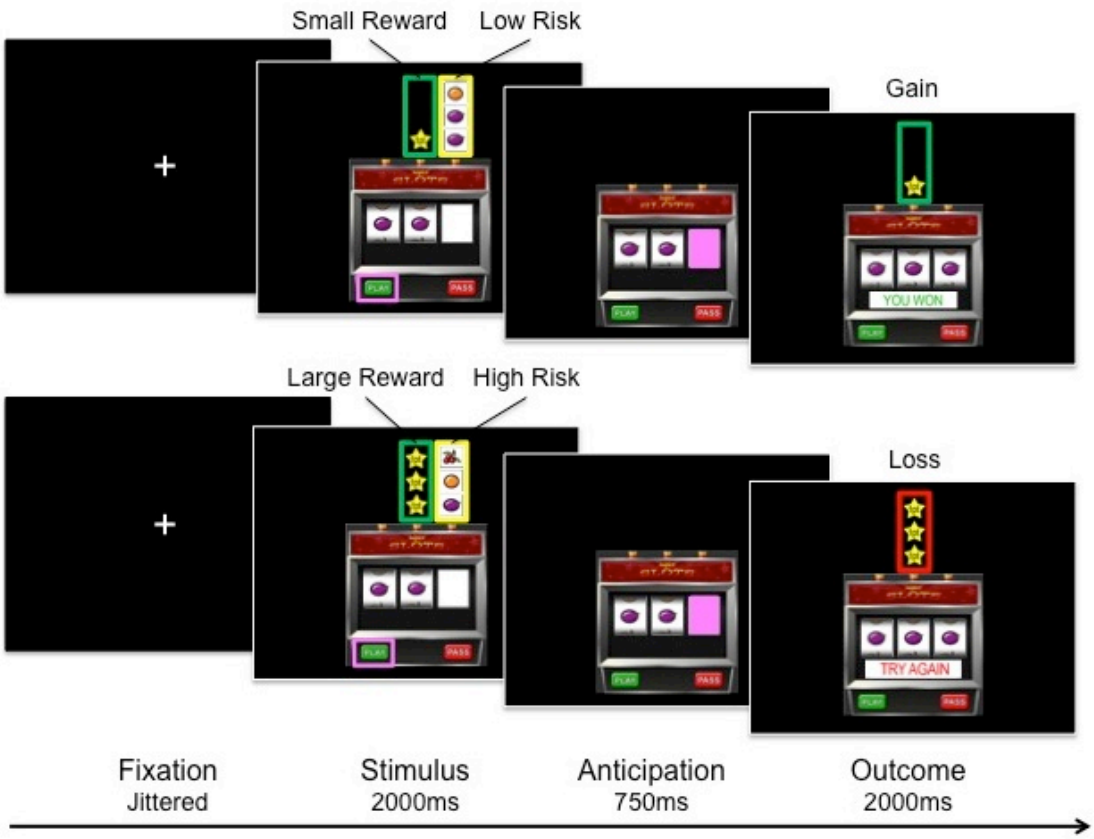

Figure 1. Examples of two Jackpot Task trials on which the participant chose to play. *Top panel:* The participant chose to play when there was a 66.7% chance to win and 1 point was at stake, and won. *Bottom panel:* The participant chose to play when there was a 33.3% chance to win and 3 points were at stake, and lost.

Analysis

Analyses were performed using SPSS software. Correlational analyses were used to test the relationships between pubertal development (i.e., PDS score), risk taking (i.e., percentage of 'play' choices on the Jackpot Task), and the various sleep measures. Multiple regression analyses were performed every time we found multiple measures that correlated with our criterions of interest. To test the effect of pubertal development on sleep and risk-taking, we performed independent-samples t-tests to compare sleep and risk taking between pre/early pubertal and mid/late pubertal girls. These groups were created based on a median split for PDS score (median: 2.4). In addition we performed independent-samples t-tests to compare sleep and risk-taking between girls who exhibited a large social jetlag and girls who exhibited a small social jetlag. These groups were based on a median split for social jetlag (median: -52.25 minutes).

Results

Puberty and sleep

Based on previous studies (e.g., Hasler et al., 2012), we expected to find that girls who are in a more advanced pubertal stage would show a later midpoint of sleep on week and weekend nights, as well as a larger discrepancy between them (i.e., social jetlag). While results of the current study did not show a correlation between pubertal stage (i.e., PDS score) and midpoints of sleep on week and weekend nights, or social jet lag (all p values > .05), a median split based on PDS score showed that mid/late pubertal girls (i.e., PDS score > 2.4) trended towards a later midpoint on weekend nights compared to pre/early pubertal girls (i.e., PDS score ≤ 2.4) ($t(46) = -1.82$, $p = .076$). This group difference was absent for midpoint on weeknights and for social jetlag (i.e., the difference between midpoint week and weekend) (See Fig. 2). These findings suggest that as girls advance through puberty their sleep shifts toward later bed and rise times, which is particularly evident when there are no sleep restrictions (i.e., on the weekend).

None of the other sleep measures (time in bed, total sleep time, sleep onset latency, number of awakenings, wake after sleep onset, sleep efficiency, sleep quality and chronotype) showed a linear relationship with pubertal stage. However, a quadratic relationship was found for the relationship between pubertal stage and (1) wake after sleep onset (WASO) on weeknights, with the PDS score explaining 12.2% of the variance in WASO (see Fig. 3a), and (2) sleep efficiency (SE) during the week, with PDS score explaining 10.2% of the variance in SE (see Fig. 3b).

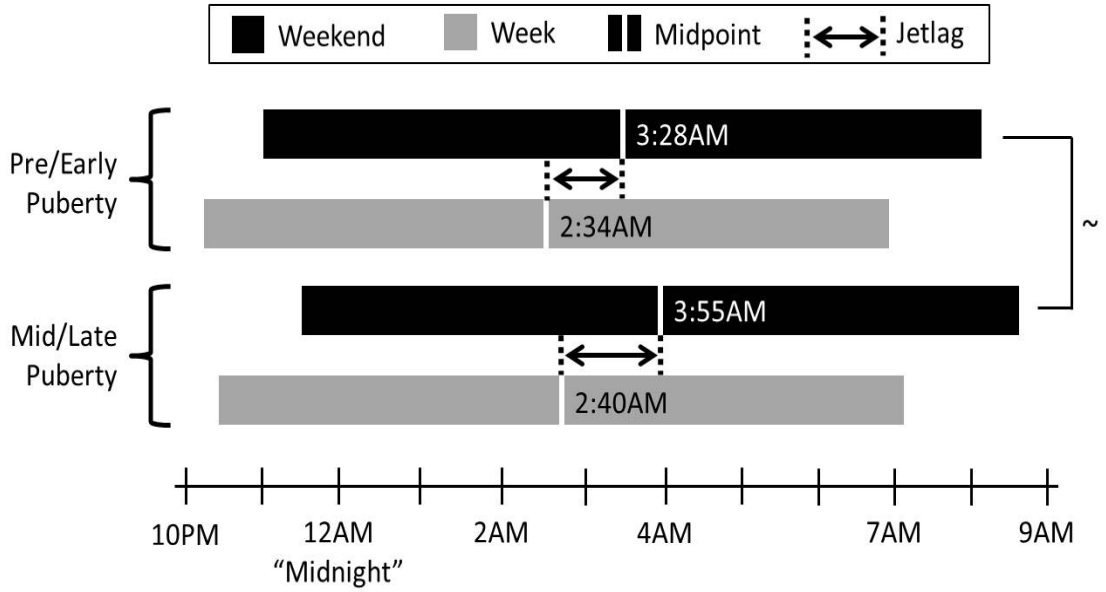

Figure 2. Midpoints for week- and weekend nights plotted separately for pre/early and mid/late pubertal girls. While the total sleep time was similar between for pre/early and mid/late pubertal girls, the midpoints on the weekend differed. The difference between midpoint on weekend and week nights (i.e., social jetlag) was similar between the two groups.

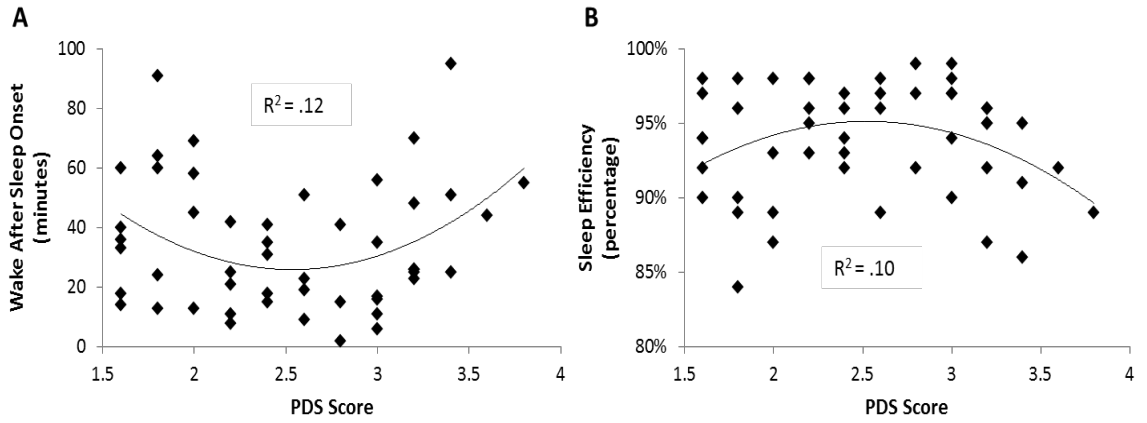

Figure 3. (a) Relationship between wake after sleep onset (WASO) during the week and puberty. *(b)* Relationship between sleep efficiency (SE) during the week and puberty.

Puberty and mood

Pubertal stage (i.e., PDS score) was negatively correlated with reported mood before bedtime on weeknights (r = -.300, p = .038), indicating that girls in later pubertal stages reported worse mood before bedtime on weeknights. There was no correlation between pubertal stage and mood before bed on weekend nights. However, a median split analysis showed that mid/late pubertal girls reported worse mood on weekend nights than pre/early pubertal girls ($t(45) = 2.32$, p = .025), in addition to weeknights ($t(46) = 2.52$, p = .015; see Fig. 4). These findings indicate that girls who are in mid/late pubertal stages report worse moods compared to their pre/early counterparts, suggesting that as individuals go through puberty their mood changes.

Puberty and risk-taking behavior

Based on previous studies in both adolescent rodents and humans, we expected to find a positive relationship between puberty and risk taking (Varlinskaya, Vetter-O'Hagen, & Spear, 2013; Vermeersch et al., 2008a; 2008b). However, in this study we did not find a significant relationship between pubertal stage and risk-taking behavior (i.e., the percentage of 'play' choices) across any of the task conditions (Low-risk/small reward: p = .67, Low-risk/large reward: p = .27, High-risk/small reward: p = .93, High-risk/large reward: p = .41). Even after conducting a median split based on PDS score no group differences were found, indicating that pre/early and mid/late pubertal girls demonstrated similar choice behavior across all conditions (see Fig. 5).

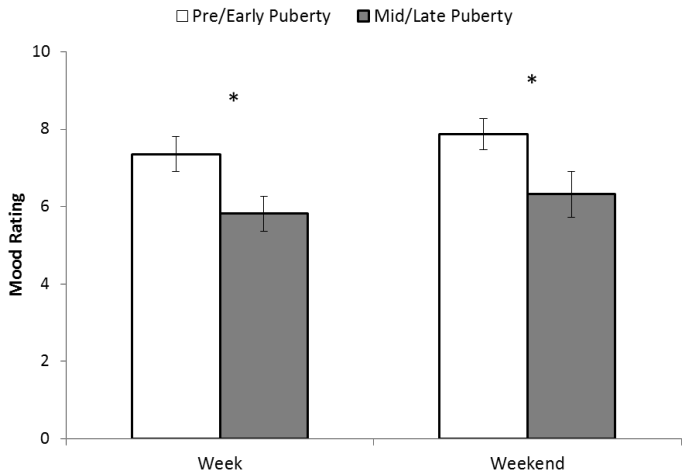

Figure 4. Mean mood ratings for week and weekend nights, plotted separately for pre/early and mid/late pubertal girls.

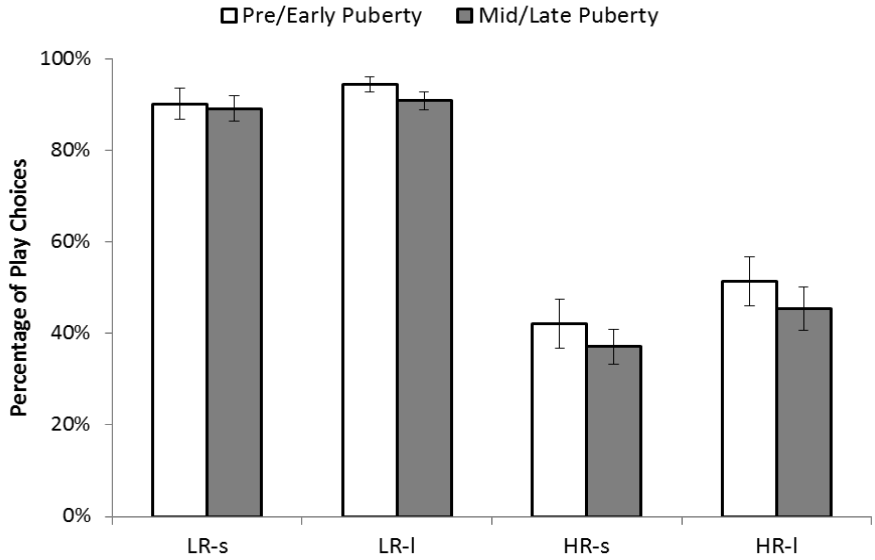

Figure 5. Risk-taking behavior plotted separately for pre/early and mid/late pubertal girls. HR-s: high-risk/small reward, HR-l: high-risk/large reward, LR-s: low-risk/small reward, LR-l: low-risk/large reward.

Sleep and risk-taking behavior

Sleep logs. Correlational analyses indicated a significant relationship between social jetlag and the percentage of 'play' choices in the high-risk/large reward (HR-l) condition (r = -.302, p = .037), suggesting that a larger discrepancy between week- and weekend midpoints was associated with more risk taking when a large reward was at stake. No relationship was found between social jetlag and risk taking in the low-risk condition (regardless of reward magnitude; all p values > .05).

A repeated-measures ANOVA with the percentage of 'play' choices as the dependent variable and risk level, reward magnitude, and group membership based on the median split of the social jetlag data showed—besides main effects of risk and reward—a marginally significant interaction between risk level and social jetlag group (F(1,46) = 3.18, p = .081). Follow-up analyses showed that in the high-risk (HR) condition, girls

with a larger social jetlag (i.e., showing a discrepancy of more than -52.25 minutes) chose to play more often compared to girls who had a smaller social jetlag ($t(46) = -2.66$, $p = .011$). This enhanced risk taking in the HR condition was particularly evident when a large reward was at stake ($t(46) = -2.77$, $p = .008$), as opposed to when a small reward was at stake ($t(46) = -1.63$, $p = .110$; see Fig. 6).

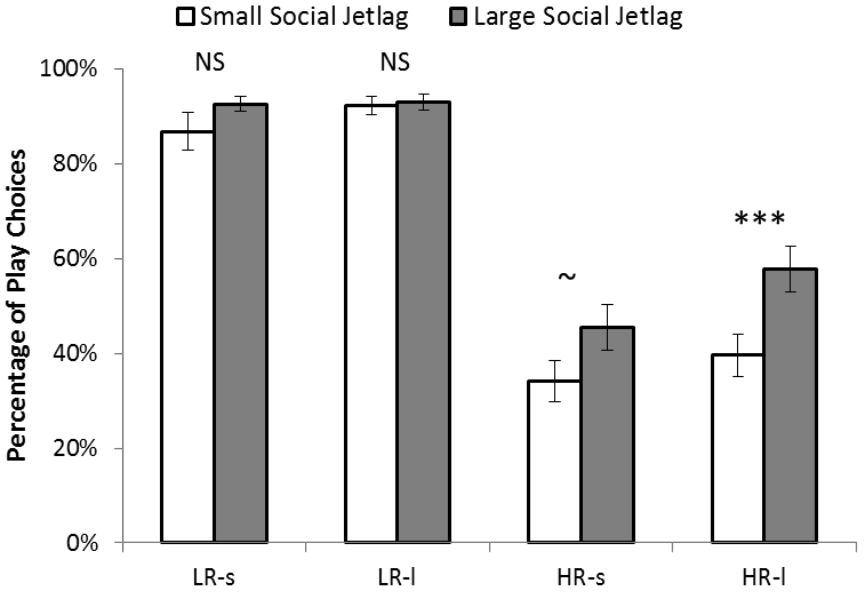

Figure 6. Risk-taking behavior plotted separately for girls exhibiting a relatively small and large social jetlag across the four different conditions: HR-s: high-risk/small reward condition, HR-l: high-risk/large reward condition, LR-s: low-risk/small reward condition, LR-l: low-risk/large reward condition.

Morningness/eveningness questionnaire (MEQ). Scores on the MEQ were negatively correlated with midpoint on weeknights ($r = -.338$, $p = .020$) and weekend nights ($r = -.363$, $p = .013$), as calculated based on the sleep logs. These findings not only indicate that girls who are more morning type are more likely to have an earlier midpoint (i.e., go to sleep earlier) on both week and weekend nights, but they also show that the two independent measures (the sleep logs and the MEQ) converge. There was no significant correlation between the MEQ score and social jetlag, indicating that chronotype was not associated with the discrepancy between week and weekend night midpoints.

Furthermore, scores on the MEQ were positively correlated with risk taking in the low-risk ($r = .366$, $p = .011$), but not the high-risk condition ($r = .049$, $p = .746$), indicating that the more morning type the girls were, the more likely they were to take risks when the chance to win was high (i.e., 67%) (See Fig. 7a). In addition, girls who reported being more morning type took a longer time deciding whether or not to play (i.e., demonstrated larger response times) in the high-risk condition ($r = .371$, $p = .010$) where the chance to win is low (i.e., 33%) (See Fig. 7b). Individual differences in both percentage of play in the low-risk condition and response time in the high-risk condition were not predicted by the age of the participant, as the regression model including both age and MEQ as independent variables showed that age was not a significant predictor for percentage of play ($t(44) = .61$, $p = .55$) nor for response time ($t(44) = .41$, $p = .68$).

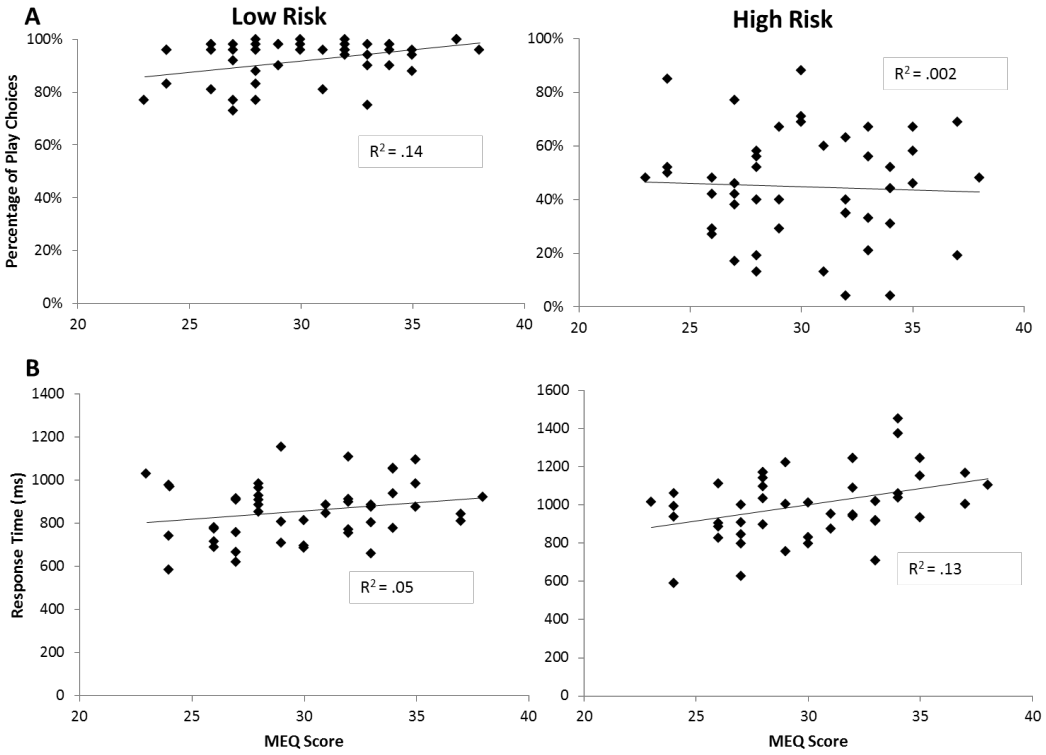

Figure 7. (a) Relationship between the Morningness/Eveningness Questionnaire (MEQ) score and risk-taking behavior in the low-risk (left) and the high-risk (right) condition. *(b)* Relationship between MEQ score and response time in the low-risk (left) and high-risk (right) conditions.

Individual-difference measures

In order to test what kind of role individual differences play in puberty, sleep and risk taking, we ran correlational analyses with self-reported personality traits. Self-reported sensation seeking (as measured by the SSS-C) was associated with pubertal measures. Specifically, girls in more advanced pubertal stages (i.e., higher PDS scores) reported more overall sensation seeking (Total score: r = .323, p = .001) and social disinhibition (SD: r = .461, p = .001). Girls who reported more drug and alcohol seeking (DAS) had shorter response times on the Jackpot task, particularly in the high-risk/small reward condition (r = -.331, p = .023), and reported worse mood before bed on weeknights (r = -.319, p = .030). Moreover, scores on the BIS-BAS correlated with both sleep and pubertal measures. Specifically, girls in more advanced pubertal stages were more likely to report a higher drive to obtain rewards (BAS-Dr: r = .387, p = .006). In addition, girls who reported more fun seeking (BAS-FS) were more likely to have larger social jetlags (r = -.416, p = .004).

Impulsivity (as measured by the BIS-11) was associated with sleep measures. Girls who reported themselves as being more impulsive showed later midpoints on the weekend (r = .312, p = .045) and tended to show larger social jetlags (r = -.293, p = .060). In particular, girls who reported more motor impulsivity (MI) exhibited larger social jetlag (r = -.363, p = .017). Furthermore, parent reports on the girls' sensitivity to rewards and to punishment (as measured by the SPSRQ-C) were associated with participant's reports on their mood as well as their response times on the Jackpot task.

Higher punishment sensitivity—as reported by the parents—corresponded with shorter response times in the low-risk condition (r = -.353, p = .019). Furthermore, girls of whom the parents reported higher punishment sensitivity and impulsivity/fun seeking behaviors were more likely to report worse mood before bed on the weekend (SP: r = -.394, p = .010; SR-I/FS: r = -.350, p = .018).

Exploratory analyses

In our study there were multiple measures that correlated with the same criterion variable: reported mood on week- and weekend nights, midpoint on week- and weekend nights, social jetlag, and risk taking (i.e., choosing to play) on the Jackpot task. To test which variable was driving the relationship with these variables, we ran additional multiple regression analyses.

Mood. According to the correlational analyses, behavioral inhibition (BIS), pubertal stage (PDS score), and drug and alcohol seeking (SSSC-DAS) explained some of the variance in reported mood on weeknights. However, only BIS survived as a significant predictor (β= -.30, t(42) = -2.19, p = .034) in the regression analysis that included all three predictors (PDS: β = -.25, t(42) = -1.86, p = .070; DAS: β = -.25, t(42) = -1.82, p = .076). The model including BIS as a single predictor explained 25.9% of the variance in mood on weeknights (F(3,42) = 4.89, p = .005). Furthermore, mood on weekend nights was explained by parent-reported sensitivity to punishment (SP) and sensitivity to reward impulsivity/fun-seeking (SR-I/FS), as well as BIS. However, only SP survived as a significant predictor (β = -.36, t(39) = -2.44, p = .019) when all predictors were added into the regression model. The model including SP as a single predictor explained 19.4% of the variance in mood on weekend nights (F(2,39) = 4.68, p = .015). These findings indicate that girls who report to be more behaviorally inhibited report worse mood on weeknights, and girls who are more sensitive to punishment (based on parent report) are more likely to report worse mood on weekend nights.

Midpoint. According to correlational analyses, chronotype (MEQ), fun seeking (BAS-FS) and choice behavior on the Jackpot task (i.e., percentage of play) in the high-risk/large reward condition (HR-l-play) explained the variance in midpoint on weeknights. However, when all predictors were added to the regression model only HR-l-play and chronotype survived as significant predictors (HR-l-play: β = -.32, t(42) = -2.39, p = .022; MEQ: β = -.34, t(42) = -2.40, p = .021). The model including HR-l-play and MEQ as predictors explained 22.1% of the variance in midpoint on weeknights (F(2,44) = 6.25, p = .004). Fun seeking (BAS-FS) did not survive as a predictor of midpoint week, possibly because girls who report higher fun seeking score higher on the MEQ (r = .302, p = .041). Furthermore, midpoint weekend was explained by chronotype (MEQ) as well as impulsivity (BIS-11-Total). However, only BIS-11-Total survived as a significant predictor (β = .32, t(38) = 2.19, p = .035), though MEQ was a marginally significant predictor (β = -.29, t(38) = -1.97, p = .057). The model including both predictors explained 19.6% of the variance in midpoint on weekend nights (F(2,38) = 4.65, p = .016). These findings suggest that girls who show more risk taking behavior (i.e., play in the HR-l condition) and report to be more evening type exhibit later midpoints on weeknights. Furthermore, girls who report to be more behaviorally inhibited and tend to be more evening type exhibit later midpoints on weekend nights.

Social jetlag. The discrepancy between week and weekend midpoints was explained by motor impulsivity (BIS-11-MI), fun seeking (BAS-FS) and choice behavior on the Jackpot task (i.e., percentage of play) in the high-risk/large reward condition (HR-l-play). However, only BAS-FS and HR-l-play survived as significant predictors (BAS-FS: β = -.34, $t(38)$ = -2.43, p = .020; HR-l-play: β = -.35, $t(38)$ = -2.66, p = .011) in the regression analysis including all three predictors. BAS-FS and HR-l-play explained 27.7% of the variance in social jetlag ($F(2,44)$ = 8. 34, p = .001). A possible explanation could be that BAS-FS and BIS-11-MI were positively correlated (r = .295, p = .055). These findings suggest that girls who report to be more fun-seeking, as well as show more risk-taking behavior on the Jackpot task tend to have larger discrepancies between their week and weekend midpoints (i.e., social jetlag).

MEQ. Response time in the high-risk condition (RT-HR), choice behavior on the Jackpot task (i.e., percentage of play) in the low-risk condition (LR-play), and self-reported fun seeking (BAS-FS) correlated with MEQ score. However, only RT-HR survived as a significant predictor (β = .31, $t(45)$ = 2.31, p = .026), and explained 13.8% of the variance in chronotype (MEQ) ($F(1, 45)$ = 7.19, p = .01). These findings indicate that girls who report being more morning type take longer to decide whether or not to play in the high-risk condition.

Together these findings imply that individual differences may play a role in risk-taking behavior, as well as the changes in sleep that occur during adolescence. Specifically, it seems that behavioral inhibition plays a role in mood regulation, as well as sleep midpoint, while fun-seeking behavior seems to play a role in social jetlag. Furthermore, girls who show more risk-taking behavior exhibit later midpoints on weeknights and a larger social jetlag. These findings suggest that there may be an underlying relationship between sleep regulation and the emergence of risk-taking behavior in adolescence.

Puberty, risk taking, and sleep

Because we did not find a relationship between pubertal development and risk-taking behavior on the Jackpot task, or any of the self-report measures on sensation seeking, impulsivity, and reward sensitivity we were unable to test for an interaction between puberty, risk taking, and sleep. Nonetheless, we revisited the relationship between social jetlag and risk-taking (in the HR-l condition) and explored whether this was moderated by pubertal stage. Results showed that this relationship was only present in the pre/early pubertal girls (r = -.396, p = .050, n = 25), but not in the mid/late pubertal girls (r = -.259, p = .232, n = 23). However, these correlations were not significantly different from one another (Fisher's Z = .504). Pubertal stage did not moderate the relationship between MEQ and risk-taking (for both RT in the HR condition and percentage of play in the LR condition). These findings indicate that in this study there is no direct or indirect (through sleep) relationship between pubertal development and risk taking.

Discussion

The goal of this study was to investigate the relationship between sleep, pubertal development and risky decision-making. We measured sleep using a 5-day self-report sleep diary (Gregory et al., 2011) and we administered the PDS (Peterson et al., 1988) to measure pubertal stage. To measure risk taking, we administered a simple decision-making task in which participants chose to either take a risk (play) or skip the trial (pass) based on information provided about the risk involved (low or high) and reward at stake (small or large). In this study, we found evidence for a relationship between pubertal development and sleep, as well as sleep and risk taking. We did not find support for a three-way relationship between sleep, puberty, and risk-taking behavior.

Puberty and sleep

Based on previous literature (Carskadon, 2011; Hasler et al., 2012) we predicted that girls who were mid/late pubertal would show a later midpoint in their sleep as compared to pre/early pubertal girls. In the current study this finding was marginally significant, indicating that there might be a relationship between sleep on the weekend and pubertal stage. This supports the hypothesis that adolescents who are in more advanced pubertal stages show a phase-delay in their sleep (Carskadon, Acebo & Jenni, 2004). While we found this relationship with midpoint on the weekend, it was not present for midpoint during the week or for social jetlag. One possible explanation for this discrepancy between sleep on weekends and during the week is that while sleep during the week is regulated by school, on weekends sleep is less, or not, restricted.

Although we did not set out to demonstrate that there is a relationship between girls who are farther along in their pubertal development and decreased mood on weeknights, we found this relationship in our study. This is consistent with previous literature that has shown that girls in later pubertal stages are more likely to report depressed mood as compared to girls in earlier pubertal stages (Oldehinkel, Verhulst & Ormel, 2011; Patton et al., 2008). Moreover, pubertal brain changes that occur at the onset of puberty have been shown to influence many emotional processes (Crone, Bullens, van der Plas, Kijkuit & Zelazo, 2008; Dahl, 2008). This suggests that biological changes associated with puberty are contributing to the decreased mood that emerges in later stages of puberty, and points to the fact that puberty is a time of emotional change. It is crucial to understand the underlying causes of changes in mood during puberty in order to target specific interventions before an individual goes in to a negative spiral of depressed mood. In future studies, it would be interesting to look at the relationship between self-reported mood and gonadal hormone concentrations, as it might offer us insight into which hormone is influencing the change in mood that occurs during puberty.

Puberty and risk taking

Previous research suggests that girls who are in later pubertal stages engage in more risk-taking behaviors (Steinberg, 2007; Vermeersch et al., 2008a). Even though previous research suggests a relationship between puberty and risk-taking behaviors, we did not find such a relationship in our sample. One explanation is that previous experiments measured puberty by using gonadal hormone concentration, whereas in our study we only used a self-report measure (PDS). While the PDS has high reliability compared to a score derived from a physical examination done by a nurse practitioner

(Shirtcliff, Dahl & Pollack, 2009), this is still a self-reported measure and it could be that the girls in our sample did not feel comfortable choosing certain items on the scale, thus skewing the self-reported data. In future studies it would be interesting to look at gonadal hormone concentrations in relation to the participant's task behavior on the Jackpot task in order to minimize this bias. Another explanation for the lack of behavioral differences could be that although pubertal development is associated with changes in the brain, as evidenced by studies that found an association between puberty and reward-related brain processes in the context of risk taking (Forbes et al., 2010; Op de Macks et al., 2011), this does not necessarily directly affect behavior in an artificial laboratory setting. In line with the hypothesis that behavioral changes occur in more naturalistic contexts and not in the laboratory, we found that girls who were in later pubertal stages reported higher levels of sensation seeking, social disinhibition and a higher drive towards seeking rewards. These findings are consistent with previous literature that has shown that adolescents have higher levels of sensation seeking (Martin et al., 2002; Spear, 2000), which plays a key role in the probability of engaging in risky behavior.

Together, these findings indicate that girls who are in a later pubertal stage tend to report worse mood before bedtime, show later midpoints of sleep, as well as increased sensation seeking, reward sensitivity, and impulsivity. These findings are in line with the literature that indicates that adolescence is a time of increased reward sensitivity, sensation seeking and phase-delay in sleep (Steinberg, 2008).

Sleep and risk taking

As expected, our findings showed that adolescents who exhibited a larger social jetlag engaged in more risk taking as measured by behavior on the Jackpot task. In addition, girls with a larger social jetlag reported higher impulsivity and fun seeking. These findings suggest that individuals with a larger social jetlag are more likely to take risks in the high-risk condition, pointing to the fact that sleep changes might have an effect on the emergence of risk-taking behavior in adolescence. These results are consistent with previous research that has shown that individuals who reported sleeping worse, less, and exhibited a larger shift in their midpoints, also reported increased risk taking (O'Brien & Mindell, 2005). Furthermore, we found that girls who have a higher MEQ score (i.e., a tendency for morningness) had earlier midpoints during the week and weekends, and that they chose to play more often in the low-risk condition. This is consistent with the literature that indicates that individuals with a tendency for morningness take less risks, whereas individuals who are more evening type tend to take more risks (Killgore, 2007). However, in the current study girls who were more evening type did not tend to take more risks.

These findings provide support for the notion that a phase-delay in sleep at puberty might contribute to the increase in risk taking during adolescence. One way that we might be able to decrease the emergence of risk taking in adolescence is if we target an individual's sleep (e.g., by changing school start times) in order for it to correspond with an adolescent's sleep preference and sleep needs. However, there may be other underlying factors that influence the increased risk taking in adolescence and these are important to take into account in to future studies as well.

Sleep, puberty, and risk taking

Previous research suggests that there might be a relationship between puberty, sleep and risk-taking (measured by reward-related brain activation) (Holm et al., 2009). However, we were unable to test this three-way relationship in our study because we did not find a relationship between pubertal development and risk-taking behavior on the Jackpot task. Nevertheless, this study does provide evidence for the relationship between sleep and risk taking, and puberty and sleep in adolescence. These findings support the belief that adolescence is a time of change and studies aimed at understanding these changes (and how they interact) are needed to create interventions that will prevent individuals from going into a negative spiral as they go through this critical period of development.

Limitations and future directions

One limitation is that this study is correlational and therefore we cannot draw conclusions as to the directionality of these findings. In addition, it is a cross-sectional study that only captures one time point in an individual's life; therefore it is difficult to draw any conclusions about *changes* across time (i.e., development). Furthermore, we used a self-reported pubertal development scale. Although the PDS is highly correlated with pubertal development (Shirtcliff, Dahl & Pollack, 2009) girls in our sample may have felt uncomfortable choosing certain items on the scale, thus skewing the data. In addition, we collected a self-reported sleep measure that only captured 5 days (3 weeknights and 2 weekend nights) of an individual's sleep. In future studies it would be critical to capture more nights of sleep (i.e., at least 10 days) in order to see fluctuations of an individual's sleep cycle.

The current findings confirm that there is a relationship between puberty and sleep, as well as a relationship between sleep and risk taking. This study has started to tease out how these three factors are related to one another; it would be interesting to see how these three factors do in fact interact, possibly using a different (more naturalistic) paradigm and/or by looking at how sleep and puberty influence the brain processes associated with risky behavior. In future studies researchers could include a hormonal concentration component to index pubertal development, as well as a longer sleep diary (e.g., 10 days) filled out by the participants to capture a more reliable sleep measure. It will be critical to capture more than one time point in an individual's life (i.e., conduct a longitudinal study) to see how sleep, puberty and risk-taking interact across development. In addition, future studies should look at individual differences in order to target those who might be at risk for excessive risk taking, as well as chronic lack of sleep.

Closing Remarks

Summary

The increased tendency to take risks during adolescence compared to any other time in life presents a societal concern that occupies the minds of many parents, teachers, law as well as policy makers, and developmental scientists. The developmental rise in risk taking not only impacts the health and welfare of adolescents, but also sets the stage for the decisions they make as adults. As such, risky decisions in adolescence can have far-reaching consequences for the overall quality of life. Given the broad range of changes that occur in adolescence, the challenge lies in the identification of contributing factors and their possible interactions. Existing neurobiological models highlight the importance of the rise in hormones during puberty, which are thought to influence how adolescents process socio-emotional information. According to these models, adolescents engage in more risk taking compared to children and adults because they process rewards differently and are more sensitive to their social environment.

In this dissertation, we set out to test whether adolescent risk taking is indeed associated with pubertal hormones, and influenced by the presence of social information. We were particularly interested in whether pubertal hormones moderate social influences on risk taking. Pubertal hormones were measured based on saliva provided by the participants. We also looked at other indicators of (pubertal) maturation: age, self-reported puberty-related physical changes, and body-mass index (BMI). To assess risk taking, we used a child-friendly, two-choice decision-making paradigm called the Jackpot task. In this task, participants were instructed to choose between taking a risk (i.e., to play) and opting out of the trial (i.e., to pass). We administered this task to participants in the MRI scanner, so that we could investigate the brain processes associated with their (risky) choices. The findings that resulted from running this task in two independent samples are summarized below.

Chapters 1 and 2 present the results based on the first version of the Jackpot task, in which participants were provided with explicit probability information: if they chose to play, the chance to win was either 33% or 67%. On each trial, they could win or lose 10 Eurocents. This version of the Jackpot task was administered in a Dutch sample of 50 10-16-year-old boys and girls (of whom 33 participants were retested ~2 years later), and 28 young adult men and women. Results showed that participants chose to play more often when the chance to win was greater (67% vs. 33%), and this did not differ with age, indicating that adolescents were equally sensitive to risk compared to adults. Furthermore, winning vs. losing after the decision to play was associated with increased activation in reward-related brain regions, such as the ventral striatum (VS), which were activated to a similar extent in both adolescents and adults.

In Chapter 1, we focused on the adolescents and investigated the relation of reward-related brain processes associated with risk taking with hormones released during puberty: testosterone and estradiol. Results of this cross-sectional study revealed that boys and girls with higher levels of testosterone demonstrated increased reward-related activation in the VS in response to winning vs. losing 10 Eurocents, particularly in the nucleus accumbens (NAc), even when controlling for age. In addition, higher levels of estradiol in girls corresponded with increased activation of dorsal striatum and (dorsolateral and medial) prefrontal regions, but these findings were less robust compared

to the testosterone finding. Of note, there were no sex differences in risk taking, or reward-related brain processes; both boys and girls engaged the striatum and medial orbitofrontal cortex in response to rewards after making a risky decision (i.e., deciding to play). These findings indicate that individual differences in testosterone level among adolescents contribute to the individual differences in reward-related brain processes involved in risk-taking behavior.

In Chapter 2, we explored other contributing factors of risk taking and associated reward-related brain processes. We looked at pubertal stage (based on self-reported puberty-related physical changes) and self-reported approach tendencies in a cross-sectional study including young adults as well as the adolescents from Chapter 1. Results from this study showed that individuals with a greater tendency to play and/or a more fun-seeking personality in every-day life engaged the VS (and the medial prefrontal cortex, mPFC) more for rewards than losses, suggesting that reward-related brain processes associated with risk taking reflect motivational processes associated with approach behavior. Furthermore, increased risk taking was associated with decreased functional connectivity between VS and anterior insula, suggesting a regulatory function of the insula in the context of risky decision-making. Individual differences in reward processing were not associated with differences in pubertal stage (but they did correspond with differences in testosterone; see Chapter 1).

We also investigated which factors contributed to changes in risk taking and reward-related brain processes over time based on a follow-up study conducted in the adolescents (two years later). These longitudinal analyses demonstrated that developmental changes in the VS response to rewards corresponded with changes in self-reported approach tendencies; individuals who reported becoming more fun-seeking with age also showed an increased VS response to receiving rewards of 10 Eurocents vs. losses of 10 Eurocents. These findings suggest that age-related changes in reward processing associated with risky decisions reflect changes in the desire for new rewards and willingness to approach potentially rewarding events on the spur of the moment. Again, no relation was found with pubertal stage (and we did not have any hormone data from the follow-up to extend our finding from Chapter 1).

Chapters 3–5 present the cross-sectional results based on a modified version of the Jackpot task, which was administered in a sample of 68 11-13-year-old girls from the United States. In this version of the task, participants played for points, which were later translated into money. On each trial, they received explicit information about the number of points at stake (i.e., they could win or lose 1 or 3 points if they chose to play), in addition to the probability of winning, which was the same as in the first version of the task (i.e., 33% or 67%). Furthermore, participants received feedback after every six trials about their cumulative performance. In the monetary context, participants saw how much money they had won; in the social context, participants saw how they ranked compared to peers who had also played the task. Based on these three pieces of information – risk level, stakes, and the type of performance feedback – participants were instructed to choose, on each trial, to take the risk (i.e., play) or opt out of the trial (i.e., pass).

In Chapter 3, we collapsed across feedback context (because there were no group differences in choice behavior between the social and monetary context) and investigated the relation between developmental differences (age, pubertal stage, hormone levels, and

BMI) and risk taking based on risk and stakes information. We also looked at the relation with reward-related brain processes associated with the choice to play. Results showed that girls with higher testosterone levels were more inclined to play, particularly on trials with the lowest expected value, and this relation was mediated by lower activation in the medial orbitofrontal cortex (mOFC) associated with the decision to pass. These findings suggest that girls with higher testosterone levels tended to value the decision to pass less, which in turn led to enhanced disadvantageous risk taking.

In Chapter 4, we compared risk taking and associated reward-related processes between the two feedback contexts (i.e., social vs. monetary context) and investigated which factors contributed to the individual differences in context sensitivity. Results showed that, across the group, risk taking and reward-related brain processes (i.e., NAc and mPFC activation) were similar between the two contexts. However, there was increased activation of anterior insula for the social vs. monetary context, suggesting that the experience of being ranked against peers was more salient for the girls compared to learning how much money they won. Furthermore, there were individual differences in sensitivity to feedback context: First, girls who reported being more susceptible to peer influence, took more time to decide (whether to play or pass) in the social context. Second, girls with higher estradiol levels tended to engage anterior insula more strongly when taking risks vs. playing it safe in the social context. Third, girls in a more advanced pubertal stage showed increased NAc activation associated with risk taking in the monetary context. Together, these findings suggest that while personality traits influenced their choice behavior (i.e., the speed at which they decided in the different contexts), puberty-related processes influenced the types of rewards (social status or money) that these girls were sensitive to.

In a separate line of research, it has become clear that adolescents experience a shift in their sleep patterns, possibly under the influence of pubertal hormones, which facilitates sleep deprivation. Sleep deprivation in adults has been shown to increase the tendency to take risks. These findings point to sleep as an additional factor that potentially contributes to adolescent risk taking. By collecting data on self-reported sleep patterns across five week and weekend nights, we took the opportunity to test the relation between sleep habits and risk taking in our sample of adolescent girls. Additionally, we explored whether pubertal stage moderated the relation between sleep and risk taking. In Chapter 5, we provided evidence for a relation between puberty and sleep, as well as for a relation between sleep and risk taking. Girls in later stages of puberty slept later compared to girls in early puberty. Furthermore, girls who had a larger discrepancy between week and weekend sleep times and/or reported being evening types engaged in more risk taking. These findings suggest that changes in sleep are indeed puberty-related. Furthermore, these findings provide evidence for the relation between irregular or later sleep and risky decision-making. While we did not find evidence for a moderating effect of puberty on the relation between sleep and risk taking, the types of sleep patterns associated with increased risk taking are particularly common during adolescence.

Future directions

While the studies included in this dissertation provide insight into some of the factors that contribute to adolescent risk taking, there are some important limitations that need to be addressed in future research to deepen our understanding of this complex period in development. First, it should be noted that we were unable to collect longitudinal hormone data. Instead, we used pubertal stage based on self-reported physical changes. While changes in pubertal stage were not related to changes in risk taking and associated reward-related brain processes as measured by this paradigm, it remains to be explored whether pubertal hormones are associated with changes in risk taking over time. To date, only one longitudinal study has investigated the role of pubertal hormones in adolescent risk taking, and found that testosterone contributes to the adolescent peak in reward-related brain activation associated with risk taking (Braams et al., in press).

Second, we focused mainly on brain regions associated with reward-related processes. However, brain regions involved in cognitive regulation (and social cognition) also contribute to risky decisions (Cascio et al., 2014; Rodrigo et al., 2014). Some neurobiological models propose that brain regions involved in cognitive-regulatory processes, located in the prefrontal cortex, are insufficiently developed in adolescence to engage in optimal emotion regulation (Somerville, Jones, & Casey, 2010; Steinberg, 2010), whereas other models argue that the protracted development of the prefrontal cortex allows for flexibility in adjustment to a changing social environment and stresses the importance of social context for adolescent risk taking (Crone and Dahl, 2012; Nelson and Guyer, 2011). Furthermore, it has been proposed that adolescents not only focus more on the present (i.e., stimulus-driven) and are less (longer-term) goal-oriented, but also show stronger conditioning in response to appetitive as opposed to aversive stimuli, which contributes to their tendency to engage in risky behaviors (Ernst, Daniele, & Frantz, 2011). Together, these models suggest that changes in cognitive-regulatory brain regions during adolescence play an important role in the developmental rise in risk taking, but more research is needed to understand their role, and to examine their influence on reward-related brain regions in the context of risky decision-making (Pfeifer and Allen, 2012). In addition, the role of pubertal maturation in emotion regulation mediated by fronto-striatal connections remains to be investigated (Ladouceur, 2012).

Third, the updated version of the Jackpot task allowed us to investigate the influence of context on risk taking and associated reward-related brain processes. By manipulating the type of cumulative performance feedback, we created a social and a monetary context in which the participants made (risky) choices. While we revealed differences in neural processing (i.e., insula activation) between the two contexts, there were no main effects of context on risk taking or reward-related processes (i.e., NAc and mPFC activation). Adjustment of the task to include more frequent feedback presentation (e.g., trial-by-trial instead of after every six trials) or to rank against familiar peers (instead of anonymous peers) could potentially influence behavior. Further insights could be gained by administering the current version of the task in older adolescent girls, who have lower self-esteem (Biro et al., 2006) and/or are perhaps more sensitive to social information (Blakemore and Mills, 2014; Knoll et al., 2015). By administering this task in clinical populations, such as adolescents with social anxiety disorder or autism, we could gain valuable insight into the neural underpinnings of the social influence on risk

taking (Caouette and Guyer, 2014), especially since individuals with autism show reduced sensitivity to social rewards (Scott-Van Zeeland et al., 2010) and blunted insula involvement (Caria and De Falco, 2015). Furthermore, this paradigm has not yet been administered in boys. Boys as well as girls show a developmental increase in risky behavior (Shulman et al., 2014). However, pubertal development is vastly different, in terms of the physical changes that occur and the hormones involved (Dorn et al., 2003, 2006; Shirtcliff et al., 2009). As such, the comparison of brain and behavior between boys and girls using this paradigm would provide additional insight into the (similarities and/or differences in the) biological mechanisms underlying adolescent risk taking.

Fourth, we found evidence that supported the role of sleep in risky decision-making, but it remains unclear whether puberty modulates this relation. To date, only one study investigated whether pubertal development moderates the relation between sleep and reward-related processes associated with decision-making (Holm et al., 2009). This study revealed that sleep patterns changed with pubertal development, and differences in sleep were associated with differences in reward processing. However, the authors did not find a moderating effect of pubertal stage. In addition, pubertal development was measured based on physical examination, the (moderating) role of pubertal hormones remains to be tested. Furthermore, the relation between sleep and reward-related brain processes associated with risk taking remains to be tested for this paradigm.

Lastly, the studies presented in this dissertation provide evidence for the role of pubertal hormones in functional brain differences associated with risk taking. However, it remains unclear how these functional differences relate to structural brain differences. Previous research has shown that there is a linear decrease in NAc volume across pubertal development in girls (Goddings et al., 2013), but the extent and direction of these volume changes also depends on the level of hormones present (Herting et al., 2014). The mapping of the functional neural differences/changes associated with risk taking onto the structural neural differences/changes during adolescence could provide additional insight into the underlying neuroendocrine mechanisms that contribute to adolescent risk taking.

Conclusion

In sum, we provided evidence for the role of testosterone in adolescent risk taking using a child-friendly decision-making task in which participants chose to play or pass based on information about risk and stakes. We also showed that the presence of status-relevant social information increased insula activation associated with risk taking, particularly in the presence of higher estradiol levels in girls. Furthermore, we extended the adult literature by providing evidence for the relation between sleep and risk taking in adolescence. Consistent with existing neurobiological models, these findings support the role of both biological and social influences on adolescent risk taking, and highlight the importance of testing their interactions using a longitudinal research design.

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Appendix A. Supplementary data associated with Chapter 1

Supplementary Table S1. Regions of activation during outcome processing: reward > loss for boys and girls separately.

Contrast	Region	MNI (x, y, z) coordinates	Brodmann area	*Z*-value	Volume[1] (=k_E value in SPM)	Uncorrected *p*
Boys: reward > loss						
	R Caudate	39 -15 -12		3.75	14	< .001
	R Putamen	18 12 -6		4.01	26	< .001
	L Putamen	-24 9 -9		3.91	34	< .001
	L Mid. Orbital Gyr.	-24 66 3	BA10	3.74	12	< .001
	L Mid. Orbital Gyr.	0 48 -6	BA10	3.32	14	< .001
	L Mid. Frontal Gyr.	-39 57 3	BA10	3.59	10	< .001
	L Cingulate Gyr.	-18 -15 36	BA24	3.74	13	< .001
	R Precentral Gyr.	45 -18 63	BA6 (70%)	3.71	16	< .001
	R Cuneus	18 -81 24	BA18	4.25	18	< .001
	L Sup. Occipital Gyr.	-21 -81 24	BA18	4.08	83	< .001
	R Inf. Occipital Gyr.	39 -81 -9	BA18	3.64	15	< .001
	R Sup. Occipital Gyr.	24 -84 18	BA18	3.82	25	< .001
	L Cerebellum	-3 -72 -12		4.51	125	< .001
Girls: reward > loss						
	Thalamus	0 -9 12		4.10	31	< .001
	R Caudate	5 18 0		4.23		< .001
	R Amygdala	18 3 -15		3.88		< .001
	L Putamen	-18 15 -5		3.85		< .001
	L Amygdala	-21 0 -12		3.97	84	< .001
	R Sup. Frontal Gyr.	33 -6 69	BA6	3.84	12	< .001
	L Sup. Frontal Gyr.	-18 24 60	BA6/8	3.89	56	< .001
	R Mid. Frontal Gyrus	39 12 54	BA6	4.11	38	< .001
	L Mid. Frontal Gyrus	-36 57 6	BA10	3.55	21	< .001
	L Inf. Frontal Gyrus	-45 45 -15	BA11	4.34	17	< .001
	R Ant. Cingulate Cortex	12 39 21	BA9	3.50	11	< .001
		3 33 12	BA24	3.52	10	< .001
	L Sup. Medial Gyr.	-3 54 15	BA9/10	3.78	69	< .001
	L Mid. Temporal Gyr.	-60 -15 -21	BA20	3.95	11	< .001
	R Linual Gyrus	12 -33 -3	BA27	4.01	16	< .001
	L Hippocampus	-24 -24 -15	BA35	4.17	26	< .001
	L Fusiform Gyrus	-45 -21 -18	BA20	4.13	92	< .001
	R Precentral Gyrus	18 -27 66	BA6 (40%)	3.87	43	< .001
	R Postcentral Gyrus	18 -39 72	BA1 (50%)	3.54		< .001
	L Calcarine Gyrus	-6 -45 6	BA29	4.17	39	< .001
	L Post. Cingulate Cortex	-9 -48 30	BA31	3.92	67	< .001
	R Sup. Parietal Lobule	39 -60 57	BA7	3.82	23	< .001
	L Inf. Parietal Lobule	-36 -75 42	BA19	3.92	26	< .001
	L Sup. Parietal Lobule	-21 -75 57	BA7	3.44	15	< .001
	R Precuneus	6 -78 54	BA7	3.94	24	< .001
	R Sup. Occipital Gyrus	9 -87 42	BA19	3.52	13	< .001
	L Mid. Occipital Gyrus	-27 -93 3	BA18	5.49	1959	< .001

[1] Volume of activation in mm^3.

Supplementary Table S2. Regions of activation during outcome processing that correlate with testosterone (T) level: reward > loss with T as predictor separately for boys, at an uncorrected threshold of $p < .001$, and for girls, at an uncorrected threshold of $p < .005$.

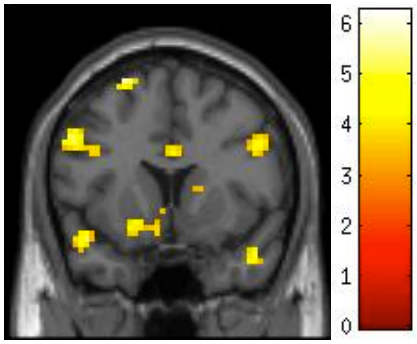
Contrast	Region	MNI (x, y, z) coordinates	Brodmann area	*Z*-value	Volume[1] (=k_E value in SPM)	Uncorrected *p*
Boys: reward > loss with T as predictor ($p < .001$)						
	R Putamen	18 9 9		3.58	13	< .001
	L Putamen	-24 9 -9		4.53	74	< .001
	L Pallidum	-21 0 -3				
	L Amygdala	-24 0 -12				
	L Thalamus	-15 -21 18		4.50	37	< .001
	L Sup. Frontal Gyrus	-21 15 66	BA6	4.61	33	< .001
	L Mid. Frontal Gyrus	-33 48 30	BA9	3.72	17	< .001
	L Inf. Frontal Gyrus	-57 15 27	BA44 (60%)	3.84	17	< .001
	L Mid. Frontal Gyrus	-42 51 0	BA10	4.36	13	< .001
	R Mid. Temp. Pole	48 12 -27	BA38	4.07	14	< .001
	L Sup. Temp. Gyrus	-51 3 -15	BA21	3.82	37	< .001
	R Mid. Temp. Gyr.	54 0 -21	BA21	4.10	36	< .001
	L Mid. Cingulate Cortex	-12 -33 36	BA31	3.95	24	< .001
Girls: reward > loss with T as predictor (p < .005)						
	L Caudate	-12 12 -12		3.01	14	= .001
	R Thalamus	6 -12 0		3.31	24	< .001
	R Pallidum	15 -9 -6		2.79		= .003
	L Mid. Front. Gyr.	-39 12 48	BA6	3.86	43	< .001
	L Inf. Front. Gyr.	-45 18 -9	BA47	3.85	61	< .001
	R Sup. Medial Gyrus	15 63 9	BA10	3.28	15	= .001
	L Sup. Medial Gyrus	-6 60 24	BA10	3.09	43	= .001
	L Mid. Temp. Gyrus	-66 -30 -12	BA21	3.21	13	= .001
	R Precentral Gyrus	24 -15 48	BA6 (40%)	3.64	14	< .001
	L Inf. Parietal Lobule	-24 -54 39	BA7	2.98	22	= .001

[1] Volume of activation in mm^3.

Supplementary Table S3. Regions of activation during outcome processing that correlate with estradiol (E) level: reward > loss with E as predictor for girls only, at an uncorrected threshold of $p < .005$.

Contrast	Region	MNI (x, y, z) coordinates	Brodmann area	*Z*-value	Volume[1] (=k_E value in SPM)	Uncorrected *p*
Girls: reward > loss with E as predictor (p < .005)						
	L Caudate	-15 15 12		3.00	17	= .001
	R Sup. Medial Gyrus	12 63 6	BA10	2.98	10	= .001
	R Ant. Cingulate Cortex	15 45 18	BA9	3.30	48	< .001
	R Inf. Frontal Gyrus	54 9 24	BA44 (40%)	2.84	12	= .002
	L Inf. Temp. Gyrus	-45 -51 -18		3.33	26	< .001

[1] Volume of activation in mm^3.



Supplementary Fig. S1. Results of the whole-brain analysis including all participants (n = 44) with testosterone level as predictor show activation in the left ventral striatum at p < .001 (uncorrected), 10 voxels.

Appendix B. Supplementary data associated with Chapter 2

Supplementary Table S1. Coordinates for the brain regions showing greater functional connectivity during rewards than losses with a left and a right ventral striatum seed. Peak voxels reported at cluster level with FDR corrected $p < .05$, > 10 contiguous voxels. SFG = superior frontal gyrus, SMA = supplementary motor area, BA = Brodmann area.

Anatomical Area		**MNI coordinates (mm)**			
	Cluster Size	x	y	z	Z-max value
Ventral Striatum (seed) Left					
L Paracingulate Gyrus	144	-6	30	33	4.01
R SMA / Medial Frontal Gyrus	10	9	-12	51	3.93
R Lateral PFC	15	51	36	24	3.58
R Inferior Frontal Gyrus / Insula	37	45	21	-6	3.71
R Precentral Gyrus	56	42	-9	42	4.21
R Inferior Parietal Lobe	22	48	-33	48	3.68
L Inferior Parietal Lobe	41	-45	-45	42	3.64
R Superior Parietal Lobe	132	27	-39	60	4.01
L Precuneus	26	-21	-66	48	3.30
R Lateral Occipital Cortex	1320	30	-81	24	5.26
L Occipital Fusiform Gyrus	188	-39	-69	-15	4.73
L Cerebellum	45	-6	-75	-27	3.54
Ventral Striatum (seed) Right					
R SFG / Paracingulate Gyrus	157	6	36	45	4.18
R Anterior Cingulate Cortex	11	12	15	33	3.47
R Lateral PFC	10	-48	9	42	3.42
R PrecentralGyrus	38	51	6	39	3.80
R PostcentralGyrus	44	36	-21	39	3.90
R Hippocampus	17	36	-21	-9	3.91
L Precuneus (BA 7)	23	-24	-57	54	3.46
R Precuneus (BA 7)	90	24	-57	48	4.22
R Lateral Occipital Cortex/ Precuneus	14	9	-78	51	3.67
R Lateral Occipital Cortex	2005	27	-81	24	5.36
L Cerebellum	15	-12	-66	-21	3.90

Supplementary Table S2. Coordinates for the brain regions showing activation for the main effect of outcome [Reward > Loss] across T1 and T2. Peak voxels are reported at cluster level with FWE corrected $p < .05$, > 10 contiguous voxels. ACC = anterior cingulate cortex, VS = ventral striatum, PCC = posterior cingulate cortex.

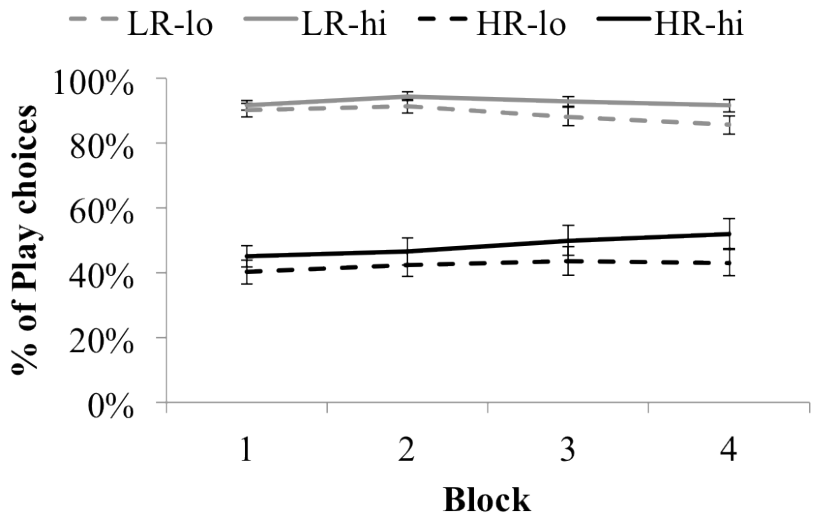
Anatomical Area		**MNI coordinates (mm)**			
	Cluster Size	x	y	z	Z-max value
Reward > Loss					
R VS (putamen)	53	15	9	-12	5.97
L VS (putamen)	26	-15	3	-12	6.02
L ACC (BA32)	69	3	48	-3	5.82
L PCC (BA29)	26	-3	-45	18	5.82
L PCC (BA23)	12	0	-27	30	5.09
R Lateral Occipital Cortex	62	30	-81	15	5.87
L Lateral Occipital Cortex	81	-24	-87	21	6.95
L Lingual Gyrus / Fusiform Gyrus	331	-15	-81	-15	7.12

Appendix C. Supplementary data associated with Chapter 3

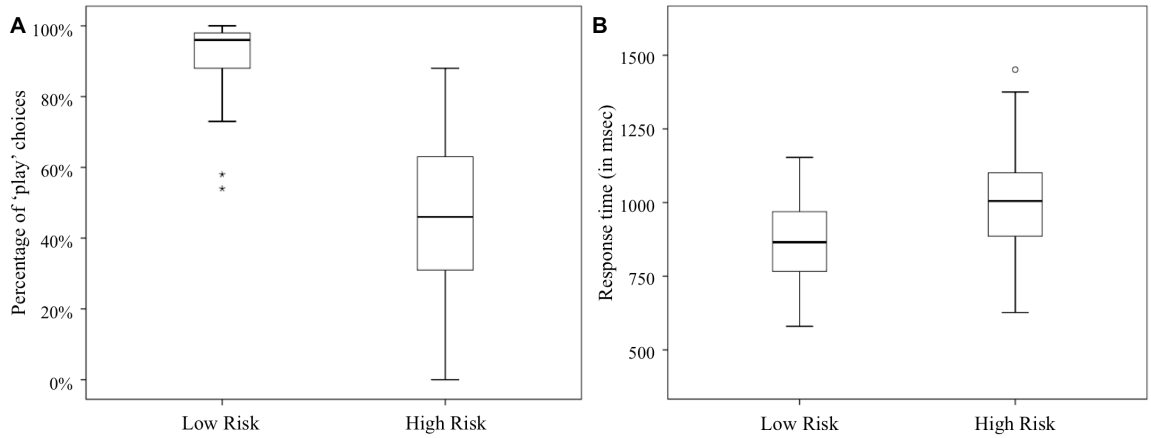
Supplementary Table S1. Personality questionnaires administered during the second lab visit, listed in the order that they were administered.

Measure:	**Source:**	**Completed by:**	**Range of possible scores (per subscale):**
Sensitivity to Punishment and Sensitivity to Reward Questionnaire for Children (SPSRQ-C)	Colder and O'Connor (2004)	Parent	15 – 75 (SP) 7 – 35 (SR-I/FS) 4 – 20 (SR-Dr) 7 – 35 (SR-RR)
Sensation Seeking Scale for Children (SSS-C)	Russo et al. (1991)	Child	0 – 12 (TAS) 0 – 7 (DAS) 0 – 7 (SD) 0 – 26 (Total)
Resistance to Peer Influence (RPI) Scale	Steinberg and Monahan (2007)	Child	10 – 40
Barratt's Impulsivity Scale, 11th edition (BIS-11)	Patton et al. (1995)	Child	8 – 32 (AI) 11 – 44 (MI) 11 – 44 (NPI) 30 – 120 (Total)
Iowa-Netherlands Comparison Orientation Scale (INCOM)	Gibbons and Buunk (1999)	Child	11 – 55
Behavioral Inhibition System/ Behavioral Approach System (BIS/BAS) Scales	Carver and White (1994)	Child	4 – 16 (BAS-Dr) 4 – 16 (BAS-FS) 5 – 20 (BAS-RR) 7 – 28 (BIS)
Social Comparison Scale (SCS)	Allan and Gilbert (1995)	Child	11 – 110
Rosenberg Self-Esteem Scale (RSES)	Rosenberg (1965)	Child	10 – 50

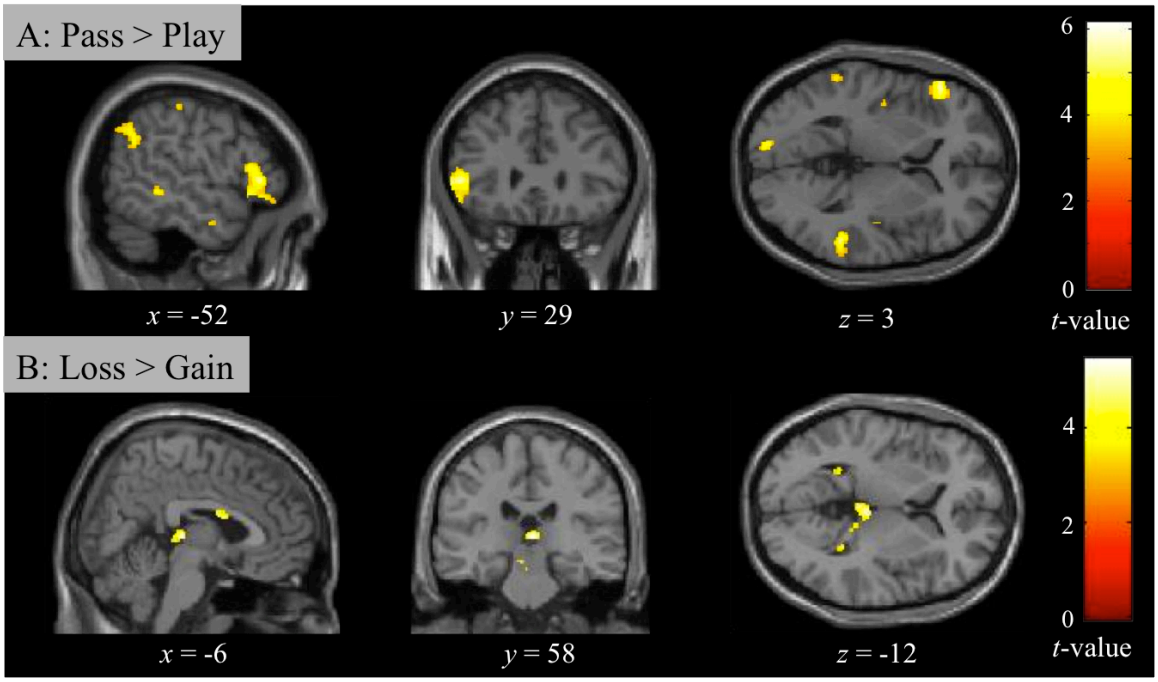
SP = sensitivity to punishment, SR = sensitivity to reward, I = impulsivity, FS = fun-seeking, Dr = Drive, RR = reward responsiveness, AI = attentional impulsivity, MI = motor impulsivity, NPI = nonplanning impulsivity, BAS = behavioral approach system, BIS = behavioral inhibition system.



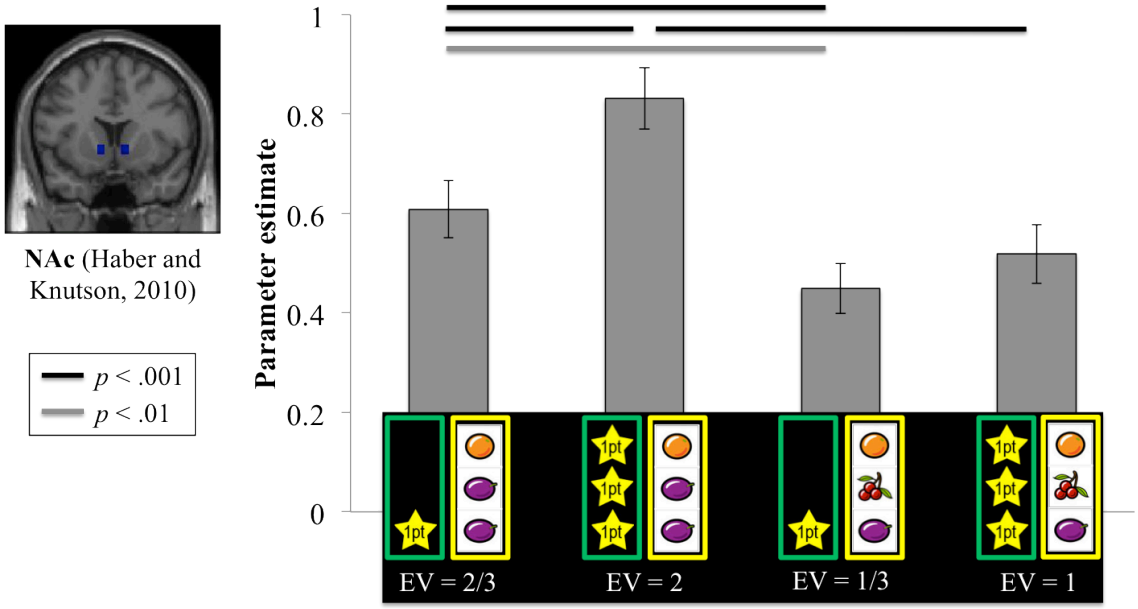
Supplementary Fig. S1. Risk taking (i.e., the percentage of play choices) across the four task blocks (of 24 trials each), plotted separately for the four task conditions.



Supplementary Fig. S2. Boxplots of risk taking (a) and response time (b) in the low-risk and high-risk conditions separately. Exclusion of the outliers for risk taking (n = 2) resulted in: M = 92.1%, SD = 7.7%, range = 73 – 100% for the low-risk condition, and M = 45.7%, SD = 22.7%, range = 0 – 88% for the high-risk condition (averaged across stakes). Exclusion of the outlier for RT (n = 1) resulted in: M = 866 ms, SD = 143 ms, range = 580 – 1160 ms for the low-risk condition, and M = 994 ms, SD = 157 ms, range = 627 – 1375 ms for the high-risk condition (averaged across stakes).

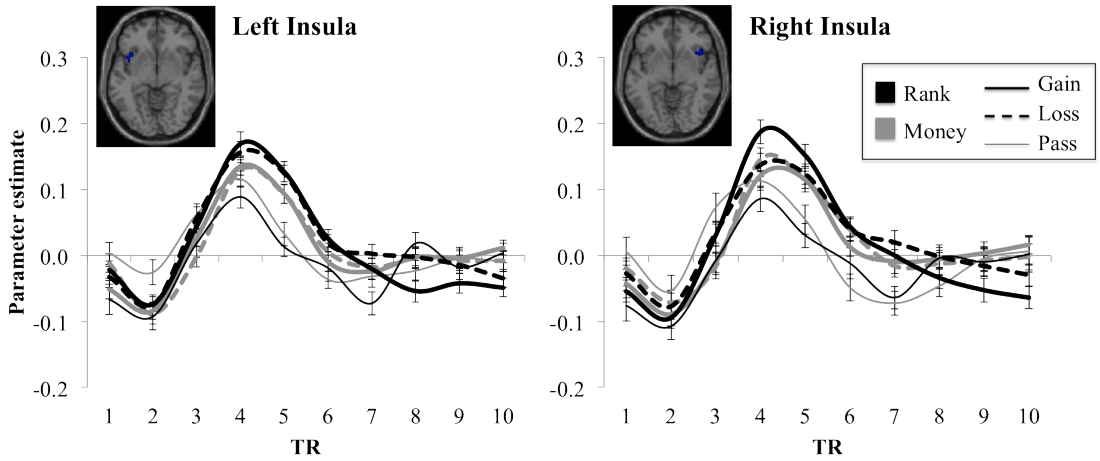


Supplementary Fig. S3. Brain regions that showed increased activation for trials on which participants made (a) Pass *vs.* Play choices, and experienced (b) Loss *vs.* Gain outcomes (after the choice to play), at p < .001 uncorrected (10 voxels).



Supplementary Fig. S4. Nucleus accumbens (Haber and Knutson, 2010) showed differential activation for all four task conditions, regardless of the choices participants made, indicating its role in tracking expected value.

Appendix D. Supplementary data associated with Chapter 4



Supplementary Fig. S1. Raw time-courses for left and right insula.