Why teens take risks ... : a neurocognitive analysis of developmental changes and individual differences in decision-making under risk

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Adolescent risky decision-making: Neurocognitive development of affective and control regions

Recent models hypothesize that adolescents risky behavior is the consequence of increased sensitivity to rewards in the ventral medial (VM) prefrontal cortex (PFC) and the ventral striatum (VS), paired with immature cognitive control abilities due to slow maturation of the dorsal anterior cingulate cortex (ACC) and lateral PFC. We tested this hypothesis with fMRI using a gambling task in which participants chose between Low-Risk gambles with a high probability of obtaining a small reward (1 Euro) and High-Risk gambles with a smaller probability of obtaining a higher reward (2, 4, 6, or 8 Euro). We examined neural responses during choice selection and outcome processing in participants from 4 age groups (pre-pubertal children, early adolescents, older adolescents and young adults). High-Risk choices increased with rewards for all ages, but risk-taking decreased with age for low reward gambles. The fMRI results confirmed that High-Risk choices were associated with activation in VMPFC, whereas Low-Risk choices were associated with activation in lateral PFC. Activation in dorsal ACC showed a linear decrease with age, whereas activation in VMPFC and VS showed an inverted-U shaped developmental pattern, with a peak in adolescence. In addition, behavioral differences in risk-taking propensity modulated brain activation in all age groups. These findings support the hypothesis that risky behavior in adolescence is associated with an imbalance caused by different developmental trajectories of affective and regulatory brain circuitry.

6.1 Introduction

From late childhood until young adulthood, teens increasingly need to rely on their own judgment in potentially risky situations, and they must learn to avoid excessive risks. The ability to make these decisions develops slowly, which can have serious consequences in daily life (Dahl & Gunnar, 2009; Steinberg et al., 2008). For example, self report and observation studies show that the number of traffic accidents peaks in adolescence, and that teens are at risk for getting involved in criminal behavior, experimentation with tobacco and alcohol, and unsafe sexual activity (Furby & Beyth-Marom, 1992; Steinberg, 2004). Even though it is difficult to examine this real-world risk-taking using laboratory tasks, these problems underline the importance of understanding the normal developmental trajectory of decision-making and its contribution to risk-taking behavior.

Tasks measuring decision-making often show a decreases in risk-taking with age (Boyer, 2006), or no age related change in performance after late childhood (Van Leijenhorst, Westenberg & Crone, 2008). However, adolescents show more risky behavior than adults when the experimental task is arousing; for example when peers are present (Gardner & Steinberg, 2005), or when it stresses affective rather than deliberative processing (Figner, Mackinlay, Wilkening, & Weber, 2009). The development of neuroimaging techniques including fMRI has led to neurobiological models that account for these findings by suggesting that risky behavior in adolescence results from the earlier functional maturation of reward-related compared to control-related brain circuitry. Affective and control related circuitry are thought to have separable contributions to decision-making, and the difference in the pattern of their development leads to an imbalance in the adolescent brain (Casey, Getz & Galvan, 2008; Ernst, Pine & Hardin, 2006; Galvan et al., 2006).

In this study, we test this model by examining the development of reward-related and control-related brain regions using fMRI and a gambling task. The developmental neuroimaging studies published to date have revealed that reward processing is associated with activation in similar brain regions in adolescents and adults, including the ventral medial prefrontal cortex (VMPFC) and the ventral striatum (VS) (Bjork et al., 2004; Ernst et al., 2005; Eshel, Nelson, Blair, Pine & Ernst, 2007; Galvan et al., 2006; May et al., 2004). In adults, these regions have been implicated in the processing of primary rewards such as a sweet taste

(McClure, Berns & Montague, 2003; O'Doherty, Deichmann, Critchley & Dolan, 2002), but also in the processing of abstract rewards such as monetary gain (Breiter, Aharon, Kahneman, Dale & Shizgal, 2001; Knutson, Adams, Fong & Hommer, 2001). Developmental studies, have reported stronger activation in the VS in response to rewards in adolescents than in adults (Ernst et al., 2005). Therefore, prior studies have suggested that brain regions associated with reward processing, show a heightened response to rewards in mid-adolescence.

The functional development of cognitive control related brain regions, associated with for example working memory, response inhibition and performance monitoring, typically follows a linear pattern (Casey, Galvan & Hare, 2005; Casey, Giedd & Thomas, 2000). In the context of decision-making tasks, these regions, including the dorsal anterior cingulate cortex (ACC) the dorsal lateral (DL) and ventral lateral (VL) PFC, show developmental changes throughout adolescence (Eshel et al., 2007; Galvan et al., 2006; Van Leijenhorst, Crone & Bunge, 2006). For example, Galvan et al. (2006) found a slow developmental trajectory for the VLPFC/lateral-OFC in a delayed two-choice task in which reward amounts were varied. The extent of activation in this region in response to rewards was larger for 7-11 year olds and 13-17 year olds than for 23-29 year olds. Similarly, Van Leijenhorst et al. (2006) found an age-related decrease in activation in the dorsal ACC associated with an increase in the ability to identify the choice option with the highest probability of resulting in a win between late childhood/ early adolescence (9-12) and young adulthood (18-25). These findings were interpreted as reflecting an immature activation pattern; children and adolescents require more activation in cognitive control related regions than adults when making decisions. In contrast, Eshel et al. (2007) found a decrease in risk-taking together with an increase in activation of the dorsal ACC and VL PFC from adolescence (9-17 years) to adulthood, and interpreted these findings in terms of an increase in the recruitment of cognitive control circuitry with increasing age, resulting in an increase in the ability to regulate impulsive risky behavior. In sum, developmental changes in cognitive control areas during decision-making have been associated with increased as well as decreased neural activation.

To date, the studies on adolescent risk-taking have focused on either the neural correlates of cognitive control (Eshel et al., 2007; Van Leijenhorst et al., 2006), or the neural correlates of reward processing

(Ernst et al., 2005; Galvan et al., 2006; Van Leijenhorst et al., 2009), but have not attempted to directly compare the relative contribution of the brain regions implicated in these processes to adolescent risk-taking behavior. In addition, not all studies have included participants from a wide age range (i.e., children, adolescents and adults), which limits the possibility to test for adolescent-specific patterns of activation and an inverted U-shaped developmental pattern. Therefore, the question whether brain regions associated with reward processing and cognitive control in a risk-taking task follow distinct developmental patterns has not yet been tested explicitly. Also, even though an adolescent specific peak in risky behavior and associated harmful consequences is well documented, not every adolescent engages in real world risky behavior. For example, Galvan, Hare, Voss, Glover & Casey (2007), found a positive relation between self reported risk perception and the response to rewards in the ventral striatum; participants who associated risky behavior with possible negative consequences showed a less pronounced neural response to rewards. Further insight into these individual differences across development is important to identify the adolescents who are at greater risk.

The goal of the present study was twofold: the first goal was to test, using fMRI, whether developmental changes in brain activation related to decision-making under risk can be characterized by a linear development pattern of control related brain regions, including dorsal ACC and lateral PFC, and a peak in adolescence in responsiveness to rewards in reward related regions, including the VMPFC and the VS. The second goal was to test the relation between brain activation and individual differences in risk-taking propensity during development. To test these hypotheses, participants from four age groups (8-10, 12-14, 16-17, 19-22-years old) participated in an fMRI study in which we used a child friendly two-choice decision-making task in which participants repeatedly chose between a low-risk gamble and a high-risk gamble, and in which the amount of reward associated with the high-risk gamble was varied (Van Leijenhorst, Westenberg & Crone, 2008). We tested for different developmental trajectories, by performing high-risk > low-risk gamble comparisons and gain > no-gain outcome comparisons, and by modeling age as a gradually increasing or decreasing predictor or as a non-linear rise-and-fall predictor.

Based on prior empirical studies, and based on the recently postulated models of adolescent risk-taking which suggest an imbalance between

the maturation of control and reward brain circuitry (Casey et al., 2008; Ernst et al., 2006; Steinberg et al., 2008), we predicted that participants would choose the high-risk gamble more often as the reward associated with it increased (Van Leijenhorst et al., 2008). In addition we predicted that rewards would elicit increased activation in VMPFC and the VS, and that activation in these regions would be associated with choices for high-risk gambles (Eshel et al., 2007; Knutson, Wimmer, Kuhnen & Winkielman, 2008). In contrast choices for low-risk gambles were expected to be associated with increased activation in lateral PFC regions (Eshel et al., 2007). We further predicted that the neural response in reward related regions and control related regions would co-vary with individual differences in risk-taking propensity. With regard to development, we expected that 1) when both choice options are similar, decision-making in younger participants would be associated with increased activation in dorsal ACC (Van Leijenhorst et al., 2006), 2) that high potential reward would be associated with a peak in activation of reward related regions in the VS and VMPFC in mid-adolescence, during both the decision and outcome phase (Ernst et al., 2005; Galvan et al., 2006; Van Leijenhorst et al., 2009), and 3) that activation in control related regions in lateral PFC would show a linear change in activation with age (Eshel et al., 2007; Galvan et al., 2006).

6.2 Method

6.2.1 Participants

Fifty-eight healthy, right-handed volunteers were included in the study. To dissociate developmental changes related to puberty and adolescence, we recruited participants from four age groups; thirteen pre-pubertal children (aged 8-10 years; 8 female; mean age 9.7, SD = 0.9), fifteen pubertal adolescents (aged 12-14 years; 8 female; mean age 13.4, SD = 0.8), fifteen post-pubertal adolescents (aged 16-17 years; 7 female; mean age = 17.1, SD = 0.7), and fifteen young adults (aged 19-26 years; 7 female; mean age = 21.6, SD = 2.08). All procedures were approved by the Leiden University Department of Psychology and the Medical Ethical Committee at the Leiden University Medical Center. All participants, or a primary caregiver in the case of minors, gave informed consent. Data for two additional participants (an 8-year-old and a 21-year-old) was excluded from the analyses because of excessive head movement. Mean head movement was .14 mm for the 8-10 year olds, .08 mm for the 12-14 year olds, .07 mm for the 16-17

year olds, and .06 mm for the 19-26 year olds. Even though mean head movement during scanning was slightly higher in the youngest age group than in the older the age groups (F (3, 57) = 12.10, $p < .001$), for none of the participants head movement during scanning exceeded 1 voxel in any direction. Participants in the three youngest age groups were screened for behavioral problems using parent-ratings on the Child Behavior Checklist (Achenbach, 1991). Scores for all participants fell within the non-clinical range.

6.2.2 The Cake Gambling Task

The present study used an adapted version of a child friendly gambling task (Van Leijenhorst et al., 2008) in which participants were asked to choose between a low-risk gamble and a high-risk gamble associated with a probabilistic monetary reward. In this gambling task, all information that was relevant for making a decision was presented to participants on every trial and no information had to be learned or retrieved over consecutive trials. The probability associated with both gambles and the associated potential rewards were presented visually. Participants saw a cake composed of six brown and pink wedges in a 4:2 ratio (see Figure 6.1A) and a pink and brown square presented at the bottom of the screen in which the reward associated with that color was presented as stacks of 50 cent coins. On each trial, one of the wedges was randomly selected by the computer. If the color of this wedge matched the color that the participant chose, the reward associated with that gamble was won; if they did not match, the gamble did not result in a reward. Participants chose between a low-risk gamble (betting on the majority color with a 66 % chance of winning) and a high-risk gamble (betting on the minority color with a 33 % chance of winning). The probabilities associated with the two choice options were kept constant but the amount of reward associated with the high-risk gamble was varied. The potential reward associated with the low-risk gamble was always 1 Euro, whereas the potential reward associated with the high-risk gamble was 2, 4, 6, or 8 Euro. The condition in which a choice had to be made between a 1 Euro low-risk gamble and a 2 Euro high-risk gamble was ambiguous, since the expected value (the probability x reward magnitude) of both choice options was equal. In the conditions in which the high-risk gamble was associated with 4 to 8 Euro, the expected value of the high-risk gamble was always higher than that of the low-risk gamble. Trials had the following structure: a fixation cross was presented for 500 ms, followed by the presentation of the cake

stimulus which remained visible for 2000 ms. During this time, participants had to make their choice via a button press with the index or middle finger of their right hand. Following the cake stimulus, a fixation cross was presented for 4000 ms after which participants were shown the outcome of the gamble for 2000 ms.

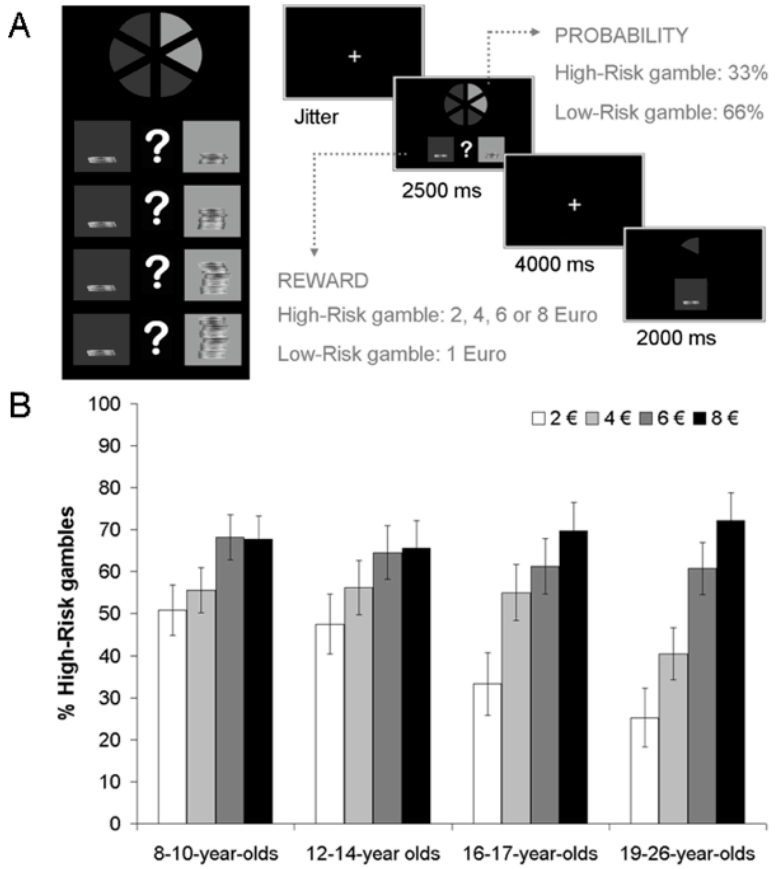

Figure 6.1 *A) The Cake Gambling Task. The left panel shows the different trial types as a function of the amount of reward associated with the High-Risk gamble. The right panel depicts trial timing for an example of a low-risk choice followed by a gain outcome. B) Behavioral Results, the percentage of choices for the High-Risk gamble shown for each Reward condition (2, 4, 6 and 8 Euro), and Age group (8-10-year-olds, 12-14-year-olds, 16-17-year-olds, and 19-26-year-olds). Error bars depict standard error. Age differences were only present for the 2-Euro condition.*

The outcome screen indicated the result of the gamble (gain or no-gain) as well as the size of the associated reward. For gain outcomes, participants saw the stack of coins they had gambled with. For no-gain outcomes, participants saw this stack of coins with a cross through it. Jittered fixation varying between 300 ms and 5250 ms in increments of 550 ms was added to the inter trial intervals using an optimization program (optseq2; see http://surfer.nmr.mgh.harvard.edu/optseq/, developed by Dale, (1999)).

6.2.3 Raven Standard Progressive Matrices

All participants completed Raven's Standard Progressive Matrices (Raven, Raven & Court, 1998) outside of the scanner in order to obtain an estimate of their ability to form perceptual relations and reason by analogy. The Raven Standard Progressive Matrices (RSPM) is a non-verbal test designed to measure general intellectual ability (Raven et al., 1998). Based on the final scores on this test, we obtained estimated IQ scores using Dutch norms. Estimated mean IQ scores all fell within the average to high-average range; 123.31 (SD = 7.86) for the 8-10 year olds, 120.60 (SD = 10.87) for 12-14 year olds, 115.20 (SD = 10.36) for 16-17 year olds, and 125.33 (SD = 7.28) for 19-26 year olds. Estimated IQ scores for 16-17 year olds were the lowest. However, only the difference between 16-17 year olds' estimated IQ scores and 19-26 year olds' estimated IQ scores reached significance ($F(1, 28) = 9.61$, $p < .01$). Because all participants' scores fell within the average to high-average range, IQ differences are not described further.

6.2.4 Procedure

Participants were prepared for the scan in a quiet laboratory. A mock scanner was used to simulate the environment and sounds of an actual MRI scanner. All participants received extensive instructions and performed 11 practice trials immediately before the scan. They were told that their goal was to win as often as possible and that at the end of the experiment they would get to keep the sum of two randomly selected outcomes (one trial per task block). We explained that there was no need to remember performance on previous trials because trials were not related, and that each trial could be chosen in the end. Therefore, all trials were equally important. We explained that gambling requires some luck, and that their winnings could be anywhere between 0 and 16 Euro. In reality, all participants were paid 5 Euro. Following

the scan, participants filled out the RSPM, and additional questionnaires which are not reported here.

6.2.5 MRI Data Acquisition

In total, 84 trials, with 21 trials per condition, were presented over the course of two event-related scans that lasted approximately 7 minutes each. Scanning was performed using a standard whole-head coil on a 3 Tesla Philips scanner at the Leiden University Medical Center (LUMC). Stimuli were projected onto a screen that participants could see via a mirror attached to the head coil. Functional data were acquired using a T2*-weighted gradient-echo echo-planar pulse sequence (38 contiguous 2.75 mm oblique axial slices, using sequential acquisition, TR = 2.2 s, TE = 30 ms, 2.75 x 2.75 mm inplane resolution, 200 volumes per run). High-resolution T2* weighed images and high resolution T1 anatomical images were collected at the end of the scan session. Head motion was restricted using a pillow and foam inserts that surrounded the head. Participants watched cartoons while structural scans were collected.

6.2.6 fMRI preprocessing and Statistical analysis

Data pre-processing and analysis was conducted using SPM5 (Wellcome Department of Cognitive Neurology). 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. Templates were based on the MNI305 stereotaxic space (Cocosco, Kollokian, Kwan & Evans, 1997). The normalization algorithm used a 12-parameter affine transformation together with a nonlinear transformation involving cosine basis functions. During normalization the data was resampled to 3 mm cubic voxels. 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 implemented in SPM5. For each participant, the fMRI time series were modeled as a series of zero duration events convolved with a canonical hemodynamic response function (HRF). We modeled the onset of the stimulus and the onset of the outcome of each trial as zero duration events. Trials for which no response was given within the 2000 ms cue window were modeled separately and were excluded from subsequent analyses. Decision-analyses related to the

stimulus distinguished high-risk and low-risk gambles for the four different reward conditions (2, 4, 6, and 8 Euro gambles). Outcome-analyses distinguished gain and no-gain outcomes for the four reward conditions (2, 4, 6, and 8 Euro) following high-risk gambles; gain and no-gain outcomes following a low-risk gamble were modeled separately. The modeled events were used as covariates in a general linear model, along with a basic set of cosine functions that high-pass filtered the data. The least-squares parameter estimates of height of the best-fitting canonical HRF for each condition were used in pair-wise contrasts. The resulting contrast images, computed on a subject-by-subject basis, were submitted to group analyses. At the group level, whole-brain contrasts between conditions were computed by performing one-tailed t-tests, treating participants as a random effect. Task-related responses were considered significant if they exceeded an uncorrected threshold of $p < .001$, with an extent threshold of 10 voxels.

To test the hypothesis that control related regions followed a linear increase or decrease with development, whereas reward related regions followed a nonlinear trend and showed a peak in adolescence, we performed separate voxelwise ANOVAs. These analyses aimed at identifying regions that showed age-related change in activation related to decision-making and during outcome processing. We tested for both linear (-3 -1 1 3 / 3 1 -1 -3 contrast) and quadratic (-1 1 1 -1 contrast) age-related patterns of change. ANOVAs were also considered significant if they exceeded an uncorrected threshold of $p < .001$, and an extent threshold of 10 contiguous voxels.

6.2.7 fMRI Results: Region of Interest Analysis

We used the MarsBaR toolbox for use with SPM5 (MarsBaR; see http://marsbar.sourceforge.net/ developed by: Brett, Anton, Valabregue & Poline (2002)) to perform region of interest (ROI) analyses to further illustrate patterns of activation in the clusters that we identified in the voxelwise analyses. We created 6 mm spherical ROIs centered at the peak active voxel for these clusters.

6.3 Results

6.3.1 Risk-taking behavior and Reaction Times (RTs)

We submitted the percentage of High-Risk gambles to a repeated

measures ANOVA with Age group as between subjects factor and Reward (2, 4, 6, 8 Euro) as within subjects factor. Risk-taking increased when the reward at stake was higher (main effect Reward, F (3, 162) = 39.13, $p < .001$). On average, risk-taking did not differ between age groups ($p = .51$), but there was a significant Age group x Reward interaction (F (9, 162) = 2.57, $p < .005$) (see Figure 6.1B.). Follow-up ANOVAs for the age groups separately showed that participants in all age groups made more High-risk decisions as rewards increased (all p's < .005). However, comparing the age groups in each reward condition separately showed no age-related differences in the percentage of High-Risk decisions for the 4, 6, and 8 Euro gambles (p's > .1). In contrast, for 2 Euro gambles this analysis revealed a decrease in risk-taking with age (p <.05), suggesting that in the most ambiguous condition older participants were more risk averse. Post hoc ANOVAs confirmed that the percentage of risk-taking in the 2-Euro condition was higher for 8-10-year-olds and 12-14-year-olds relative to 19-26-year-olds, whereas the 16-17-year-olds did not differ from the younger and older age groups.

To test for age-related differences in response times, we submitted participants' average RTs to a repeated measures ANOVA with Reward (2, 4, 6, or 8) and Choice (High-Risk, Low-Risk) as within subjects factors and Age group as between subjects factor. Ten participants were excluded from this analysis due to missing observations in one or more of the conditions (2 pre-pubertal children, 1 pubertal adolescent, 4 post-pubertal adolescents, and 3 young adults). The analysis showed that average RTs did not differ between Age groups ($p = .21$), or between High-Risk and Low-Risk decisions ($p = .33$). RTs varied as a function of the amount of reward at stake as revealed by a main effect of Reward (F (3, 132) = 4.68, $p = .004$). RTs for 2 Euro gambles were slower compared to 6 Euro ($p < .05$) or 8 Euro ($p < .001$) gambles. This pattern of results did not differ as a function of Age (Reward x Age Group, $p = .36$) (see Supplemental Figure 6.1).

Taken together, there were no age differences in risk-taking when the reward at stake was high, however, for the more ambiguous 2 Euro gambles participants were more risk averse as they were older. There were no age differences in response times, suggesting that age differences in neural responses cannot be explained by differences in reaction times or impulsive responding.

6.3.2 fMRI results

The fMRI results are described in two sections; first we describe the results of the analyses during the decision phase, then we describe the analyses related to the outcome processing.

6.3.3 Brain regions involved in High-Risk versus Low-Risk decisions

We first identified brain regions underlying risk-taking behavior across age groups. We performed a general linear model analysis on the functional data modeled at the onset of the stimulus, and computed a voxelwise contrast of High-Risk > Low-Risk decisions across reward conditions. This analysis revealed three significant clusters in the medial PFC; one cluster in the dorsal medial PFC (peak at -12, 51, 18, z = 3.62) , $t(1, 57) = 3.85$, $p < .001$, one in the ventral medial PFC (peak at -6, 60, -6, z = 3.96) , $t(1, 57) = 4.26$, $p < .001$, and one cluster in the subgenual ACC (peak at -3, 21, -6, z = 4.34) , $t(1, 57) = 4.75$, $p < .001$. The reverse contrast of Low-Risk > High-Risk decisions resulted in a cluster of activation in right DLPFC (peak at 39, 24, 36, z = 4.49), $t (1, 57) = 4.94$, $p < .001$ (see Figure 6.2A). These results are consistent with the dual process hypothesis which suggests that activation in reward related areas in the medial PFC is associated with risky decisions, whereas activation in control areas in the lateral PFC is associated with cautious decisions. All significant clusters and corresponding MNI coordinates are reported in Supplemental Table 6.1.

6.3.4 Effects of reward magnitude on risk-taking

Second, we tested which brain regions involved in risk-taking were modulated by the amount of reward at stake. We performed voxelwise ANOVAs testing for linear changes in activation as a function of reward size on the High-Risk > Low-Risk contrast across participants. The ANOVA testing for a linear increase in activation as a function of increasing reward (-3 -1 1 3 contrast) revealed significant clusters of activation in the right putamen (peak at 24, 15, 3, z = 4.40), $t(1, 212) = 4.51$, $p < .001$, and bilateral amygdala (peaks at -24, 0, -18, z = 3.88 and 15, -6, 18, z = 3.59), $t(1, 212) = 3.95$, $p < .001$ and $t(1, 212) = 3.65$, $p < .001$, respectively (see Figure 6.2B). The ANOVA testing for a linear decrease in activation as a function of the amount of reward (3 1 -1 -3 contrast) did not result in any significant clusters. These analyses are consistent with the hypothesis that subcortical affective areas are

sensitive to the reward that is associated with a risk. All significant clusters and corresponding MNI coordinates are reported in Supplemental Table 6.2.

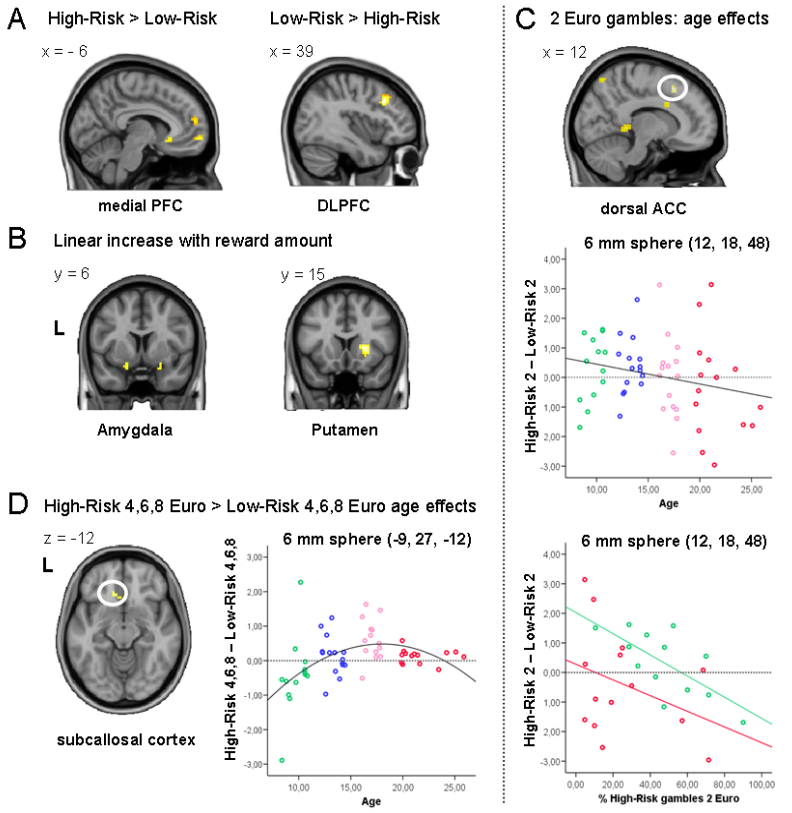

Figure 6.2 *A) Whole-brain results for the contrast of High-Risk and Low-Risk gambles for all participants combined modeled at the time the gamble options were presented. B) Regions for which the contrast of High-Risk > Low-Risk gambles showed a parametric increase with the amount of reward. C) Dorsal ACC region which showed a linear decrease with age in the 2 Euro condition, when corrected for individual differences in risk-taking (top scatter plot), and plotted for the children (green) and adults (red) as a function of risk-taking in the 2 Euro condition (bottom scatter plot). D) Region which shows an adolescent specific peak in activation for the High-Risk > Low-Risk contrast for high reward (4, 6, and 8 Euro) gambles combined. All images are thresholded at p < .001 uncorrected, 10 contiguous voxels. In scatter plots, data for 8-10-year-olds is presented in green, for 12-14-year-olds in blue, for 16-17-year-olds in pink, and for 19-26-year-olds in red.*

6.3.5 Neural correlates of age-related differences in risk-taking

To identify age-related differences in brain regions associated with risk-taking, we modeled a linear increase (-3, -1, 1, 3), linear decrease (3, 1, -1, -3) and adolescent specific peak (-1 1 1 -1) as a function of Age group. We first tested these patterns in an ANOVA for High-Risk > Low-Risk decisions across all reward conditions. The linear decrease ANOVA resulted in a small cluster of activation in the dorsal ACC (peak at 12, 9, 27, z = 3.90), $t(1, 54) = 4.22$, $p < .001$, and a larger cluster in the central opercular cortex/postcentral gyrus (peak at 51, -6, 21, z = 4.44), $t(1, 54) = 4.90$, $p < .001$. No regions showed a linear increase with age or a peak in adolescence. Second, because we only found age-related differences in performance in the 2 Euro condition, but not in the higher reward conditions, we repeated these ANOVAs for the 2 Euro condition separately and for the higher reward conditions (4, 6, 8 Euro) combined.

Contrary to our expectations, the analysis for the 2 Euro condition did not result in any significant clusters when testing for age differences. However, the significant differences in performance between the age groups in the 2 Euro condition could be a confounding factor. When we added the percentage of High-Risk gambles in the 2 Euro condition as a covariate factor to the ANOVA, we found a significant cluster in the dorsal ACC (peak at 12, 18, 48, z = 3.83), $t(1, 54) = 4.14$, $p < .001$ (see below for performance regressions, and Figure 6.2C), but only at a lower threshold ($p < .005$). The relation between age versus performance is described in more detail below.

The same analysis for the higher reward conditions mirrored the results found for all reward amounts combined, showing a linear decrease with age in the same regions in the dorsal ACC (peak at 12, 9, 27, z = 4.46), $t(1, 52) = 4.95$, $p < .001$, and central opercular cortex (peak at 54, -3, 12, z = 4.41), $t(1, 52) = 4.88$, $p < .001$. Again no regions showed a linear increase with age, but for these high reward conditions (4, 6 and 8 Euros combined) we found a small cluster in the medial OFC/ subcallosal cortex which showed a peak in activation for adolescents compared to children and adults (peak at -9, 27, -12, z = 3.55), $t(1, 52) = 3.80$, $p < .001$ (see Figure 6.2D). All significant clusters and corresponding MNI coordinates are reported in Supplemental Table 6.3. The results of the analyses comparing the different age groups from late childhood through early adulthood are consistent with the hypothesis

that risky decisions are associated with more ACC activation in children, and with the hypothesis that risk-taking is associated with more activation in affective areas within the VMPFC in adolescents compared to children and young adults, but only when gambles are associated with a high potential reward.

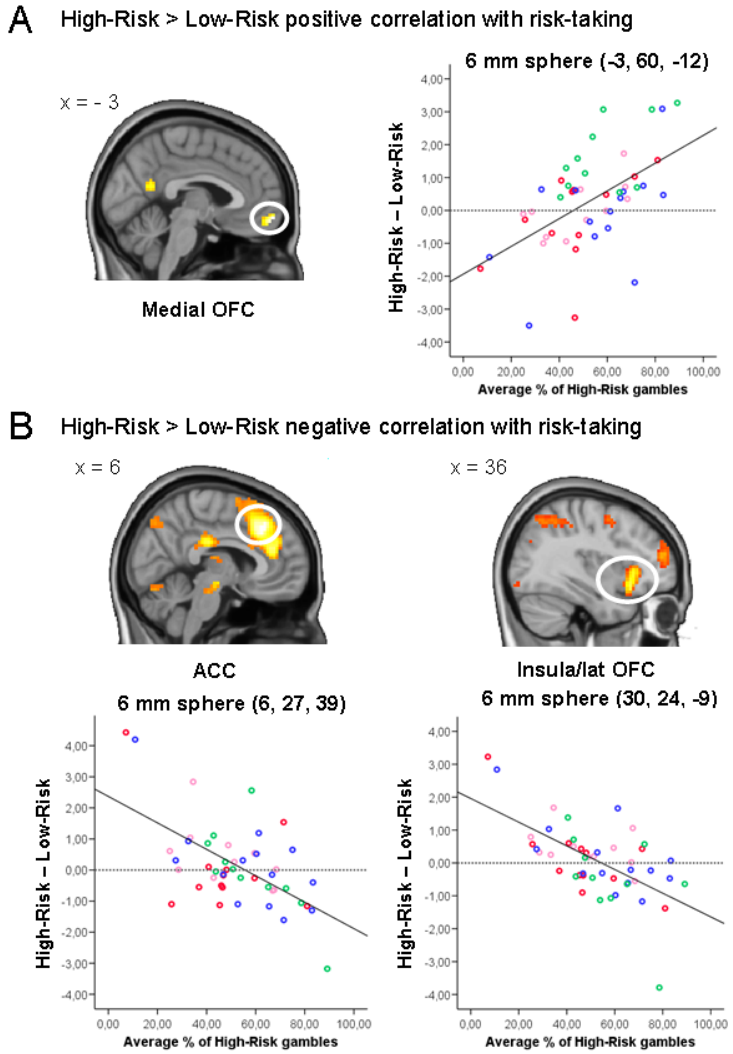

Figure 6.3 *A) Clusters of activation in the ventral medial PFC/medial OFC that show a positive correlation with risk-taking. B) Clusters of activation in dorsal ACC and Insula that show a negative correlation with risk-taking. All images are thresholded at p < .001 uncorrected, 10 contiguous voxels. In scatter plots, data for 8-10-year-olds is presented in green, for 12-14-year-olds in blue, for 16-17-year-olds in pink, and for 19-26-year-olds in red.*

6.3.6 Individual differences in Risk-taking

More detailed analyses on individual participants' behavioral data revealed that there were large individual differences in risk-taking within all age groups (see Supplemental Figure 6.2 for scatter plots). The second goal of this study was therefore to identify brain regions that contribute to these individual differences in the tendency to gamble. To this end, we added the average percentage of High-Risk choices as a regressor to the analysis on the contrast of High-Risk > Low-Risk decisions.

As can be seen in Figure 6.3A, one region in the ventral medial PFC (peak at -3, 60, -12, z = 5.07), $t(1, 56) = 5.74$, $p < .001$, was more active in the High-Risk > Low-Risk contrast for those participants who chose the High-Risk gambles more often. In contrast, a large region in the dorsal medial PFC (with sub-clusters in the paracingulate gyrus; peak at 6, 27, 39, z = 6.13, $t(1, 56) = 7.36$, $p < .001$; and ACC; peak at 9, 36, 18, z = 5.49, $t(1,56) = 6.35$, $p < .001$), showed the opposite pattern; this region was more active in the High-Risk > Low-Risk contrast for individuals who chose the Low-Risk gambles more often (see Figure 6.3B). The latter contrast also showed increased activation in bilateral DLPFC, lat-OFC/Insula, and parietal cortex[1] (see Supplemental Table 6.4 for coordinates).

Together, the results are consistent with the hypothesis that activation in reward related areas within the medial PFC co-varies with risk-taking behavior, whereas activation in control areas in dorsal medial PFC and lateral PFC co-varies with risk-averse behavior[2].

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[1] Additional analyses for the regions that were found in the general High-Risk vs. Low-Risk contrast (dorsal medial PFC, ventral medial PFC and subgenual ACC for High-Risk > Low-Risk and DLPFC for Low-Risk > High-Risk) showed that the ventral medial PFC cluster (peak at -6, 60, -6), which partly overlaps with the ventral medial PFC area identified in this regression analysis, showed a positive correlation with risk-taking as well.

[2] The pronounced brain-behavior relations may explain why the developmental differences in the 2 Euro condition above could not be revealed; possibly, in this condition individual difference in performance are a stronger predictor of brain activity than differences in age. It should be noted that the correlation of risk-taking in the 2 Euro condition and average risk-taking across all reward conditions was high (r = .56, p < .001), therefore, the same analyses for the 2 Euro condition mirror the effects across reward conditions.

6.3.7 Brain regions related to the processing of outcomes of High-Risk gambles

To identify regions which respond to the receipt of a reward following High-Risk gambles, we performed a GLM analysis on the functional data modeled at the onset of the outcome, and computed the voxelwise contrast of Gain > No-Gain outcomes following High-Risk decisions across age groups. This analysis revealed large clusters of activation in the medial PFC and ventral striatum (see Figure 6.4A). The peak active voxel for the medial PFC cluster was located more ventral (peak at -3, 45, -6, z = 6.27), $t(1, 43) = 8.08$, $p < .001$, and in addition we located a more dorsal sub-cluster (peak at 6, 51, 3, z = 6.37) , $t(1, 43) = 8.29$, $p < .001$. Activation in the ventral striatum peaked in the left NAcc (peak at -9, 9, -9, z = 5.73), $t(1, 43) = 7.08$, $p < .001$, and right NAcc (peak at 9, 15, -6, z = 6.30, $t(1, 43) = 8.14$, $p < .001$. No significant clusters were found for the reverse No-Gain > Gain contrast. All clusters and corresponding MNI coordinates are reported in Supplemental Table 6.5.

6.3.8 Effects of reward magnitude on outcome processing

To identify brain regions which respond to parametric changes in the amount of reward, we tested for a linear change in activation as a function of increasing reward (-3 -1 1 3 contrast) in voxelwise ANOVAs on the Gain > No-Gain outcome contrast. The ANOVA testing for a linear increase in activation revealed significant clusters in the right putamen (peak at 24, 9, 0, z = 3.01 t (1, 209) = 3.05, $p = .001$ and right VS/NAcc (peak at 9, 6, -12, z = 3.51 t (1, 209) = 3.57, $p < .001$ (see Figure 6.4B). The ANOVA testing for a linear decrease in activation as a function of the amount of reward associated with the decision (3 1 -1 -3 contrast) did not result in any significant clusters.

6.3.9 Neural correlates of age-related differences in outcome processing

Our final analyses tested for age-related differences in neural responses to the outcome of High-Risk gambles (see Supplemental Figure 6.3 for Gain > No-gain contrast plotted for the age groups separately). We tested for three patterns of age-related change: linear increase (-3, -1, 1, 3), linear decrease (3, 1, -1, -3) and a peak in adolescence (-1 1 1 -1) on the Gain > No-Gain outcomes across reward amounts. No regions were found that showed a linear change with development. In contrast, the peak model revealed activation in the caudate (peak at 21, 18, 9, z =

3.26 $t(1, 40) = 3.52$, $p = .001$) (see Figure 6.4C.), suggesting a peak in the responsiveness of this region to gains in adolescence.

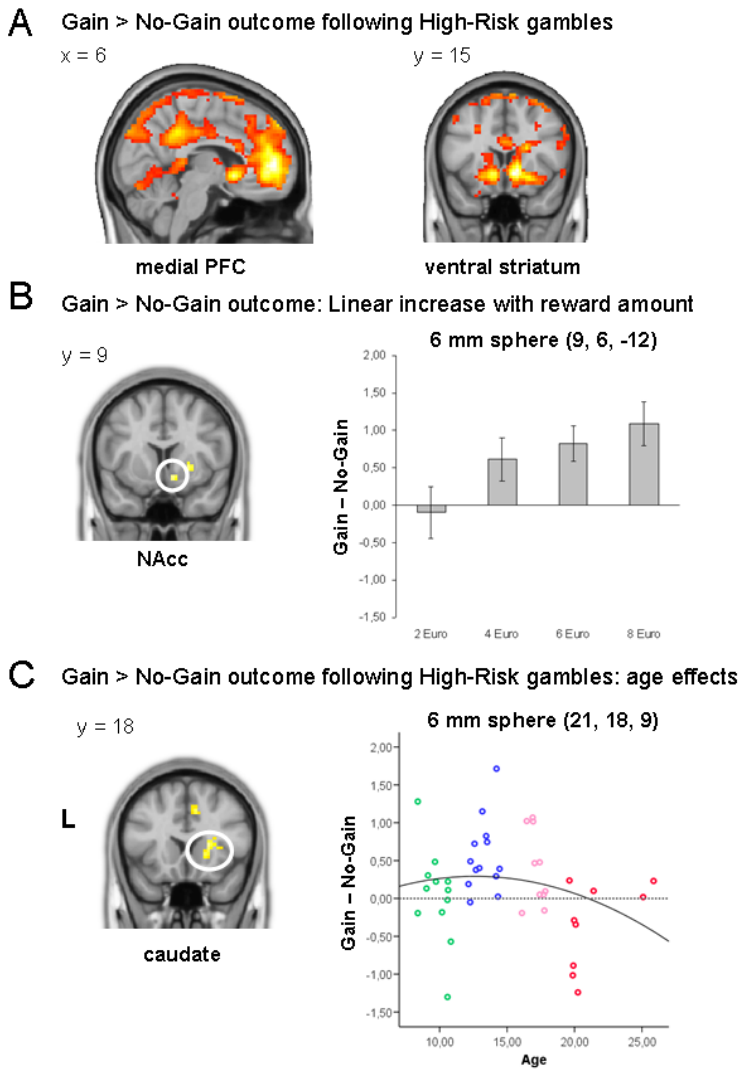


Figure 6.4 *A) Whole-brain results for the contrast of Gain > No-Gain outcomes following High-Risk decisions for all participants combined modeled at the time the outcome was presented. B) Regions for which the contrast of Gain > No-Gain outcomes showed a parametric increase with the amount of reward. C) A region in the ventral striatum showed an adolescent specific peak in activation for the Gain > No-Gain contrast. All images are thresholded at p < .001 uncorrected, 10 contiguous voxels. In scatter plots, data for 8-10-year-olds is presented in green, for 12-14-year-olds in blue, for 16-17-year-olds in pink, and for 19-26-year-olds in red.*

Together, the results from the outcome analyses are consistent with the hypothesis of increased activation in the striatum for gain outcomes, and with the hypothesis that this region is more responsive in mid-adolescence.

6.4 Discussion

The main goal of this study was to test for two different patterns of functional brain development that have been proposed to account for adolescent risk-taking: an inverted U-shaped pattern for reward related regions with a peak in adolescence, and a linear pattern for regions associated with cognitive control. Recent models of adolescent risk-taking have described risk-taking in adolescence as a consequence of these different developmental trajectories (Casey et al., 2008; Ernst et al., 2006; Steinberg et al., 2008). Behaviorally, we found no age-related differences in risk-taking behavior for gambles associated with high rewards; all participants were more likely to take risks as the potential reward increased. These results are consistent with prior studies which showed that the ability to incorporate reward and probability information in decisions under risk is already mature by late childhood (Van Leijenhorst et al., 2008). Interestingly we found a linear decrease in risk-taking for ambiguous gambles; when the expected values of two choices were equal, and both options were associated with low reward, adults preferred to choose the low-risk gamble, whereas younger participants were more likely to choose the high-risk gamble. The finding that adults are risk averse in ambiguous risky situations is consistent with studies that have shown that adults often make risk-averse decisions in the context of potential gains (Tversky & Kahneman, 1981), and with dual process models such as "Fuzzy-trace theory" (Reyna & Rivers, 2008). The latter theory offers an explanation for this finding by proposing that adult decision making in ambiguous situations is dependent on intuitive, rather than computational processes. This intuitive decision-making is thought to develop slowly, and because of this slow development, children rely more on computational strategies when making decisions, and their choices can therefore appear more rational (Reyna & Ellis, 1994; Rivers, Reyna & Mills, 2008).

The fMRI data associated with the decision and outcome phase of gambles resulted in two main findings: First, across ages, risky choices were associated with activation in the medial PFC and the ventral

striatum, whereas cautious choices were associated with activation in the lateral PFC. These results support the hypothesis that the relative weight of reward related regions (medial PFC and ventral striatum) and cognitive control related regions (lateral PFC) contributes to decision-making under risk, in such a way that more activation in reward related regions is associated with risk-taking, whereas more activation in control related regions is associated with cautious behavior. Second, the results of our tests for linear and non-linear age-related changes are consistent with the hypothesis that the relative weight of control related regions and reward related regions changes across development (Casey et al., 2008; Ernst et al., 2006; Galvan et al., 2006; Steinberg et al., 2008), and are in favor of models that hypothesize that risky behavior in adolescence is a consequence of the different developmental trajectories for reward related and control related brain regions (Casey et al., 2008; Galvan et al., 2006; Steinberg et al., 2008).

6.4.1 Control related changes

Consistent with the prediction that cognitive control regions follow a linear change with development, we found a linear decrease in activation with age associated with risky choices in the dorsal ACC. This is consistent with our earlier finding that this region was more active in 9-12 year old participants compared to adults when participants had to identify the most likely outcome in a two-choice task which measured the ability to judge probability (Van Leijenhorst et al., 2006). The finding that there is more activation in control related regions in children and adolescents compared to adults is also consistent with the results reported by Galvan et al. (Galvan et al., 2006) who found a linear decrease in activation in the VLPFC with age in a delayed two-choice task in which reward amounts were varied, and with the finding that activation in regions related to cognitive control often shows a shift from diffuse to focal activation (Durston et al., 2006).

A different pattern, however, was reported by Eshel and colleagues (2007), who used a similar paradigm to the one used in the present study. Eshel et al found more activation in the dorsal ACC and VLPFC for risky choices together with less risky behavior in adults compared to adolescents. These authors interpreted this increase in activation in these regions as reflecting an increased recruitment of cognitive control related regions associated with the regulation of risky decisions. One explanation for these contrasting findings could be found by examining

differences in the tasks that have been used. First, we aimed to control for differences in working memory ability between children, adolescents and adults by instructing participants that trials were not related and that therefore participants would not have to remember their choices and the outcomes of previous trials. In addition, participants were told that only two gambles would be randomly chosen by the computer at the end of the experiment that would determine their prize money. In contrast, in the Eshel et al study participants were paid based on their cumulative earnings; increased recruitment of ventral PFC regions and ACC could reflect differences in the strategies used by adolescents and adults in the context of these different task demands. Second, we only varied the amount of reward associated with the high-risk gamble but not the probabilities associated with both choice options; in all high-reward conditions the high-risk gamble was also associated with the highest expected value. In the Eshel et al. study, both the probability and the magnitude of reward was varied, and importantly, the expected value of the low-risk choice option was higher than that of the high-risk choice option. It is possible that in the Eshel et al. study adults had a more accurate representation of the expected value associated with the two choice options (Levin, Weller, Pederson & Harshman, 2007), and consequently chose the options with the highest expected value more often (which were the low-risk choices). Possibly, activation in ACC and VLPFC could reflect processes important for forming this reward representation. For example, Smith et al. (2009) adapted the task used by Eshel et al (2007), and demonstrated that different PFC regions specifically respond to reward, risk and probability. That is, regions in the VMPFC responded to reward, and activation in dorsal ACC was interpreted in terms of response conflict.

The decrease in ACC activation with age observed in the present study could reflect a decreased need for cognitive control with increasing age. No regions showed a linear increase in activation with age, this finding could be interpreted as a reflection of the relatively low task demands in the current study. In all age groups, DLPFC activation was associated with low-risk choices. Even though DLPFC is one of the last regions to mature both structurally (Gogtay et al., 2004) and functionally (Bunge & Wright, 2007), the finding that the different age groups do not differ in recruitment of this region is consistent with previous studies. These have shown that children recruit lateral PFC regions and perform similar to adults when task demands are low, but differ from adults when the task is more difficult (Crone, Wendelken, Donohue, Van

Leijenhorst & Bunge, 2006). In future studies it would be interesting to examine developmental changes in the effects of task difficulty and working memory demands on the recruitment of control related circuitry in a decision-making context (Geier & Luna, 2009).

6.4.2 Reward related changes

Consistent with the prediction that reward related regions follow a non-linear change with development, a region in VMPFC and in the VS showed a peak in activation in adolescence, both during the decision phase of trials and during the outcome phase. This is the first study to report this peak in relation to risky choices in a decision-making paradigm. The Galvan et al. (2006) study compared children (7-11 years), adolescents (13-17 years) and adults (23-29 years), but used a delayed response two-choice task in which participants did not have to weigh probabilities and rewards. The Eshel et al. (2007) study did use an active gambling task, but these researchers only compared adolescents to adults, which did not enable them to test for a peak in brain responsiveness to risk and reward in adolescence. The comparison of adolescents and adults did not result in differences between these age groups in activation in the VS during the decision phase (Eshel et al., 2007). However, the processing of reward outcomes in these participants was associated with more activation in the VS in adolescents compared to adults (Ernst et al., 2005). These finding are consistent with prior results, showing that the neural response to rewards is larger during the outcome phase of trials than during the decision phase (Van Leijenhorst et al., 2009). Finally, the brain region that showed a peak in activation in adolescence during the decision phase was more anterior (VMPFC/subcallosal cortex) compared to the region that showed this peak during the outcome phase (VS/caudate).

6.4.3 Individual differences

One interesting finding in the current experiment is that the behavioral data do not reveal a peak in risk-taking in adolescence. This finding is not uncommon, other studies have also failed to report this peak behaviorally (Van Leijenhorst et al., 2008), and more often linear changes in risk-taking behavior (Crone, Bullens, Van der Plas, Kijkuit & Zelazo, 2008) are reported (see also Boyer (2006) for a review). These findings reflect the difficulty of showing deviant adolescent behavior in a controlled experimental setting. Importantly, when

differences in behavior are small, or even absent, fMRI can reveal a difference in the neural correlates of this behavior across development and can help build hypotheses. To better understand the relation between risk-taking behavior as it is observed in everyday life and the developmental changes in brain circuitry important for decision-making observed in the laboratory, future studies could benefit from examining how individual differences in behavior relate to changes in brain function across development.

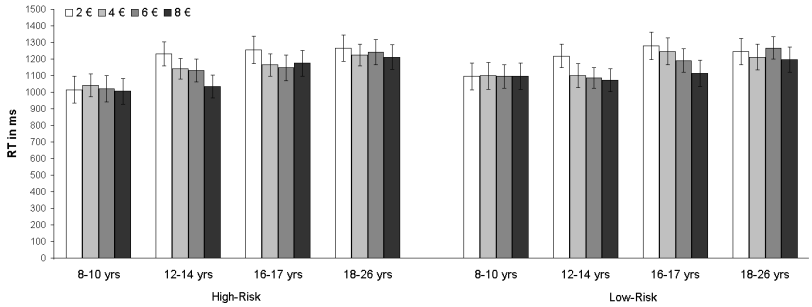
In the present study individual differences in risk-taking behavior in the task were associated with activation in regions in medial PFC, and not with activation in the VS. Interestingly, activation in control related regions in dorsal medial PFC showed a negative correlation with risk-taking behavior, whereas activation in reward related regions in VMPFC showed a positive correlation with risk-taking. These findings suggest the possibility that the function of these regions is associated with participants' behavioral preferences. A similar dissociation between dorsal and ventral MPFC regions activation in relation to risk preference in adults has been reported recently by Xue et al. (2009). These authors suggest that a strong reward related signal in VMPFC could cause risky behavior, whereas a strong signal in dorsal medial PFC could act as a warning signal to prevent risky behavior. The results from the present study extend these findings and suggest that the relation between activation in these regions and behavior could be related to participants' subjective experience. The VMPFC regions that show a positive correlation with risk-taking were more active when risk averse participants avoided the high-risk option, but showed the opposite pattern for participants who preferred the high-risk gamble on most trials risk; for these participants VMPFC was most active when they chose the high-risk option. Together with the finding that activation in VMPFC regions in all participants is associated with High-Risk choices and with the receipt of gain feedback, these individual differences data stress the need for a better understanding of the role of sub regions of VMPFC and their development (Kringelbach & Rolls, 2004; O'Doherty, 2007; Wallis, 2007).

A question that we could not address in this study but that will be important to examine in future studies is whether monetary rewards hold comparable subjective value for children, adolescents and adults. It could be that the peak in reward related regions in adolescence is observed because the potential monetary reward is more important for

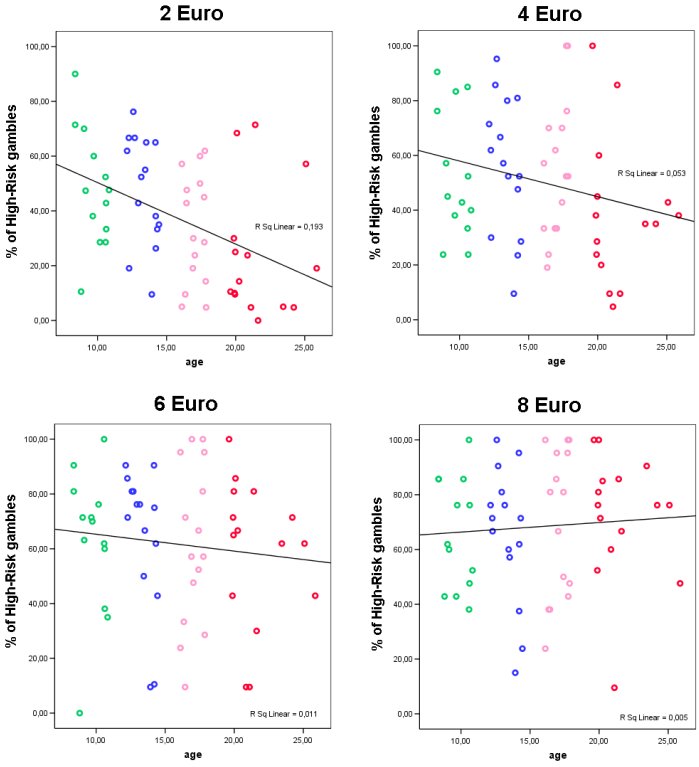
adolescents compared to children and adults. However, the observation that similar brain regions respond to parametric changes in reward value in all age groups and the finding that response time profiles are similar across age groups argue against this possibility. Nonetheless, this will be an important issue to tackle in future experiments.

6.4.4 Conclusion

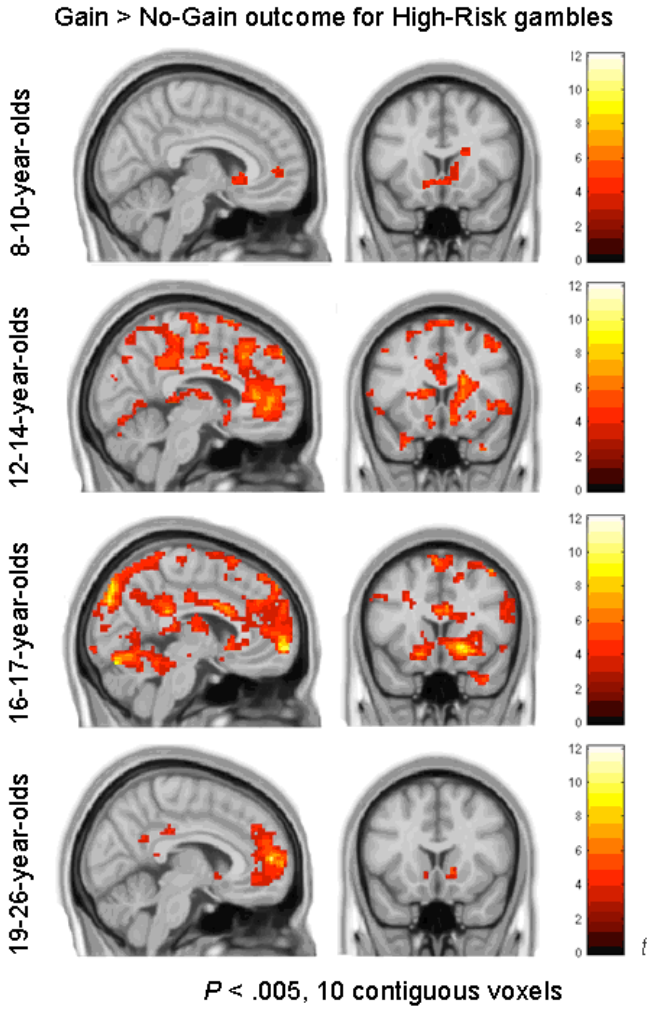
In summary, the current findings demonstrate that brain regions implicated in reward processing and cognitive control in decision-making under risk follow distinct developmental trajectories. Reward related regions show an increased sensitivity to rewards in adolescence and follow an inverted U-shaped developmental pattern, whereas cognitive control related regions mature slowly and follow a linear development. In addition, patterns of activation in dorsal and ventral medial PFC are related to individual differences in risk-taking propensity. These findings support the hypothesis that risky behavior in adolescence follows from an imbalance caused by different developmental trajectories of motivational and regulatory brain circuitry (Casey et al. 2008; Galvan et al. 2006; Steinberg et al. 2008). Importantly, the relative contributions of reward related and control relate regions to decision-making vary with individual differences in risk-taking propensity in all age groups. Future studies should take individual differences into account in order to identify those adolescents who are at risk.



Supplemental Figure 6.1 *Average Reaction times (RT) for High-Risk and Low-Risk gambles shown for each Reward condition (2, 4, 6 and 8 Euro), and Age group (8-10-year-olds, 12-14-year-olds, 16-17-year-olds, and 19-26-year-olds). Error bars depict standard error.*



Supplemental Figure 6.2 *Average % of High-Risk gambles shown for each Reward condition (2, 4, 6 and 8 Euro) and each participant. Data for 8-10-year-olds is presented in green, for 12-14-year-olds in blue, for 16-17-year-olds in pink, and for 19-26-year-olds in red. The Age x Risk correlation was significant in the 2 Euro condition.*



Supplemental Figure 6.3 *Whole-brain results for the contrast of Gain > No-Gain outcomes following High-Risk decisions for the separate age groups [MNI 9, 15, -6]. All images are thresholded at p < .005 uncorrected, 10 contiguous voxels.*

Supplemental Table 6.1 *Activation related to high-risk and low-risk decisions for 8-10, 12-14, 16-17 and 19-26 year olds, at p < .001 uncorrected; with extent threshold of 10 voxels.*

Contrast	Region	MNI coordinates x	y	z	Z-value	Cluster size (voxels)	Cluster corrected
H-R > L-R							
All ages	R Occipital Pole	12	-102	12	4.57	130	$p < .001$
	L Subcallosal cortex	-3	21	-6	4.34	18	$p = .10$
	L Occipital Pole	-12	-105	3	4.34	20	$p = .09$
	L Frontal pole/VMPFC	-6	60	-6	3.96	12	$p = .17$
	L Paracingulate gyrus	-12	51	18	3.62	23	$p = .07$
8-10 yrs		no significant clusters					
12-14 yrs		no significant clusters					
16-17 yrs	L Subcallosal cortex	-3	27	-6	3.85	14	$p = .05$
19-26 yrs	R Anterior cingulate gyrus	12	42	3	3.70	13	$p = .04$
L-R > H-R							
All ages	R Middle frontal gyrus	39	24	36	4.49	54	$p = .009$
	R Superior parietal lobe	24	-42	39	4,15	13	$p = .16$
8-10 yrs		no significant clusters					
12-14 yrs		no significant clusters					
16-17 yrs	L Postcentral gyrus	-33	-33	54	4.73	34	$p = .004$
	R Lateral occipital cortex	18	-72	45	4.23	33	$p = .005$
	L Lateral occipital cortex	-15	-72	45	3.89	13	$p = .06$
	R Middle frontal gyrus	33	0	57	3.88	11	$p = .08$
	L Superior parietal lobe	-21	-48	60	3.44	13	$p = .06$
19-26 yrs	R Lateral occipital cortex	45	-69	33	3.78	12	$p = .05$
	R Middle frontal gyrus	33	30	48	3.65	11	$p = .06$
	R Central opercular cortex	48	-6	6	3.65	11	$p = .06$
	L Postcentral gyrus	-6	-36	69	3.64	16	$p = .03$

Supplemental Table 6.2 *Linear changes in activation for High-Risk > Low-Risk contrast related to reward magnitude across age, at p < .001 uncorrected; with extent threshold of 10 voxels.*

Contrast	Region	MNI coordinates x	y	z	Z-value	Cluster size (voxels)	Cluster corrected
Increase (-3 -1 1 3)							
All ages	R Putamen	24	15	3	4.40	47	$p = .02$
	L Superior temporal gyrus	-57	-39	9	4.16	228	$p < .001$
	L Parahippocampal gyrus	-27	-36	-15	4.12	38	$p = .03$
	L Superior parietal lobe	-24	-48	63	4.03	128	$p < .001$
	R Parietal operculum cortex	39	-30	21	3.96	47	$p = .02$
	L Parahippocampal gyrus	-24	0	-18	3.88	39	$p = .03$
	L Superior parietal lobe	-30	-48	63	3.81	46	$p = .02$
	R Superior temporal gyrus	63	-24	15	3.70	16	$p = .13$
	R Posterior cingulate gyrus	15	-15	39	3.64	12	$p = .19$
	R Superior frontal gyrus	21	-6	63	3.62	17	$p = .12$
	R Amygdala	15	-6	-18	3.59	46	$p = .02$
	R Middle temporal gyrus	60	-54	3	3.56	37	$p = .03$
Decrease (3 1 -1 -3)							
all ages		no significant clusters					

Supplemental Table 6.3 *Changes in activation for High-Risk > Low-Risk contrast related to linear and non-linear age changes, at p < .001 uncorrected; with extent threshold of 10 voxels.*

Contrast	Region	MNI coordinates x	y	z	Z-value	Cluster size (voxels)	Cluster corrected
Increase with age (-3 -1 1 3)							
all rewards	no significant clusters						
2 Euro	no significant clusters						
4, 6, 8 Euro	no significant clusters						
Decrease with age (3 1 -1 -3)							
All rewards							
	R Postcentral gyrus	51	-6	21	4.44	96	$p = .001$
	R Parahippocampal gyrus	21	-15	-24	4.07	19	$p = .09$
	R Anterior cingulate gyrus	12	9	27	3.90	14	$p = .14$
	R Lateral occipital cortex	36	-63	3	3.53	10	$p = .21$
2 Euro	no significant clusters						
4, 6, 8 Euro	R Anterior cingulate gyrus	12	9	27	4.46	19	$p = .08$
	R Central opercular cortex	54	-3	12	4.41	102	$p < .001$
	R Hippocampus	27	-15	-21	3.65	10	$p = .19$
Peak in adolescence (-1 1 1 -1)							
all rewards	no significant clusters						
2 Euro	no significant clusters						
4, 6, 8 Euro	L Subcallosal cortex	-9	27	-12	3.55	10	$p = .19$

Supplemental Table 6.4 *Regions showing a positive or negative correlation with the average % of High-Risk gambles across age, at p < .001 uncorrected; with extent threshold of 10 voxels.*

Contrast	Region	MNI coordinates x	y	z	Z-value	Cluster size (voxels)	Cluster corrected
Positive correlation							
all ages	L Frontal pole/VMPFC	-3	60	-12	5.07	42	$p = .02$
	L Middle temporal gyrus	-57	-9	-18	4.94	127	$p < .001$
	L Inferior frontal gyrus	-54	27	12	4.59	35	$p = .03$
	R Superior temporal gyrus	54	0	-15	4.42	223	$p < .001$
	L Superior temporal gyrus	-66	-36	3	4.30	51	$p = .01$
	L Precuneus cortex	-6	-57	18	3.95	31	$p = .04$
	R Supramarginal gyrus	66	-24	33	3.89	19	$p = .09$
	L Superior frontal gyrus	-21	30	39	3.89	12	$p = .17$
	R Parietal operculum cortex	51	-30	18	3.75	11	$p = .19$
	L Posterior cingulate gyrus	-15	-45	36	3.67	18	$p = .09$
Negative correlation							
all ages	R (Para)cingulate gyrus	6	27	39	6.13	1067	$p < .001$
	R Orbital frontal cortex	30	24	-9	6.0	291	$p < .001$
	L Superior parietal lobe	-30	-60	48	5.24	995	$p < .001$
	L Inferior frontal gyrus	-36	6	27	5.23	231	$p < .001$
	R Posterior cingulate gyrus	6	-24	27	5.11	141	$p < .001$
	L Anterior Insula	-30	18	3	4.88	129	$p < .001$
	R Lateral occipital cortex	30	-63	45	4.63	480	$p < .001$
	R Basal ganglia	12	3	-6	4.45	45	$p = .01$
	L Frontal pole	-30	48	18	4.20	142	$p < .001$
	R Frontal pole	36	51	15	4.16	113	$p < .001$
	R Occipital pole	30	-90	-9	3.85	24	$p = .06$
	R Middle frontal gyrus	33	0	51	3.71	32	$p = .03$
	L Occipital pole	-27	-96	0	3.71	46	$p = .01$
	L Lateral occipital cortex	-36	-78	-15	3.69	14	$p = .14$
	R Middle frontal gyrus	51	15	42	3.64	16	$p = .12$
	R occipital pole	24	-102	0	3.38	12	$p = .17$

Supplemental Table 6.5 *Activation related to Gain feedback following high-risk gambles across age groups and for 8-10, 12-14, 16-17 and 19-26 year olds separately, at p < .001 uncorrected; with extent threshold of 10 voxels.*

Contrast	Region	MNI coordinates x	y	z	Z-value	Cluster size (voxels)	Cluster corrected
Gain > No-Gain							
all ages	L Frontal medial cortex	-3	45	-6	6.27	10993	$p < .001$
	R Nucleus Accumbens	*9*	*15*	*-6*	*6.30*		
	L Nucleus Accumbens	*-9*	*9*	*-9*	*5.73*		
	R Paracingulate gyrus	*6*	*51*	*3*	*6.37*		
	R Inferior temporal gyrus	63	-42	-15	5.71	394	$p < .001$
	L Inferior temporal gyrus	-57	-27	-21	4.94	365	$p < .001$
	L Occipital pole	-27	-102	-6	4.74	65	$p = .005$
	R Putamen	30	-15	-3	3.68	55	$p = .009$
	L Precentral gyrus	-45	-12	36	3.44	17	$p = .12$
	L Postcentral gyrus	-57	-12	36	3.44	15	$p = .14$
8-10 yrs	no significant clusters						
12-14 yrs	L Precentral gyrus	-6	-24	69	4.83	755	$p < .001$
	R Frontal pole	15	48	42	4.80	422	$p < .001$
	L Anterior cingulate gyrus	-9	42	3	4.53	644	$p < .001$
	L Middle frontal gyrus	-39	39	36	4.51	40	$p = .001$
	R Orbital frontal cortex	21	36	-12	4.46	119	$p < .001$
	L Lateral occipital cortex	-45	-66	45	4.41	126	$p < .001$
	L Caudate	-12	12	12	4.33	31	$p = .003$
	R Inferior temporal gyrus	60	-45	-18	4.32	29	$p = .003$
	R Middle frontal gyrus	42	12	48	3.99	28	$p = .004$
	R Supramarginal gyrus	60	-33	45	3.97	15	$p = .03$
	R Middle frontal gyrus	33	33	48	3.96	40	$p = .001$
	L Amygdala	-18	3	-15	3.96	34	$p = .002$
	R Frontal pole	48	48	15	3.95	26	$p = .005$
	L Middle temporal gyrus	-60	-33	-18	3.85	46	$p < .001$
	R Lateral occipital cortex	48	-66	33	3.81	45	$p < .001$
	Superior frontal gyrus	0	12	69	3.79	28	$p = .004$
	R Middle frontal gyrus	45	33	33	3.75	20	$p = .01$
	L Central opercular cortex	-54	3	3	3.74	18	$p = .02$
	L Middle frontal gyrus	-36	9	51	3.69	11	$p = .05$
	L Parahippocampal gyrus	-24	-18	-33	3.66	22	$p = .009$
	L Middle frontal gyrus	-33	18	-30	3.49	14	$p = .03$

	R Anterior insula	42	18	0	3.47	14	$p = .03$
	R Lateral occipital cortex	51	-72	-12	3.45	10	$p = .06$
16-17 yrs	L Posterior cingulate gyrus	-6	-39	27	4.96	1730	$p < .001$
	L Hippocampus	-30	-12	-24	4.82	295	$p < .001$
	R Paracingulate gyrus	15	45	9	4.59	332	$p < .001$
	L Postcentral gyrus	-33	-30	60	4.57	28	$p = .001$
	R Central opercular cortex	57	3	9	4.55	16	$p = .006$
	R Putamen	18	15	-6	4.53	144	$p < .001$
	R Middle frontal gyrus	45	27	36	4.48	26	$p = .001$
	L Lateral occipital cortex	-51	-78	-3	4.45	278	$p < .001$
	R Supramarginal gyrus	33	-42	36	4.34	41	$p < .001$
	L Putamen	-18	18	-12	4.26	68	$p < .001$
	L Frontal pole	-39	48	12	4.26	12	$p = .01$
	L Paracingulate gyrus	-3	39	30	4.23	248	$p < .001$
	R Orbital frontal cortex	36	36	-18	4.16	10	$p = .02$
	L Superior frontal gyrus	-24	30	48	4.12	14	$p = .009$
	L Frontal pole	-24	42	-12	4.08	26	$p = .001$
	R Superior frontal gyrus	15	18	48	3.99	10	$p = .02$
	R Anterior cingulate gyrus	6	6	30	3.97	53	$p < .001$
	L Superior frontal gyrus	-6	18	66	3.95	36	$p < .001$
	R Caudate	12	-12	18	2.87	50	$p < .001$
	R Temporal pole	18	9	-30	3.85	18	$p = .004$
	R Lateral occipital cortex	54	-66	27	3.80	38	$p < .001$
	L Lateral occipital cortex	-51	-75	21	3.65	10	$p = .02$
	R Thalamus	9	-30	12	3.65	26	$p = .001$
	R Occipital pole	12	-96	-6	5.74	13	$p = .01$
	R Lateral occipital cortex	33	-90	-9	5.64	22	$p = .002$
	R Frontal pole	36	45	-3	5.62	33	$p < .001$
	R Supramarginal gyrus	45	-30	36	3.56	20	$p = .002$
	R Angular gyrus	54	-51	45	3.39	39	$p < .001$
19-26 yrs	R Frontal pole	9	63	6	4.85	356	$p < .001$
	L Frontal pole	-39	42	-3	4.72	62	$p < .001$
	L Supramarginal gyrus	-57	-36	48	4.20	11	$p = .01$
	R Lateral occipital cortex	51	-66	27	3.80	23	$p = .001$
	L Lateral occipital cortex	-39	-63	24	3.79	37	$p < .001$
	L Precuneus cortex	-15	-63	39	3.74	11	$p = .01$
	L Lateral occipital cortex	-33	-81	42	3.70	22	$p = .001$

No-Gain > Gain

all ages	no significant clusters
8-10 yrs	no significant clusters

12-14 yrs	no significant clusters
16-17 yrs	no significant clusters
19-26 yrs	no significant clusters