ELSEVIER

Neuropsychologia 44 (2006) 2158–2170

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

Neural correlates of developmental differences in risk estimation and feedback processing

Linda van Leijenhorst [a,b,c,*], Eveline A. Crone [a,c], Silvia A. Bunge [a,d]

[a] *Center for Mind and Brain, University of California at Davis, USA*
[b] *Department of Psychology, University of Amsterdam, The Netherlands*
[c] *Department of Psychology, Leiden University, The Netherlands*
[d] *Department of Psychology, University of California at Davis, USA*

Received 9 July 2005; received in revised form 9 January 2006; accepted 1 February 2006
Available online 30 March 2006

Abstract

The primary aim of this study was to compare the neural substrates of decision-making in middle-aged children and adults. To this end, we collected fMRI data while 9–12-year-olds and 18–26-year-olds performed a simple gambling task. The task was designed to tap two important aspects of decision-making: risk estimation and feedback processing. We examined how orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), and dorsolateral prefrontal cortex (DLPFC) contributed to risk estimation, and how ventrolateral and medial prefrontal cortices (VLPFC and medial PFC) contributed to negative feedback processing in children and adults. Region of interest analyses revealed differences in brain activation between children and adults for ACC and lateral OFC. ACC was recruited more for high-risk than for low-risk trials, and this difference was larger for children than for adults. In contrast, children and adults did not differ in activation for OFC or DLPFC. These data suggest that children's decision-making under uncertainty is associated with a high degree of response conflict. Both age groups exhibited bilateral VLPFC (BA 47) and medial PFC/ACC (BA 6/ BA 32 (dorsal) and 24 (ventral)) activation associated with negative feedback processing. Relative to adults, children engaged lateral OFC more strongly for negative relative to positive feedback. These results indicate that children may find negative feedback more aversive than adults do. In summary, children aged 9–12 years and adults recruit similar brain regions during risk-estimation and feedback processing, but some key differences between the groups provide insight into the factors contributing to developmental changes in decision-making.
© 2006 Elsevier Ltd. All rights reserved.

Keywords: Development; Decision-making; Somatic marker; Neuroimaging; Feedback

1. Introduction

Decision-making, which involves the ability to choose between competing actions that are associated with uncertain benefits and penalties, is a key component of human cognition and behavior. Throughout childhood, we learn and develop the ability to make choices that are beneficial in the long run. The ability to make decisions that require the delay of gratification to receive a larger reward in the future begins to emerge during the pre-school period (Mischel, Shoda, & Rodriguez, 1989). Interestingly, the ability to delay gratification at age four was found to be predictive of socially competent behavior in adolescence (Mischel et al., 1989). Even though 4-year-olds can choose delayed over immediate rewards (e.g., Prencipe & Zelazo, 2005; Thompson, Barresi, & Moore, 1997), children show difficulties with delay of gratification that may persist into adolescence on tasks in which one must make a decision between immediate and future reward (e.g., Crone & Van der Molen, 2004; Hooper, Luciana, Conklin, & Yarger, 2004; Overman, 2004). Thus, the ability to make advantageous decisions under conditions of uncertainty does not fully develop until early adulthood.

The mechanisms underlying developmental changes in decision-making are not well understood. The interpretation of behavioral findings is difficult because of the complexity of many decision-making tasks. For example, most decision-making tasks not only require an estimation of risk (Critchley, Mathias, & Dolan, 2001), but also require participants to process performance feedback (O'Doherty, Critchley, Deichmann,

* Corresponding author at. Wassenaarseweg 52, 2300 RB Leiden.
E-mail address: lleijenhorst@fsw.leidenuniv.nl (L. van Leijenhorst).

0028-3932/$ – see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2006.02.002

& Dolan, 2003), and keep an appropriate strategy on-line (Barraclough, Conroy, & Lee, 2004). Developmental changes have been observed in all of these functions, namely risk estimation, feedback monitoring, and strategy (or task-set) maintenance. Behavioral data indicate that children and adolescents make more disadvantageous decisions, suggesting that they are prone to risk-taking (Crone et al., 2003; Overman, 2004). Additionally, when it is necessary to learn from external feedback, young children are more likely than older children to perseverate in their behavior, which suggests that they may also be less able to use the informative value of performance feedback than older children and adults in order to change their behavior (Kirkham & Diamond, 2003). Finally, a large body of evidence indicates that there are developmental improvements in the ability to keep relevant information online (e.g., Barcelo, 1999; Barcelo & Knight, 2002; Casey, Giedd, & Thomas, 2000; Diamond, 2002; Thomas et al., 1999). Thus, to learn more about the factors contributing to developmental changes in decision-making, it is necessary to examine how separable cognitive functions contribute to the complex process of decision-making.

Our understanding of the processes underlying decision-making in adults has benefited from investigations of its neural underpinnings. Brain imaging techniques are especially valuable when overt behavior is difficult to interpret, because different underlying mechanisms may contribute to observed differences in behavior (see Casey, Davidson, & Rosen, 2002; Van der Molen & Molenaar, 1994). Neuroimaging studies in healthy adults and neuropsychological studies in patients with real-life decision-making problems have shown that two key components of decision-making – risk estimation and processing performance feedback – are subserved by different regions within the prefrontal cortex (PFC) (e.g., Bechara, Damasio, Damasio, & Anderson, 1994; Breiter, Aharon, Kahneman, Dale, & Shizgal, 2001; Cohen, Heller, & Ranganath, 2005; Ernst et al., 2005; Knutson, Adams, Fong, & Hommer, 2001; Rolls, 2000). More specifically, these studies show that orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) are important for risk anticipation, whereas ventrolateral PFC (VLPFC) is engaged when participants receive negative performance feedback.

In several patient studies, Bechara et al. (1994), Bechara, Tranel, Damasio, and Damasio (1996); Bechara, Damasio, Tranel, and Damasio (1997), and Bechara, Tranel, and Damasio (2000) have shown that patients with OFC damage make disadvantageous choices on the Iowa Gambling Task. The Iowa Gambling Task mimics real-life decision-making, in that it features immediate and future rewards and punishments. These studies showed that healthy control participants learned to make advantageous choices over the course of the task, favoring larger gains in the future over smaller but more immediate gains, whereas OFC patients selected only those options that result in immediate reward. These findings have been taken as evidence that OFC subserves risk estimation by generating autonomic responses, but that it does not subserve feedback processing. More recent studies have suggested a somewhat different account of OFC function, by showing that OFC patients make disadvantageous choices on the Iowa Gambling Task only when reversal learning is required, i.e., when they must learn to adjust their responses after the reinforcement values of stimuli have been reversed (Fellows & Farah, 2003, 2005; Maia & McClelland, 2004, 2005; Rolls, 1999). Both accounts, however, suggest that OFC is important for learning to make decisions by weighing possible outcomes (risk estimation).

A number of imaging studies have implicated OFC in decision-making under conditions of uncertainty (Ursu & Carter, 2005). Some studies suggest that OFC is important for risk estimation (Cohen et al., 2005; Ursu & Carter, 2005). Additionally, some studies suggest that OFC is responsible for processing negative performance outcomes (Elliott, Friston, & Dolan, 2000; Kahn et al., 2002; Rogers et al., 1999). However, the anterior, ventral portion of VLPFC (BA 47), which is sometimes considered to be part of lateral OFC, is more consistently reported as being related to receiving punishment feedback (O'Doherty, Kringelbach, Rolls, Hornak & Andrews, 2001; O'Doherty, Critchley, Deichmann, Dolan, 2003; Rogers et al., 2004).

In addition to OFC, several other regions, including anterior cingulate cortex and midbrain regions (in particular, the nucleus accumbens and ventral striatum), are reported as being important for uncertain decision-making (Paulus, Hozack, Frank, & Braun, 2002; Rodriguez, Aron, & Poldrach, 2005; Rogers et al., 2004; Volz Schubotz, & Von Cramon, 2003). ACC is associated with the detection of response conflict and the monitoring of performance (Carter et al., 1998; Ernst et al., 2004; Gehring & Knight, 2000; Holroyd, Nieuwenhuis, Mars, & Coles, 2004; O'Doherty et al., 2001; Van Veen & Carter, 2002). Midbrain regions are thought to be associated with the prediction of errors (Rodriguez et al., 2005) or responsive to the magnitude of reward (Galvan et al., 2005).

Adaptive decision-making requires not only emotional evaluation, but also the weighing of positive and negative consequences of several potential actions. Therefore, it is not surprising that dorsolateral PFC (DLPFC), a region associated with response selection (e.g., Bunge, Hazeltine, Scanlon, Rosen, & Gabrieli, 2002; Critchley et al., 2001; McClure, Laibson, Loewenstein, & Cohen, 2004; Rowe, Toni, Josephs, Frackowiack, & Passingham, 2000), and working memory requirements of decision-making tasks (Bechara, Tranel & Damasio, 1998; Fellows & Farah, 2005; Manes et al., 2002), is active when subjects make rational decisions, such as when they decide to wait for future rewards (Fellows & Farah, 2005; McClure et al., 2004). The framework provided by these studies in adults allows us to investigate specific hypotheses regarding developmental changes in decision-making.

Recent advances in developmental neuroimaging have made it possible to relate changes in prefrontal activity to the development of cognitive functions. fMRI studies of cognitive control have reported activation in similar brain regions for middle-aged children and adults (e.g., Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Casey et al., 1995, 2000, 2002; Klingberg, Forssberg, & Wessterberg, 2002). Interestingly, even though children show activity in similar regions, the pattern of activation often differs between children and adults, suggesting that the development of cognitive functions is related to a refinement in the organization or efficiency in the recruitment of the prefrontal cortex (Casey et al., 2002). Relative to cognitive con-

trol, decision-making has received considerably less attention in the developmental neuroimaging literature (see Happeney, Zelazo, & Stuss, 2004). To date, only three studies have examined decision-making in adolescents and adults (Bjork et al., 2004; Ernst et al., 2005; May et al., 2004), and no fMRI studies have yet examined decision-making in children under the age of 12 years.

The present study compares the neural substrates of decision-making in 9–12-year-olds and young adults, using a children's gambling task designed to tap two important aspects of decision-making: risk estimation and feedback processing. Because the current fMRI study is the first to investigate decision-making in children, we have chosen to adapt for children a paradigm designed by Critchley et al. (2001) for use in adults. The *cake task* allows us to examine developmental differences in subcomponents of decision-making, including risk estimation and feedback processing. The stimuli in this task resemble "wheels of fortune" that have been used in the adult neuroimaging literature (e.g., see Breiter et al., 2001; Ernst et al., 2004).

In our child-friendly task, the stimuli represent cakes that are part chocolate-flavored and part strawberry-flavored. Participants are asked to look at a given cake stimulus, and decide whether a piece of chocolate or strawberry cake is most likely to be randomly selected by a computer. The proportion of chocolate/strawberry pieces differs between cakes, resulting in low-risk decisions (for example, one chocolate piece and eight strawberry pieces) and high-risk decisions (for example, four chocolate pieces and five strawberry pieces). Performance feedback, indicating gain or loss, follows each decision.

This study focused on the contributions of OFC, ACC, DLPFC, and the midbrain to risk estimation in children and adults, as well as the contributions of VLPFC and medial PFC to feedback processing. Such a region-of-interest (ROI) approach allowed us to examine changes across development in the relative contribution of these regions to decision-making. Additionally, we examined the extent to which children and adults rely on the same or different brain regions during risk estimation and feedback processing. We focused primarily on negative feedback, because of its importance in updating behavior, but examined the neural correlates of positive > negative feedback as well.

We had two predictions about the development of decision-making. The first prediction was that children have difficulty anticipating risks because the network relying on prefrontal cortex (DLPFC and OFC) and its connections with ACC is not fully developed yet. Such a finding would be consistent with the literature showing that children do not experience warning signals in gambling tasks in a similar way as adults do (e.g., Hooper et al., 2004; Steinberg, 2005). We expected that adults would engage OFC and ACC (e.g., Cohen et al., 2005) as well as DLPFC (McClure et al., 2004) more for high-risk than low-risk decisions. If children exhibit immature risk estimation, we would expect them to exhibit less activation of OFC (associated with affective judgements) and more ACC activation (associated with detection of response conflict), compared to adults. However, if children differ from adults in the way they make rational judgements, we would expect to see less DLPFC (control) and more ACC (conflict) activation.

The second prediction was that children would differ from adults with respect to the impact of negative and positive feedback on their behavior. We expected that if children were to differ from adults in feedback processing, negative feedback would result in a different pattern of neural activity for children than for adults. This finding would be consistent with the literature showing that children fail to process negative feedback (e.g., Kirkham & Diamond, 2003) or process this feedback less efficiently (Crone & Van der Molen, 2004). We expected that adults would engage OFC (Breiter et al., 2001), VLPFC (in particular BA 47), and medial PFC when processing negative versus positive feedback (e.g., Holroyd et al., 2004; O'Doherty et al., 2003). If children experience the negative outcomes of their decisions differently from adults, we would expect to find a different pattern of OFC, VLPFC, and medial PFC activation related to loss or punishment feedback in children compared to adults.

2. Materials and methods

2.1. Participants

Twenty-six paid volunteers participated in the study. These participants consisted of 14 right-handed, healthy young adults (9 females; ages 18–26 year; mean age = 21.5 year, S.D. = 2.2) from the University of Davis and 12 right-handed, healthy children (7 females; ages 9–12 year; mean age = 11.3 year, S.D. = 0.9). The primary caregiver of each child gave informed consent. Participants' consent was obtained according to the declaration of Helsinki (BMJ 1991; 302: 1194), and the study was approved by the Internal Review Board at the University of California at Davis.

2.2. Task

Participants learned to perform the cake task prior to scanning. Each trial started with a 500 ms fixation cross, followed by a stimulus that was presented for 3500 ms, followed by a feedback stimulus that was presented for 2000 ms (see Fig. 1). The stimulus consisted of a round cake presented at the center of the screen, made up of nine wedges, each of which were either said to be chocolate-flavored (brown wedges) or strawberry-flavored (pink wedges), followed after 2000 ms by the presentation of a question mark and a piece of strawberry and chocolate cake at the foot of the cake (Fig. 1). At this point, participants were instructed to indicate by a left or right button press which flavor – strawberry or chocolate – the computer would be most likely to select, given the fact that its choice was random. To ensure that the youngest participants would understand this instruction, all participants were told to think of the computer as someone who picks a piece of cake with their eyes closed. The proportion of strawberry/chocolate wedges varied across stimuli, resulting in low-risk decisions (cakes composed of nine pieces, of which one or two pieces had contrasting flavor) and high-risk decisions (cakes composed of nine pieces, of which three or four pieces had a contrasting flavor) (see Critchley et al., 2001). Participants used the middle and index fingers of their left hand to respond. The valence of the feedback participants received always was the consequence of the combination of the computer's random choice for either strawberry or chocolate and the subject's decision. If these two matched, subjects received positive feedback (gained one point), if they did not match, subjects received negative feedback (lost one point).

2.3. Data acquisition

Over the course of three event-related scans, participants performed a total of 162 experimental trials, in which high-risk and low-risk trials were intermixed. The visual stimuli were projected onto a screen that participants could see via a mirror attached to the head coil. During each scan, subjects performed 27 trials for each risk condition (54 trials total). Across the two scans, there were equal numbers of trials of each type requiring left-button and right-button responses. The order of trial types within each scan was determined with an algorithm

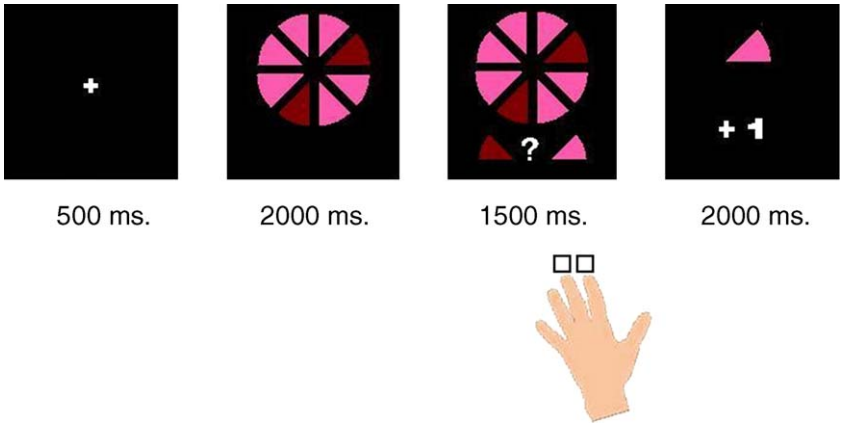

Fig. 1. Task example of a low-risk trial. Participants viewed the cue for 2000 ms, followed by the cue and target. Participants had 1500 ms to give a response, after which gain or loss feedback was presented for 2000 ms, along with the choice of the computer. Gain was indicated by +1 and loss was indicated by −1.

designed to maximize the efficiency of recovery of the BOLD response (Dale, 1999). For each condition, the order in which the stimuli were presented was pre-randomized and was the same for all participants. Periods of fixation lasting between 2 and 8 s, jittered in increments of 2 s, were interleaved with the experimental trials, as determined by the optimization program.

Scanning was performed with a standard whole-head coil on a 1.5 Tesla GE scanner at the UCD Imaging Research Center. Functional data were acquired using a gradient-echo echo-planar pulse sequence (TR = 2 s, TE = 40 ms, 24 oblique slices, 3.44 mm × 3.44 mm × 5 mm, 0 mm inter-slice gap, 240 volumes per run). The first four volumes of each scan were discarded to allow for T1-equilibration effects. High-resolution T1 weighed anatomical images were collected. Head motion was restricted using a pillow and foam inserts that surrounded the head. All children were trained in a mock scanner at the UCD Imaging Research Center prior to the actual scan.

2.4. fMRI data analysis

Data were pre-processed using SPM2 (Wellcome Department of Cognitive Neurology, London). Images were corrected for differences in timing of slice acquisition, followed by rigid body motion correction. Structural and functional volumes were spatially normalized to T1 and EPI templates, respectively. The normalization algorithm used a 12-parameter affine transformation together with a nonlinear transformation involving cosine basis functions, and resampled the volumes to 3 mm cubic voxels. Templates were based on the MNI305 stereotaxic space (Cosoco, Kollokian, Kwan, & Evans, 1997), an approximation of Talairach space (Talairach & Tourneaux, 1988). Functional volumes were spatially smoothed with an 8 mm FWHM isotropic Gaussian kernel.

Statistical analyses were performed on individual subjects' data using the general linear model in SPM2. The fMRI time series data were modeled by a series of events convolved with a canonical hemodynamic response function. The cue and feedback portions of each trial were modeled as single events in two separate models: one event-related design time-locked with the cue presentation, and one event-related model time-locked with feedback presentation. Both designs included four conditions: high-risk positive feedback, high-risk negative feedback, low-risk positive feedback, and low-risk negative feedback trials. Error trials, defined as those trials where the participant did not make the choice that was most likely to result in gain, were modeled separately and were excluded from the fMRI analyses. The correct trial functions were used as covariates in a general linear model, along with a set of cosine functions that high-pass filtered the data, and a covariate for session effects. The least-squared 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, contrasts between conditions were computed by performing one-tailed *t*-tests on these images, treating subjects as a random effect. Task-related responses were considered significant if they consisted of at least five contiguous voxels that exceeded an uncorrected threshold of $p < .001$, unless reported otherwise.

We employed a fast event-related design in the interest of keeping the study as short as possible for the children. As such, it is likely that risk estimation effects were confounded by feedback effects and vice versa. Additionally, a consequence of the way participants tend to perform the task is that negative feedback occurs more often following high-risk than following low-risk choices, and vice versa for positive feedback. Consequently, any effect of negative feedback could be influenced by the uncertainty associated with high-risk trials. For these reasons, our analyses were performed on a selection of trials, to eliminate the effect that the stimuli may have. The comparison of high- versus low-risk decisions was based only on trials followed by positive feedback, thereby holding feedback constant. Similarly, the comparison of positive and negative feedback was based on high-risk trials only, thereby holding risk anticipation constant.

ROI analyses were performed to characterize rule sensitivity of five a priori predicted regions – OFC, VLPFC (BA 47), DLPFC medial PFC/ACC, and midbrain – based on contrasts for risk-taking and feedback processing separately. Averaging the signal across voxels, as is done in ROI analyses, captures the central tendency and tends to reduce uncorrelated variance. Thus, ROI analyses have greater power than whole-brain statistical contrasts to detect effects that are present across a set of voxels. ROI analyses were performed with the Marsbar toolbox in SPM2 (Brett, Anton, Valabregue, & Poline, 2002; http://marsbar.sourceforce.net/). ROIs that spanned several functional brain regions were subdivided by sequentially masking the functional ROI with each of several anatomical Marsbar ROIs.

Two contrasts were used to generate functional ROIs: high-risk versus low-risk trials (risk analysis), and negative versus positive feedback trials (feedback analysis). These contrasts were generated from all participants with an F-threshold of $p < .001$. An ROI of ACC was identified from the risk analysis, and VLPFC and medial PFC ROIs were identified from the feedback analysis. Additionally, if an a priori ROI was active for a contrast in only one of the two age groups, this region was selected to test for significant differences between groups (DLPFC and OFC for the risk analysis, and OFC for the feedback analysis). In the case of the midbrain, it was not possible to create an ROI based on either a general or a specific contrast. As such, we created a 15 mm spherical ROI centered on MNI coordinates 0, −15, −9 [*x*, *y*, *z*], on the basis of a study by Aron et al. (2004).

For ROI analyses, effects were considered significant at an alpha of .05. Following correction for multiple comparisons across ROIs (five in total), all critical effects, i.e., Age Group × Condition interactions, survived when the *p*-value was lowered to $p < .01$ ($p = .05/5$ ROIs).

3. Results

3.1. Performance

Accuracy was defined as the percentage of choices favoring the option with the greatest likelihood of reward. On average,

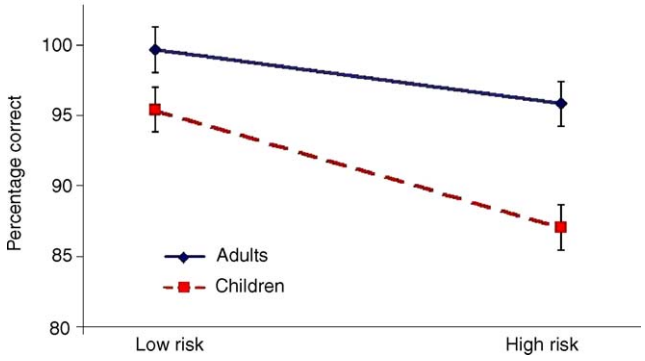

Fig. 2. Accuracy for adults and children, for high-risk and low-risk choices. Accurate responses were those trials that were most likely to result in a reward.

children and adults performed accurately on ±91% and ±98% of trials, respectively. A 2 (Age Group) × 2 (high-risk versus low-risk Condition) ANOVA resulted in a main effect of Age Group ($F(1, 24) = 14.63$, $p < .001$), showing that children made more errors than adults. There was also a main effect of Condition ($F(1, 24) = 26.19$, $p < .001$), indicating that participants made more errors on high-risk than low-risk trials. There was a marginally significant Age Group × Condition interaction ($F(1, 24) = 3.63$, $p = .07$, see Fig. 2), indicating that children were more prone than adults to make a greater number of errors on high-risk compared to low-risk trials.

3.2. ROI analyses

3.2.1. Risk estimation

We examined the effects of risk estimation in OFC and DLPFC ROIs derived from the contrast of high-risk versus low-risk in adults. Because these ROIs were defined on the basis of the fact that they were modulated by risk estimation in adults, our analyses focused on whether a similar modulation was also observed in children (Fig. 3). Both ROI analyses revealed a main effect of Condition, showing that activation was higher in DLPFC ($F(1, 24) = 7.80$, $p < .01$), and OFC ($F(1, 24) = 5.81$, $p < .05$) for high-risk compared to low-risk trials, but there were no interactions with Age Group (both F's < 1). The absence of interactions with Age Group suggests that children did not differ from adults in terms of DLPFC or OFC activation on high-risk compared to low-risk trials.

We additionally examined the effects of risk estimation in an unbiased ROI of medial PFC/ACC, derived from the F-test of high-risk versus low-risk based on all participants (Fig. 3). The 2 (Age Group) × 2 (Condition) ANOVA for medial PFC/ACC resulted in a main effect of Condition ($F(1, 24) = 14.31$, $p < .001$), demonstrating greater activation for high-risk than low-risk trials. This analysis also revealed an Age Group × Condition interaction ($F(1, 24) = 5.23$, $p < .001$). Post hoc comparisons for separate age groups showed that children activated medial PFC/ACC more for high-risk than for low-risk trials ($F(1, 11) = 10.51$, $p < .001$), whereas this difference was absent in adults ($F(1, 13) = 2.58$, $p = .13$). Thus, children showed greater modulation with respect to risk estimation in medial PFC/ACC than adults, but no age differences were observed in

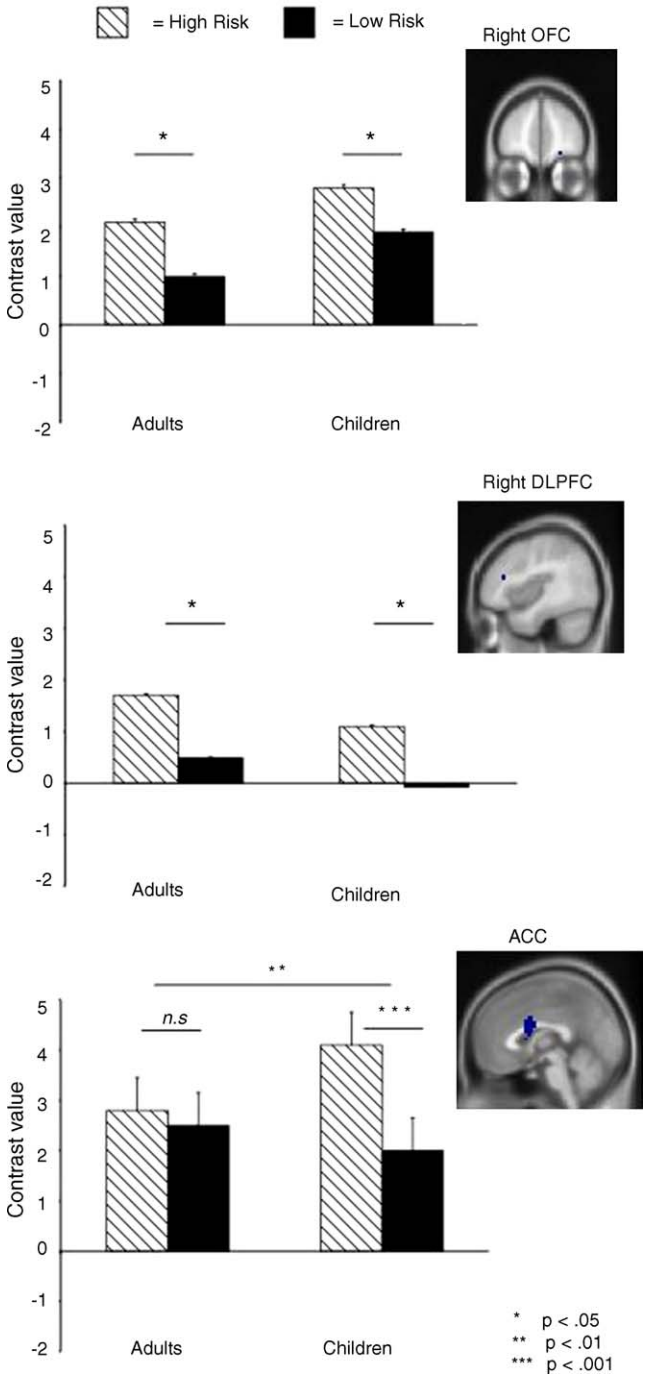

Fig. 3. Activation profiles for ROIs derived from high-risk vs. low-risk contrast. The contrast for OFC (22, 50, −14 [x, y, z]) and DLPFC (42, 30, 18 [x, y, z]) was based on a high-risk > low-risk contrast in adults, and the contrast for ACC (0, 6, 20 [x, y, z]) was based on an F-contrast based on all participants.

OFC or DLPFC. Finally, an analysis for midbrain was performed for the spherical ROI based on Aron et al. (2004). This region was not influenced by the task manipulations, all p's > .10.

3.2.2. Feedback

We performed ROI analyses on medial PFC and right VLPFC (BA 47) regions identified from an F-contrast of negative ver-

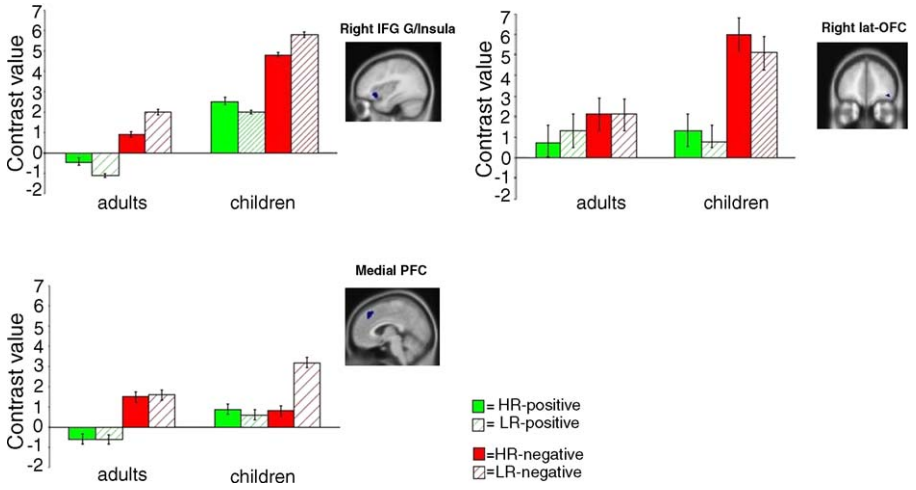

Fig. 4. Activation profiles for ROIs derived from gain vs. loss contrast. The contrasts for VLPFC (−20, 12, −20 [*x*, *y*, *z*]) and medial PFC (−22, 18, 50 [*x*, *y*, *z*]) were based on an F-contrast based on all participants. The contrast for OFC (40, 46, −12 [*x*, *y*, *z*]) was based on loss > gain in children.

sus positive feedback based on all participants. The 2 (Age Group) × 2 (Condition) ANOVA for medial PFC revealed more activity in this region for negative feedback compared to positive feedback ($F(1, 24) = 20.16$, $p < .001$), but there was no interaction with Age Group ($F < 1$). The same ANOVA for right VLPFC also showed more activity in this region for negative feedback compared to positive feedback ($F(1, 24) = 38.06$, $p < .001$), but again, there was no interaction with Age Group ($F < 1$). Thus, both children and adults recruited medial PFC and VLPFC more strongly for negative than positive feedback.

An additional ROI analysis focused on the lateral OFC ROI that was derived from the contrast of negative versus positive feedback in children only, and the analysis tested whether this region was also active in adults. The 2 (Age Group) × 2 (Condition) ANOVA resulted in main effects of Age Group, $F(1, 24) = 4.87$, $p < .05$) and Condition ($F(1, 24) = 26.00$, $p < .001$), and an Age Group × Condition interaction ($F(1, 24) = 10.15$, $p < .005$). Post hoc comparisons revealed that both adults ($F(1, 13) = 5.95$, $p < .05$) and children ($F(1, 11) = 17.82$, $p < .001$) engaged lateral OFC more strongly for negative compared to positive feedback, but that children showed more activation than adults for negative feedback ($F(1, 25) = 5.14$, $p < .05$), such that children showed a greater difference between negative and positive feedback than adults did ($F(1, 25) = 3.39$, $p = .09$).

As noted above, the feedback analysis focused on the comparison between negative and positive feedback in response to high-risk trials only. In the high-risk condition – and even more so in the low-risk condition – positive feedback was more likely to occur than negative feedback; therefore it is possible that activation for negative > positive feedback is actually related to the feedback being unexpected rather than negative. To examine this issue, we also analyzed positive and negative feedback trials following low-risk trials. If activation associated with negative feedback is related to the feedback being unexpected, then this activation should be larger following low-risk trials, because the probability of negative feedback is lowest in this condition. However, we found no differences in activation for positive and negative feedback trials followed by high-risk trials compared to positive and negative feedback trials followed by low-risk trials (all F's < 1; see Fig. 4). This result suggests that the negative feedback-related activation is in fact related to the type of feedback provided, rather than to the low frequency of this type of feedback.

3.3. Whole-brain analysis

In addition to the ROI analyses, an exploratory whole-brain analysis was performed. These analyses indicate that children and adults showed largely overlapping patterns of activation in the expected brain regions. Fig. 5 shows the glass brain images for both comparisons, and Fig. 6 shows an overlap of the two main comparisons: high-risk > low-risk, and negative feedback > positive feedback. For the high-risk > low-risk comparison, adults recruited right DLPFC (BA 9), bilateral ACC (BA 24/33), and right VLPFC (BA 47), and children recruited ACC and right VLPFC. When the statistical threshold was lowered to $p < .005$ uncorrected, adults additionally recruited right OFC (BA 11). Additional regions that were active for this contrast are reported in Table 1. The results of the reverse comparison (low-risk > high-risk), while not a focus of the current study, are also reported in Table 1.

For the negative feedback > positive feedback comparison (see Table 2), regions activated by adults and children included bilateral VLPFC (BA 47), and medial PFC/ACC (BA 6) at a threshold of $p < .001$ (uncorrected). When the threshold was lowered to $p < .005$ (uncorrected), children additionally recruited a region in right lateral OFC (BA 11). The reverse contrast (positive > negative feedback, Table 1) resulted in a network of regions, including the expected regions for reward processing: bilateral ventromedial PFC (VMPFC) and left caudate nucleus

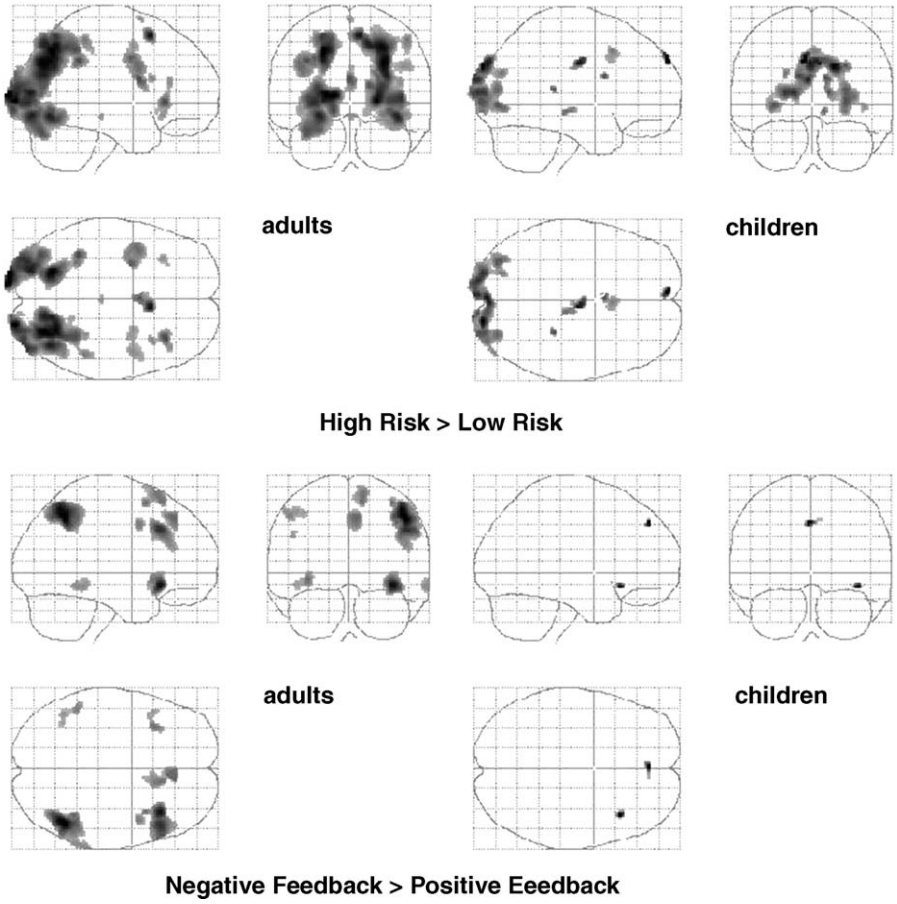

Fig. 5. Glass brain activation profiles for high-risk vs. low-risk contrast and negative vs. positive feedback trials in children and adults.

(Knutson et al., 2001; O'Doherty et al., 2003; Rogers et al., 2004). Additional activations are reported in Table 2.

4. Discussion

In this study, we used fMRI to test whether risk estimation and feedback processing are sensitive to developmental change. We performed ROI analyses to focus on several subregions of PFC that have been associated with these functions in previous studies. Specifically, we examined how OFC, ACC, DLPFC, and midbrain contributed to risk estimation, and how VLPFC and medial PFC contributed to negative feedback processing. ROI analyses revealed differences in the patterns of brain activation of children and adults in these regions of a priori interest, while the whole-brain data indicate overlapping patterns of brain activation associated with risk estimation and feedback-processing for children and adults, suggesting that both age groups performed the task in a similar way. The differences are important, as they provide us with insight into the relative contributions of different brain regions to the development of decision-making abilities. For both risk anticipation and negative feedback processing, we observed greater engagement in both ACC and lateral OFC among children than in adults. These findings suggest that children use these regions less efficiently.

4.1. Performance

Children and adults were highly comparable in terms of performance. Importantly, the groups did not differ in performance on low-risk trials, excluding the possibility that children did not understand the task instructions. Participants from both groups tended to choose the option that had the highest likelihood of resulting in reward; thus, few choices resulted in loss (see also Critchley et al., 2001). Both groups, however, made slightly more choices that were likely to result in loss on the high-risk trials, and there was a trend towards a disproportionately larger number of disadvantageous choices on high-risk trials for children compared to adults. These data suggest that, consistent with the literature, children were more prone than adults to take risks on high-risk trials (e.g., Ernst et al., 2005; Overman, 2004). Additionally, response selection demands may have been larger for children on high-risk than low-risk trials, because the perceptual conflict was larger (see Bunge, Dudukovic et al., 2002; Ridderinkhof & Van der Molen, 1995).

4.2. Risk estimation

Consistent with our expectations, right OFC (BA 11), bilateral ACC (BA 24/33) and, right DLPFC (BA 9) were engaged more strongly when participants made high-risk relative to low-

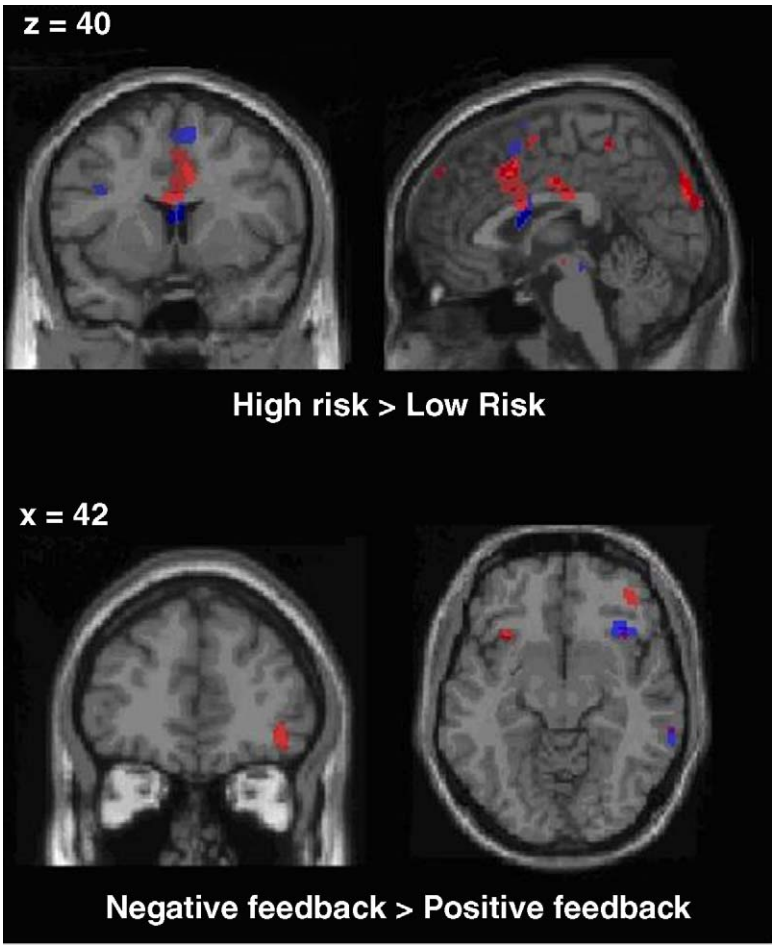

Fig. 6. Neural correlates of risk estimation (high-risk followed by positive feedback > low-risk followed by positive feedback), and negative feedback processing (high-risk followed by loss > high-risk followed by gain) in children and adults ($p < .005$). Activation for children is displayed in red, and activation for adults is displayed in blue. High-risk trials were associated with increased medial PFC/ACC activation in both children and adults. Negative feedback trials were associated with increased activation in bilateral VLPFC (BA 47), and children additionally activated right lateral OFC for negative feedback trials.

risk decisions. These findings are consistent with previous neuroimaging studies that have shown increased OFC activation when healthy adults make risky decisions (Breiter et al., 2001; Cohen et al., 2005; Ernst et al., 2005; Rogers et al., 2004; Ursu & Carter, 2005), as well as with non-human primate studies showing that OFC is important for reversal learning (Fellows & Farah, 2003, 2005; see also Maia & McClelland, 2004, 2005; Rolls, 1999; Schoenbaum, Chiba, & Gallagher, 2000), and reward expectation (Tremblay & Schultz, 1999). Contrary to expectations, an ROI analysis targeting the midbrain showed that this region was not affected by the risk manipulation. Parts of the midbrain have been associated with error prediction (Rodriguez et al., 2005), and therefore it was expected to be active in the high-risk condition. However, the results showing that midbrain was not active in this task is consistent with previous studies in which this region has been shown to be sensitive to differences in reward amount (e.g., Galvan et al., 2005), whereas in this study the reward or punishment were always associated with winning or losing one credit.

In summary, children and adults exhibited similar patterns of activation in OFC and DLPFC in relation to risk estimation, but children recruited ACC more strongly for high-risk choices relative to low-risk choices than adults did. The similarities of OFC and DLPFC activation between the groups may reflect the marginal performance differences between children and adults on this simple decision-making task. It would be helpful to manipulate risk level more extensively in future studies, for example, to include trials where the chances of obtaining reward are low but the reward itself is large (e.g., Ernst et al., 2005; Rogers et al., 2004). We predict that excessive risk-taking in children relative to adults would be associated with under-recruitment of DLPFC, a region implicated in the weighing of response options (McClure et al., 2004), and/or under-recruitment of OFC, a region implicated in the anticipation of choice outcomes (Rogers et al., 2004). It should, however, be noted that this was the first fMRI study examining decision-making in children younger than 12 years of age. We have shown that children aged 9–2 year recruit many of the same regions that have been linked to risk estimation in adults, albeit with some differences in sensitivity to uncertainty and risk. The sensitivity of these regions to different levels of uncertainty and risk in children should be validated in future research.

Within the current theoretical framework (Carter et al., 1998; Ernst et al., 2004), the finding that children showed greater mod-

Table 1
Risk estimation-elicited activation for high-risk and low-risk trials for both age groups

Contrast	Region	Talairach coordinates			Brodman area	*Z*-value	Volume* (=k_E value in SPM)	Uncorrected *p*
HR_pos > LR_pos Adults								
Medial PFC	R OFC	22	50	−14	11	2.98		<.005
	R superior frontal gyrus	8	14	56	6	4.37	57	<.001
Lateral PFC	R inferior frontal gyrus	34	28	0	47	3.83	42	<.001
	R DLPFC	42	30	18	46	3.06	160	<.005
	L medial frontal gyrus	−30	−2	38	6	3.61	110	<.001
	L DLPFC	−42	4	32	9	3.49		<.001
Cingulate cortex	L/R anterior cingulate	0	6	20	33	3.76	27	<.001
Parietal cortex	R parietal, precuneus	28	−74	34	19	4.61	2415	<.001
	R superior parietal	26	−64	46	7	4.53		<.001
	L superior parietal	−22	−68	44	7	4.67	586	<.001
	L parietal, precuneus	−20	−74	34	19	3.72		<.001
	R inferior parietal	48	−40	52	40	3.33	8	<.001
Occipital cortex	L cuneus	−14	−104	6	18	4.69	1339	<.001
	L occipital	−24	−86	8	19	4.32		<.001
	L occipital	−26	−84	−10	18	4.25		<.001
	R cuneus	22	−98	2	18	4.68	2415	<.001
HR_pos > LR_pos Children								
Medial PFC	R medial frontal gyrus	2	14	44	6	3.44	65	<.001
	L superior frontal gyrus	−8	62	36	9	4.28	24	<.001
Basal ganglia	R caudate	28	−34	12		3.69	12	<.001
Cingulate cortex	R cingulate gyrus	6	−14	34	24	4.06	47	<.001
	R cingulate gyrus	8	14	36	32	3.25	65	<.001
	L cingulate gyrus	−2	8	24	24	3.67	22	<.001
Occipital cortex	R occipital	18	−94	32	19	4.22	1389	<.001
	L occipital	−2	−90	34	19	4.08		<.001
LR_pos > HR_pos Adults								
Medial PFC	R anterior PFC	16	58	20	10	3.47	16	<.001
Lateral PFC	L insula	−36	−28	16	13	3.38	10	<.001
Parietal cortex	L inferior parietal	−66	−32	28	40	4.68	91	<.001
	R inferior parietal	58	−24	24	40	4.52	145	<.001
Temporal cortex	R middle temporal gyrus	58	−64	8	37	4.05	143	<.001
	L middle temporal gyrus	−58	−68	8	37	3.68	21	<.001
	L angular	−52	−72	32	39	3.5	71	<.001
Cingulate cortex	R anterior cingulate	12	46	−10	29	3.2	5	<.001
Somatosenosry cortex	L precentral gyrus	−24	−24	58	4	3.93	63	<.001
Occipital cortex	L superior occipital	−46	−80	34	19	3.43	71	<.001
LR_pos > HR_pos Children								
Parietal cortex	L parietal, angular	−44	−68	34	39	3.16	5	<.001

HR: high-risk, LR: low-risk, pos: positive feedback.
* Volume of activation in mm^3.

ulation of ACC for high-risk relative to low-risk choices than adults suggests that children experience greater conflict associated with high-risk trials. ACC is thought to be important for detecting response conflict, monitoring performance, and/or anticipating uncertain outcomes (Critchley, Corfield, Chandler, Mathias, & Dolan, 2000; O'Doherty et al., 2001; Van Veen & Carter, 2002). The ACC activation in the present study suggests that performance monitoring for high-risk decisions is more effortful for children compared to adults. This enhanced ACC activation is likely to reflect the fact that children have greater difficulty making the right decision under uncertainty, even if, as in the case of this simple task, they choose advantageously most of the time. Instead or additionally, greater ACC response in children may reflect less efficient performance monitoring in children, even though the high-risk versus low-risk contrast was estimated purely on the basis of correctly performed trials. Arguing against this interpretation, it has been found that the error-related negativity (a brain potential observed in the encephalogram in response to errors) becomes larger over the course of adolescence (e.g., a flanker task in Davies, Segalowitz, Gavin, 2004). This latter finding supports the view that children over-recruit ACC on this task because they have greater difficulty than adults in choosing the less risky option.

4.3. Feedback processing

Both adults and children recruited bilateral VLPFC (BA 47) for negative versus positive feedback processing. This result is consistent with previous studies on adults showing that this region is active following punishment (e.g., O'Doherty et al.,

Table 2
Feedback-elicited activation (positive > negative and negative > positive) for both age groups

Contrast	Region	Talairach coordinates			Brodman area	*Z*-value	Volume* (=k_E value in SPM)	Uncorrected *p*
Negative > positive FB Adults								
Lateral PFC	L IFG	−34	20	−6	47	3.78	78	<.001
	R IFG	36	24	−10	47	4.63	213	<.001
	R DLPFC	48	24	36	9	4.37	447	<.001
	L DLPFC	−46	18	30	9	3.32	14	<.001
	R medial frontal gyrus	36	12	58	6	3.77	22	<.001
	R inferior frontal gyrus	44	6	40	6	3.66	45	<.001
Medial PFC	R superior frontal gyrus	12	26	60	6	3.75	161	<.001
Temporal	R inferior temporal gyrus	64	−46	−12	20	3.53	54	<.001
Parietal	R inferior Parietal	46	−56	48	40	4.86	900	<.001
	L inferior Parietal	−50	−46	48	40	3.59	103	<.001
	L superior Parietal	−44	−58	50	7	3.44		<.001
Negative > positive FB Children								
Lateral PFC	R IFG	40	22	−12	47	3.59	13	<.001
Medial PFC	L medial frontal gyrus	−2	46	42	8	3.53	12	<.001
	R superior frontal gyrus	8	46	44	8	3.12		<.001
	R lateral OFC	40	46	−12	11	2.88	30	<.005
Positive > negative FB Adults								
Medial PFC	R VMPFC	4	50	−10	10	4.9	1598	<.001
	L VMPFC	−4	50	−16	11	4.67		<.001
Lateral PFC	R DLPFC	20	38	18	9	3.62	8	<.001
	L IFG	−20	12	−20	47	4.42	1097	<.001
	L insula	−34	−42	22	13	3.72	62	<.001
	L superior frontal gyrus	−22	6	68	6	3.57	28	<.001
	L medial frontal gyrus	−22	18	50	6	4.18	1079	<.001
	R medial frontal gyrus	22	28	36	8	3.72	10	<.001
Basal ganglia	L caudate	−12	22	4		3.83	1598	<.001
Somatosensory cortex	R postcentral gyrus	48	−18	44	3	4.94	3817	<.001
	R precentral gyrus	66	−4	26	6	4.88		<.001
	R postcentral gyrus	54	−18	54	3	4.8		<.001
Parietal cortex	L parietal, sub-gyral	−26	−46	56	7	3.4	16	<.001
Temporal cortex	R middle temporal gyrus	62	0	−8	21	4.47	325	<.001
	R superior temporal gyrus	68	−18	0	22	3.83		<.001
	Parahippocampal gyrus	20	−8	−24	35	4.88	3214	<.001
	L posterior cingulate	−12	−60	14	30	5.04	8525	<.001
	L middle temporal gyrus	−48	−76	10	39	4.03	101	<.001
	L superior temporal gyrus	−60	−30	14	42	4.22	260	<.001
	L parahippocampal gyrus	−22	0	−12	34	4.55	1097	<.001
	L fusiform gyrus	−44	−36	−24	36	3.4	6	<.001
Occipital cortex	L superior occipital	−40	−84	36	19	3.98	91	<.001
	L occipital	−20	−90	40	19	3.74		<.001
Positive > negative FB Children								
Lateral PFC	L medial frontal gyrus	−20	−2	38	6	3.26	6	<.001
Basal ganglia	L caudate	−6	20	8		3.66	5	<.001
Cingulate cortex	R cingulate gyrus	12	−40	44	31	3.33	10	<.001
Parietal cortex	L inferior parietal	−66	−26	32	40	3.54	26	<.001
Occipital cortex	L occipital	−10	−82	20	18	3.23	6	<.001

* Volume of activation in mm^3.

2003), and following negative feedback indicating a rule reversal (Cools, Clark, Owen, & Robbins, 2002; Cools, Clark, & Robbins, 2004). In our study, adults also exhibited activation in medial PFC/ACC (BA 6/BA 32 (dorsal) and 24 (ventral)). This finding is consistent with previous results by Holroyd et al. (2004), who have suggested that the medial PFC/ACC is active when individuals receive negative feedback as well as when they make an error. However, it should be noted that this interpretation is not universally accepted, and follow-up research by this group has failed to replicate this effect (Nieuwenhuis, Slagter, Alting von Geusau, Heslenfeld, & Holroyd, 2001). Also, the medial PFC region reported here is more anterior than the medial PFC/ACC region reported by Holroyd et al. (2004).

Children additionally recruited a region in right lateral OFC (BA 11) in response to negative versus positive feedback. In adults, this region was only slightly more active follow-

ing negative than positive feedback, broadly consistent with the view that this region is important for processing magnitude of both positive and negative outcomes (Breiter et al., 2001).There was no difference between age groups for positive feedback in this region, indicating that right lateral OFC was more strongly attuned to negative feedback for children than adults.

Lateral OFC and VLPFC (BA 11/47) are thought to process negative feedback for the purpose of adjusting behavior to optimize performance (Cools et al., 2002; Kringelbach & Rolls, 2004). In a prior developmental study in which participants had to use performance feedback to improve their performance, we examined how children adjust their behavior based on positive and negative feedback in a stimulus-response mapping task (Crone & Van der Molen, 2004). On a proportion of the trials, participants received standard response-dependent feedback (i.e., negative feedback after an incorrect response, and positive feedback after a correct response). In a second condition, intermixed with the response-dependent condition and unknown to the participants, participants received positive and negative feedback that was unrelated to their actual performance. Heart rate was measured as an index of feedback processing. In this prior study, we found that heart rate slowed following negative performance feedback, and that the amount of slowing was the same for all age groups for informative feedback. However, participants older than 12 did not show this slowing to uninformative negative feedback, whereas children younger than 12 did. These findings suggest that children under the age of 12 year have difficulty distinguishing between relevant and irrelevant feedback for the purpose of performance adjustment. Behavioral studies have consistently shown that children perform worse than adults on complex decision-making tasks (Crone et al., 2003; Kerr & Zelazo, 2004; Overman, 2004). This might be in part because they fail to distinguish between informative and uninformative feedback, or because they are less able than adults to adjust their behavior on the basis of negative feedback (Kirkham & Diamond, 2003). The enhanced activation in lateral OFC observed in children in the present study in response to negative feedback suggests that children may be generally more sensitive to negative feedback than adults, regardless of whether or not the feedback is meaningful. This finding could be further investigated in future research by manipulating the magnitude of positive and negative feedback.

5. Conclusion

These data indicate that the neural correlates of risk estimation and feedback processing are dissociable in children as well as in adults. First, it is important to note that the children recruited partially overlapping brain regions relative to adults, showing that children aged 9–12 year performed the task in a similar way to adults. The differences in the pattern of brain activity (i.e., the relative contribution of the brain regions involved) that were found between 9–12-year-olds and young adults, for lateral OFC and ACC in particular, contribute to our understanding of the role that these different processes play in the development of decision-making over childhood.

Acknowledgements

This research was funded by NSF grant 00448844. We would like to thank Maurits van der Molen, Richard Ridderinkhof, Stefan Ursu, Mariëtte Huizinga, and Sander Nieuwenhuis for helpful comments, Sarah Donohue for assistance with subject recruitment, and Michael Souza for his assistance with the ROI analyses.

References

Aron, A. R., Shohamy, D., Clark, J., Myers, C., Gluck, M. A., & Poldrack, R. A. (2004). Human midbrain sensitivity to cognitive feedback and uncertainty during classification learning. *Journal of Neurophysiology*, *92*, 1144–1152.

Barcelo, F. (1999). Electrophysiological evidence of two different types of error in the Wisconsin Card Sorting Test. *Cognitive Neuroscience*, *10*, 1299–1303.

Barraclough, D. J., Conroy, M. L., & Lee, D. (2004). Prefrontal cortex and decision making in a mixed-strategy game. *Nature Neuroscience*, *7*, 404–410.

Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*, *50*, 7–15.

Bechara, A., Damasio, H., Tranel, D., & Anderson, S. W. (1998). Dissociation of working memory from decision-making within the human prefrontal cortex. *The Journal of Neuroscience*, *18*, 428–437.

Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1997). Deciding advantageously before knowing the advantageous strategy. *Science*, *275*, 1293–1295.

Bechara, A., Tranel, D., & Damasio, H. (2000). Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. *Brain*, *123*, 2189–2202.

Bechara, A., Tranel, D., Damasio, H., & Damasio, A. R. (1996). Failure to respond autonomically to anticipated future outcomes following damage to the prefrontal cortex. *Cerebral Cortex*, *6*, 215–225.

Barcelo, F., & Knight, R. T. (2002). Both random and perseverative errors underlie WCST deficits in prefrontal changes. *Neuropsychologia*, *40*, 349–356.

Bjork, J. M., Knutson, B., Fong, G. W., Caggiano, D. M., Bennett, S. M., & Hommer, D. W. (2004). Incentive-elicited brain activation in adolescents: Similarities and differences from young adults. *Journal of Neuroscience*, *24*, 1793–1802.

Breiter, H. C., Aharon, I., Kahneman, D., Dale, A., & Shizgal, P. (2001). Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron*, *30*, 619–639.

Brett, M., Anton, J.-L., Valabregue, R., Poline, J.-B. (2002). Region of interest analysis using an SPM toolbox. Eight International Conference on Functional Mapping of the Human Brain, June 2–6, Sendai, Japan. *NeuroImage*, 16, 2 (abstract).

Bunge, S. A., Dudukovic, N. M., Thomason, M. E., Vaidya, C. J., & Gabrieli, J. D. E. (2002). Immature frontal lobe contributions to cognitive control in children: Evidence from fMRI. *Neuron*, *33*, 301–311.

Bunge, S. A., Hazeltine, E., Scanlon, M. D., Rosen, A. C., & Gabrieli, J. D. (2002). Dissociable contributions of prefrontal and parietal cortices to response selection. *Neuroimage*, *17*, 1562–1571.

Bush, G., Vogt, B. A., Holmes, J., Dale, A. M., Greve, D., Jenike, M. A., et al. (2002). Dorsal anterior cingulate cortex: A role in reward-based decision making. *Proceedings of the National Academy of Sciences U S A*, *99*, 523–528.

Carter, C., Braver, T. S., Barch, D. M., Botvinick, M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the on-line monitoring of performance. *Science*, *280*, 747–749.

Critchley, H. D., Corfield, D. R., Chandler, M. P., Mathias, C. J., & Dolan, R. J. (2000). Cerebral correlates of autonomic cardiovascular arousal: A

functional neuroimaging investigation in humans. *Journal of Physiology*, 259–270.

Cools, R., Clark, L., Owen, A. M., & Robbins, T. W. (2002). Defining the neural mechanisms of probabilistic reversal learning using event-related functional magnetic resonance imaging. *Journal of Neuroscience*, *22*, 4563–4567.

Cools, R., Clark, L., & Robbins, T. W. (2004). Differential responses in human striatum and prefrontal cortex to changes in object and rule relevance. *The Journal of Neuroscience*, *24*, 1129–1135.

Casey, B. J., Cohen, J. D., Jezzard, P., Turner, R., Noll, D. C., Trainor, R. J., et al. (1995). Activation of prefrontal cortex in children during a nonspatial working memory task with functional MRI. *NeuroImage*, *2*, 221–229.

Casey, B. J., Davidson, M., & Rosen, B. (2002). Functional magnetic resonance imaging: Basic principles of an application to developmental science. *Developmental Science*, *5*, 301–309.

Casey, B. J., Giedd, J. N., & Thomas, K. M. (2000). Structural and functional brain development and it's relation to cognitive development. *Biological Psychology*, *54*, 241–257.

Cohen, M. X., Heller, A. S., & Ranganath, C. (2005). Brain connectivity with anterior cingulate and orbitofrontal cortices during decision-making. *Cognitive Brain Research*, *23*, 61–70.

Cocosco, C. A., Kollokian, V., Kwan, R. K. S., & Evans, A. C. (1997). Brain Web: Online interface to a 3D MRI simulated brain database. *Neuroimage*, *5*, S425.

Critchley, H. D., Mathias, C. J., & Dolan, R. J. (2001). Neural activity in the human brain relating to uncertainty and arousal during anticipation. *Neuron*, *29*, 537–545.

Critchley, H. D., Mathias, C. J., Josephs, O., O'Doherty, J., Zanini, S., Dewar, B., et al. (2003). Human cingulate cortex and autonomic control: Converging neuroimaging and clinical evidence. *Brain*, *126*, 2139–2152.

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

Crone, E. A., Van Veen, F. M., Van der Molen, M. W., Van Beek, B., Somsen, R. J. M., & Jennings, J. R. (2003). Cardiac concomitants of feedback processing. *Biological Psychology*, *64*(1–2), 143–156.

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

Davies, P. L., Segalowitz, S. J., & Gavin, W. J. (2004). Development of error-monitoring event-related potentials in adolescents. *Annals of the New York Academy of Sciences*, *1021*, 324–328.

Diamond, A. (2002). Normal development of prefrontal cortex from birth to young adulthood: Cognitive functions, anatomy, and biochemistry. In D. T. Stuss & R. T. Knight (Eds.), *Principles of Frontal Lobe Function* (pp. 466–503). London: Oxford University Press.

Elliott, R., Friston, K., & Dolan, R. (2000). Dissociable neural responses in human reward systems. *Journal of Neuroscience*, *20*, 6159–6165.

Ernst, M., Nelson, E. E., Jazbec, S., McClure, E. B., Monk, C. S., Leibenluft, E., et al. (2005). Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. *NeuroImage*, *25*, 1279–1291.

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

Fellows, L. K., & Farah, M. J. (2003). Ventromedial frontal cortex mediates affective shifting in humans: Evidence from a reversal learning paradigm. *Brain*, *126*, 1830–1837.

Fellows, L. K., & Farah, M. J. (2005). Different underlying impairments in decision-making following ventromedial and dorsolateral frontal lobe damage in humans. *Cerebral Cortex*, *15*, 58–63.

Galvan, A., Hare, T. A., Davidson, M., Spicer, J., Glover, G., & Casey, B. J. (2005). The role of ventral frontostriatal circuitry in reward-based learning in humans. *The Journal of Neuroscience*, *25*, 8650–8656.

Gehring, W. J., & Knight, R. T. (2000). Prefrontal-cingulate interactions in action monitoring. *Nature Neuroscience*, *3*, 516–520.

Happeney, K. H., Zelazo, P. D., & Stuss, D. T. (2004). Development of orbitofrontal function: Current themes and future directions. *Brain and Cognition*, *55*, 1–10.

Holroyd, C. B., Nieuwenhuis, S., Mars, R. B., & Coles, M. G. H. (2004). Amterior cingulated cortex, selection for action and error processing. In M. I. Posner (Ed.), *Cognitive Neuroscience of Attention* (pp. 219–231). New York: Guilford Press.

Hooper, C., Luciana, M., Conklin, H. M., & Yarger, R. (2004). Adolescents' performance on the Iowa Gambling Task: Implications for the development of decision-making and ventromedial prefrontal cortex. *Developmental Psychology*, *40*, 1148–1158.

Kahn, I., Yeshurun, Y., Rotshtein, P., Fried, I., Ben-Bashat, D., & Hendler, T. (2002). The role of the amygdala in signaling prospective outcome of choice. *Neuron*, *33*, 983–994.

Kerr, A., & Zelazo, P. D. (2004). Development of 'hot' executive function. The children's gambling task. *Brain and Cognition*, *55*, 148–157.

Kirkham, N. Z., & Diamond, A. (2003). Sorting between theories of perseveration: Performance in conflict tasks requires memory, attention and inhibition. *Developmental Science*, *6*, 474–476.

Klingberg, T., Forssberg, H., & Wessterberg. (2002). Increased brain activity in frontal and parietal cortex underlies the development of visuo-spatial working memory capacity during childhood. *Journal of Cognitive Neuroscience*, *14*, 1–10.

Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *The Journal of Neuroscience*, *21* (RC159 1 of 5).

Kringelbach, M. L., & Rolls, E. T. (2004). The functional neuroanatomy of the human orbitofrontal cortex: Evidence from neuroimaging and neuropsychology. *Progress in Neurobiology*, *72*, 341–372.

Maia, T. V., & McClelland, J. L. (2004). A reexamination of the evidence for the somatic marker hypothesis: What participants really know in the Iowa gambling task. *Proceedings of the National Academy of Sciences of the United States of America*, *101*, 16075–16080.

Maia, T. V., & McClelland, J. L. (2005). The somatic marker hypothesis: Still many questions but no answers. Response to Bechara et al. *Trends in Cognitive Sciences*, *9*, 162–164.

Manes, F., Sahakian, B., Clark, L., Rogers, R., Antoun, N., Aitken, M., et al. (2002). Decision-making following damage to the prefrontal cortex. *Brain*, *125*, 624–639.

May, J. C., Delgado, M. R., Dahl, R. E., Stenger, V. A., Ryan, N. D., Fiez, J. A., et al. (2004). Event-related functional magnetic resonance imaging of reward-related brain circuitry in children and adolescents. *Biological Psychiatry*, *55*, 359–366.

McClure, S. M., Laibson, D. I., Loewenstein, G., & Cohen, J. D. (2004). Separate neural systems value immediate and delayed monetary rewards. *Science*, *306*, 503–507.

Mischel, W., Shoda, Y., & Rodriguez, M. (1989). Delay of gratification in children. *Science*, *244*, 933–938.

Nieuwenhuis, S., Slagter, H. A., Alting von Geusau, N. J., Heslenfeld, D. J., & Holroyd, C. B. (2001). Knowing good from bad: Differential activation of human cortical areas by positive and negative outcomes. *European Journal of Neuroscience*.

O'Doherty, J., Critchley, H., Deichmann, R., & Dolan, R. J. (2003). Dissociating valence of outcome from behavioral control in human orbital and ventral prefrontal cortices. *Journal of Neuroscience*, *23*, 7931–7939.

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

Overman, W. H. (2004). Sex differences in early childhood, adolescence, and adulthood, on tasks that rely on orbitofrontal cortex. *Brain and Cognition*, *55*, 134–147.

Paulus, M. P., Hozack, N., Frank, L., & Brown, G. G. (2002). Error rate and outcome predictability affect neural activation in prefrontal cortex and anterior cingulate during decision-making. *NeuroImage*, *15*, 836–846.

Paulus, M. P., Hozack, N., Zauscher, B., McDowell, J. E., Frank, L., Brown, G. G., et al. (2001). Prefrontal, parietal, and temporal cortex networks underlie decision-making in the presence of uncertainty. *NeuroImage*, *13*, 91–100.

Prencipe, A., & Zelazo, P. D. (2005). Development of affective decision making for self and other: Evidence for the integration of first- and third-person perspectives. *Psychological Science*, *16*, 501–505.

Ridderinkhof, K. R., & Van der Molen, M. W. (1995). A psychophysiological analysis of developmental differences in the ability to resist interference. *Child Development*, *66*, 1040–1056.

Rodriguez, P. F., Aron, A., & Poldrack, R. (2005). Ventral-striatal/nucleus-accumbens sensitivity to prediction errors during classification learning. *Human Brain Mapping*, *9* (E-pub ahead of print).

Rogers, R., Everitt, B. J., Baldacc hino, A., Blackshaw, A. J., Swainson, R., Wynne, K., et al. (1999). Dissociable deficits in decision making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to the prefrontal cortex, and tryptophan depleted normal volunteers: Evidence for monoaminergic mechanisms. *Neuropharmacology*, *20*, 322–339.

Rogers, R. D., Ramnani, N., Mackay, C., Wilson, J. L., Jezzard, P., Carter, C. S., et al. (2004). Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. *Biological Psychiatry*, *55*, 594–602.

Rolls, E. T. (1999). *The Brain and Emotion*. Oxford: Oxford University Press.

Rolls, E. T. (2000). The orbitofrontal cortex and reward. *Cerebral Cortex*, *20*, 284–294.

Rowe, J. B., Toni, I., Josephs, O., Frackowiak, R. S., & Passingham, R. E. (2000). The prefrontal cortex: Response selection or maintenance within working memory? *Science*, *5471*, 1656–1660.

Schoenbaum, G., Chiba, A. A., & Gallagher, M. (2000). Changes in functional connectivity in orbitofrontal cortex and basolateral amygdala during learning and reversal training. *Journal of Neuroscience*, *20*, 5179–5189.

Steinberg, L. (2005). Cognitive and affective development in adolescence. *Trends in Cognitive Sciences*, *9*, 69–74.

Talairach, J., & Tourneaux, P. (1988). *Co-Planar Stereotactic Atlas of the Human Brain*. New York: Thieme.

Thompson, C., Barresi, J., & Moore, C. (1997). The development of future-oriented prudence and altruism in preschoolers. *Cognitive Development*, *12*, 199–212.

Thomas, K. M., King, S. W., Franzen, P. L., Welsh, T. F., Berkowitz, A. L., Noll, D. C., et al. (1999). A developmental functional MRI study of spatial working memory. *NeuroImage*, *10*, 327–338.

Tremblay, L., & Schultz, W. (1999). Relative reward preference in primate orbitofrontal cortex. *Nature*, *398*, 704–708.

Ursu, S. T., & Carter, C. S. (2005). Outcome representations, counterfactual comparisons and the human orbitofrontal cortex: Implications for neuroimaging studies of decision-making. *Cognitive Brain Research*, *23*, 51–60.

Van der Molen, M. W., & Molenaar, P. C. M. (1994). Cognitive psychophysiology: A window to cognitive development and brain maturation. In G. Dawson & K. W. Fisher (Eds.), *Human Behavior and the Developing Brain*. New York: Guilford Publications.

Van Veen, V., & Carter, C. S. (2002). The anterior cingulate as a conflict monitor: fMRI and ERP studies. *Physiology and Behavior*, *77*, 477–482.

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