Behavioral/Systems/Cognitive

Developmental Differences in Posterior Mesofrontal Cortex Recruitment by Risky Rewards

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Might increased risk taking in adolescence result in part from underdeveloped conflict-monitoring circuitry in the posterior mesofrontal cortex (PMC)? Adults and adolescents underwent functional magnetic resonance imaging during a monetary game of "chicken." As subjects watched ostensible winnings increase over time, they decided when to press a button to bank their winnings, knowing that if they did not stop pursuing money reward before a secret varying time limit, they would "bust" and either lose the money accrued on the current trial (low-penalty trials) or forfeit trial winnings plus a portion of previous winnings (high-penalty trials). Reward accrual at risk of low penalty (contrasted with guaranteed reward) activated the PMC in adults but not in adolescents. Across all subjects, this activation (1) correlated positively with age but negatively with risk exposure and (2) was greater when subjects busted on the previous low-penalty trial. Reward accrual at risk of high penalty was terminated sooner and recruited the PMC in both adults and adolescents when contrasted with guaranteed reward. Predecision PMC activation in the high-penalty trials was significantly reduced in trials when subjects busted. These data suggest that (1) under threat of an explicit severe penalty, recruitment of the PMC is similar in adolescents and adults and correlates with error avoidance, and (2) when potential penalties for a rewarding behavior are mild enough to encourage some risk taking, predecision PMC activation by a reward/risk conflict is sensitive to previous error outcomes, predictive of risk-aversive behavior in that trial, and underactive in adolescents.

Key words: **adolescence; development; reward; risk taking; decision making; cortex**

Introduction

Adolescents are risk takers (Baumrind, 1987; Shedler and Block, 1990; Spear, 2000) who suffer elevated mortality from behavioral causes (Centers for Disease Control and Prevention; www.cdc.gov). We sought to ascertain whether adolescents show reduced risk-elicited recruitment of behavior-monitoring circuitry in the posterior mesofrontal cortex (PMC). The PMC encompasses the supragenual anterior cingulate cortex (Brodmann's area 24) and extends superiorly and posteriorly to Brodmann's areas 8, 6, and 32. Because of its abundant corticocortical and corticolimbic connections (Paus, 2001), the PMC is extensively recruited during preresponse conflict (Ridderinkhof et al., 2004), error monitoring (Ridderinkhof et al., 2004; Ullsperger and von Cramon, 2004), and error avoidance (Magno et al., 2006).

The cortical gray matter/white matter ratio decreases from early adolescence to adulthood (for review, see Durston et al., 2001; Casey et al., 2005), with reductions in gray matter (Sowell et al., 1999) and cortical synaptic (Huttenlocher and Dabholkar, 1997) density and increases in myelination (Barnea-Goraly et al., 2005). These maturational changes occur more slowly in the frontal cortex compared with other cortical regions. Because frontocortical gray matter development has been linked to improved cognitive functioning (Shaw et al., 2006) and increasingly focal activations by cognitive tasks (Durston and Casey, 2006), some portion of increased adolescent risk-taking may arise from incomplete maturation of cortical regions that control behavior.

Many risky behaviors, such as unprotected sexual activity, street racing, and drug use, have potential for both reward and punishment, in which the likelihood and severity of a bad outcome often rises with the magnitude of potential benefit. To determine how the PMC of adults and adolescents responds to this contingency, we introduce here a monetary game of "chicken," in which the probability of a negative outcome increased with reward magnitude. Subjects pressed a button to accumulate money but were required to voluntarily stop reward accrual before a covert varying time limit was reached. Failure to stop reward accrual before the secret time limit resulted in either forfeiture of the winnings of that trial or forfeiture of trial winnings plus some previous winnings. This task was designed to model how adolescents typically make risky decisions when potential reward is explicit but specific odds of a bad outcome are uncertain.

Because regions of the PMC recruited by predecision conflict overlap with regions recruited by response error feedback (Ridderinkhof et al., 2004), our task exploited the human tendency to preserve small gains by avoiding risky alternatives (Kahneman

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and Tversky, 1979) to probe predecision conflict while suppressing individual differences in (1) the incidence of errors (that would complicate interpretation of between-subject differences in PMC activation), (2) the timing of motor behavior, or (3) the overall task winnings (that would frame outcomes of individual trials differently across subjects). We hypothesized that (1) the PMC would be activated during reward accrual at risk of penalty (contrasted with safe reward trials in which there is no conflict or risk); (2) the PMC signal would increase predecision; (3) the risk-elicited PMC activation would correlate negatively with actual duration of risk-taking; and (4) adolescents would show reduced PMC activation during risky reward accrual compared with adults.

Materials and Methods

All procedures were reviewed and approved by the Institutional Review Board of the National Institute on Alcohol Abuse and Alcoholism.

Subjects

Twenty young adults age 23–33 (10 male; mean age, 28.5 ± 3.2) and 20 adolescents age 12–17 (10 male; mean age, 14.3 + 1.6) participated with written informed consent. All subjects were right-handed. Subjects were free of any physical or mental illness, as determined by structured clinical interviews for DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders IV*) and a physical exam.

Risk-taking task

Stimuli were projected onto a screen placed at the foot of the magnetic resonance imaging (MRI) scanner bed and were viewed using a mirror mounted on the head coil. Risk-taking task (RTT) trials were a fixed 14 s in duration and were presented continuously with no intertrial interval. In each trial, subjects were required to press a button on a small button box twice per trial (Fig. 1). A counter reading "Total Earnings: $x.xx" in black letters was continuously displayed in the upper middle of the screen that summarized the subject's cumulative winnings across trials. The background color of the screen (white, green, yellow, or red) signified each of four trial types of the task (control, nonrisk reward, low-risk reward, and high-risk reward, respectively). This color scheme, which reflected the relative potential penalties for proceeding at a traffic light, was intended to facilitate task comprehension by children in future comparisons across clinical groups. Trial order was pseudorandomly determined and identical for every subject. In each of three scanning runs, subjects completed eight trials of each type (total $n = 24$ per trial type). Trial events and behavioral contingencies were as follows.

Motor control trials. The trial began with the cumulative earnings counter in black characters on an all white background. Two seconds into the trial, a dollar sign "$" appeared at the bottom middle of the screen, at which time subjects were instructed to press the response button. After responding, "Earnings this trial: $0.00" was displayed in the center of the screen, and the $ disappeared from the lower-middle half of the screen. Four to 10 s later (a pseudorandomized even distribution of 4, 6, 8, or 10 s after presentation of the $ cue), the word "press" appeared in the same place as the original dollar sign, at which time the subject was instructed to press the button the second time. The second press caused the word press to disappear. Twelve seconds after trial onset, the words "No earnings this trial" appeared in the middle of the screen to confirm no winnings in the control trial.

No-penalty trials. The trial began with the cumulative earnings counter in black characters on an all green background (Fig. 1). Two seconds later, a $ cue appeared at the bottom middle of the screen, at which time subjects were instructed to press the response button. After responding, the subject began accruing earnings. This was indicated in two ways. First, the "Earnings this trial:" money counter was displayed in the center of the screen, and just below it, a numerical counter began sequentially advancing like the display on a gasoline pump. The rate of earnings accumulation per second accelerated across the trial in an exponential function. Second, a horizontal bar positioned to the lower left of the screen simultaneously appeared and lengthened in a rightward direction

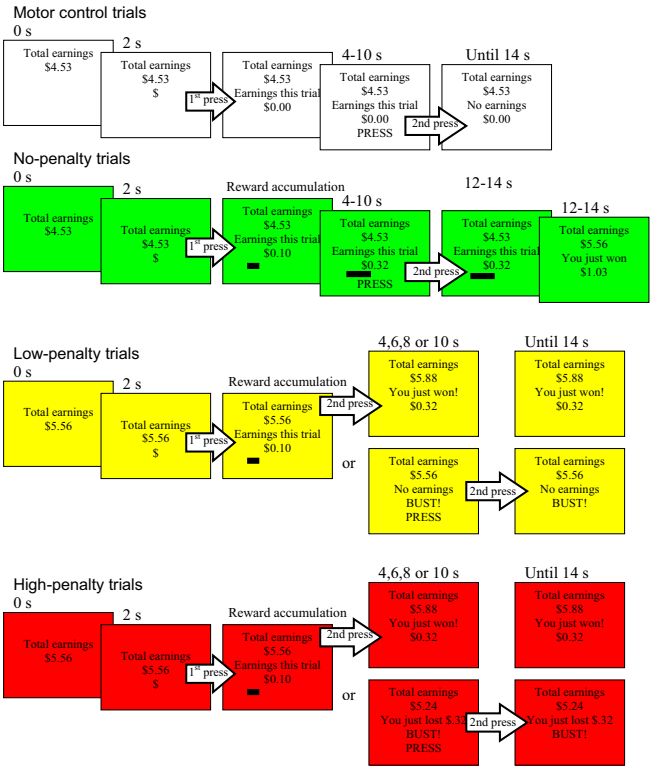

Figure 1. Diagram of the RTT. The RTT presented subjects with four types of pseudorandomly presented trials (duration 14 s; $n = 24$ each). In motor control trials, subjects pressed on cue twice (to the $ cue and to the word press) for no incentive. In no-penalty trials, subjects began accruing money after pressing in response to the $ cue and accumulated winnings throughout the trial with no chance of penalty. In low-penalty trials, each trial was assigned a secret time limit of either 4, 6, 8, or 10 s after the $ cue, during which the subject was allowed to accumulate money. If the subject voluntarily stopped reward accrual before the secret time limit (top bifurcated outcome), he or she added accrued trial winnings to total winnings. If he or she failed to stop reward accrual before the secret time limit (bottom bifurcated outcome), he or she busted and forfeited all winnings in that trial and was instructed to press a second time. In high-penalty trials, subjects were also required to terminate reward accrual before the secret varying time limit, but busts resulted in subtraction of trial-accumulated winnings from previous winnings.

toward the middle of the screen in proportion to the accumulated earnings. This bar was added to enhance the salience of the reward. Four to 10 s later (a pseudo-randomized even distribution of 4, 6, 8, or 10 s after presentation of the $ cue), the word press appeared in the same place as the original dollar sign, at which time the subject was to press the button the second time. The second press caused the word press to disappear. Meanwhile, the money counter and animated bar continued advancing throughout the trial, until 10 s after trial onset, at which time the cumulative earnings counter was increased by the earnings of that trial, and the words, "You just won $x.xx" appeared below the cumulative counter. An attentive subject who pressed the button immediately after appearance of the $ cue could win a maximum of $1.06 across the 10 s of potential accrual time. Conversely, failure to press to the $ cue resulted in no winnings. There was no risk of loss of any accrued winnings.

Low-penalty trials. The screen was drawn with the cumulative earnings counter in black characters on a yellow background. Two seconds later, a $ cue appeared at the bottom middle of the screen, at which time subjects were instructed to press the response button. After registering this press, the subject began accruing earnings as in the no-penalty trials: (1) the "Earnings this trial:" money counter was continually displayed in the center of the screen; (2) just below it, the numerical counter was sequentially advancing like the display on a gas pump; (3) the rate of earnings advancement accelerated across the seconds of the trial in an exponential function; (4) a horizontal bar positioned to the lower left of the screen lengthened in a rightward direction toward the middle of the screen in

proportion to the accumulated earnings. However, the duration during which the subject was allowed to accrue winnings was variable and covert. To earn money in the low-penalty trial, the subject was required to voluntarily press the button a second time to terminate accrual of winnings before a secret time limit was reached. The secret time limit ranged from 4 to 10 s after the presentation of the $ cue, with time limits having the same even distribution of delay as "press" cues in the control and no-penalty reward trials. If the subject emitted his/her second button press before the secret time limit of that trial, accrual stopped, the animated bar stopped lengthening, and the cumulative earnings counter advanced to reflect the winnings of that trial. If the covert time limit was reached without the subject having freely pressed the button a second time, the subject "busted" and won no money for the trial. The words "No earnings this trial" and "BUST" appeared in place of the trial counter, along with the word press to elicit a second motor response. The second press caused the word press to disappear. The cumulative earnings counter did not change value after a bust.

High-penalty trials. The screen was drawn with the cumulative earnings counter in black characters on a red background. This trial type was identical to the low-penalty trial type in all respects with one difference. Whereas busts in the low-penalty reward trials simply resulted in no winnings for that trial, if a subject busted in the high-penalty reward trial (by not pressing the button a second time before the covert time limit), he or she would have the winnings on the trial counter at the time of the bust deducted from previous cumulative winnings on the total earnings counter. This represented a parametric doubling of the bust penalty.

Prescan task training

To avoid confounds by possible developmental differences in learning the operational contingencies of the four types of task trials, subjects were trained in the task before scanning. Each subject was read an instruction script (supplemental material, available at www.jneurosci.org) that explicitly explained the contingencies of all four screen color-coded trial types. Subjects were not told of the specific distribution of possible bust times (4–10 s). Subjects then performed a practice session with the task that enabled detection of possible bust times. All subjects busted at least once in the practice session. Finally, to enhance the salience of the task, subjects were shown an envelope stuffed with cash and were reminded that they would actually receive their task winnings out of the envelope after scanning.

Functional MRI acquisition

Imaging was performed using a 3T General Electric (Milwaukee, WI) MRI scanner and a standard quadrature head coil. We collected 24 3.8-mm-thick axial slices sequentially from inferior to superior, with a 1 mm gap. This montage encompassed the upper half of the cerebellum up through the entire cerebrum. In-plane resolution was 3.75×3.75 mm. Functional scans were acquired using a T2*-sensitive echoplanar sequence [repetition time (TR), 2000 ms; echo time (TE), 40 ms; and flip angle = 90°]. Functional scanning was completed in three runs, with a 2–3 min break between each run during scanning protocol setup. To allow for signal stabilization before events of each run, six dummy acquisitions were obtained before task onset. A total of 690 volumes were collected. Structural scans were acquired using a T1-weighted magnetization-prepared rapid acquisition gradient echo sequence (TR, 100 ms; TE, 7 ms; flip angle, 90°) that facilitated localization and coregistration of functional data. To minimize head movement during task performance, each subject's head was restrained with a Vacu-Fix System deflateable head motion restraint (S&S X-Ray Products, Houston, TX).

Functional MRI analysis

Preprocessing. Analyses of the blood oxygen-level dependent (BOLD) signal were conducted using Analysis of Functional Neural Images (AFNI) software. Echoplanar image volumes were preprocessed in AFNI as follows: (1) voxel time series were interpolated to correct for nonsimultaneous slice acquisition within each volume (using sinc interpolation and the most inferior slice as a reference); (2) volumes were concatenated across the three task runs; (3) volumes were corrected for head motion in three-dimensional space. The third from final volume collected during the RTT task was used as the reference volume. Motion-correction estimates indicated that no participant's head moved >1.5 mm in any dimension from one volume acquisition to the next. Across the entire task, no participant's head moved >3 mm overall in any dimension. Visual inspection of each subject's reconstructed brain images across the time series confirmed minimal residual head motion after the volume correction. We applied a 4 mm full-width at half-maximum isotropic smoothing kernel. Finally, a despiking algorithm was applied to the data on a voxelwise basis to smooth out deviations in signal >2.5 SD from the mean, followed by a bandpass filtering algorithm that smoothed cyclical fluctuations in signal that were not temporally indicative of a hemodynamic response (either >0.011/s or <0.15/s).

Individual subject statistical maps. The multiple regression model featured six trial-wise regressors of interest (motor control, no-penalty, low-penalty wins, low-penalty busts, high-penalty wins, high-penalty busts). These were convolved with a gamma variate function that modeled a prototypical hemodynamic response time locked to the presentation of the cue ($) which elicited the first press of a trial (the onset of reward accrual in no-penalty, low-penalty, and high-penalty trials) and lasted 14 s. Wins and busts for each of the low- and high-penalty trial classes were entered into the model as separate regressors to test for differential activation between trials with successful versus bust outcomes. Event-related activations were isolated by inclusion of additional covariate regressors modeling residual motion after volume correction and baseline and linear trends for each of the three runs.

Event-related modeling was limited to a single event (the $ cue) in each trial because of physiological and conceptual considerations of the temporal configuration of the task. Notably, reward-termination presses in penalty trials typically occurred within a narrow range of 3–5 s after the response to begin money accrual, too soon to engender a distinct hemodynamic response separable from that initiated predecision. Second, the task did not feature a discrete "feedback" event that was both informative and temporally similar across trial types. Subjects were trained to know likely consequences of motor-control and no-penalty trials at trial onset, whereas in penalty trials, bust versus successful outcome notifications were temporally contiguous with the predecision period.

Activations were defined by four linear contrasts (LCs) of BOLD activity between opposing trial types as follows. First, to examine activation by the prospect of an instrumental response for reward itself (with no probability of penalty), we contrasted no-penalty (reward) trials from motor control trials. Second, to examine activation by the addition of a potential low-magnitude penalty (not winning any money on the trial) for trying to accumulate money, we contrasted low-penalty trials with no-penalty trials. Third, to examine activation by the addition of a potential high-magnitude penalty for trying to win excess money (not winning plus subtracting current trial winnings from previous winnings), we contrasted high-penalty trials with no-penalty trials. Finally, to examine the effect of doubling the magnitude of potential aversive outcomes while pursuing reward, we contrasted high-penalty trials with low-penalty trials.

Groupwise statistical maps. For each subject, the anatomical maps of *t* statistics representing each of these LCs were transformed into *z* scores and warped into common stereotactic (Talairach) space. Individual warped maps were then combined into a group map using a voxelwise random-effects analysis. For each contrast, activations were identified using AFNI plug-in programs AlphaSim, 3dmerge, and 3dExtrema, in which (1) voxels each exceeded a statistical significance threshold of $p < 0.0001$, (2) activated voxels were part of a contiguous cluster of sufficient size to obtain a family-wise corrected type I error rate ≥0.05 using Monte Carlo simulation, and (3) activated voxels represent the peak activation within a 20 mm radius.

Group Difference Maps. We restricted our consideration of group activation differences to voxels within the PMC and mesial orbitofrontal cortex (mOFC), regions extensively shown to be involved in reward and/or risk conflicts in laboratory tasks (Bechara et al., 2000; Ridderinkhof et al., 2004). We calculated a voxelwise statistical map of the differences in activation between adolescents and adults. First, individual subject time series data were normalized by conversion to percentage of signal change. Second, we performed voxelwise *t* tests of the event-related β coefficients calculated from the general linear model (using contrasts

of the regression model). We applied a false discovery rate detection (ANFI plug-in 3dFDR) to mOFC and PMC voxels ($n = 2412$), removing from consideration voxels >5% probability of a false positive group difference.

Volume of interest analysis of signal change in the PMC. To characterize differences between adolescents and adults in BOLD signal change in the PMC, we drew a volume of interest (VOI) mask in the midsaggital plane that encompassed the bulk of the activation maxima of predecision conflict activation as diagrammed in Ridderinkhof et al. (2004) and extended the mask laterally for a width of 5 mm (for mask diagram, see Fig. 5*B*, inset). Signal data were extracted from the time series as follows: (1) signal at each voxel was converted to a percentage of signal change from the mean for that voxel across the entire time series; (2) signal was averaged by trial type and spatially translated into Talairach space; (3) signal change values were calculated from the average across the VOI mask at the acquisition observed to be the peak of the hemodynamic response after the event of interest; (4) group differences in percentage of signal change across averaged trials were compared using ANOVA and *t* tests. In these analyses, age group (two levels, adolescents and adults) was a between-subject factor, and penalty magnitude (two levels, low and high) and time (six levels, postbaseline acquisitions across the trial) were within-subject factors.

Behavior analysis

In each trial type, we assessed attention to (and motivation by) the task as the mean reaction time (RT) to respond to the $ cue in each of the four trial types. Group differences in mean RT were assessed with *t* tests. In low-penalty and high-penalty trials, we measured risk-taking as the mean elapsed time between the first and second presses in trials in which the subject did not bust. For the penalty trial types, seconds of reward accrual, as well as number of busts, were compared in mixed-model ANOVA, with penalty severity (low and high) and time (three levels, runs 1–3) as within-subject factors, and age group as the between-subject factor. Finally, task earnings were compared in mixed model ANOVA, with time (three levels, runs 1–3) as the within-subject factor, and age group as the between-subject factor

Psychometric measures

In a postscan questionnaire, subjects ranked their relative preferences for playing the four different trial types, then rated on a scale of 0–3 how "happy," "anxious," "excited," and "bored" they were when playing each type. In addition, the questionnaire asked subjects whether they adopted any specific strategy in the penalty trials, and if so, to describe their strategy in prose. A rater blind to each subject's identity rated the prose responses and classified strategy as "none," "static," (if the subject described a strategy of always stopping at a certain point), or "dynamic" (if the subject described a strategy of adjusting reward accrual behavior from trial to trial based on recent penalty trial outcomes). Group comparisons were performed using *t* tests and χ^2 tests.

Results

Task behavior

Adolescents took longer to respond to the first-press cue ($) that initiated the trial than adults in all trial types, with significantly slower RTs ($p < 0.05$) in motor control, no-penalty, and high-penalty trials (Fig. 2*A*). There were no main or interactive effects of age group ($p > 0.40$), however, on reward accrual duration (risk exposure), incidence of busts (31.8% of low-penalty trials; 20.0% of high-penalty trials), or task winnings (mean, $34.56 ± 2.1). On average, adolescent and adult subjects terminated reward accrual after the possibility of busts began in low-penalty trials but terminated accrual at the time the possibility of busts began in the high-risk trials (Fig. 2*B*). Seconds of reward accrual (risk exposure) decreased across the experiment in low ($F_{(2,76)} = 3.684$; $p < 0.05$) but not high-penalty trials. Subjects terminated reward accrual sooner in high-penalty compared with low-penalty trials ($F_{(1,38)} = 38.594$; $p < 0.0001$), with trial-by-trial variation (SD) in successful reward accrual times significantly greater in low-risk compared with high-risk trials ($F_{(1,38)} = 5.899$; $p < 0.05$). This did not differ by age group.

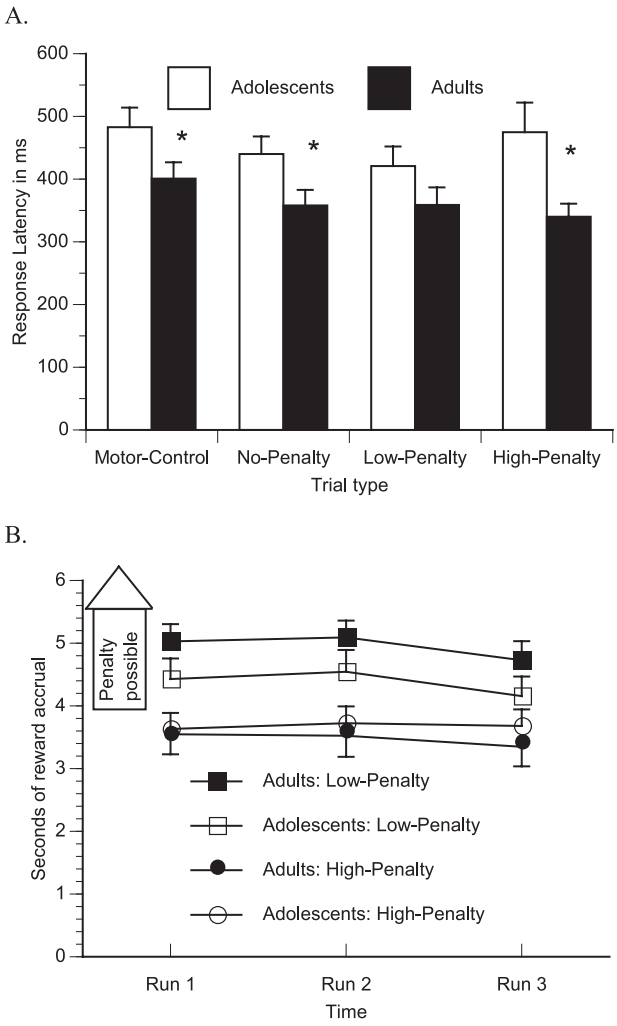

Figure 2. RTT behavior. ***A***, Mean time to respond with the first press to the $ cue was significantly slower in adolescents in motor control, no-penalty, and high-penalty trial types. ***B***, Reward accrual time (and therefore risky reward pursuit) did not significantly differ between adults and adolescents. Both groups on average terminated accrual in the high-penalty trials before penalty outcomes could occur. Error bars indicate SEM. * $p < 0.05$.

Psychometric measures

In the postscan questionnaire ranking of relative preference for playing the different trial types, almost every subject (97.4%) ranked the no-penalty (guaranteed reward) trial type his or her favorite to play, and of those, 68.4% ranked the low-penalty trial second favorite, with no age differences in rankings of first- and second-favorite trial types. From there, opinion diverged, with 16 subjects preferring playing the motor-control trials over the high-penalty trials, and others ($n = 21$) the reverse. When subjects were grouped into two categories based on their order of preference for the motor-control trials relative to high-penalty trials, a χ^2 analysis showed that more adolescents preferred the high-penalty over the motor-control trials than did adult respondents. ($p < 0.05$).

There were no age group differences in ratings (scale 0–3) of either excited or bored playing any of the four trial types. Adults showed an orderly increase in reportedly feeling anxious from motor control to no-penalty, to low-penalty, to high-penalty tri-

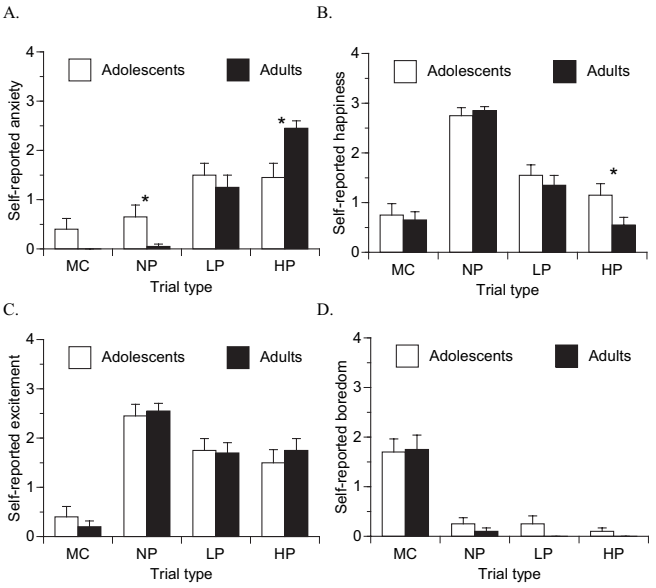

Figure 3. Affect ratings reported on postscan questionnaire. ***A–D***, Self-reports (scale 0–3) of feeling anxious (***A***), happy (***B***), excited (***C***), and bored (***D***) when playing the motor control (MC), no-penalty (NP), low-penalty (LP), and high-penalty (HP) trials of the RTT. The group by trial type interaction effect on anxiety ratings (but not the other mood ratings) was significant ($p < 0.0001$), where self-reported anxiety reflected the magnitude of potential penalty in adults but not adolescents. Group-wise differences ($p < 0.05$) are indicated by an asterisk. All 20 adult subjects reported "0" boredom in penalty trials. Error bars indicate SEM.

als, but adolescents did not (Fig. 3*A*) (age group by trial type interaction $F_{(3,111)} = 8.232$; $p < 0.0001$). Adults were more anxious than adolescents ($p = 0.004$) when playing high-penalty trials but less anxious than adolescents playing no-penalty trials ($p = 0.021$). Finally, 53% of subjects reported a strategy of always stopping reward accrual at a certain point in penalty trials, 18% subjects reported an adjusting strategy based on previous trial presentations or outcomes, whereas 29% of subjects reported adopting no strategy. The distribution of reported strategy did not differ by age group.

Brain activations by linear contrasts between trial types

Reward accrual in no-penalty trials, contrasted with nonincentive motor control trials, activated the occipital cortex in both groups (Table 1). Reward accrual at risk of low penalty contrasted with reward at no risk of penalty activated the PMC, bilateral insula, thalamus, midbrain, occipital cortex, parietal cortex, and striatum in adults but showed no suprathreshold brain activation in adolescents (Fig. 4*A*,*B*; Table 2). A voxelwise *t* test of activation illustrated a significant decrement in PMC activation by this contrast in adolescents compared with adults (Fig. 4*C*). Reward accrual at risk of high penalty contrasted with reward at no risk of penalty activated the PMC, thalamus, midbrain, occipital cortex, parietal cortex, and striatum in both adolescents and adults (Fig. 4*D*,*E*; Table 3). Reward accrual at risk of high penalty contrasted with accrual at risk of low penalty activated the occipital and parietal cortex in both adolescents and adults (Table 4). Suprathreshold PMC activation by penalty increase was detectable, however, when both groups were consolidated to increase statistical power in a *post hoc* omnibus analysis.

In each of low- and high-penalty trials, an LC between trials in which the subject busted versus trials in which the subject won money did not reveal any suprathreshold activation. Finally, in a follow-up study of nine additional healthy adults, we confirmed that PMC activation by the reward/penalty conflict was also evident when the screen background colors denoting the task contingencies were reversed, where for example, a white background was shown during high-penalty trials, and a yellow background was shown during no-penalty trials (i.e., guaranteed reward).

Signal change in a PMC VOI

We analyzed BOLD signal change in a VOI drawn a priori across the intrahemispheric fissure in the PMC that encompassed a cluster of activation maxima diagrammed in a review of previous predecision conflict experiments (Ridderinkhof et al., 2004) (Fig. 5*B*, inset). There were no age group differences in signal change across acquisitions of the trial in motor control and nonpenalty trials. In an omnibus ANOVA across acquisitions of both penalty trial types, there were significant main effects of group ($F_{(1,38)} = 5.683$; $p < 0.05$; adolescents less than adults) and time ($F_{(1,38)} = 47.565$; $p < 0.00001$; signal increase in both types of penalty trials) on BOLD signal, but no main effect of penalty severity (low versus high)(Fig. 5). There were also significant interaction effects of penalty by age group ($F_{(1,38)} = 4.998$; $p < 0.05$; reduced overall signal in low-penalty trials in adolescents, but not in high-penalty trials), time by age group ($F_{(5,190)} = 2.893$; $p < 0.05$; reduced signal increase over time in adolescents compared with adults in both risk trial types collapsed), and penalty by time ($F_{(5,190)} = 7.798$; $p < 0.00001$; greater signal increase over time in high-penalty trials compared with low-penalty trials in both subject groups collapsed). The penalty by time by group interaction was not significant. When low- and high-penalty trial types were analyzed singly, however, there was a significant age group by time interaction effect on BOLD signal change during each of low-penalty ($F_{(5,190)} = 2.325$; $p < 0.05$) and high-penalty ($F_{(5,190)} = 2.918$; $p < 0.05$) trials (Fig. 4*A*,*B*, respectively), with blunted or delayed signal increase in adolescents.

We calculated predecision PMC activation as the BOLD signal increase from the acquisition at trial onset to the acquisition spanning the time point when subjects on average stopped accruing reward and when busts could occur (4 s after reward accrual onset, or 6 s into the trial). In low-penalty trials, predecision signal increase correlated positively with age across all participants, both in bivariate correlation (Spearman $r = 0.32$; $p < 0.05$) and after controlling for individual differences in reward accrual time (risk exposure) and task vigilance, as assessed by latency to respond to the cue to initiate the trial (partial correlation $\beta =$

Table 1. Activations by a linear contrast between nonpenalty versus motor control trial conditions

		Talairach coordinates				
	Region	*x*	*y*	*z*	*t* value	Uncorrected p^a
Adults	R middle occipital gyrus	38	−79	10	6.605	<0.00001
	R inferior parietal lobule	26	−49	48	6.409	<0.00001
Adolescents	R middle occipital gyrus	49	−68	15	5.995	<0.00001

R, Right; L, left.

[a]Voxel coordinates listed in all tables were the peak of a contiguous cluster sufficient to obtain a family-wise corrected type I error rate of $p < 0.05$ using Monte Carlo simulation.

0.45; $p < 0.001$) (Fig. 5*C*). Predecision signal increase inversely correlated with reward accrual time, both in bivariate correlation (Spearman $r = -0.33$; $p < 0.05$) and after controlling for age and task vigilance ($\beta = -0.38$; $p < 0.05$) (Fig. 5*D*).

None of these relationships were evident in high-penalty trials (all $r/\beta < 0.1$). However, subjects who preferred playing motor-control trials (for no money) over the high-penalty trials (risk avoiders) showed a trend toward reduced reward accrual time in high-penalty trials (3.25 vs 3.92 s; $p = 0.062$) and attained peak signal change 2 s sooner than other subjects (group by time interaction effect; $F_{(5,185)} = 2.813$; $p < 0.05$). Mood adjective ratings did not correlate with PMC signal change in any trial type, nor did the PMC signal change differ in subjects who described a specific gameplay strategy.

Predecision PMC activation and errors in the current penalty trial

To examine whether blunted predecision PMC recruitment in penalty trials might relate to a greater incidence of error (bust) outcomes, we compared predecision activation between successful versus busted trials. Two adults and one adolescent never busted in high-penalty trials, and two adolescents avoided busting in low-penalty trials, and were excluded from analyses where required. Across both low- and high-penalty trials, there was a significant main effect of current trial outcome ($F_{(1,34)} = 5.796$; $p < 0.05$) with lower predecision signal increases before busts. A significant penalty by outcome interaction effect indicated that reduced prebust signal increase was specific to busts in high-penalty trials ($F_{(1,34)} = 6.969$; $p < 0.05$). There were no interaction effects of age group and outcome.

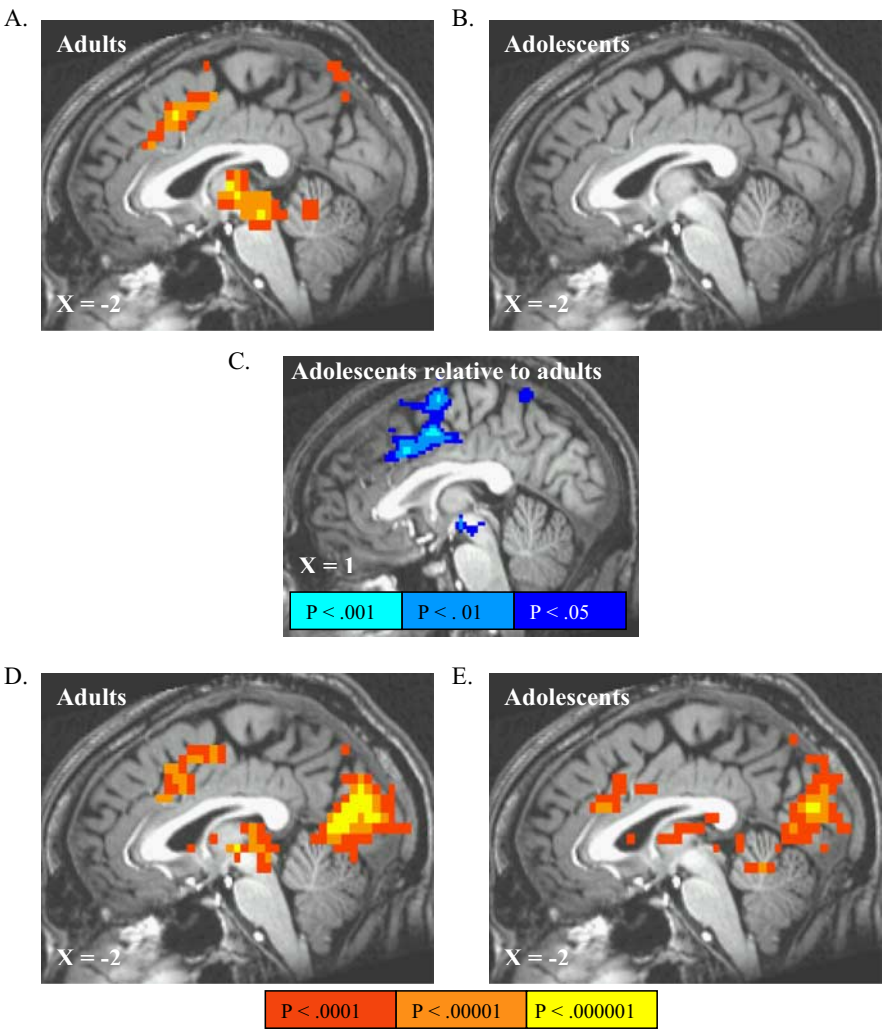

Figure 4. Brain activation by risky versus nonrisky reward accrual. ***A***, ***B***, Adults (***A***) but not adolescents (***B***) showed significant recruitment of the PMC during accrual of reward at risk of forfeiture of reward for that trial (low penalty) contrasted with reward accrual at no risk of forfeiture. ***C***, This resulted in a net activation decrement among adolescents when adults and adolescents were compared in a voxelwise *t* test. ***D***, ***E***, Accruing reward at the risk of forfeiture of reward for that trial plus loss of an identical amount of previous winnings (high penalty) contrasted with accruing certain reward, activating the PMC in both adults (***D***) and adolescents (***E***), with no group activation differences.

In low-penalty trials analyzed singly, there was neither a significant main effect of current trial outcome (Fig. 6*A*) nor an outcome by age group interaction on predecision PMC signal change. In high-penalty trials analyzed singly, the main effect of current trial outcome was significant, with lower activation before busts than before successful outcomes ($F_{(1,34)} = 10.954$; $p < 0.01$) (Fig. 6*B*) but no outcome by age group interaction. There was no significant self-reported strategy type by outcome interaction effect on predecision activation during either low- or high-penalty trials.

PMC activation and behavior change as a function of previous penalty trial outcome

To determine whether error outcomes in a penalty trial prompted more conservative behavior in the subsequent trial of that type, we compared mean reward accrual time between (nonbust) trials that followed a bust in the previous trial with (nonbust) trials that followed a previous win. Across both low- and high-penalty trial types, there was a main effect of previous outcome ($F_{(1,34)} = 5.465$; $p < 0.05$), with reduced reward accrual in trials that followed one or more (consecutive) busts. There was a trend for this behavior difference to be specific to the low-penalty trials (previous-outcome by penalty effect; $F_{(1,34)} = 3.104$; $p = 0.087$).

In low-penalty trials analyzed singly, there was a main effect of previous trial outcome, with lower mean reward accrual time in trials that followed one or more consecutive bust outcome(s) in the previous trial(s) ($F_{(1,36)} = 9.995$; $p < 0.01$) (Fig. 6*C*). The previous-outcome by age group interaction effect on reward accrual was not significant. In high-penalty trials, there was neither a main effect of previous trial outcome nor a previous outcome by age group interaction effect on reward accrual time (Fig. 6*D*).

To assess differential predecision BOLD signal increases in the PMC as a function of previous trial outcome, both the time series and VOI analyses were reperformed, where instead of penalty trial outcomes delineated based on the outcome of the current trial, trials within each of low- and high-penalty trial types were recoded based on whether the subject busted or won money in the previous trial of that type. In the time series analyses of both

Table 2. Activations in adults by a linear contrast between low-penalty versus no-penalty trial conditions

	Talairach coordinates				
Region	*x*	*y*	*z*	*t* value	Uncorrected *p*
R anterior insula	30	19	0	8.715	<0.000001
PMC	−4	15	39	8.636	<0.000001
L midbrain	−8	−30	−9	8.309	<0.000001
L thalamus	−8	−15	5	8.445	<0.000001
L inferior temporal gyrus	−41	−68	0	7.746	<0.000001
L nucleus accumbens	−15	11	−4	7.698	<0.000001
L insula gyrus	−34	11	5	7.694	<0.000001
L precuneus	−11	−71	53	7.515	<0.000001
R superior frontal gyrus	23	11	53	7.468	<0.000001
L middle frontal gyrus	−23	0	48	7.403	<0.000001
R anterior cingulate	11	19	24	7.217	<0.000001
R mesofrontal cortex	4	4	58	6.921	<0.00001
R middle occipital gyrus	49	−64	−4	6.866	<0.00001
L superior parietal lobule	−26	−60	44	6.493	<0.00001
L inferior frontal gyrus	−41	0	29	6.217	<0.00001
R caudate head	11	11	0	6.199	<0.00001
R inferior frontal gyrus	45	4	24	5.998	<0.00001
R superior temporal gyrus	41	−56	15	5.908	<0.0001
R precuneus	15	−60	29	5.862	<0.0001
R middle frontal gyrus	34	38	29	5.805	<0.0001
R parahippocampal gyrus	19	−38	5	5.453	<0.0001
R superior parietal lobule	30	−56	53	5.193	<0.0001

Adolescents had no activations. R, Right; L, left.

Table 3. Activations by a linear contrast between high-penalty versus no-penalty trial conditions

		Talairach coordinates				
	Region	*x*	*y*	*z*	*t* value	Uncorrected *p*
Adults	R cuneus	15	−68	10	12.404	<0.000001
	L cuneus	−11	−56	5	10.483	<0.000001
		0	−86	20	7.646	<0.000001
	L thalamus	−8	−26	−4	9.497	<0.000001
	R thalamus	11	−15	−4	9.117	<0.000001
	L nucleus accumbens	−15	11	−4	9.085	<0.000001
	R PMC	8	4	58	8.795	<0.000001
	R caudate head	12	9	−1	8.549	<0.000001
	L middle frontal gyrus	−30	0	53	8.042	<0.000001
	R superior parietal lobule	15	−71	44	7.492	<0.000001
	L superior occipital gyrus	−30	−75	24	7.385	<0.000001
	L middle occipital gyrus	−45	−71	5	7.181	<0.000001
	L PMC	0	15	34	7.019	<0.00001
	R middle occipital gyrus	38	−75	0	6.529	<0.00001
	R cerebellum	23	−60	−14	6.163	<0.00001
	L postcentral gyrus	−49	−30	48	6.157	<0.00001
	L superior parietal lobule	−11	−68	58	6.003	<0.00001
	R superior parietal lobule	26	53	48	5.734	<0.0001
	L precentral gyrus	−49	0	29	5.721	<0.0001
	R middle temporal gyrus	38	−56	10	5.652	<0.0001
	L superior frontal gyrus	−8	−8	68	5.295	<0.0001
Adolescents	R lingual gyrus	19	−56	0	10.363	<0.000001
		11	−94	0	6.483	<0.00001
	L PMC	−11	19	29	8.766	<0.000001
	L lingual gyrus	−15	−64	0	8.550	<0.000001
	R cuneus	8	−75	15	8.233	<0.000001
	R insula	34	8	0	8.013	<0.000001
	R precuneus	4	−75	44	7.594	<0.000001
	R PMC	8	11	44	6.969	<0.00001
		11	26	20	6.512	<0.00001
	R thalamus	8	−8	5	6.795	<0.00001
	L middle temporal gyrus	−30	−68	24	6.724	<0.00001
	L putamen	−19	15	−1	6.650	<0.00001
	L parahippocampal gyrus	−19	−38	5	6.580	<0.00001
	R precuneus	27	−71	34	6.542	<0.00001
	R superior frontal gyrus	26	41	24	5.887	<0.0001
	Posterior cingulate cortex	0	−30	39	5.766	<0.0001

R, Right; L, left.

Table 4. Activations by a linear contrast between high-penalty versus low-penalty trial conditions

		Talairach coordinates				
	Region	*x*	*y*	*z*	*t* value	Uncorrected *p*
Adults	R cuneus	15	−71	15	9.735	<0.000001
	R lingual gyrus	11	−53	5	9.082	<0.000001
	L cuneus	−15	−68	10	8.710	<0.000001
Adolescents	L lingual gyrus	−19	−64	5	8.302	<0.000001
	R lingual gyrus	11	−64	0	8.058	<0.000001
	L cuneus	−8	−86	10	7.544	<0.000001
	R cuneus	15	−83	34	7.239	<0.000001
	L precuneus	−15	−86	39	7.139	<0.000001
Adolescents plus adults	R PMC	10	21	26	5.595	<0.00001

R, Right; L, left.

low- and high- penalty trials, the LC between postbust versus postwin trials (again, each time locked to reward accrual onset) did not reveal activation or deactivation. Activated PMC voxels in adults and adolescents were evident only at a very relaxed threshold ($p < 0.01$, uncorrected).

In the VOI analysis across both penalty trial types, however, there was a significant main effect of previous outcome on predecision PMC increase ($F_{(1,34)} = 6.227$; $p < 0.05$), where signal increases were higher in trials that followed a bust compared with a win. There were no interaction effects of penalty magnitude or age group. In low-penalty trials, predecision signal increase was significantly higher in trials that followed a bust compared with a win (main effect of previous outcome; $F_{(1,36)} = 4.509$; $p < 0.05$) (Fig. 6*E*). There was no previous outcome by age group interaction effect. In the high-penalty trials, there was a trend for busting in the previous trial to correlate with increased predecision PMC activation in the subsequent trial (main effect of previous outcome; $F_{(1,35)} = 3.903$; $p = 0.056$) (Fig. 6*F*). There was no previous outcome by age group interaction effect.

Finally, in an exploratory analysis, we determined whether previous outcome-based differences in predecision PMC activation differed as a function of subjects' self-reported strategy types (none, static, dynamic). In low-penalty trials, mean signal increases were higher after busts compared with wins in subjects who reported either no strategy or a dynamic strategy, whereas subjects reporting a static strategy (always stopping at a certain time) showed no difference in predecision signal increase between trials that followed wins and trials that followed busts (previous outcome by strategy type interaction effect; $F_{(2,34)} = 3.286$; $p < 0.05$) (supplemental Fig. 1*A*, available at www.jneurosci.org as supplemental material). This pattern was less pronounced in high-penalty trials, with no significant previous outcome by strategy type interaction effect (supplemental Fig. 1*B*, available at www.jneurosci.org as supplemental material).

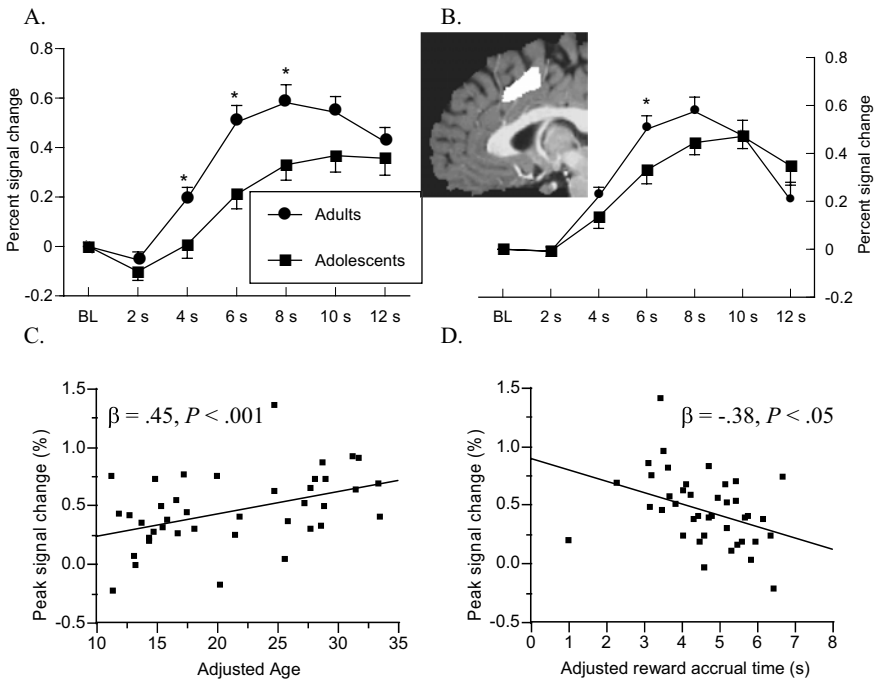

Figure 5. Trial-wise BOLD signal in a region of the PMC previously reported to be activated by a variety of predecision conflict imaging paradigms (shown in white in the inset of the brain image). Signal change did not differ between adults and adolescents in motor control and no-penalty reward trials. ***A***, ***B***, In both low-penalty (***A***) and high-penalty (***B***) trials, there were significant group by time interaction effects on BOLD signal, with reduced or delayed signal increases in adolescents. Asterisks denote significant signal differences ($p < 0.05$) at individual time points. Error bars indicate SEM. ***C***, In low-penalty trials, when subjects took more risks, age correlated positively with peak predecision PMC signal increases (leverage plot) after controlling for RT to initiate the trial (task engagement) and individual differences in reward accrual time (risk-taking). ***D***, Reward accrual time negatively correlated with PMC signal after controlling for age and RT to initiate the trial (leverage plot).

Discussion

Pursuing reward at risk of penalty (relative to guaranteed reward) activated the PMC only in adults during low-penalty trials, and in both adults and adolescents during high-penalty trials. There were no age differences in error outcomes or earnings, where both adolescents and adults generally avoided risk to preserve small gains. Increasing potential penalties from nonwins to actual monetary losses activated regions of the visual cortex reported to be activated by threatening images (Bradley et al., 2003) but only marginally activated the PMC over the activation achieved during low-penalty exposure. This increased activation was detected only when both groups were statistically consolidated for the time series analysis and in the penalty by time effect in the VOI analysis.

The RTT as a probe of PMC activation

Based on the patterns of task behavior, we posit that the threat of money loss in high-penalty trials engendered a cognitively facile, risk-avoidant strategy to preserve gains obtained in other trial

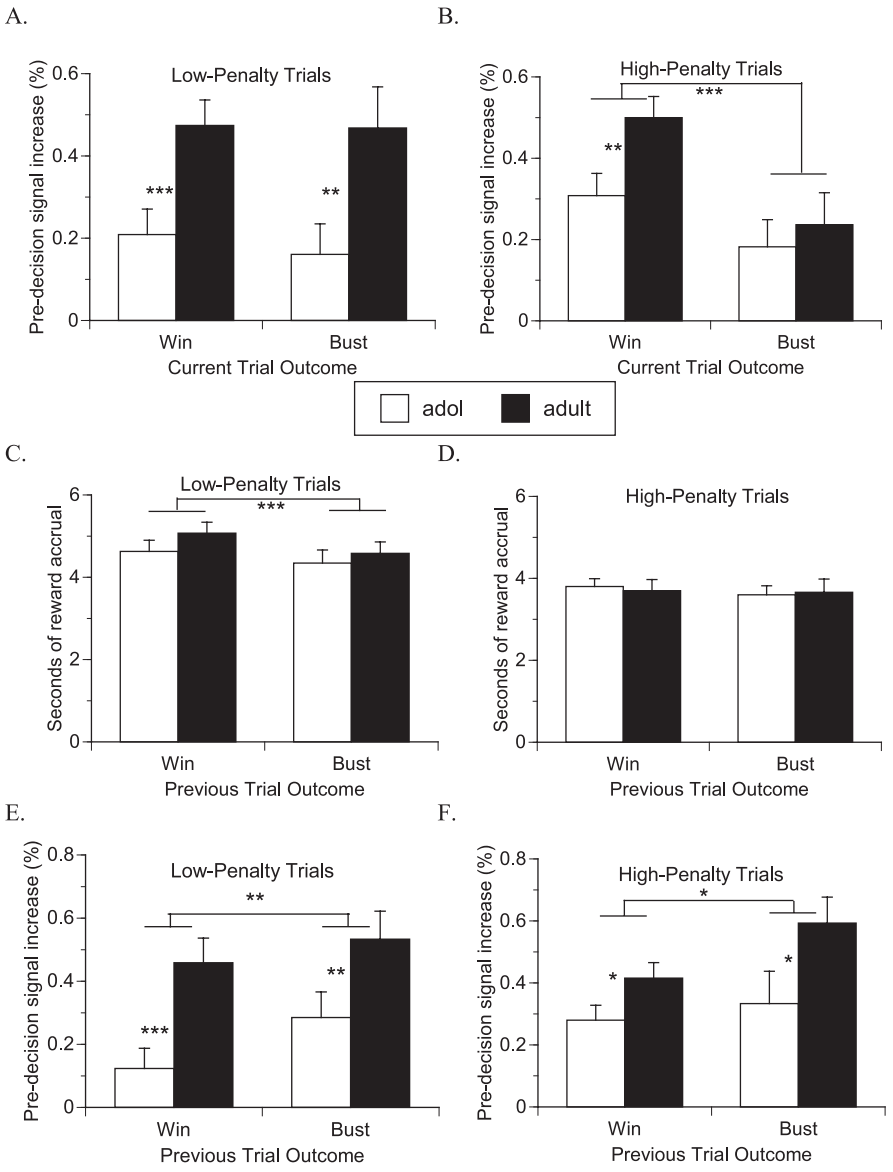

Figure 6. ***A–F***, Behavior change and predecision PMC signal change in penalty trials as a function of error outcomes in the current (***A***, ***B***) or previous (***C–F***) penalty trial of that type. ***A***, In low-penalty trials, predecision PMC signal change did not differ between win and bust outcomes but was significantly lower in adolescents in both successful and busted trials. ***B***, In high-penalty trials, predecision PMC signal increase was lower in trials when subjects ultimately busted compared with trials with wins. ***C***, ***D***, Duration of risky reward accrual (in nonbusted trials) was reduced in low-penalty trials that followed a bust in the previous low-penalty trial (***C***) but did not differ in (nonbusted) high-penalty trials as a function of previous high-penalty trial outcome (***D***). ***E***, ***F***, Predecision PMC signal increase was significantly greater in low-penalty trials that were preceded by a bust in the previous low-penalty trial (***E***), and there was a trend for greater activation in high-penalty trials that followed a bust in the previous high-penalty trial (***F***). There were no interaction effects of age group on error-related behavior or signal change differences. $^{*}p < 0.10$; $^{**}p < 0.05$; $^{***}p < 0.01$. Error bars indicate SEM.

crual behavior would thus make the low-penalty trials more sensitive to developmental differences.

Because PMC signal increases in penalty trial types began before busts could occur, we posit that its activation was driven by upstream cognitive and emotional processing related to predecision conflict, specifically error avoidance (Magno et al., 2006), because subjects could essentially "opt out" of the possibility of penalty altogether. Because PMC activation in high-penalty trials was robust but was not correlated with the timing of motor behavior, it does not seem likely that PMC activation by penalty trials was simply an epiphenomenon of downstream ballistic antecedents of a motor response. Moreover, in low-penalty trials, the time to reward termination also inversely correlated (−0.479) with predecision PMC signal increase as measured 2 s earlier, at the midpoint of "safe" reward accrual. This is further in advance of the timing of posterior mesocortical signal increases elicited by voluntary motor activity in conflict-free paradigms (Cunnington et al., 2003).

Predecision PMC signal increases in penalty trials related to actual task behavior in several ways. First, in low-penalty trials, when subjects assumed more risk, predecision signal change was greatest in subjects who avoided risk. Second, subjects who preferred playing nonincentive motor-control trials over playing high-risk trials showed a more rapid increase in PMC signal in the high-risk trials. Third, predecision PMC signal increases were greater in penalty trials that followed a bust in the previous trial of that type compared with trials after a win. This echoes data from other fMRI decision-making paradigms, in which PMC activation has been linked specifically to error notifications (Ullsperger and von Cramon, 2004).

Finally, in high-penalty trials, predecision PMC signal increases were lower in busted trials. We did not hypothesize a difference between PMC signal increases before wins versus busts because we assumed that subjects would be uniformly motivated to avoid busting in every penalty trial. Indeed, because busts occurred almost entirely in trials with the earliest assigned bust time (4 s) after $ cue presentation, negative outcomes were externally and pseudorandomly imposed on the subjects. Accordingly, the linear contrast between successful versus busted trials did not activate PMC voxels in either low- or high-penalty trials. The VOI analysis of high-penalty trials, however, revealed a lower predecision PMC signal increase from baseline when subjects busted compared with when they stopped reward accrual in time. This suggests that PMC recruitment correlates with successful error avoidance under certain task conditions.

types, and this reduced sensitivity to developmental differences. Critically, mean reward accrual time in (nonbusted) high-penalty trials was briefer than the shortest accrual time at which busts could occur (4 s), with less trial-to-trial variance in accrual times compared with low-penalty trials. In addition, whereas reward accrual in low-penalty trials differed as a function of an error in the previous trial, reward accrual times did not differ after busts versus wins in high-penalty trials. In contrast, subjects were less motivated to avoid penalties for incorrect decisions when these resulted in mere forfeiture of current-trial winnings, and this resulted in a more dynamic, risky strategy in low-penalty trials. Greater extent and trial-to-trial differences in reward ac-

Developmental differences in PMC recruitment by the risky rewards

A developmental difference in PMC activation by a reward/penalty conflict was evident both in the time series contrast between low-penalty and no-penalty trials, where adults as a group showed significant activation but adolescents did not and in the VOI analysis of the hemodynamic response in low-penalty trials singly. Moreover, PMC activation increased with age across all participants in the low-penalty trials, especially after controlling for individual differences in actual risk-taking behavior as well as task engagement. There were no age group differences in exposure to busts (errors) to confound interpretation of age group differences in PMC activation by risky reward accrual. Because there were no age group differences in previous trial error effects (bust versus win) on either reward-accrual behavior or on predecision PMC activation in the subsequent trial, this suggests that age-related differences in PMC activation in low-penalty trials did not simply result from a relative ambivalence to error notifications in the adolescents.

A dissociation between PMC recruitment and error avoidance was evident in low-penalty trials, where adolescents showed blunted activation of PMC but were as adept as adults in avoiding penalty outcomes. Although the correlation between PMC activation and risk termination suggests that individual differences in PMC activity relate to differences in risk exposure, the adolescents' performance in the low risk trials shows that control of risky behavior can be implemented in the absence of robust PMC activation. We offer two possible explanations for this dissociation. One possibility is that PMC recruitment is required for successful penalty avoidance but must only exceed a modest threshold, especially when subjects use a rule-based strategy.

A more parsimonious explanation, however, is that individual differences in PMC activation by this task reflected primarily differences in recruitment of circuitry governing affective/motivational components of decision-making under risk, which may not correlate with or determine the actual decision. Calculation-based processing more proximal to (and predictive of) actual choice behavior may reside in other cortical regions, such as the parietal lobe (Sugrue et al., 2005). When performing Stroop and GoNogo tasks, subjects with lesions in the PMC were still able to modulate behavior with parametric modulation of task difficulty and also showed posterror slowing similar to controls (Fellows and Farah, 2005). Conversely, in normal controls, errors coupled with monetary loss activated the PMC more than verbal feedback alone (Taylor et al., 2006), suggesting that PMC activation is sensitive to the motivational aspects of decision making. Finally, in subject debriefing, adults reported an orderly increase in self-reported anxiety in accord with penalty magnitude across trial types, but adolescents did not.

Alternatively, if we assume that self-referential circuitry is also recruited during conflict in risky decision-making paradigms, it is also possible that the deficient PMC activation we see in adolescence resulted in part from developmentally reduced processing of self-involvement (agency) in the decision making. Notably, dorsal regions of the PMC activated by potential penalties in our task were also activated by self-referential versus other-referential negatively valenced judgments (Moran et al., 2006). Developmental differences between adolescents and adults in appraisal of self as the agent of action have been suggested (Harter, 1999).

Conclusions and future directions

This study had two key limitations. As in a game of chicken, risky reward accrual (predecision processing) and outcome notification (error processing) were contiguous in penalty trials, and precluded delineation of specific hemodynamic responses to the two components of risky decision making. The time course of the PMC BOLD response indicated that predecision activation saturated PMC by the time subjects stopped reward in time or busted. Future experiments could jitter the interval between risky reward accrual and discrete feedback of outcomes. Second, our task did not include parametric modulation of risk itself (defined as the probability of a negative outcome), because the distribution of bust times was identical in the two error trial types. Future adaptations of this paradigm could factorially modulate both penalty magnitude and outcome uncertainty.

In conclusion, these findings collectively indicate that when humans assume some risk of penalty in pursuit of an explicit reward, the recruitment of mesofrontal circuitry extensively implicated in decision-making increases from adolescence to adulthood. Conversely, this developmental difference is reduced when potential penalties are sufficiently severe. This complex pattern suggests that while adolescents possess functional error-monitoring circuitry, this circuitry is less sensitive to potential penalties in scenarios that hold potential for both positive and negative outcomes. This developmental difference may account in part for the increased propensity of adolescents and young adults to engage in risky behaviors. Although adolescents performed adequately in the simple task we used (which presented explicit penalty possibilities and outcomes), developmental decrements in PMC recruitment may be critical in more complex or ambiguous real-world situations involving both potential penalty and benefit. Future experiments could assess gender differences in PMC recruitment as well as differences from controls in pathological subject populations.

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