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Neurobiology of Decision-Making in Depressed Adolescents: an fMRI Study

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Abstract

Objective—Despite evidence that impaired reward- and risk-related behavior during adolescence can have potentially serious short- and long-term consequences, few studies have investigated the impact of depression on reward-related selection in adolescents. This study examined the relationship between reward-related behavior and prefrontal activations in depressed and healthy adolescents during a decision-making task.

Method—Twenty-two adolescents with no personal or family history of psychiatric illness and 22 adolescents with major depressive disorder were administered a monetary two-option decision-making task, the Wheel of Fortune, using a functional magnetic resonance imaging protocol. The analysis was focused on the selection phase, i.e., the first phase of the decision-making process, which typically includes two more phases, the anticipation of outcome and the feedback.

Results—Similar prefrontal regions were activated in healthy and depressed adolescents during reward-related selection. However, in a contrast involving the selection of high-risk (low-probability/high-magnitude reward) vs. equal-risk (50% chance of reward) options, healthy adolescents showed greater activation than patients in the right lateral orbitofrontal cortex (OFC), whereas participants with depression showed greater activation than healthy subjects in the left dorsal OFC and right caudal anterior cingulate cortex. In addition, healthy adolescents, but not participants with depression, showed a negative correlation between high-risk behavior and neuronal activation in pre-specified prefrontal regions.

Conclusions—These results suggest subtle changes in the neural responses to reward selection in depressed adolescents. In addition to the replication of these findings in larger samples, the association of these neuronal changes with treatment response and prognosis should be examined.

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Keywords

Neurobiology; Decision-Making; Depressed; Adolescents; fMRI

Introduction

Decision-making is a higher-order cognitive function in humans, and it involves the ability to choose between competing actions that are associated with varying levels of risk and reward. The ability to make optimal decisions is less well-developed in children and adolescents than in adults[1–7], probably a reflection of immature brain function, particularly of the prefrontal cortex. In addition, ongoing brain maturational changes during adolescence might explain the increased vulnerability for psychiatric disorders,[8] such as depression[9]. Of interest, depression does compromise decision-making, a contributor to the severe consequences of this disorder, including suicide.[10] It is also interesting to note that major depressive disorder (MDD) and decision-making share common neurobiological substrates, such as the anterior cingulate cortex (ACC),[11,12] which may explain why impaired decision-making is commonly observed in MDD.[13] Therefore, a better understanding of the neurobiology of decision-making in adolescent depression might be helpful in developing more targeted interventions and in reducing the morbidity and mortality associated with this disorder.[9,12]

One approach to understanding the neurobiology of decision-making in depression is to examine the neuronal responses to reward-related choices.[11,14] Conceptual models emphasize disrupted reward function as a neural characteristic of low mood and anhedonia in depression, and functional neuroimaging studies in adult depressed patients report alterations in the reward system.[14] Although there is a growing literature on the brain activation patterns associated with reward-related behavior in healthy youngsters,[15–21] only two neuroimaging studies examined reward-related behavior in depressed youth.[22,23] These studies did not assess neural responses during the selection of options of different incentive values, which is the first step in the decision-making process.[11] The selection phase also provides the opportunity to examine the association between manifest behavior (execution of the preferred option) and neural responses. In contrast, only subjective reports can serve as behavioral measures during the anticipation and feedback phases of the decision-making process.[11]

To the best of our knowledge, neural responses to the selection of reward-related options have not been reported in depressed youth. However, one study compared the neural responses during the selection phase in healthy adolescents and adults[16] using the Wheel of Fortune (WOF) task, which allows the separate analysis of reward-selection from other phases of decision-making.[24] This study reported an inverse relationship between risky behavior and prefrontal activations in both adolescents and adults, confirming the role of prefrontal cortex in decision-making.[11,16] Similar results were reported in a study of healthy adolescents.[25] Administration of the WOF paradigm revealed greater activation of the orbitofrontal cortex (OFC), but reduced activation of the rostral ACC in adult depressed participants compared with healthy controls during the selection phase.[26]

To date, pediatric studies of depression have examined brain activation patterns during the anticipation and receipt of rewards, using imaging paradigms other than the WOF.[22, 23] In one study using a card-guessing paradigm, depressed adolescents showed greater activation in the medial PFC (mPFC; Brodmann's area 10) than healthy controls during the outcome phase.[22] In another study using a similar card-guessing paradigm, depressed youth showed decreased ACC responses compared to healthy controls during both anticipation and

feedback phases. In addition, diagnostic status interacted with the probability and magnitude of reward to predict activation in specific regions of the OFC.[23] Finally, reduced activation in the ACC (particularly the rostral region) was observed during anticipation and feedback phases in adult depressed patients vs. healthy controls.[12,14,26]

In studies that directly compared healthy adolescents and adults, activation of the ACC and/or OFC was reported to be greater in adults than in adolescents during the decision-making process.[15,16,18] This pattern of differential activation of prefrontal regions between adolescents and adults may be due to the maturational brain changes occurring during adolescence.[2–5] More specifically, age-related immaturity in the ACC and OFC might be associated with suboptimal conflict-resolution and response-prevention[16] (both of which are key components of decision-making), respectively, whereas immaturity in the mPFC may underlie compromised self-awareness and error-monitoring.[11,27,28] It is possible that the cognitive and affective changes observed in depression might compound these effects of neural immaturity, thereby increasing the risk for serious consequences such as substance use and suicidal behavior.[9,10] However, it is not known whether the reward-related selection process will induce a pattern of prefrontal dysfunction in depressed adolescents similar to that observed during reward-anticipation and reward-outcome in earlier pediatric studies,[22,23] or comparable to the observed pattern of responses during the selection phase in depressed adults.[26]

The present work is part of an ongoing study on the neurobiological substrates of decision-making in adolescent depression and their association with longitudinal clinical course. The WOF task was employed to examine the relationships between choices of probabilistic rewards and activations in prefrontal regions, while keeping constant the expected value of the reward. Keeping the reward magnitude constant across low- and high-risk selections provides an opportunity to examine the association between manifest behavior and neural responses to reward-selection. Although there are no previous data on prefrontal activation in response to reward-selection in depressed adolescents, we predicted that depressed and healthy adolescents would differ on prefrontal activation in response to reward-selection. In addition, we hypothesized that risk-taking behavior would show a weaker correlation with prefrontal activation in depressed adolescents compared to healthy adolescents because of the reported reduced variability in prefrontal responses to reward in depressed individuals.

Method

Due to space limitations, the methods are described briefly and additional details are provided in Supplement 1, available online.

Participants

The participants included 22 adolescents with MDD (average age = 15.0 ± 2.1; M/F = 12/10)[13] and 22 age- and gender-matched controls with no personal or family history of psychiatric illness (average age = 16.0 ± 2.1; M/F = 11/11).

Of the 22 depressed adolescents, two had a comorbid anxiety disorder and three had attention-deficit hyperactivity disorder. The participants were recruited from local schools and mental health programs, through advertisements in local newspapers and by word-of-mouth. The age range was comparable in both groups (i.e., 12 – 20 years), and the number of Caucasians (n = 16) and non-Caucasians (n = 6) was similar in both groups. All participants were in Tanner Stage III, IV or V of pubertal development (Tanner Stage V: controls = 68%; depressed = 70%).[29,30] Controls had higher socioeconomic status (SES) scores (50.4 ± 7.9) than depressed youth (39.6 ± 11.0) (t = 3.19; p = 0.003). The groups did not differ significantly on IQ scores (controls = 109 ± 22.3; depressed 102 ± 14.0). All

participants were medically healthy and free from alcohol or illicit drug use, as determined by physical examination, full chemistry panel, thyroid function tests, electrocardiogram and urine drug screens. Prior to performing the research procedures, all participants signed an informed consent form (adolescents under 18 years signed an assent form and parents signed the informed consent document), approved by the local Institutional Review Board.

Diagnostic Evaluation

Psychiatric disorders were assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children - the Present and Lifetime Version (K-SADS-PL).[31] The K-SADS-PL was administered separately to the adolescent and the parent, and both were re-interviewed to resolve any discrepancies. Summary scores were tabulated based on the information obtained from both informants. The Family History-Research Diagnostic Criteria (FH-RDC) was used for the evaluation of psychiatric disorders in family members.[32] The FH-RDC is sensitive for obtaining information from knowledgeable relatives.[33] SES was assessed with the Hollingshead Four-Factor Index of Social Status,[34] and the Intelligence Quotient (IQ) was estimated from Vocabulary and Block Design scores using the Wechsler Intelligence Scale for Children (WISC IV) for ages <16 years,[35] and Wechsler Adult Intelligence Scale III for ages ≥16 years.[36]

Behavioral Task

The WOF is a computerized two-choice decision-making task involving probabilistic monetary rewards with varying levels of risk (for a more detailed description of the task, see the Online Supplement).[24] This task has been used in other studies of adolescents and adults,[16,24–26,37,38] and it allows an analysis of reward-selection separately from the other phases of decision-making. The WOF task used in the current study was comprised of two monetary and one plain/control wheels (see Figure 1). The monetary wheels were composed of two slices, each representing an option. One monetary wheel, the 2575 wheel, presented two options of different probability of win (risk),a *low* (25%) probability and a *high* (75%) probability and different reward, a *high*-magnitude ($6 or $3) and a *low*-magnitude (i.e., $2 or $1)] option. The other monetary wheel, the 5050 wheel, presented two options of equal-risk (50%) and equal reward ($1/1). For the 2575 wheel, the low (25%) probability condition was always associated with the higher reward ($6 or $3) and the high (75%) probability condition with the lower reward ($2 or $1). The proportional variations in the probability of winning and magnitude of reward in the two options of the 2575 wheel (i.e., $6/$2 and $3/$1) were set so that the expected value (EV) was the same for these two options. For example, in the $3/$1 wheel, selection of the high-risk option with 25% probability of winning $3 (EV = 3*0.25 = 0.75) was equal to the selection of low-risk option with 75% probability of winning $1 (EV = 1*0.75 = 0.75); and for the $6/$2 wheel, the selection of the high-risk option with 25% probability of winning $6 (6*0.25 = 1.50) was identical to the selection of low-risk option with 75% probability of winning $ 2 (2*0.75 = 1.50). The plain wheel was included to control for the visual and motor aspects of the task. The order of presentation for all conditions was fully randomized. The task did not include a jittered inter-trial interval (i.e., there was no non-task baseline)

The task comprised four runs of 7.8 minutes each. Thirty-nine trials or wheel types were presented in each of the four runs [i.e., twenty-four 2575 wheels, eight 5050 wheels and seven plain/control wheels]. Each trial consisted of 3 phases; selection, anticipation, and feedback [(4 seconds duration in each phase); see Figure 1]. Because the task is relatively complicated and the primary aim of this paper was to compare behavioral and neurobiological aspects of risk-taking behavior in healthy and depressed adolescents, only the selection phase is reported here. Data from the other phases of decision-making will be presented in subsequent publications. Subjects were instructed to try to win as much money

as possible. Their compensation was up to $50 for participation in the neuroimaging study, and additional compensation was based on earnings in 2 of 4 randomly selected runs. The task was administered using the E-Prime software.[39]

Imaging Parameters and Processing

Functional magnetic resonance imaging (fMRI) technique was used to measure regional blood oxygen level dependent (BOLD) signal during performance of the task. A General Electric 1.5 Tesla scanner was employed and gradient echo planar images (EPI) were acquired in 26, 5 mm sagittal slices per brain volume. The following imaging parameters were used: EPI gradient echo pulse sequence, TR = 2000 ms; TE = 20 ms; Flip = 90°; slice spacing = 0; field of view = 200 mm; matrix = 64 mm × 64 mm. The raw fMRI data acquired from each subject were slice-time corrected and converted to ANALYZE image format using Analysis of Functional NeuroImages (AFNI) software.[40] The first 6 scans (or images acquired during the first 12 s) were deleted to remove potential artifacts related to signal stabilization. The stimulus onsets of all data were included in the design with "hemodynamic response function (HRF) only" option in the Statistical Parametric Mapping software – Version 2 (SPM2).[41] At the individual subject level (i.e., time series), event-related response amplitudes were estimated, employing the General Linear Model (GLM) in SPM2 for each of the two active (2575 and 5050) and plain/control wheel conditions. A mean image was generated from the realigned functional volumes to determine parameters for spatial normalization into Montreal Neurological Institute (MNI) standardized space employed in SPM2.[41] Normalized images were then smoothed with a 10×10×10 mm Gaussian kernel. Finally, the smoothed images were filtered using a Butterworth low pass filter with a cut-off frequency of 0.15 to remove any high frequency noise.

A Visual Basic for Applications (VBA) macro was run on the E-Prime task data to obtain scan-onset vectors that were used to model the design matrix. The fMRI design was specified in the scans with the vectors obtained from the above step. The mean image generated in the realignment step is the mean of all functional scan volumes within the run, which were imported into the design matrix with a standard SPM2 high-pass filter of 128 seconds and no global scaling. Percent signal change was measured in each *a priori* ROI constructed from the Wake Forest University (WFU) Pick Atlas, and signal change was measured based on contrasting the beta images within the two groups with respect to the session/run effect image in all the voxels of the ROI, not just the peak voxels.

Statistical Analysis

At the individual level, three sets of analyses were conducted with events during the reward-selection phase: (1) high-risk (25% probability) choice events vs. low-risk (75% probability) choice events from the 2575 wheel; (2) high-risk (25% probability) choice events vs. equal-risk (5050 wheel) control event; and (3) risk/reward (2575 wheel) choice event vs. control (plain wheel) control event.

Although the contrast activations were collected brain-wide, this report considered three *a priori* prefrontal regions (divided into right and left) that have been linked consistently to incentive and cognitive-conflict processing,[4,42–47] the dorsal ACC (BA 24, 32), the OFC (BA 11, 47), and the mPFC (BA 8, 10). Voxel-wise *t*-tests were performed within the anatomically-defined region of interest (ROI) masks based on the standard WFU Pickatlas toolbox. The statistical threshold for significance within each ROI was set at $p < .05$ after small volume correction. For all group-level analyses, a random effects model was employed using the analysis of variance (ANOVA) in SPM2. Bonferroni's method was used to correct for multiple comparisons between pre-specified ROIs by multiplying *p* values with the number of ROI comparisons in each of the three contrasts. Independent sample t-

tests compared the reaction times and the selection rates of high- vs. low-risk options between the two groups. Spearman Rank Test was used to assess the correlation between percent BOLD signal change for the specified contrasts and high-risk behavior (frequency of low-probability/high-reward selections, i.e., 25% choices). Fisher r- to -z test was conducted to examine group differences in correlation coefficients for the relationship between percent BOLD signal change and high-risk selections. Initially, univariate analyses were performed to examine the relationships between sociodemographic factors (namely, age, gender, ethnicity, Tanner Stage, IQ, and SES) and percent BOLD signal change in response to high-risk behavior. Significant variables were then entered into a multiple regression model.

Results

Behavioral Performance

The groups did not differ on behavioral performance. For further details, see the Online Supplement.

ROI-based Brain Activation Patterns in Healthy and Depressed Groups

High-risk (25%) choice events vs. low-risk (75%) choice events contrast—This contrast produced no between-group differences in activation of the pre-specified ROIs. Within-group analysis revealed bilateral activation of the ACC, mPFC, and OFC in healthy adolescents (see Figure 2a, top section; and Table 1). In the depressed group, only right OFC was activated, while right ACC and left OFC showed a trend ($p \leq .10$) (see Figure 2a, bottom section; and Table 1). The reverse contrasts did not show any significant activation in either group.

High-risk (25%) choice events vs. equal-risk (50/50) probability contrast—The healthy > depressed comparison yielded activation of the right ventrolateral OFC ($t = 2.28$; $p = 0.01$). The reverse contrast (depressed > healthy) produced activation of the right caudal ACC ($t = 2.39$; $p = 0.01$), and left dorsal OFC ($t = 2.09$; $p = 0.02$). Within-group analysis showed activation of the left dorsal ACC, right ACC, right mPFC, and right ventrolateral OFC in healthy adolescents (see Figure 2b, top section). The depressed group manifested activation only in the left mPFC (see Figure 2b, bottom section). No significant activation occurred in the reverse contrast in either group.

Risk/reward (2575) wheel vs. control (plain) wheel contrast—This contrast revealed no between-group differences in any of the pre-specified ROIs. The within-group analysis revealed activation of the right dorsal ACC, left mPFC, and right OFC in healthy adolescents (see Figure 2c, top section). Depressed adolescents demonstrated activation of the right ACC, and right OFC (see Figure 2c, bottom section). No activations were observed in the reverse contrast in either group.

Correlations between Functional ROIs and Risk-related Behavior

In healthy subjects, the proportion of high-risk (25% probability) choice correlated negatively with percent BOLD signal change in the left ACC ($r = -0.63$, $p = 0.002$), right ACC ($r = -0.57$, $p = 0.008$), right OFC ($r = -0.51$, $p = 0.02$), left OFC ($r = -0.49$, $p = 0.02$), and left mPFC ($r = -0.51$; $p = 0.02$). All correlations remained significant after controlling for age, gender, ethnicity, IQ or SES. However, only left and right ACC survived Bonferroni's correction (see Figure 3). There were no significant correlations between high-risk behavior and neuronal activation patterns in the depressed group (r values ranging from −0.03 to −0.22). Fisher r- to –z test showed significant differences in correlation coefficients between healthy and depressed groups in the left and right ACC ($p = .004$, FDR = .022; and $p = .008$, FDR = .022, respectively), and left mPFC ($p = .02$, FDR = .03).

Relationship between Sociodemographic Factors and Change in BOLD Signal

The only significant relationship between prefrontal activation and sociodemographic factors was found in healthy adolescents who showed a negative correlation between SES and percent change in BOLD signal in the right and left ACC (Spearman's $r = -0.63$, $p = 0.006$; and $r = -0.62$; $p = 0.007$, respectively), and right and left mPFC (Spearman's $r = -0.87$, $p = 0.0001$; and $r = -0.57$, $p = 0.01$, respectively) in the monetary 2575 wheel vs. control wheel condition. There were no significant correlations between percent change in BOLD signal in the pre-specified ROIs and Tanner Stage or IQ scores.

Discussion

This study compared neurobiological substrates associated with the selection of probabilistic monetary rewards in healthy and depressed adolescent volunteers. Reward-related behavior in both groups was associated with activation of similar prefrontal regions that mediate response-inhibition and the coding of reward values (lateral OFC), as well as conflict and error-monitoring (dorsal ACC and mPFC).[16] A direct comparison of these two groups showed few significant differences; in the contrast comparing the high-risk vs. the less-challenging equal-risk conditions, healthy adolescents had greater activation than depressed participants in the right lateral OFC, whereas depressed adolescents showed greater activation than healthy subjects in the left dorsal OFC and right caudal ACC. Since the right lateral OFC mediates inhibitory control and the caudal ACC is involved in conflict-monitoring,[16] these findings suggest that, during risky decision-making, healthy adolescents employed the brain regions involved in inhibitory control whereas depressed adolescents engaged areas involved in conflict-monitoring. The reduced inhibitory control, as reflected by reduced activation of the right lateral OFC in depressed adolescents, may provide a potential neurobiological surrogate for impulsivity, which is frequently associated with suicidal behavior and substance abuse among depressed youngsters. Taken together, these findings suggest that the depressed adolescents in this study may have used more emotional judgment during the selection of high-risk options compared to healthy adolescents. This hypothesis could be confirmed by self-reports on how the participants determined their choices, but, unfortunately, self-reports were not collected.

In contrast to a previous report,[22] depressed adolescents did not show greater activation of the mPFC than healthy controls in the present study. These contradictory findings might be explained by methodological differences between the two studies. The current study assessed neural responses during the selection phase, while the previous study measured neural responses during the feedback phase. Given the social cognitive functions of the mPFC,[27,28] increased activation of this region in response to rewards in depressed adolescents suggests that these adolescents may be comparing themselves to others instead of enjoying the reward.[22]

In the present study, SES and prefrontal activation were correlated in the healthy adolescents but not in the depressed youth. This may be explained by lesser variance in SES and prefrontal activation in the depressed group (depressed adolescents had significantly lower SES scores than controls, and within-group analyses showed less robust prefrontal activation in this cohort). Among healthy adolescents, the negative correlation between SES and prefrontal activation suggests that adolescents of lower SES may be more conflicted than higher-SES youth when making choices involving monetary rewards, because small gains or losses likely have a greater subjective value in low-SES than high-SES participants. There was no relationship between pubertal status and prefrontal activations. This could be explained by the relative lack of variance in pubertal maturation in the sample, with the majority of participants being in Tanner Stage V. Future investigations should recruit

adolescents across pubertal states and also include gonadal hormonal measures in order to examine the association between pubertal status and the neurobiology of decision-making.[17]

Among healthy adolescents, a risky choice (a low-probability but high-magnitude reward) was associated with less prefrontal activation, confirming that differences in prefrontal function may be associated with risk-taking behavior.[18] The lack of relationship between these two measures of prefrontal function and risky choice in depressed adolescents may also reflect relatively less variability in prefrontal responses during the selection of rewards in this group. Although the behavioral performance was comparable in healthy and depressed adolescents, the within-group analyses of prefrontal activations were less robust in the depressed group as compared to healthy controls

The findings from this study should be interpreted in the context of methodological limitations. The sample consisted of adolescent volunteers with stringent eligibility criteria, and the results might not be generalizable to adolescents in the community. Also, the temporal dissociation of the BOLD responses during the selection phase vs. the anticipation phase cannot be estimated due to the lack of a jittered inter-trial interval in the paradigm. In addition, the separation of selection and anticipation phases may seem to be difficult to achieve because anticipation is probably present even before the selection since it contributes to the selection of choices. Similarly, the dissociation of the neuronal responses associated with reward-selection from the responses associated with the feedback phase from the preceding trial may also be difficult to achieve. However, the brain regions involved in feedback (i.e., ventral striatum and mPFC) are different from the regions involved in the reward-selection (i.e., lateral PFC and OFC).[26] Hence, the neuronal activity associated with reward-selection is unlikely to be confounded by the neuronal responses associated with feedback phase from the preceding trial in the regions examined. Finally, it is difficult to disentangle neuronal activity associated with the selection of reward-level and that associated with probability-level (i.e., a high-risk/low-probability choice always was associated with a reward of larger magnitude, whereas a low-risk/high-probability choice was always associated with a reward of smaller magnitude). Despite these limitations, this is one of the few studies to report patterns of prefrontal activation in response to varying levels of risk and reward in healthy and depressed adolescents without the confounding effects of variable reaction times and expected values.

The results from the present study indicate that reward-related behavior engages similar prefrontal monitoring regions (i.e., ACC, mPFC, and OFC) in healthy and depressed adolescents. There were, however, subtle differences between the groups, with healthy adolescents primarily recruiting prefrontal regions involved in inhibitory control and depressed adolescents engaging areas involved in conflict-monitoring. Also, the lack of a relationship between high-risk behavior and prefrontal activation in depressed adolescents suggests that the variability in prefrontal responses to risky behavior may be reduced in adolescent depression. These findings might be helpful to identify potential biomarkers for targeted interventions in youngsters suffering from depression. Of note, the current findings are based on initial results from an ongoing longitudinal study. Longitudinal information likely will provide a better understanding of the components of reward-related decision-making and their relationship to the clinical course of depression or prognosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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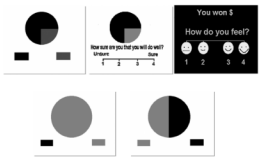

Figure 1.
The Wheel of Fortune (WOF) task depicting the (a) selection (4s), (b) anticipation (4s), and (c) feedback (4s) phases of the 25/75 wheel (top section). Note: The bottom section shows the plain/control wheel (left), and the 50/50 wheel (right).

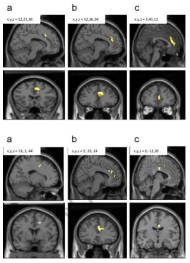

Figure 2.

Peak voxels in the right anterior cingulate cortex in healthy and depressed adolescents

a. High-risk (25% probability) vs. low-risk (75% probability) choice contrast

b. High-risk (25% probability) vs. equal-risk (50/50 probability) choice contrast

c. Reward-related behavior (25/75 probability) versus control (plain wheel) choice contrast

Healthy Controls (Top Section)

- **a** 25% vs. 75%
- **b** 25% vs. 50%
- **c** 25/75 vs. control

Depressed Adolescents

- **a** 25% vs. 75%
- **b** 25% vs. 50%
- **c** 25/75 vs. control

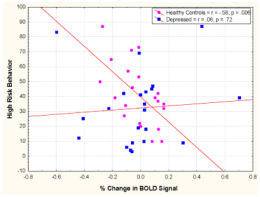

Figure 3.
Correlation between %change in blood-oxygen-level-dependent (BOLD) signal in the right anterior cingulate cortex and high-risk behavior in the risk/reward (25/75 wheel) vs. control/plain wheel contrast in healthy and depressed adolescents.

Table 1

Region of interest (ROI) group activations in healthy and depressed adolescents in the high-risk (25%) vs. low-risk (75%) contrast.

	L-ACC					R-ACC				
	Equivk	***p* voxel**	**t**	**x, y, z**	**Signal Change - Range (SD)**	**Equivk**	***p* voxel**	**t**	**x, y, z**	**Signal Change - Range (SD)**
Healthy Adolescents	27	0.004	2.99	−3, 36 28	−0.09—0.13 (0.06)	69	0.001	5.09	12,36,24	−0.11—0.12 (0.06)
Depressed Adolescents	10	0.018	2.26	−6, 48, 4	−6.64—0.38 (1.42)	25	0.012	2.40	9, 33, 24	−1.69—0.29 (0.38)

	L-OFC					R-OFC				
	Equivk	***p* voxel**	**t**	**x, y, z**	**Signal Change - Range (SD)**	**Equivk**	***p* voxel**	**t**	**x, y, z**	**Signal Change - Range (SD)**
Healthy Adolescents	34	0.003	3.07	−39, 15, −16	−0.11—0.34 (0.11)	106	0.003	3.22	27, 27, −12	−0.12—0.36 (0.11)
Depressed Adolescents	6	0.010	2.53	−36, 30, −4	−0.33—0.40 (0.16)	43	0.006	2.79	33, 42, −16	−1.84—0.25 (0.42)

	L-mPFC					R-mPFC				
	Equivk	***P*voxel**	**t**	**x, y, z**	**Signal Change - Range (SD)**	**Equivk**	***p* voxel**	**t**	**x, y, z**	**Signal Change - Range (SD)**
Healthy Adolescents	9	0.003	3.14	−12, 66, 16	−0.12—0.16 (0.08)	51	0.001	3.83	45, 48, 4	−0.06—0.13 (0.07)
Depressed Adolescents	18	0.022	2.16	−6, 51, 4	−0.25—0.49 (0.18)	21	0.017	2.30	15 54 4	−0.17—2.44 (2.35)

Note: ROI activation in the contrast 25% (high-risk) versus 75% (low- risk) probability. The ROIs include the left and right anterior cingulate cortices (L-ACC, R-ACC); left and right orbitofrontal cortices (L-OFC, R-OFC), and left and right medial prefrontal cortices (L-mPFC; R-mPFC). Results show significant activations ($p < 0.05$ small volume corrected) based on peak voxels within the pre-specified ROIs in response to high-risk versus low-risk selections. Statistics for ROI activations that survived multiple comparisons are bolded. Equivk is the cluster size of voxels, and *x, y, z* (mm) are the coordinates of the peak voxel based on the brain template provided by the Montreal Neurological Institute (MNI). The range and SD of percent change in blood-oxygen-level-dependent (BOLD) signal change in ROIs is documented to show the degree of variation in the two groups. No ROI showed significantly more activation during low-risk (75% probability) than during high- risk (25% probability) selections.