# **FAST-TRACK REPORT**

# Risk-taking and the adolescent brain: who is at risk?

# Adriana Galvan,<sup>1</sup> Todd Hare,<sup>1</sup> Henning Voss,<sup>2</sup> Gary Glover<sup>3</sup> and B.J. Casey<sup>1</sup>

1. Sackler Institute for Developmental Psychobiology, Weill Medical College of Cornell University, USA

2. Department of Radiology, Weill Medical College of Cornell University, USA

3. Center for Advanced Magnetic Resonance Technology, Stanford University, USA

## Abstract

Relative to other ages, adolescence is described as a period of increased impulsive and risk-taking behavior that can lead to fatal outcomes (suicide, substance abuse, HIV, accidents, etc.). This study was designed to examine neural correlates of risk-taking behavior in adolescents, relative to children and adults, in order to predict who may be at greatest risk. Activity in reward-related neural circuitry in anticipation of a large monetary reward was measured with functional magnetic resonance imaging, and anonymous self-report ratings of risky behavior, anticipation of risk and impulsivity were acquired in individuals between the ages of 7 and 29 years. There was a positive association between accumbens activity and the likelihood of engaging in risky behavior across development. This activity also varied as a function of individuals' ratings of anticipated positive or negative consequences of such behavior. Impulsivity ratings were not associated with accumbens activity, but rather with age. These findings suggest that during adolescence, some individuals may be especially prone to engage in risky behaviors due to developmental changes in concert with variability in a given individual's predisposition to engage in risky behavior, rather than to simple changes in impulsivity.

# Introduction

Relative to other ages, adolescence has been described to be a period of increased risk-taking (Spear, 2000), yet not all adolescents are risk-takers. Individual differences in taking risks has been recognized in psychology for some time (Benthin, Slovic & Severson, 1993). Some theorists have postulated that dopaminergic mesolimbic circuitry, implicated in reward processing, underlies risky behavior (Blum, Braverman, Holder, Lubar, Monastra, Miller, Chen & Comings, 2000) and that individual differences in this circuitry might relate to the propensity to engage in risky behavior (O'Doherty, 2004). Increased activity of this circuitry, especially the nucleus accumbens region, is associated with risky choices in adults on monetary-risk paradigms (Montague & Berns, 2002; Matthews, Simmons, Lane & Paulus, 2004; Kuhnen & Knutson, 2005). Adolescents show exaggerated accumbens activity to rewarding outcomes relative to children or adults (Ernst, Nelson, Jazbec, McClure, Monk, Leibenluft, Blair & Pine, 2005; Galvan, Hare, Parra, Penn, Voss, Glover & Casey, 2006). However, it remains unclear

whether accumbens activity may serve as a biological marker for the likelihood of an individual to engage in risky behavior in everyday life or explain how this tendency may change across development.

#### **Methods**

#### Participants

Twelve right-handed healthy adults (six female, ages 23–29 with mean age of 25.3 years), 12 adolescents (six female, ages 13–17 with mean age of 16 years), and 13 children (seven female, ages 7–11 with mean age 9.8 years) were included in the fMRI experiment (Galvan *et al.*, 2006). A separate statistical analysis of developmental neural activity with these subjects was reported previously (Galvan *et al.*, 2006). A subset of these individuals: ten adults, seven adolescents and nine children completed all ratings and were included in the current analysis. Only subjects who completed the questionnaires were included in the analysis reported in this paper.

Address for correspondence: B.J. Casey, The Sackler Institute for Developmental Psychobiology, Weill Cornell Medical College of Cornell University, 1300 York Ave, Box 140, New York 10021, USA; e-mail: bjc2002@med.cornell.edu

Subjects had no history of a neurological or psychiatric disorder and children and adolescents had an IQ of greater than 89. After complete description of the study to the subjects, written informed consent was obtained for a protocol approved by the Institutional Review Board of Weill Cornell Medical College of Cornell University. Adolescents and children were simulated in a mock scanner prior to image acquisition to acclimatize them to the scanner environment.

#### Risk-taking and impulsivity measures

#### Risk-taking assessment

A modified version of the Cognitive Appraisal of Risk Activities (CARE) (Fromme, Katz & Rivet, 1997) was used to assess evaluation of risks and perception of consequences. Participants were asked to provide ratings on six factors, including Risky Sexual Behavior, Heavy Drinking, Illicit Drug Use, Aggressive and Illegal Behaviors, Irresponsible Academic/Work Behaviors, and High Risk Sports. There were a total of 34 items. For each item, participants were asked to provide three ratings from 1 to 7 (1 = Not likely at all; 7 = Extremely likely): (1) the likelihood of engaging in this activity in the next 6 months; (2) the likelihood of a negative consequence and (3) the likelihood of a positive consequence. This risk-taking measure was originally developed in a sample of young adults and test-retest reliability and construct validity of the measure have been established (Fromme et al., 1997) and the measure has shown high degrees of validity in older adults and in clinical samples (Fromme et al., 1997).

Given some adult-specific questions on the CARE questionnaire, a child appropriate version was developed and administered to the children in the study. The CARE-C version did not include questions regarding sexual and substance abuse-related behavior, but all other parameters were kept constant. In order to compare the different age groups, each subject's raw score was normalized by dividing by the number of questions that were answered.

#### **Risk** perception

A shortened, modified version (Gardner & Steinberg, 2005) of the Benthin Risk Perception Measure (Benthin *et al.*, 1993) was used to assess risk preference. This measure assesses both risk perception (the extent to which one perceives a given activity as having the potential for adverse consequences) and risk preference (whether one believes the benefits inherent in an activity outweigh the costs, or vice versa) (Gardner & Steinberg,

2005). Participants were presented with six hypothetical scenarios involving risky behavior. These scenarios included: drinking alcohol, using fireworks, vandalizing property, riding in a car with a drunk driver, smoking cigarettes, and stealing from a store. They were then presented with four questions for each scenario and asked to provide a rating from 1 to 7: (1) If you did this activity, how scary are the things that could happen? (1 = Risks)are not scary at all; 7 = Risks are very scary); (2) If you did this activity, how much are you at risk for something bad happening? (1 = I would be very much at risk; 7 = Iwould not be at risk); (3) How would you compare the benefits (or pleasures) of this activity with the risks (1 =Risks much greater than the benefits; 4 = Risks equal the benefits; 7 = Benefits are much greater than the risks); (4) If something bad happened because of this activity, how serious would it be? (1 = Not at all serious; 7 =Very serious). A higher rating for each scenario is associated with a greater risky behavior than a lower rating.

#### Impulsivity

The Connors Impulsivity Scale – Revised (Connors, Sitarenios, Parker & Epstein, 1998) was used as a measure of impulsive behavior. A modified version of the scale with 15 items was employed. Participants were asked to consider their behavior during the past month and rate each behavior according to a 0-3 Likert scale (0 = not at all true to 3 = very much true).

## fMRI paradigm

Participants were tested using an adapted version of a delayed response two-choice task previously used in nonhuman primates (Cromwell & Schultz, 2003) and described previously (Galvan, Hare, Davidson, Spicer, Glover & Casey, 2005) in an event-related fMRI study. In this task, three cues were each associated with a distinct reward value that was counterbalanced across subjects. Subjects were instructed to press either their index or middle finger to indicate the side on which a cue appeared when prompted, and to respond as quickly as possible without making mistakes.

The stimulus parameters were as follows. One of three pirate cartoon images was presented in pseudorandom order on either the left or right side of a centered fixation for 1000 msec. After a 2000-msec delay, subjects were presented with a response prompt of two treasure chests on both sides of the fixation (2000 msec) and instructed to press a button with their right index finger if the pirate was on the left side of the fixation or their right middle finger if the pirate was on the right side of the fixation. After another 2000-msec delay, reward feedback of either a small, medium or large amount of coins was presented in the center of the screen (1000 msec). Each pirate was associated with a distinct reward amount. There was a 12-sec intertrial interval (ITI) before the start of the next trial. Total trial length was 20 sec. Subjects were not rewarded if they failed to make a response or if they made an error; in both cases, they received an error message at the time they would normally receive reward feedback.

Subjects were guaranteed \$50 for participation in the study and were told they could earn up to \$25 more, depending on performance (as indexed by reaction time and accuracy) on the task. Although the reward amounts were distinctly different from one another, the exact value of each reward was not disclosed to the subject because during pilot studies, subjects reported counting the money after each trial and we wanted to avoid this possible distraction. Stimuli were presented with the integrated functional imaging system (IFIS) (PST, Pittsburgh) using an LCD video display in the bore of the MR scanner and a fiber optic response collection device.

The experiment consisted of five runs of 18 trials (six each of small, medium and large reward trials), which lasted 6 min and 8 s each. Each run had six trials of each reward value presented in random order. At the end of each run, subjects were updated on how much money they had earned during that run. Prior to beginning the experiment, subjects were shown the actual money they could earn to ensure motivation. They received detailed instructions that included familiarization with the stimuli employed. For instance, subjects were shown the three cues and three reward amounts they would be seeing during the experiment. They were not told how the cues related to the rewards. We explicitly emphasized that there were three amounts of reward, one being small, another medium and another large. These amounts are visually obvious in the experiment as the number of coins in the stimuli increases with increasing reward.

#### Image acquisition

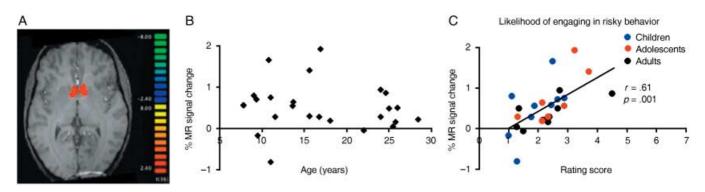
Imaging was performed using a 3T General Electric (Milwaukee, WI) MRI scanner using a quadrature head coil. Functional scans were acquired using a spiral in and out sequence (Glover & Thomason, 2004). The parameters were: repetition time (TR) = 2000 ms, echo time (TE) = 30 ms,  $64 \times 64$  matrix, 29 5-mm coronal slices,  $3.125 \times 3.125$ -mm in-plane resolution, flip 90 for 184 repetitions, including four discarded acquisitions at the beginning of each run. Anatomical T1 weighted in-plane scans were collected (TR = 500 msec, TE = minimum,  $256 \times 256$ , FOV = 200 mm, 5-mm slice thickness) in the same locations as the functional images in addition to a

3-D data set of high resolution SPGR images (TR = 25, TE = 5, 1.5-mm slice thickness, 124 slices).

#### Image analysis

The Brainvoyager QX (Brain Innovations, Maastricht, The Netherlands) software package was used to perform a random effects analysis of the imaging data. Before analysis, the following preprocessing procedures were performed on the raw images: 3-D motion correction to detect and correct for small head movements by spatial alignment of all volumes to the first volume by rigid body transformation, slice scan time correction (using sinc interpolation), linear trend removal, high-pass temporal filtering to remove non-linear drifts of three or fewer cycles per time course, and spatial data smoothing using a Gaussian kernel with a 4-mm FWHM. Estimated rotation and translation movements never exceeded 2 mm for subjects included in this analysis. Functional data were co-registered to the anatomical volume by alignment of corresponding points and manual adjustments to obtain optimal fit by visual inspection and were then transformed into Talairach space. Talairach transformation was performed in two steps using the BrainVoyager QX software package (Brain Innovations, Maastricht, The Netherlands). The first step consisted of rotating the 3-D data set for each subject to be aligned with the stereotaxic axes. For this step the location of the anterior commissure (AC) and the posterior commissure (PC) as well as two rotation parameters for midsagittal alignment was specified manually. In the second step the extreme points of the cerebrum were specified. These points together with the AC and PC coordinates were then used to scale the 3-D data sets into the dimensions of the standard brain of the Talairach and Tournaux atlas. Functional voxels were interpolated from the acquisition voxel size of 48.83 mm<sup>3</sup> to a resolution of 1 mm<sup>3</sup> during Talairach transformation. The nucleus accumbens was defined by Talairach coordinates in conjunction with reference to the Duvernoy brain atlas (Talairach & Tournoux, 1988; Duvernoy, 1999).

Statistical analyses of the imaging data were conducted using a general linear model (GLM) on the whole brain and are described in detail elsewhere (Galvan *et al.*, 2006). We focused on activation in the nucleus accumbens in anticipation (e.g. following large reward cue) of large reward outcomes during late trials of the experiment, given previous findings showing robust responses across developmental populations to this condition. The early and late trials were defined as the first and last runs (18 trials each), respectively, of the experiment, as described previously (Galvan *et al.*, 2005). Our imaging analyses were driven largely by behavioral data



**Figure 1** (*A*) The localization of nucleus accumbens activity in anticipation of reward. (*B*) Percent change in fMRI signal in accumbens in anticipation of large relative to small reward as a function of age. The percent MR signal change corresponds to a ~5–6 hemodynamic lag following the behavioral response. (*C*) The association between accumbens activity to reward and likelihood of engaging in risky behavior as a function of age group.

reported previously (Galvan *et al.*, 2005) showing that reaction times between the different reward values (small, medium and large) did not differ significantly until the last run (late trials).

The GLM comprised all runs (the full trial) [185 (5 runs  $\times$  37 subjects) z-normalized functional time courses] and was conducted with reward value as the primary predictor. The predictors were obtained by convolution of an ideal boxcar response (assuming a value 1 for the volume of task presentation and a value of 0 for the remaining time points) with a linear model of the hemodynamic response and used to build the design matrix of each time course in the experiment. Only correct trials were included and separate predictors were created for error trials. Post-hoc contrast analyses were then performed based on *t*-tests on the beta weights of predictors to identify a region of interest in the nucleus accumbens, given our a priori hypothesis. Contrasts were conducted with a random effects analysis. Percent changes in peak MR signal (for the entire trial relative to a brief fixation period preceding trial onset) for each subject were calculated using event-related averaging over significantly active voxels. Corrections for multiple comparisons were based on Monte Carlo simulations, which were run using the AlphaSim program within AFNI (Cox, 1996), to determine appropriate contiguity thresholds to achieve a corrected alpha level of p < .01 (Forman, Cohen, Fitzgerald, Eddy, Mintun & Noll, 1995) based on a search volume of 450 mm<sup>3</sup> for the nucleus accumbens.

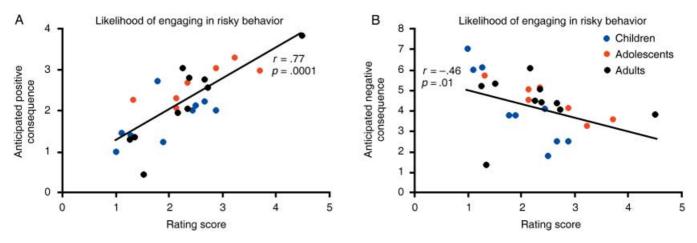
## Results

Enhanced accumbens activity [right (x = 6, y = 5, z = -2) and left (x = -8, y = 6, z = -2)] was shown for a reward

 Table 1
 Activations to reward versus baseline

| Region                           | Talairach $(x, y, z)$ | T stat | Cluster<br>size |
|----------------------------------|-----------------------|--------|-----------------|
| Greater activation to reward     |                       |        |                 |
| Right Nucleus Accumbens          | 6, 5, -2              | 4.25   | 14              |
| Left Nucleus Accumbens           | -8, 6, -2             | 4.36   | 11              |
| Right Orbital Frontal Cortex     | 46, 31, 1             | 3.61   | 16              |
| Right Inferior Frontal Gyrus     | 44, 33, 26            | 4.5    | 8               |
| Right Inferior Parietal Lobule   | 43, -49, 38           | 3.99   | 34              |
| Right Putamen                    | 25, 8, 5              | 7.26   | 9               |
| Cingulate Cortex                 | 2, -8, 34             | 2.18   | 5               |
| Right Caudate                    | 13, 5, 17             | 2.2    | 5               |
| Greater activation to baseline   |                       |        |                 |
| Ventral Medial Prefrontal Cortex | 1, 32, -1             | 5.09   | 22              |
| Left Superior Frontal Cortex     | -22, 32, 42           | 4.59   | 20              |
| Temporal Lobe                    | 45, -5, -11           | 5.86   | 27              |
| Right Superior Parietal          | 16, -49, 54           | 4.75   | 23              |
| Anterior Cingulate Cortex        | 5, 29, 33             | 2.24   | 5               |
| Cerebellum                       | 6, -43, -33           | 2.71   | 10              |

relative to baseline contrast, with reward value as the primary predictor, across all subjects and runs of the experiment for the entire trial relative to the 2-s intertrial interval preceding the start of the next trial (see Figure 1 and Supplemental Table 1) that varied across development (Figure 1b). The percent MR signal change corresponds to a ~5–6 hemodynamic lag following the behavioral response. This activity was positively correlated with individuals' anonymous ratings of risk-taking behavior and of anticipated positive or negative consequences of such behavior. Specifically, there was an association between accumbens activity and the likelihood of engaging in risky behavior in the near future (r = .61, p = .001, Figure 1c). Within each age group, there was a significant association between accumbens activity and the likelihood



**Figure 2** (*A*) The association between likelihood to engage in risky behavior and anticipation of positive consequences across age groups with children (r = .62, p = .07) depicted in blue, adolescents (r = .81, p = .02) in red, and adults (r = .85, p = .002) in black. (*B*) The association between likelihood to engage in risky behavior and anticipation of negative consequences across age groups with children (r = -.92, p = .0001) depicted in blue, adolescents (r = -.92, p = .003) in red, and adults (r = -.3, p = .93) in black.

of engaging in risky behavior in adults (r = .69, p = .02) and adolescents (r = .77, p = .04) and a trend towards significance in children (r = .6, p = .08).

Anticipated consequences of risky behavior was related to accumbens activity as well. There was a positive correlation between individuals' ratings of the anticipation of a positive consequence and accumbens activity (r = .44, p = .02), such that individuals who anticipated positive consequences of engaging in risky behavior activated this region more. This pattern appeared to change across development, as adults (r = .64, p = .04) and adolescents (r = .78, p = .03) showed an association between accumbens activity and anticipated positive consequences of risk-taking, but children did not (r = .42, p = .27). There was a negative correlation between individuals' ratings of the anticipation of a negative consequence and accumbens activity (r = -.62, p = .001) such that individuals who anticipated negative consequences of engaging in risky behavior activated this region less. This pattern also appeared to change across development, with children and adolescents showing a tighter coupling between accumbens activity and anticipated negative consequences of risk-taking (r = -.73, p = .02 and r = -.83, p = .02,respectively) than adults (r = -.51, p = .12). The correlation between accumbens activity and both likelihood of engaging in risky behavior and anticipated consequences, survived multiple comparisons correction (p < .05/5 =< .01), controlling for both age (r = .74, p = .001) and gender (r = .71, p = .001).

Across the entire sample, the likelihood of engaging in risky behavior correlated with the anticipation of a positive consequence (r = .77, p = .0001) and anticipation of a negative consequence (r = -.46, p = .01), see Figure 2). Adolescents (r = .81, p = .02) and adults (r = .85, p = .002) showed a positive correlation between the likelihood of engaging in risky behavior and anticipation of a positive consequence, while children showed a trend towards significance (r = .62, p = .07). Children (r = -.92, p = .0001) and adolescents (r = -.92, p = .003) showed a negative correlation between the likelihood of engaging in risky behavior and anticipation of a negative consequence, but adults did not (r = -.3, p = .93). Children (r = -.69, p = .03) and adolescents (r = -.77, p = .04)also showed a negative correlation between negative and positive consequences, but adults did not (r = -.12, p = .74).

There were no correlations between accumbens activity and the Connor's Impulsivity Scale (r = -.15, p = .49) or the Benthin risk perception measure (r = -.13, p = .52) across individuals. However, the impulsivity measure showed a negative correlation with age (r = -.47, p =.02), but the Benthin risk perception measure showed no such correlation (r = .16, p = .44). Neither of these scales correlated with likelihood of engaging in risky behavior as measured by the CARE (p > .25). There were no gender differences in the data. However, a larger sample would be needed to adequately address this question.

#### Discussion

This study examined whether individual differences in the likelihood of engaging in risky behaviors is associated with patterns of brain activity in reward-related circuitry in anticipation of reward. The findings suggest that individual differences in neurobiological substrates of reward and risk-taking might influence subsequent 'real-life' risky behavior, and that this is true across development.

First, these data show that whether an individual anticipates the potential consequences as positive or negative is related to both accumbens activity and the likelihood of engaging in risky behavior. For instance, individuals who expected a negative consequence to result from a risky behavior showed diminished accumbens activity in anticipation of reward (relative to other subjects) and were less likely to engage in risky behavior. Conversely, individuals who anticipated a positive consequence were more likely to engage in risky behavior. Second, the data suggest a developmental shift in reward-related accumbens activity and in how the perception of positive or negative consequences of risky behavior might influence actual engagement in risky behavior. Specifically, for children and adolescents, less risky behavior was associated with anticipated negative consequences while anticipated negative consequences did not seem to influence the likelihood of engaging in risky behaviors in adults. For adults and likewise for adolescents, risky behavior was associated with anticipated positive consequences consistent with previous adult studies (Fromme et al., 1997). These developmentally distinct findings suggest that engagement in risky behavior is associated with anticipated negative consequences in children and anticipated positive consequences in adults which are changing during adolescence. This potential shift in anticipation of consequences of risky behavior may underlie adolescent tendencies toward risky behaviors as immediate positive outcomes associated with social status among peers, substance use and sexual encounters may outweigh potential long-term negative consequences. Alternatively, individual differences in the perception of costs versus benefits of a risky behavior may determine whether the adolescent engages in the behavior. As such, a study of adolescents using a different costs and benefits scale showed that in general, the costs adolescents anticipate are more important than the anticipated benefits in determining risky health-compromising behaviors (Small, Silverberg & Kerns, 1993). When probed more carefully, data from the same sample show that the adolescents who did not engage in risky behaviors anticipated significantly more costs to the behaviors relative to their risk-taking peers (Small et al., 1993). Evidence in support of this notion in our own data comes from the finding that adolescents (and children) showed an inverse correlation between negative and positive consequences, such that those more likely to anticipate negative consequences

anticipated less positive consequences to result from engaging in risky behavior.

Adolescent behavior has been described as impulsive and risky, yet there appear to be different developmental trajectories for these behaviors. Specifically, a review of the imaging literature suggests that impulsivity is associated with immature ventral prefrontal development and gradually diminishes from childhood to adulthood (Casey, Galvan & Hare, 2005). In the current study, there was a negative correlation between impulsivity ratings and age, but no correlation between impulsivity ratings and ratings of risk-taking or accumbens activity. In contrast, risk-taking is associated with an increase in accumbens activity (Montague & Berns, 2002; Matthews, Simmons, Lane & Paulus, 2004; Kuhnen & Knutson, 2005) that is exaggerated in adolescents, relative to children and adults (Ernst et al., 2005; Galvan et al., 2006). Thus adolescent choices and behavior cannot be explained by impulsivity or protracted development of the prefrontal cortex alone, as children would then be predicted to be greater risk-takers.

In a previous study (Galvan et al., 2006), we showed developmental changes during adolescence in regions associated with reward sensitivity and risk-taking (e.g. Kuhnen & Knutson, 2005). Together with the current findings, these data suggest that individuals prone to risky behavior are at further risk during adolescence when neural systems underlying risky behaviors undergo significant development. Collectively, these data suggest that although adolescents as a group are considered risk-takers (Spear, 2000; Gardner & Steinberg, 2005), some adolescents will be more prone than others to engage in risky behaviors, putting them at potentially greater risk for negative outcomes. These findings underscore the importance of considering individual variability when examining complex brain-behavior relationships related to risk-taking and reward processing in developmental populations. Further, these individual and developmental differences may help explain vulnerability in some individuals to risk-taking associated with substance use, and ultimately, addiction.

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