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A unique adolescent response to reward prediction errors

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Previous work has shown that human adolescents may be hypersensitive to rewards, but it is not known which aspect of reward processing is responsible for this. We separated decision value and prediction error signals and found that neural prediction error signals in the striatum peaked in adolescence, whereas neural decision value signals varied depending on how value was modeled. This suggests that heightened dopaminergic prediction error responsivity contributes to adolescent reward seeking.

Adolescence is a unique period in psychological development that is characterized by increased risky choices and actions as compared with children and adults. This may reflect the relatively early functional development of limbic affective and reward systems in comparison with prefrontal cortex[1], causing adolescents to make poor decisions and risky choices more often than both children (who are not yet fully sensitive to rewards) and adults (who are sensitive to rewards, but have the ability to exert control over reward-driven urges).

According to behavioral decision theories, choices are driven by the value assigned to each potential choice (decision value)[2]. The decision value is computed by a system in the medial prefrontal cortex that serves as a common pathway for value representation[3,4]. However, to behave adaptively in a changing or noisy world, these values must be updated on the basis of experience. Reward prediction error signals reflect the difference between the expected value of an action and the actual outcome of the action[5] and are coded by phasic activity in the mesolimbic dopamine system[6]. In functional magnetic resonance imaging, they are usually observed in the ventral striatum, reflecting dopaminergic output[7]. The nature of prediction error signals in children or adolescents is unknown. Adolescents may have a hypersensitive striatal response to reward[8,9], although this finding is somewhat inconsistent[10,11]. Using a probabilistic learning procedure[12], we examined whether adolescence is associated with unique changes in either decision value or prediction error signals (**Fig. 1** and **Supplementary Methods**). We estimated both decision value and prediction error signals on each trial during learning using a simple learning model[5]. Using parametric fMRI analyses, we identified brain regions whose response was modulated in accordance with these signals and examined how this response changed with age from childhood to adulthood. We examined both linear effects (which reflect general maturational or developmental trends) and quadratic effects (which reflect adolescent-specific effects) with age. To the best of our knowledge, these results represent the first examination of these subcomponents of decision-making across development.

Behaviorally, all participants became more accurate and faster with training for predictable stimuli, but not for random stimuli (interaction: accuracy, $F_{5,210} = 9.85$, $P < 0.0001$; response times, $F_{5,210} = 6.60$, $P < 0.0001$; **Supplementary Table 1** and **Supplementary Fig. 1**). There was a reward × age interaction for response times ($F_{2,42} = 5.03$, $P = 0.01$). *Post hoc* tests indicated that adolescents were the only age group to respond significantly more quickly to stimuli associated with large rewards as compared with small rewards (adolescents, $t_{15} = 3.24$, $P = 0.006$; children, $t_{17} = -0.32$, $P = 0.75$; adults, $t_{10} = 1.90$, $P = 0.09$).

We modeled the fMRI data to allow separate estimation of the neural responses to stimulus and feedback (**Supplementary Methods**, **Supplementary Figs. 2–4** and **Supplementary Tables 2** and **3**) and examined how neural correlations with model-based decision signals (decision value and prediction error) were related to age. We analyzed quadratic trends in positive prediction error at feedback and identified two regions in which adolescents had a hypersensitive response as compared with the other age groups: the striatum and the angular gyrus. An area in the medial prefrontal cortex showed a negative linear

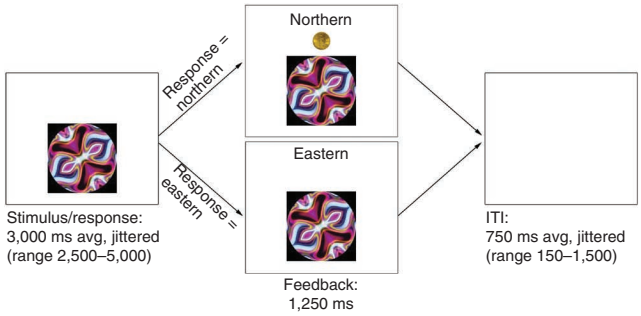

Figure 1 Experimental design. 45 healthy participants (18 children aged 8–12, 16 adolescents aged 14–19, and 11 adults aged 25–30) performed a probabilistic learning task during fMRI acquisition. Written informed consent was obtained. Participants classified abstract stimuli into one of two categories (Northern and Eastern) and were given feedback displaying the correct response at the end of each trial. If their response matched the outcome, feedback included a monetary reward. We paid participants according to the reward they received to ensure motivation. There were two stimulus types, predictable (associated 83% of the time with one of the two categories) and random (associated 50% of the time with each category). There were also two rewards, large ($0.25) and small ($0.05).

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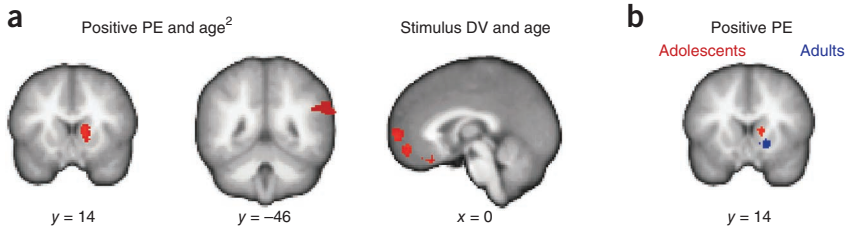

Figure 2 fMRI results. (**a**) Regions showing correlations with age when correcting at the whole-brain level ($z > 2.3$, $P < 0.05$). The striatal and angular gyrus regions were negatively correlated with age squared (age^2). Because the mean age^2 was subtracted from each value before squaring, age^2 was lowest for adolescents and the negative correlation reflected greater signals for adolescents. The region in the medial prefrontal cortex was negatively correlated with age (**Supplementary Table 4**). DV, decision value; PE, prediction error. (**b**) Striatal ROI analyses cluster-mass corrected at $z > 2.3$, $P < 0.05$. When looking at the striatal response to prediction error separately for the three age groups, we found that different striatal regions were active for adolescents (red) and adults (blue). Children showed no activity, even when lowering the threshold to uncorrected $P < 0.05$ (**Supplementary Figs. 8** and **9**).

effect of age on stimulus decision value, such that younger participants had a stronger decision value signal in this region as compared with older participants; this region has been strongly associated with goal-oriented stimulus value in previous work in adults (**Fig. 2a** and **Supplementary Table 4**)[13]. Thus, although response to unpredictable positive feedback peaked in adolescence, sensitivity to stimulus value decreased linearly with age (**Supplementary Fig. 5**).

Given that decision value develops through error-driven learning in the model, it was surprising that decision value showed a different age-related trajectory than prediction error. However, as a result of the structure of the task, it is possible that choice was driven by other factors beyond reinforcement learning (for example, explicit memory). To clarify these results, we used a second model that computed decision value in a more integrative fashion as the proportion of previous trials on which the optimal response was chosen for each stimulus (A. Lin, R. Adolphs and A. Rangel, unpublished observations; **Supplementary Methods**). We analyzed prediction error values from this model and found that they mirrored the results of our initial analyses, showing regions in the striatum and parietal cortex, along with ventral lateral prefrontal regions, in which neural response to prediction error peaked in adolescence. Analysis of decision value from this model indicated that there were both linear and nonlinear relationships between age and neural activity in a number of regions, including the lateral parietal cortex and striatum (**Supplementary Fig. 6** and **Supplementary Table 5**). Exploratory (non-independent) region of interest (ROI) analyses indicated that the neural response to decision value in this model appeared to increase between childhood and adolescence, but then reached an asymptote between adolescence and adulthood (**Supplementary Fig. 7**). These results suggest that the peak prediction error response in adolescence was robust to different models, whereas age-related changes in decision value signals were sensitive to model specification.

Previous work found that the ventral striatum is consistently sensitive to unexpected positive feedback, as reflected in model-based reward prediction error signals[7]. We examined the localization of prediction error–related responses for each age group separately in an independent anatomical ROI that included the bilateral caudate, putamen and nucleus accumbens using the original reinforcement learning model (**Fig. 2b**). Striatal regions significantly related to positive prediction error did not overlap for adolescents and adults (cluster-mass corrected at $z > 2.3$, $P < 0.05$). Although we found activity in the ventral striatal region of adults that has been consistently found when examining prediction error in adults, activity in adolescents occurred in a more dorsal region. We found no activity in the striatum of children that was related to positive prediction error.

Previous studies found that reward-related neural activity was increased during adolescence[8,9]. Our results extend this, as we found that the increase was specific to prediction error, as compared with valuation signals. The developmental differences in prediction error response probably reflect differences in phasic dopamine signaling[14]. If correct, this explains the risky reward-seeking behavior that is often observed in adolescents. The increased risky behavior in adolescence could reflect either a decreased sensitivity to potentially negative outcomes or an increased sensitivity to potentially positive outcomes. We believe that our data are consistent with the latter; that is, increased prediction error signals (putatively reflecting greater phasic dopamine signals) reflect a greater effect of positive outcomes[15], which results in an increased motivation to obtain positive outcomes (and thus greater risk-taking). Thus, an overactive dopaminergic prediction error response in adolescents could result in an increase in reward-seeking, particularly when coupled with an immature cognitive control system[1].

Our findings may shed light on why previous studies have yielded inconsistent effects of age on reward processing. First, not all studies compared adolescents with both children and adults, meaning that the possibility of nonlinear relationships with age could not be noted. Furthermore, the definition of adolescent has not been consistent across studies. Second, it is important to note that the probabilistic learning task that we used was not a risky decision making task per se, and is therefore different from other tasks that have been used in studies of reward and risk-taking. Third, our results suggest that a proper understanding of developmental changes in reward processing requires the use of model-based approaches and decomposition of individual trial components (stimulus, choice and feedback).

Adolescence is a unique period in psychological development and the risky, reward-seeking behavior that occurs during this period can result in substantial morbidity and mortality, including accidental death and the onset of drug addiction. Understanding the neural basis of adolescent decision-making is a critical challenge. Our results suggest that enhanced prediction error signals contribute to adolescent reward-seeking, which provides a target for future studies of this important period in development.

Note: Supplementary information is available on the Nature Neuroscience website.

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AUTHOR CONTRIBUTIONS

J.R.C. helped design the experiments, conducted data acquisition and analyses, and wrote the manuscript. R.F.A., R.M.B. and S.Y.B. designed the experiments. F.W.S. contributed to data acquisition. B.J.K. and R.A.P. designed the experiments and helped write the manuscript.

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