ADAPTIVE ADOLESCENT FLEXIBILITY: NEURODEVELOPMENT OF DECISION-MAKING AND LEARNING IN A RISKY CONTEXT

BY

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THESIS

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Abstract

Research on adolescence has largely focused on the particular biological and neural changes that place teens at risk for negative outcomes linked to increases in sensation-seeking and risky behavior. However, there is a growing interest in the adaptive function of adolescence, with work highlighting the dual nature of adolescence as a period of potential risk and opportunity. We examined how behavioral and neural sensitivity to risk and reward vary as a function of age using the Balloon Analog Risk Task (BART). Seventy-seven children and adolescents (ages 8-17 years) completed the BART during an fMRI session. Results indicate that adolescents show greater exploration and learning across the task. Furthermore, older participants showed increased neural responses to reward in the OFC and ventral striatum, increased activation to risk in the right SFG and MCC, as well as increased functional OFC-mPFC coupling in both risk and reward contexts. Age-related changes in regional activity and inter-regional connectivity explain the link between age-related increases in flexible exploration and learning. These results support the idea that adolescents' sensitivity to risk and reward supports adaptive behavioral approaches for reward acquisition.

To all my friends and family.

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CHAPTER 1

INTRODUCTION

Adolescence has been largely recognized as a period of heightened risk and poor decision-making; however, adolescence is also a period of opportunity for learning and skill acquisition. While neurodevelopmental research has begun to shed light on neural mechanisms that support changes in risk-taking and sensation-seeking behaviors during adolescence (Steinberg et al., 2008), empirical work and theoretical models of adolescent brain development suggests these behaviors are the result of deficient or ineffective circuitry (see Telzer, 2015). Several neurobiological models have proposed that early-maturing subcortical regions coupled with slower-developing prefrontal regions underlies increased risk taking during adolescence (Steinberg, 2010; Ernst et al., 2006; Casey et al., 2008), comparing adolescent behavior to a car in full throttle but with ineffective breaks (Steinberg, 2010). While these heuristics are useful tools (see Casey, 2015; but see Pfeifer & Allen, 2016), they can pathologize adolescence as a period of deficiency and overlook the potentially adaptive role of adolescence as a period of opportunity for learning and the acquisition of new ideas, skills, and interests (Crone & Dahl, 2012).

Emerging evidence supports the idea of adolescence as a period of exploration and flexibility. Adolescent rodents (Pattwell et al., 2012), non-human primates (Spear, 2000), and humans (Humphreys et al., 2013) show behavioral patterns that support increased exploration, even at potential risk to their health and reproductive success. For instance, human adolescents show age-related increases in risk taking as well as adolescent-specific increases in learning in a risk-taking context (Humphreys et al., 2016), and adolescents show greater tolerance for

ambiguity during risk taking than do adults (Tymula et al., 2012), which might promote learning and exploration of the environment during this adolescence. Adolescent mice also show increased flexibility and learning when pursuing rewards (Johnson & Wilbrecht, 2011). This flexibility supports adolescents' learning of the environment and helps them gain access to food and reproductive opportunities (Vigilant et al., 2015). In light of this research, some have suggested that the unique configuration of adolescent neural systems serves an adaptive function necessary for appropriate development (Casey, 2015; Crone & Dahl, 2012).

While no empirical studies have explored the neurodevelopment of learning and flexible behavior in risky contexts, some initial evidence highlights the potentially adaptive function of still-developing neural states for learning. While the heuristic models utilized in adolescent neurodevelopmental research generally highlight the maladaptive nature of delayed prefrontal development (see Casey, 2015), slower maturation of the PFC may actually promote an individual's ability to flexibly adapt to new contexts. For instance, early adversity (e.g., maternal deprivation, neighborhood violence) is associated with accelerated life history trajectories (Ellis et al., 2009) including early transition to adult-like PFC functioning (Gee et al., 2013). While this acceleration is hypothesized to serve a compensatory role, early transition to adult neural states is also associated with developmental trade-offs that can result in suboptimal outcomes such as decreases in plasticity and academic achievement (Shaw et al., 2006), suggesting that later-developing PFC function may be adaptive and support learning and skill acquisition.

Despite this initial evidence, we know relatively little about neurodevelopmental mechanisms which support age-related changes in flexibility and learning. To address this gap, we examined exploration and learning in the context of risk and reward contingencies. Youth ages 8-17 years completed the Balloon Analog Risk Task (BART; Lejuez et al., 2002) during an

fMRI session. The BART mirrors real-world behavior in that risky behavior is rewarded up until a point, but then becomes detrimental to the individual's goals. The task creates a context for investigating learning and exploration since participants can use feedback they receive on each trial to modify or reinforce their behavior (Humphreys et al., 2016). We examined age-related changes in risk-taking behavior across the task, as well as age-related differences in neural activation and connectivity in motivational (e.g., ventral striatum and orbitofrontal cortex) and regulatory (e.g., lateral PFC and anterior cingulate) regions involved in learning and goal-directed behavior. We hypothesized that adolescents would be more likely than younger participants to explore the task, and that this exploration would allow them to better learn the parameters of the task. Adolescents could then utilize this learning to guide their risk-related behavior in pursuit of rewards. We further hypothesized that neurodevelopmental changes in motivational and regulatory regions would mediate these age-related increases in flexible behavior and learning.

CHAPTER 2

METHODOLOGY

Participants

Eighty healthy children and adolescents completed an fMRI scan. Two participants were excluded due to excessive head motion (>2.0 mm slice-to-slice on ≥10% of slices) during the session, and an additional participant was excluded due to processing errors, leaving 77 participants in the final sample (41 female; M_{age}=14.23 years, *SD*=2.76, *range*=8.1-17.7 years). Participants (54 European-American, 18 African-American, 1 Asian-American, 2 Latin-American, and 3 mixed/multiple ethnicity) provided written consent and assent in accordance with the University of Illinois' Institutional Review Board.

Risk and Reward Task

Participants completed a version of the Balloon Analog Risk Task (BART), a well-established experimental paradigm (Lejuez et al., 2002; Qu et al., 2015; Telzer et al., 2015) that measures participants' willingness to take risks in the pursuit of rewards. Prior to the scan, participants were shown a box of age-appropriate prizes and were told that the more points they earned on the task, the more prizes that they could select at the end of the neuroimaging session. In reality, all participants were allowed to choose 3 prizes regardless of the number of points they earned. During the scan, participants were presented with a series of 24 balloons that they could choose to pump up in order to accrue points (Figure 1). Each pump increased the risk that the balloon would explode, and if the balloon exploded, participants lost all points they had accrued from that balloon. At any point after the first pump, participants could choose to cash out their points for that balloon, which were added to their total for the task. The running total of points earned was presented on the screen as a points meter. Participants were instructed that

their goal was to earn as many points as they could during the task. Each event (e.g., larger balloon following a pump, new balloon following cashed or exploded trial) was separated with a random jitter (500-4000 ms). Balloons were presented in a fixed order, with the explosion rate ranging from four to ten pumps, although this was not made explicit to participants. The task was self-paced and would not advance unless the participant made the choice to either pump or cash-out.

Behavior Modeling. We measured several indices of behavior to tap risk behavior, exploration, and learning on the task. *Risk Behavior* represents participants' willingness to engage in risk taking. This was calculated as the average number of pumps on cashed trials. The number of pumps on explosion trials was not included since those trials end before participants have reached their maximum tolerance for risk (Lejuez et al., 2002). This metric has been used widely as an index of risk taking and is associated with higher levels of self-reported risk-taking behavior in the real world both concurrently and longitudinally (Lejuez et al., 2002; Qu et al., 2015; Telzer et al., 2015).

We measured *Exploratory Behavior,* which was calculated as the standard deviation of pumps, and represents how willing participants are to probe the limits of balloons before cashing out. A greater standard deviation of pumps represents more exploratory behavior across the task.

We modeled *Learning* which is indexed by participants' feedback sensitivity, or how likely participants are to use information from the previous trial to guide their behavior on each subsequent trial and to adapt when their current behavior is resulting in maladaptive outcomes (Humphreys et al., 2015). To obtain this index, we used hierarchical linear modeling (Raudenbush & Byrk, 2002), in which trials (24 total) were nested within participants, and the outcome variable was the number of pumps on a given trial. We modeled whether the number of

pumps on a given trial varied depending on the outcome of the previous trial. Consistent with prior studies (Mata et al., 2012; Ashenhurst et al., 2014), our Level 1 equation was:

$$\text{Number of Pumps}_{ij} = b_{0j} + b_{1j}(\text{Explosion}_{(N-1)}) + b_{2j}(\text{Explosion}_{(N)}) + b_{3j}(\text{Trial Number}) + \varepsilon_{ij}$$

Total pumps on a particular trial (i) for a particular adolescent (j) was modeled as a function of the average number of pumps across the task (b_{0j}) and whether the previous trial (b_{1j}) was an explosion or cash-out (coded $\text{Explosion}_{(N-1)} = 0$; $\text{Cash-Out}_{(N-1)} = 1$). In addition, we included two controls, including whether the current trial resulted in an explosion or a cash-out (b_{2j}; coded $\text{Explosion}_{(N)} = 1$; $\text{Cash-Out}_{(N)} = 0$), and the trial number (b_{3j}).

In order to use the *Learning* index in our neural and behavioral analyses, we extracted empirical Bayes estimates for each participant. Empirical Bayes estimates are optimally weighted averages that combine individual average slopes by combining estimates from both the individual and the group, and "shrink" individual specific estimates towards the overall mean (Diez-Roux, 2002). The extracted estimate represents individual differences in how participants change their subsequent behavior (both magnitude and direction) based on the type of feedback they received on the prior trial. Larger positive values (e.g. > 0) are indicative of greater learning (i.e., participants increase pumps following a cashed balloon but decrease points following an exploded balloon), while values closer to zero indicate little or no learning (i.e., participants increased or decreased their pump behavior at random with respect to previous feedback). While negative values (e.g. < 0) are possible, this would indicate that participants were increasing pumps after explosions and decreasing pumps after cash-outs, an especially irrational strategy.

Additional behavioral measures included *Number of Explosions*, or the number of times participants pumped balloons until they popped, as well as *Total Points*, which represents participants' successful acquisition of resources. Higher total point values are indicative of more optimal behavior on the task.

fMRI Data Acquisition

Imaging data were collected using a 3 Tesla Siemens Trio MRI scanner. The BART included T2*-weighted echoplanar images (EPI) (slice thickness=3 mm; 38 slices; TR=2sec; TE=25msec; matrix=92x92; FOV=230 mm; voxel size 2.5x2.5x3mm^3). In addition, structural scans consisted of a T2*weighted, matched-bandwidth (MBW), high-resolution, anatomical scan (TR=4sec; TE=64msec; FOV=230; matrix=192x192; slice thickness=3mm; 38 slices) and a T1* magnetization-prepared rapid-acquisition gradient echo (MPRAGE; TR=1.9sec; TE=2.3msec; FOV=230; matrix=256x256; sagittal plane; slice thickness=1mm; 192 slices). To maximize brain coverage, MBW and EPI scans were obtained using an oblique axial orientation.

fMRI data preprocessing and analysis. Preprocessing and data analysis utilized Statistical Parametric Mapping (SPM8; Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK) software package. Preprocessing steps involved spatial realignment to correct for head motion (included participants had no motion in excess of 1.5mm between-slice motion); coregistration of all images to the high-resolution T1* MPRAGE structural scan; and segmentation into grey matter, white matter, and cerebrospinal fluid. Transformation matrices used in MPRAGE segmentation were applied to MBW and EPI images to warp them into the standard stereotactic space defined by the Montreal Neurological Institute (MNI) and the International Consortium for Brain Mapping. EPI images were smoothed using an 8mm Gaussian kernel, full-width-at-half maximum to increase signal-to-noise ratios in the functional

images. The general linear model in SPM8 was then used to convolve each trial with a canonical hemodynamic response function. Low-frequency drift across the time series was removed using a high-pass temporal filter with a 128s cutoff, and a restricted maximum likelihood algorithm with an autoregressive model order of 1 was used to estimate serial autocorrelations.

The BART was modeled using an event-related design with trial duration corresponding to participant response time on a given pump or cash-out, or using the average RT across the task on explosions. Fixed-effects models included a general linear model for each condition of interest, which included pump decisions, cash-out decisions, and explosion events. We modeled pump decisions separately for trials that ended in cash-outs and trials that ended in explosions. Because the number of pumps is artificially constrained on balloons that end in explosions, analyses were only performed with pump decisions on balloons that ended in cash-outs, as done in prior research (Lejuez et al., 2002; Telzer et al., 2015). The jittered inter-trial periods were not modeled and served as the implicit baseline for the task. A parametric modulator (PM) was included for each of the three conditions of interest, and represents the pump number for a balloon at each pump or cash-out decision. All the PM values were mean centered by balloon, such that for each balloon, all PM values summed to 0. The PM served to control for differences across pumps within a balloon trial. Contrasts were then computed at the individual level for each condition of interest.

In addition, we examined neural connectivity by conducting psychophysiological interaction (PPI) analyses. We used structurally-defined regions of interest (Wake Forest University PickAtlas, Maldjian et al., 2003) as the seed regions, including the medial orbitofrontal cortex (mOFC) and bilateral ventral striatum (VS). These regions have been strongly implicated in reward-related associative learning, being involved in the formation and

manipulation of stimulus-reward expectations (Gottfried et al., 2003; Schoenbaum & Roesch, 2005; Kelley, 2004), and as such may be involved in developmental processes which support exploration and learning. PPI analyses utilized a generalized form of context-dependent PPI form the automated generalized PPI (gPPI) toolbox in SPM (McLaren et al., 2012). Deconvolved time series were extracted from the mOFC and VS ROI for each participant to create the physiological variables. Each trial type was then convolved with the canonical HRF to create the psychological regressor. Finally, the physiological variable was multiplied with the time series from the psychological regressors to create the PPI term. This interaction term was then used to identify regions that covary with the seed region in a task-dependent manner. Each participant has a regressor computed that represents the deconvolved BOLD signal, which was included alongside each psychological and PPI term for each event type to create a gPPI model.

Random effects, group-level analyses were run on all individual subject contrasts using GLMFlex, which corrects for variance-covariance inequality, removes outliers and sudden activation changes in the brain, partitions error terms, and analyzes all voxels containing data (http://mrtools.mgh.harvard.edu/index.php/GLM_Flex). Because not all participants had sufficient explosion events to model successfully, group level analyses focused on pump and cash-out decisions. Group-level analyses involved whole-brain regressions using age as a continuous covariate. Correction for multiple comparisons was run using a Monte Carlo simulation through 3dClustSim from the AFNI software package (Ward, 2000) using the group-level brain mask. The simulation resulted in a voxel-wise threshold of $p<.001$ and a minimum cluster size of 34 voxels for the whole brain, corresponding to $p<.05$, Family-Wise Error (FWE) corrected.

CHAPTER 3

RESULTS

Behavioral Results

Age-Related Increases in Risk, Exploration, and Learning. We ran bivariate correlations between age of participants and behavioral indices of interest (see Table 1 for means, SDs, ranges, and correlations between all study variables). Age was associated with more risk behavior (i.e., higher average pumps; $r = .36$, $p = .001$), exploratory behavior (i.e., greater SD in pumps; $r = .34$, $p = .003$), and learning (i.e. pumping more after a cash-out and less after an explosion; $r = .51$, $p < .001$). Moreover, increased learning was associated with greater levels of exploration ($r = .67$, $p < .001$) and higher points earned ($r = .50$, $p < .001$), suggesting a potential utility of exploration for learning and its downstream influence on how participants acquire adaptive outcomes.

Exploration and Learning Explain Age differences in Risk-Taking Behavior. Next, we examined whether older subjects' increased exploration and learning explained the link between age and risk taking during the BART. In other words, does the propensity of older individuals to explore and learn the task environment explain why they tend to take more risks across the task? We standardized all variables of interest and performed mediation analyses as outlined by Hayes (Hayes, 2013), examining whether participants' exploratory behavior and learning account for the association between age and risk behavior. Using 1000 sample bootstrapping, we calculated the magnitude and significance of the indirect effect, and calculated a bias-corrected confidence interval (CI). As shown in Figure 2, we found that both exploratory behavior and learning significantly mediate the relationship between age and risk behavior

during the task, suggesting that older adolescents' greater risk-taking behaviors is explained, in part, because they are exploring and learning the parameters of the task to a greater extent.

We also examined whether the increased propensity to explore and take risks benefits participants, or whether the associated costs of increased explosions would offset their higher rates of pumping. We found that participants' risk behavior mediates the relationship between exploratory behavior and the total number of points that participants earned. Risk behavior also mediates the relationship between learning and total points (Figure 2). In other words, participants who show heightened levels of exploration and learning are more likely to earn more points because they engage in greater amounts of risk behaviors. Together, results demonstrate that older participants' show increases in exploration, learning, and risk taking across the task, and that these behavioral patterns serve an adaptive function with respect to resource acquisition.

fMRI Results

Age-related Differences in Risk- and Reward-Related Neural Activity. We examined the effects of age on our conditions of interest by entering age as a continuous regressor in whole-brain regression analyses (for main effects without age, see Table 2). Areas showing age-related increases in risk-related activity (i.e., during pumps) included regions of the mid-cingulate cortex (MCC), right superior frontal gyrus (SFG), and bilateral calcarine gyrus. For reward-related activity (i.e., during cash-outs), we found age-related increases in the VS and medial OFC. No regions showed significant age-related decreases during risk or reward (Table 3; Figure 3).

Linking Age-related Neural Activation with Learning and Exploratory Behavior. Next, we examined whether regions showing age-related increases in activation were associated with exploratory behavior and learning. To do so, we extracted parameter estimates of signal

intensity from the regions which showed significant age effects and performed mediation analyses to examine whether activity in these regions explained the link between age and exploratory behavior as well as age and learning. Correlation analyses indicated that all regions showing age-related increases in activation were related to both exploratory behavior and learning (Table 4). However, mediation analyses indicate that only activity in the MCC during risk (indirect effect: B =.12, SE = .05, 95% CI [.04, .24]) and medial OFC during reward (indirect effect: B = .12, SE = .06, 95% CI [.03, .27]) significantly explained the link between age and exploratory behavior. Moreover, reward-related activity in the medial OFC was the only region to significantly explain the link between age and learning (indirect effect: B = .11, SE = .05, 95% CI [.03, .23]). These findings suggest that developmental differences in these regions support increased exploration and learning within the task environment observed in older adolescents.

Functional Connectivity

Age-related Changes in Connectivity during Risk and Reward. Next, we ran PPI analyses using our medial OFC and VS seed regions (for main effects without age, see Table 2). We entered age as a regressor in whole-brain PPI analyses. We found that the medial OFC shows age-related increases in functional connectivity with the mPFC during risk and with the mPFC and PCC during reward (Table 3; Figure 4). There were no regions that showed age-related decreases in connectivity with the medial OFC during either condition. When using the VS seed in a whole-brain PPI analysis, we found no regions that showed age-related change in VS connectivity.

Links between Age-related Neural Connectivity and Behavior. Finally, we examined whether age-related differences in OFC-mPFC connectivity explain age-related differences in

exploratory behavior and learning. Correlation analyses indicate that all regions showing age-related increases in OFC connectivity were related to both exploratory behavior and learning (Table 4); however, only age-related increases in OFC-mPFC functional connectivity significantly explain the link between age and learning (indirect effect: B = .12, SE = .05, 95% CI [.04, .25]).

CHAPTER 4

DISCUSSION

A major focus of research on neural development during adolescence has been the neural mechanisms that support changes in risk taking and sensation seeking (Casey, 2015). However, much of the theoretical and empirical work on adolescent neural development has highlighted aspects of adolescent neural circuitry which are deficient or ineffective, while ignoring potentially adaptive roles for developing neural circuits (Telzer, 2015; Casey, 2015). In contrast, we focused on aspects of adolescent neurodevelopment that might support exploration and learning and in turn, adaptive outcomes. Our findings highlight adolescence as a period of behavioral and neural flexibility, which leads to increases in exploration and learning within risky contexts. Additionally, this flexibility can drive behaviors that extract adaptive outcome from these contexts, suggesting that a more-nuanced view of adolescence is warranted. Instead of characterizing still-developing neural systems as deficient, developmentally appropriate neural circuitry can play an adaptive role in adolescent behavior.

Consistent with prior research, we found that participants showed age-related increases in risk taking. Supporting the theory that increased exploration of the environment, even at potential risk, supports adaptive behavior, we found that age-related increases in exploratory behavior and learning explained older adolescents' tendency to take more risks, and greater risk taking was linked to greater acquisition of points. While previous work has suggested the potential utility of risk taking during adolescence (Spear, 2000), the current literature generally discusses and tests how increased risk taking during adolescence is impulsive and irrational behavior driven by increases in sensitivity to motivational stimuli (see Steinberg et al., 2008;

Casey, 2015). Results in the present study suggest that risk taking may emerge, in part, from a drive for exploration and learning during adolescence. Such learning and exploration may play adaptive roles in adolescent skill acquisition, establishment of new social networks, and identity formation.

Context is an important determinate of whether a propensity to take risks is adaptive or maladaptive (Humphreys et al., 2013). In an uncertain environment, a drive for exploration and learning may lead to increased risk taking, which in turn may help the individual to increase the likelihood of attaining adaptive outcomes. When we consider the evolutionary history of adolescence, it is likely that there are trade-offs on a population level for a developmental period marked by increased risk and exploration, where the risk of exposure to detrimental outcomes is weighted against the opportunities for food and mate resources that exploration promotes (Spear, 2000). The present study suggests that older adolescents are more willing to engage in these trade-offs between risk taking and exploration than are younger participants, behavior which may result in adaptive outcomes.

At the neural level, we found that age-related increases in both motivational and regulatory neural systems supported flexible behavior and learning. Motivational regions included the ventral striatum and orbitofrontal cortex. The ventral striatum, a region with a high density of dopaminergic neurons, has been classically implicated in reward anticipation and reactivity and shows heightened activation during adolescence (Galvan et al., 2005; Galvan et al., 2006; see Telzer, 2015). The OFC's role in reward processing involves assigning and updating the relative reward value of actions and stimuli (O'Doherty et al., 2001; Gottfriend et al., 2003). The present study's findings of age-related increases in these two regions during reward acquisition fits well with previous research. Furthermore, we found that OFC reward-

related activity explained links between age and increases in both learning and exploration, which supports previous research implicating the OFC in reward-related learning (Schoenbaum & Roesch, 2005). Reward-related activity in the OFC may help adolescents track the motivational salience of points in the task as well as integrate reward (i.e. cash-outs) and punishment (i.e. explosion) feedback from the task into their cost-benefit representations for future risk taking.

We also found age-related increases in regulatory regions during risk decisions, including the mid-cingulate cortex and superior frontal gyrus. The MCC has been implicated in action selection (Vogt, 2005; Shackman et al., 2011), while dorsolateral prefrontal regions, which include the SFG, play a role in higher-order cognitive control and goal maintenance (Ridderinkhof et al., 2004; Braver et al., 2009). Risk-related activity in the MCC explained age-related increases in exploratory behavior, suggesting that increased MCC activity in older participants may reflect greater flexible enactment of exploration behavior that integrates task feedback. Developmental increases in reward-related activation in the OFC may reflect greater valuation of reward which drives changes in future behavior, while increases in regulatory and action-selection regions may support increases in goal-directed behavior enactment. Changes in these neural systems supports both learning and risk taking by increasing attention to certain stimuli, weighting information gained in rewarding contexts more so than children. This weighted information is in turn used to a greater degree to direct behavior during this period of development. However, an over-weighting of reward-related information likely also is responsible for adolescents sometimes pursuing rewarding contexts without complete regard for the potential negative consequences. These results highlight the importance of two types of neural systems in supporting flexible behavior and reflect a growing understanding that complex

behaviors are not supported by the development of single brain regions, but rather a system of regions that play particular computational roles in the service of behavior.

Finally, to examine connectivity of circuits that may be important for exploration and learning behavior, we examined how age-related changes in functional connectivity between motivational and regulatory regions support flexible behavior. We found age-related increases in functional connectivity between the medial OFC and regions of the mPFC during both risk and reward conditions. Medial regions of the OFC show both structural (Öngür & Price, 2000) and positive functional (Kahnt et al., 2012) connectivity to regions of the mPFC. Regions of the dorsal mPFC have been implicated in associative learning and response adaptation (Euston et al., 2012) and are sensitive to risk conditions (Van Leijenhorst, et al., 2010). In the present study, age-related increases in OFC-mPFC connectivity provide a mechanism for age-related increases in learning, suggesting that increased OFC-mPFC functional connectivity reflects a more-integrated motivational-regulatory system, with greater intercommunication between regions involved in reward processing and regions involved in action updating and selection. This supports previous findings that still-developing top-down regulation of the mPFC is associated with adaptive outcomes (Gee et al, 2013), and that similar to other forms of physiological development (e.g. pubertal and reproductive timing), acceleration of neural development likely will involve trade-offs which curtail extended learning and plasticity (Ellis et al., 2009). The present study further suggests that the development of exploration and learning do not only depend on localized activational increases, but also on how neural regions interact, which underscores the importance of circuit-based understandings of neurodevelopmental processes (Casey, 2015).

Mapping the functional significance of system-level neurodevelopmental changes for adolescent behavior is an important future step for the examination of the neurobiological mechanisms driving the increases in exploration, risk taking, and learning that characterize adolescence. When studying complex processes, such as risky decision-making, both localized and circuit-based changes should be considered as possible supporting mechanisms for behavior changes seen across development (Casey, Somerville, & Galvan, 2016). While research localizing function to particular brain regions has greatly contributed to our understanding of neural function, the brain operates as an integrated circuit, and studying developmental changes in individual regions may have a finite utility. Future research should also examine how the processes of exploration, risk taking, and learning change within individuals over time. Longitudinal examination of these behavioral and neurodevelopmental processes can help to examine how individual differences in these trajectories contribute to differences in adaptive and maladaptive outcomes across adolescence.

CHAPTER 5

CONCLUSIONS

In summary, our findings support a new perspective of the behavioral and neurobiological changes which characterize adolescence. Development of motivational and regulatory neural circuitry supports adolescents' exploration and learning, which contributes to increases in risk taking. However, in contrast with much of the literature on adolescent development concerning risk behavior, we found that risky decisions emerge in part through adolescents' increased drive for exploration and learning, which suggests an adaptive role for still-developing neural circuitry. These results complement findings in non-human models which suggest that adolescent animals (Johnson & Wilbrecht, 2011; Vigilant et al., 2015) show unique behavioral patterns which support exploration and flexibility in service of adaptive goals. This adaptive role for developing neural circuitry also supports previous suggestions that accelerated development may actually be detrimental and linked to negative outcomes (Ellis et al., 2009). Instead of a one-to-one correspondence between maturity and function, normative development may rely on neural and behavioral states that happen in a particular, developmentally-appropriate fashion. Our findings underscore the importance of paying greater attention to the potentially adaptive roles that still-developing neural circuitry can have for adolescent behavior and the contexts in which these propensities for exploration and learning may be appropriately channeled.

CHAPTER 6

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FIGURES AND TABLES

Figure 1. Balloon Analog Risk Task. Participants can choose to Pump to increase the size of the balloon or to Cash Out in order to add points to their Points Meter. However, if participants pump too many times, the balloon will explode.

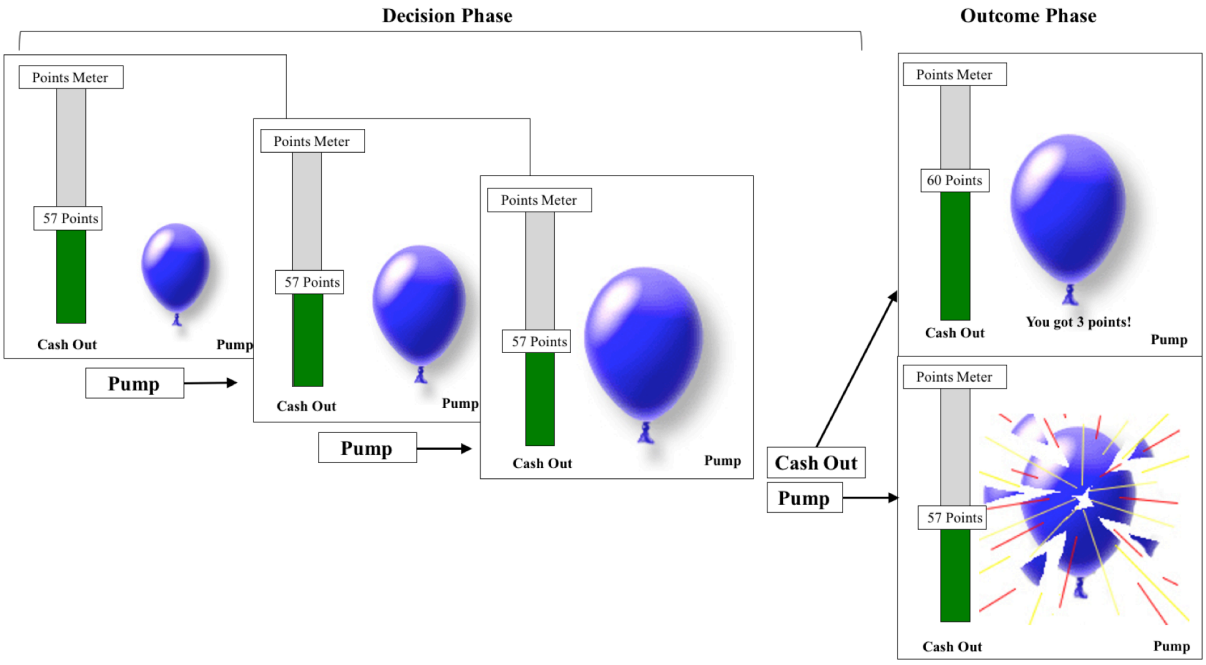

Figure 2. A) Exploration and **B)** Learning mediate the link between age and risk behavior, which is associated with more total points. Direct effects are indicated by the coefficients (greyed-out) above the dashed lines. For the path from Exploration/Learning to Risk Behavior coefficients to the left are for the first model and coefficients to the right are for the second. For indirect effects, coefficients are standardized with the SD in parentheses, and all other coefficients are standardized. * p < .05, ** p < .01, ** p < .001

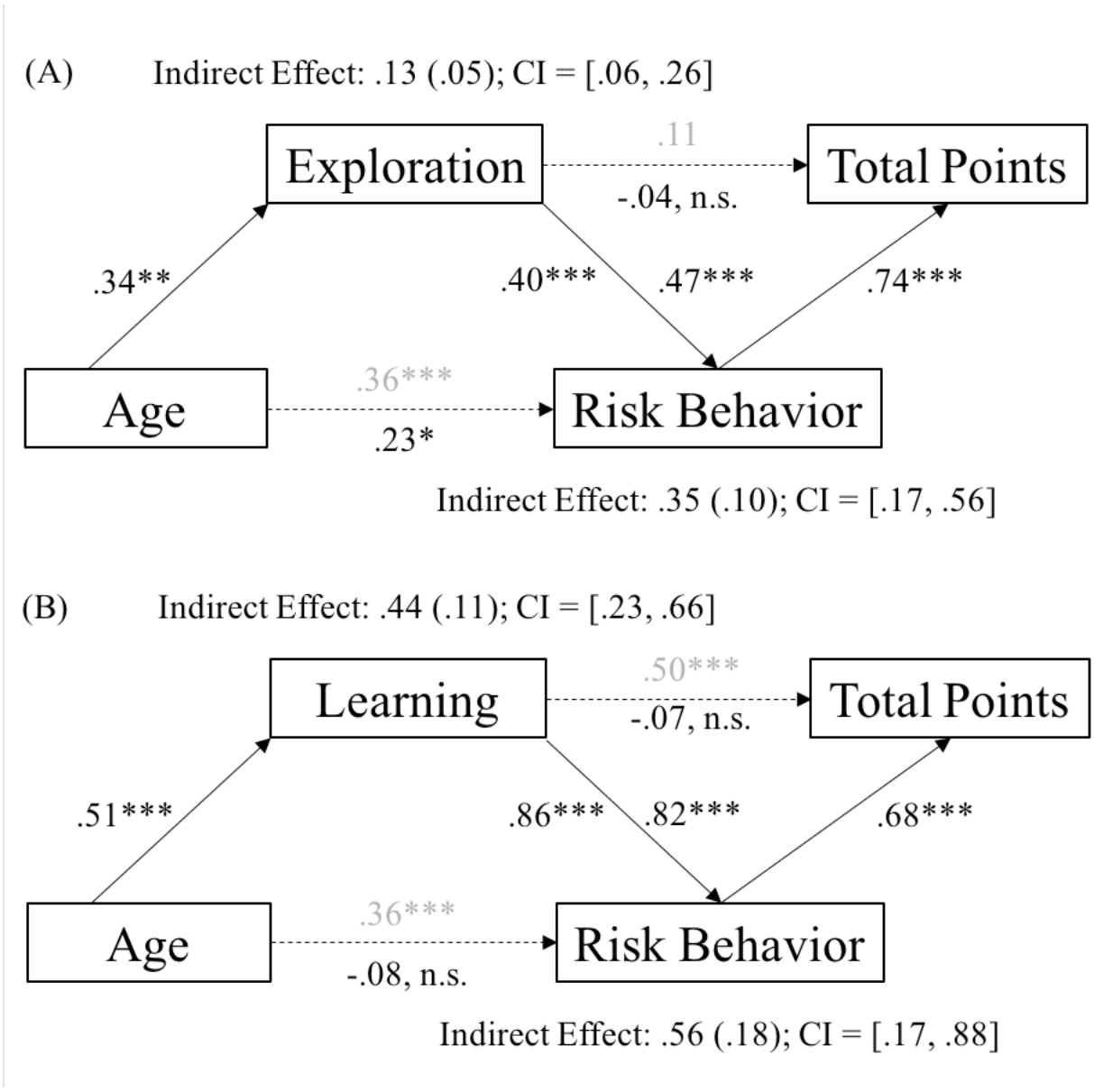

Figure 3. A) During reward (e.g. cash-outs), we found age-related increases in VS and medial OFC activation. **B)** During risk (e.g. pumps), we found age related increases in MCC and R SFG activation.

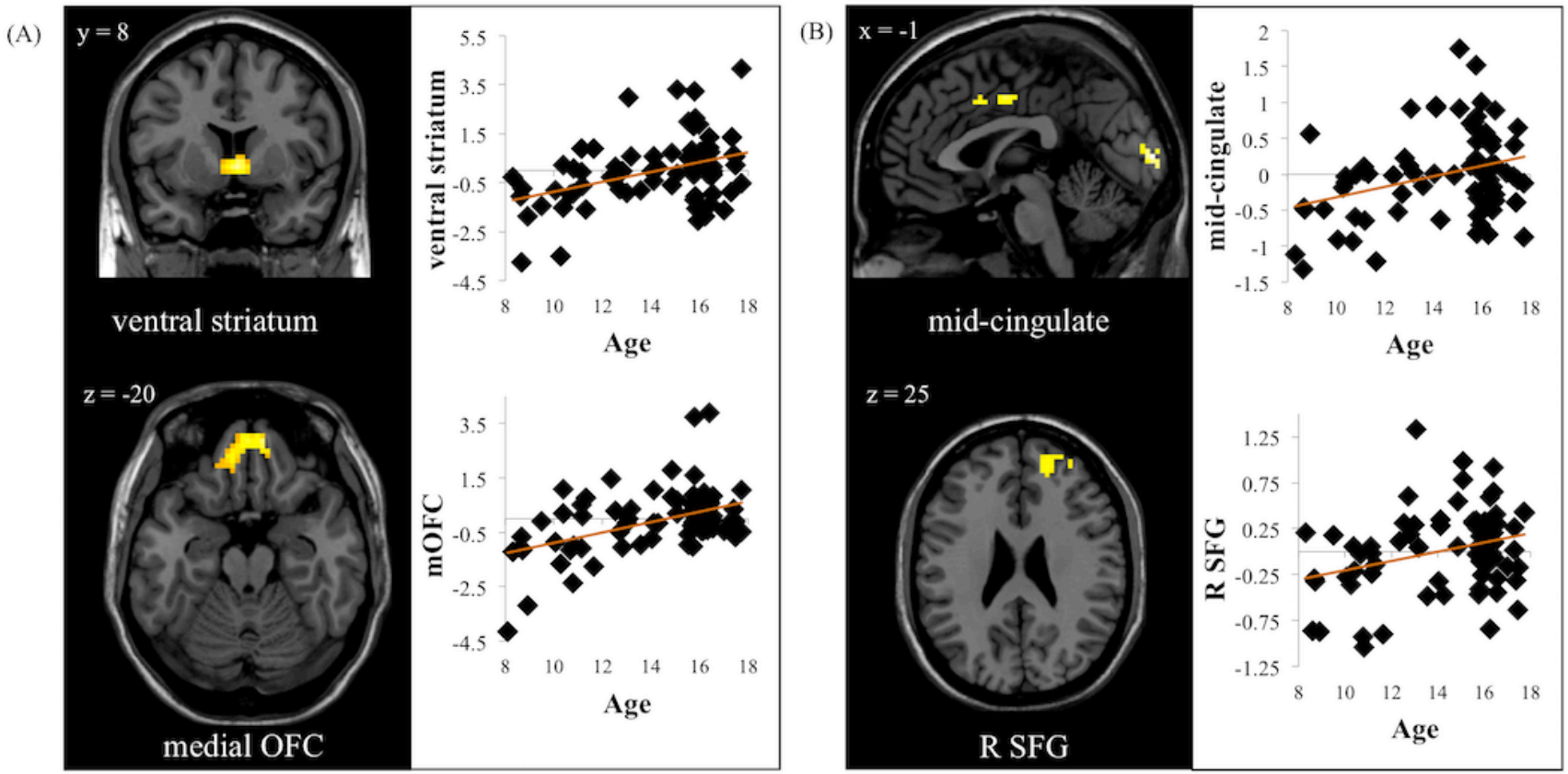

Figure 4. A) We found age-related increases in both mPFC and PCC functional connectivity with OFC during reward, and **B)** mPFC functional connectivity with OFC during risk.

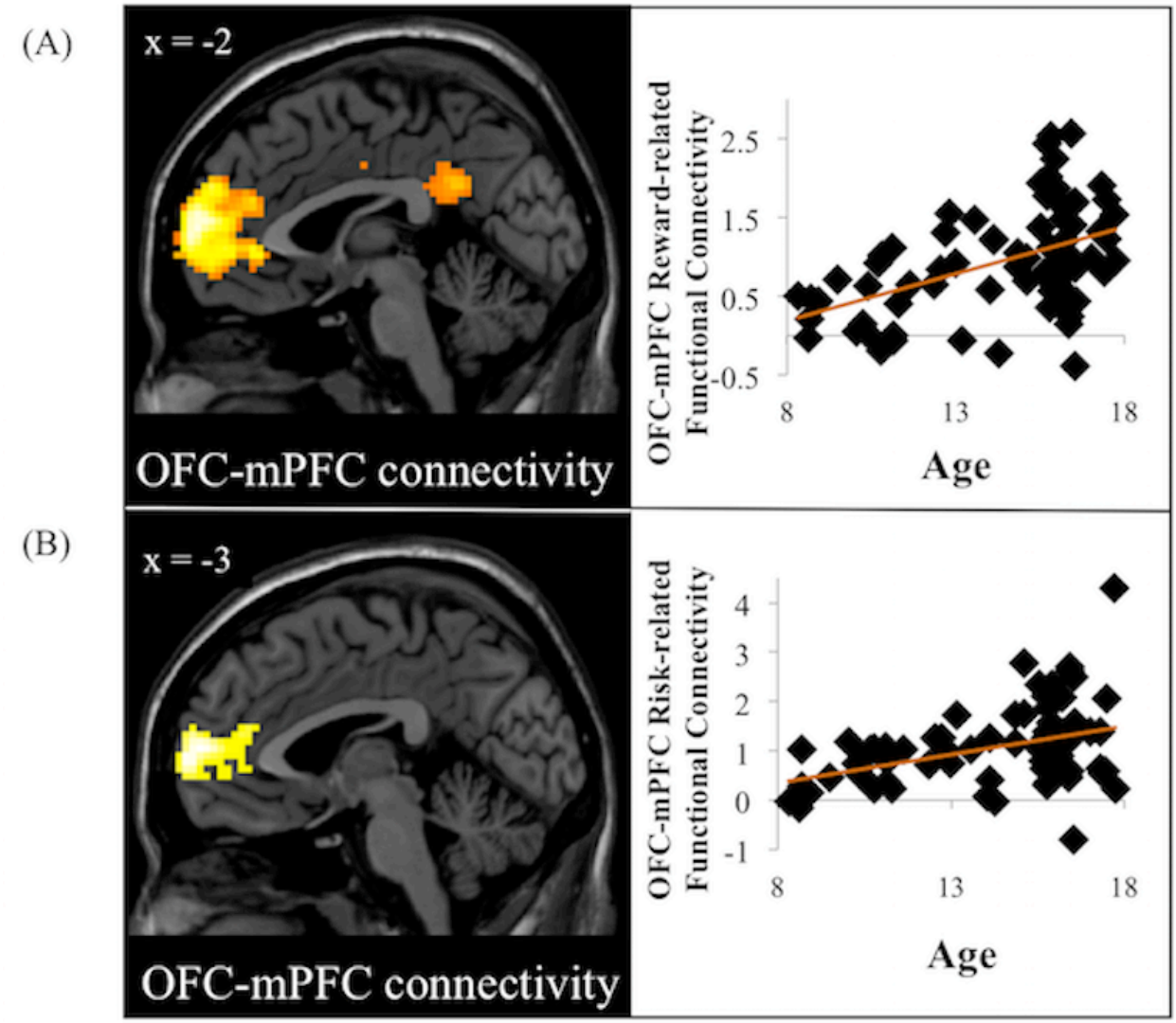

Table 1. Descriptives and Correlations for Study Variables of Interest

Variable	*M*	*SD*	*Range*	1	2	3	4	5	6
1. Age	14.10	2.76	8.10-17.7	1	.36***	.34***	.51***	.21^{+}	.36***
2. Risk Behavior	4.50	0.77	2.78-6.21		1	.47***	.82***	.63***	.83***
3. Exploratory Behavior	1.39	0.46	0.51-2.77			1	.67***	.11	.56***
4. Learning	-0.87	0.32	0.24-1.32				1	.50***	.74***
5. Total Points	81.83	8.32	63-106					1	.12
6. Number of Explosions	5.48	2.41	1-12						1

Note: $^{+}$<.1, * <.05, **<.01 ***<.005. Numbers along the diagonal represent Pearson's correlations.

Table 2. Neural Regions Showing Significant Activation During Risk and Reward in the Main Effects and PPI analyses.

Anatomical Region	+/-	BA	x	y	z	t	k
Main Effect							
Risk							
L Insula	+		-30	20	7	8.82	479
R Insula	+		33	23	7	5.94	219
ACC	+	24/32	3	26	31	8.00	710
L MFG	+	9	-33	53	25	5.06	120
R MFG	+	9/46	36	44	34	4.86	53
L Postcentral Gyrus	+		-63	-22	25	6.15	258
L IFG (pars triangularis)	-	45	-36	11	28	-5.67	171
R IFG (pars triangularis)	-	45	48	29	22	-4.38	155
PCC	-	23/31	6	-46	34	-5.13	438
Reward							
L Insula[a]	+		-30	17	1	11.30	32470
R Insula[a]	+		33	23	-2	11.07	
ACC[a]	+	24/32	3	29	31	10.83	
R Ventral Striatum[a]	+		21	11	-2	8.42	
L Ventral Striatum[a]	+		-18	14	-5	7.92	
R MFG[a]	+	9	33	-70	31	7.42	
L MFG[a]	+	9/46	-45	41	22	6.75	
R lateral OFC[a]	+	11	21	41	-20	6.76	
L lateral OFC	+	11	-27	50	-14	6.61	93
Medial OFC	-	11	-6	56	-8	-4.56	65
PPI (medial OFC Seed)							
Risk							
Ventromedial PFC	+	10/11	0	50	-17	17.20	44147
PCC	+	23/31	0	-49	37	12.61	
R Amygdala	+		21	-7	-17	7.57	
L Amygdala	+		-21	-10	-17	8.51	
L SFG	+	8/9	-18	35	43	9.56	
R SFG	+	8	24	32	46	8.30	
L Ventral Striatum	+		-9	14	-8	8.06	
Reward							
Ventromedial PFC[b]	+	10/11	-3	50	-17	14.30	49598
Ventral Striatum[b]	+		0	8	-8	5.90	
Superior Medial PFC[b]	+	9/10	-9	44	46	9.38	
PCC[b]	+	23/31	-3	-49	25	12.92	
R IFG[b]	+	45	51	32	-8	8.86	
L IFG[b]	+	45	-51	29	-2	8.33	
PPI (VS Seed)							
Risk							

Table 2 (cont.)

Anatomical Region	+/-	BA	x	y	z	t	k
R Caudate[c]	+		0	-10	10	14.38	56455
L Caudate[c]	+		-12	-7	13	12.02	
L Amygdala[c]	+		-18	-1	-14	11.48	
R Amygdala[c]	+		18	5	-14	10.34	
dACC[c]	+	24/32	-3	32	28	11.52	
PCC[c]	+	23/31	3	-27	25	11.77	
Reward							
R Caudate[d]	+		6	-10	10	11.78	49598
L Putamen[d]	+		-18	11	7	11.41	
R Putamen[d]	+		21	15	-5	11.35	
L Amygdala[d]	+		-18	-1	-14	9.34	
PCC[d]	+	23/31	0	-40	22	10.13	
dACC[d]	+	24/32	3	32	31	9.62	

Note: L and R refer to left and right hemispheres; + and – refer to positive or negative activation; BA refers to Brodmann Area of peak voxel; k refers to the number of voxels in each significant cluster; t refers to peak activation level in each cluster; x, y, and z refer to MNI coordinates. Superscripts (e.g. a, b, etc.) indicate that peak voxels are part of a contiguous cluster. ACC = Anterior Cingulate Cortex, dACC = dorsal ACC, MFG = Middle Frontal Gyrus, IFG = Inferior Frontal Gyrus, PCC = Posterior Cingulate Cortex,; OFC = Orbitofrontal Cortex, PFC = Prefrontal Cortex.

Table 3. Neural Regions Showing Age-related Increases During Risk and Reward in Activation and PPI analyses.

Anatomical Region	+/-	BA	x	y	z	t	k
Activation							
Risk							
R SFG	+	9	15	47	25	3.63	42
MCC	+	31	0	-10	43	3.79	67
R Motor Cortex	+	4	24	-25	61	4.12	82
Calcarine Gyrus	+	17	0	-99	7	4.45	50
Reward							
R Ventral Striatum	+		3	8	-2	4.64	50
R medial OFC[e]	+	11	9	53	-20	4.46	76
L medial OFC[e]	+	11	-9	41	-17	4.00	
R Cerebelum	+		24	-70	-38	3.89	55
PPI (medial OFC Seed)							
Risk							
Superior Medial PFC	+	9/10	-3	56	10	4.31	299
Reward							
Superior Medial PFC[f]	+	9/10	-6	59	10	5.85	891
rACC[f]	+	32	6	32	-2	5.40	
L SFG	+	9	-18	38	43	4.05	42
PCC	+	23/31	3	-49	28	4.02	112
R Cerebelum	+		30	-85	-32	4.78	42

Note: L and R refer to left and right hemispheres; + and – refer to positive or negative association; BA refers to Brodmann Area of peak voxel; k refers to the number of voxels in each significant cluster; t refers to peak activation level in each cluster; x, y, and z refer to MNI coordinates. Superscripts (e.g. a, b, etc.) indicate that peak voxels are part of a contiguous cluster. SFG = Superior Frontal Gyrus, MCC = Mid-Cingulate Cortex, OFC = Orbitofrontal Cortex, PFC = Prefrontal Cortex, rACC = rostral Anterior Cingulate Cortex, PCC = Posterior Cingulate Cortex

Table 4. Associations between neural regions showing age-related increases in activation and task behavioral indices.

Neural Regions	Age	Risk Behavior	Exploratory Behavior	Learning
Activation				
Risk				
MCC	.40***	.20^{+}	.40***	.35***
R SFG	.39***	.28*	.23*	.31***
Reward				
Medial OFC	.46***	.41***	.33***	.42***
Ventral Striatum	.46***	.18	.24*	.28*
PPI (medial OFC seed)				
Risk				
Medial PFC	.45***	.25*	.19^{+}	.30**
Reward				
Medial PFC	.52***	.33***	.31**	.35***
PCC	.42***	.27*	.21^{+}	.28*

Note: $^{+}$<.1, * <.05, **<.01 ***<.001.