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Adolescent risk-taking and resting state functional connectivity

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ABSTRACT

The existing literature on the role of emotion regulation circuits (amygdala-prefrontal cortex) in the adolescent brain yields mixed results, particularly on the role of these regions in the context of reward sensitivity and risk-taking behavior sensitivity and risk-taking behavior. Here, we examined functional connectivity in the resting state in 18 risk-taking (RT) adolescents compared with 18 non-risk-taking (NRT) adolescents as defined by the Youth Risk Behavior Surveillance Survey. Separate seed-based correlations with bilateral amygdala and bilateral nucleus accumbens used as the seed were performed to determine functional connectivity using functional magnetic resonance imaging (fMRI). The results showed greater connectivity between the amygdala (seed region) and the right middle frontal gyrus, left cingulate gyrus, left precuneus and right inferior parietal lobule in RT adolescents than in NRT adolescents. Likewise, there was greater connectivity between the nucleus accumbens (seed region) and the right middle frontal gyrus in RT adolescents compared with NRT adolescents. These findings suggest that risk-taking behavior in adolescents is associated with hyperconnectivity during the resting state in networks associated with emotion regulation, reward sensitivity, executive control, and the default mode.

1. Introduction

Risk-taking behavior is a growing concern in today's adolescent population. The Youth Risk Behavior Surveillance Survey of high school students in 2011 reported that in the 30 days preceding the survey, 38.7% drank alcohol, and 23.1% used marijuana (Eaton et al., 2012). The survey further revealed that 15.3% of adolescents had four or more sexual partners in their lifetime, and 32.8% had been in a physical fight in the last 12 months (Eaton et al., 2012). Emerging evidence in the neuroimaging literature suggests that a combination of developing brain regions and aberrant network connectivity among these regions may be moderating adolescent decision-making and risk-taking (Wetherill et al., 2012). One such brain network is the emotion-regulation network (Perlman et al., 2012).

Emotion regulation is commonly thought to consist of a regulatory feedback loop whereby limbic regions (such as the amygdala) provide input to prefrontal cortex (PFC) regions (including the dorsolateral PFC in adults (Staudinger et al., 2011) and the ventrolateral PFC in children and young adults (McRae et al., 2012)), which in turn provide reciprocal input back to limbic regions allowing for regulation of emotional reactivity, i.e., emotion regulation (Levesque et al., 2004). Disruptions in brain regions within the regulatory loop can lead to antisocial and risk-seeking behaviors. For example, Joseph et al. (2009) showed that high sensation-seeking adults exhibited greater neural activity in PFC regions related to processing emotion including in the insula and medial orbital frontal cortex (OFC) as compared with participants defined as low sensation-seekers.

Emotion regulation as it relates to risk-taking behavior is shown in adults to consist of cognitive control over emotional responses with the net effect of a reduction in reward-circuitry activation (Martin and Delgado, 2011). The behavioral findings on the association between emotion regulation and risk-taking in adolescents suggest that the ability to make effective decisions in the context of risk may be affected by states of heightened arousal (Rivers et al., 2008; Spear, 2009). Studies that have examined emotional response and regulation in adolescents reveal behavioral and neural patterns distinct from those of children and adults in limbic, PFC, and reward-circuitry regions (Ernst et al., 2005; Galvan et al., 2006; Guyer et al., 2008).

Many researchers have used functional connectivity analysis to investigate the relationship among regions involved in emotion regulation. Functional connectivity is defined as a temporal correlation of a neurophysiological index measured in brain areas, such as the blood-oxygen-level-dependent (BOLD) signal (Biswal et al., 1997). The relationship between neuronal activation patterns of differing brain regions is described by the level of functional connectivity between the regions (van den Heuvel and Hulshoff Pol, 2010). Functional networks among brain regions observed

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during rest (i.e., the resting state) are shown to correspond closely to the networks of those regions when a task is carried out (Smith et al., 2010; Kannurpatti et al., 2012). Such observations suggest that knowledge of the intrinsic organization of brain regions informs neuronal activation patterns when the brain is engaged in a task.

Studies that look at connectivity and activation patterns in regions related to emotion regulation in adolescents have not denoted a clearly defined pattern of connectivity. Resting-state connectivity in regions related to emotion regulation including the amygdala and ventromedial PFC (vmPFC) has been shown to be significantly weaker in children compared with adults (Qin et al., 2012). However, in a recent study in which participants were shown emotional faces (happy vs. scared), functional connectivity observed from childhood through early adulthood showed a switch from positive amygdala-PFC connectivity to negative connectivity around the age of 10 (Gee et al., 2013).

Thus far, most existing studies that have examined functional connectivity in adolescents have focused on task-dependent responses, with few evaluating its relationship to risky behavior. Some findings have shown a reduction in connectivity in areas of emotion regulation related to risky behavior for adolescents engaged in emotion-related tasks (Hare et al., 2008), particularly in adolescents with clinical disorders associated with risky behavior. One such study examined functional and structural amygdala-PFC connectivity in youth with conduct disorder and psychopathic traits (Marsh et al., 2011). Findings from this study showed reduced functional connectivity between the amygdala and the orbitofrontal cortex (OFC) during a task where participants were asked to make moral judgments. Interestingly, a similar amygdala-OFC disconnection has been observed in adults with borderline personality disorder and is suggested to be related to an inability of the OFC to down-regulate amygdalar response to aversive stimuli (New et al., 2007). Reduced functional connectivity between the amygdala and the rostral anterior cingulate during a learning task was also observed in youth with conduct disorder (Finger et al., 2012). Other studies, however, found increased activation in fronto-limbic regions to be associated with risk. For example, Silveri et al. (2011) found enhanced activation in subjects performing a visual Stroop Task in the ventral cingulate cortex (connected to the amygdala) and the middle frontal gyrus in adolescents who had a family history of substance abuse compared with adolescents who did not. The authors suggested that enhanced activation may be the result of neuronal inefficiency, such as a disproportionate amount of activation for a given task in these regions.

Taken together, these studies suggest that aberrant functional connectivity may be a hallmark of behavioral problems/disorders, particularly in adolescents. However, a clear pattern of functional connectivity associated with risk-taking behavior needs to be established. In the present study, we used resting state functional connectivity to assess the regions responsible for emotion regulation in a risk-taking adolescent population. Given the role of reward-circuitry/reward sensitivity in adolescent risk-taking behavior, we examined these regions as well.

The focus of our investigation was on intrinsic organization related to emotion regulation and reward sensitivity. Thus, we determined resting state functional connectivity with the amygdale (i.e., as the seed region) given its role in emotion. Previous studies in healthy adults have suggested that the amygdala (including its subdivisions) has distinct functional connectivity patterns throughout the brain, which highlight its diffused role in emotional input (Roy et al., 2009). Investigations of resting state functional connectivity between the amygdala and regions of the PFC have revealed aberrant connectivity patterns in adult with posttraumatic stress disorder (Brown et al., 2014) and major depressive disorder (Yue et al., 2013), as well as in adolescents suffering from depression (Connolly et al., 2013). Studies have shown a reduction in task-based functional connectivity between the amygdala and the PFC for adolescents with clinical diagnoses such as conduct disorder. However, the focus of our study is in developing adolescents who engage in risk-taking behavior. Specifically, those who do not yet meet criteria for any disorders such as substance use problems and have no history of psychopathology/behavioral disorders. This allows for the possibility to determine potential pre-morbid processes that may reflect vulnerability to later pathology. Silveri et al. (2011) showed increased fronto-limbic activation in those with an increased risk for substance abuse (i.e., family history). Similarly, we also expect that resting state functional connectivity between the amygdala and PFC areas in risk-taking (RT) adolescents to be greater compared with that in non-risk-taking (NRT) adolescents. This would suggest that altered resting state functional connectivity associated with early risk-taking is a vulnerability factor that preceded problematic behavior such as substance dependence. To investigate the role of reward sensitivity/reward-seeking behavior, we determined resting state functional connectivity with the nucleus accumbens, a key region of the ventral striatum involved in the brain's reward circuitry. Given the extant literature, which describes a hyperactive reward-circuitry as a hallmark of the adolescent brain, we likewise expect resting state functional connectivity between the nucleus accumbens and PFC areas in RT adolescents to be greater than that in NRT adolescents. Elucidating these neural mechanisms as they relate to adolescent risk could lead to a better understanding of the neurocognitive profile and mechanisms of risk-taking, which can inform risk-prevention strategies for adolescents.

2. Methods

Written parental informed consent and assent were obtained from all subjects in accordance with the Institutional Review Board (IRB) of our academic institutions, The University of Texas at Dallas and The University of Texas Southwestern Medical Center at Dallas.

2.1. Participants

Eighteen RT participants were age- and sex-matched to 18 NRT participants (12–17 years old). Risk-taking behavior was assessed using the Youth Risk Behavior Surveillance Survey (YRBSS) and included items related to sexual activity, substance use, or violent behavior (Eaton et al., 2012). Those who endorsed any risk-taking item were categorized in the RT group. Those in the NRT group did not endorse any risk-taking item. The eligibility requirements included the following: aged 12–17 years, right-hand-dominant, no history of brain injury or brain-related illness, no MRI contraindications (e.g., metal implants, claustrophobia, pregnancy), no Axis I disorders, and no current use of psychoactive medications. Adolescents who reported current illicit drug use other than marijuana in the last 60 days were excluded to control for any observable effects of illicit drugs on brain activation. Two members of the RT group reported regular alcohol use at a rate of once per week for no more than a year. One member of the RT group reported regular marijuana at this same level of frequency/duration. Participants were screened for psychiatric disorders using the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime (KSADS-PL) diagnostic (Kaufman et al., 1997) interview, and substance use history was obtained via a substance use history questionnaire. Both groups were matched on age (mean age per group: 14 years) and gender (8 males per group). The two groups were significantly different in mean income levels, with the NRT group having significantly higher income ($p < 0.05$) (Table 1).

Table 1
Subject characteristics and household income, mean (SD).

	N	Age	Gender (M/F)	Household income
NRT Group	18	14.0 (1.7)	10/8	$94,600 ($39,300)*
RT Group	18	14.0 (1.6)	10/8	$66,235 ($29,637)*

* Significant difference at $p < 0.05$, missing data from 3 in NRT group, 1 in RT group.