Research paper

Neural correlates of RDoC reward constructs in adolescents with diverse psychiatric symptoms: A Reward Flanker Task pilot study

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ARTICLE INFO

Keywords:
Positive valence system
Anhedonia
Adolescence
fMRI
RDoC

ABSTRACT

Background: There has been growing interest under the Research Domain Criteria initiative to investigate behavioral constructs and their underlying neural circuitry. Abnormalities in reward processes are salient across psychiatric conditions and may precede future psychopathology in youth. However, the neural circuitry underlying such deficits has not been well defined. Therefore, in this pilot, we studied youth with diverse psychiatric symptoms and examined the neural underpinnings of reward anticipation, attainment, and positive prediction error (PPE, unexpected reward gain). Clinically, we focused on anhedonia, known to reflect deficits in reward function.

Methods: Twenty-two psychotropic medication-free youth, 16 with psychiatric symptoms, exhibiting a full range of anhedonia, were scanned during the Reward Flanker Task. Anhedonia severity was quantified using the Snaith-Hamilton Pleasure Scale. Functional magnetic resonance imaging analyses were false discovery rate corrected for multiple comparisons.

Results: Anticipation activated a broad network, including the medial frontal cortex and ventral striatum, while attainment activated memory and emotion-related regions such as the hippocampus and parahippocampal gyrus, but not the ventral striatum. PPE activated a right-dominant fronto-temporo-parietal network. Anhedonia was only correlated with activation of the right angular gyrus during anticipation and the left precuneus during PPE at an uncorrected threshold.

Limitations: Findings are preliminary due to the small sample size.

Conclusions: This pilot characterized the neural circuitry underlying different aspects of reward processing in youth with diverse psychiatric symptoms. These results highlight the complexity of the neural circuitry underlying reward anticipation, attainment, and PPE. Furthermore, this study underscores the importance of RDoC research in youth.

1. Introduction

The NIMH Research Domain Criteria (RDoC) initiative uses a transdiagnostic approach to identify core constructs in five functional domains that potentially contribute to psychopathology; these domains are thought to reflect common psychological and neurobiological mechanisms of dysfunction across psychiatric illnesses (Cuthbert and Insel, 2013; Insel et al., 2010). The positive valence system (PVS) is one such domain responsible for responses to pleasure and includes reward motivation, reward attainment, and reward learning (Morris and Cuthbert, 2012). The neural circuitry supporting these reward processes matures during adolescence (Paus, 2005), with this period often characterized by increased risk-taking and reward-seeking behaviors (Casey et al., 2010). Relatedly, alterations in the reward network have been associated with the early emergence of psychiatric symptoms during this sensitive period of development (Paus et al., 2008).

Anhedonia, a reduced capacity to experience pleasure, is a known prodromal symptom for various psychiatric illnesses, including depression (Dryman and Eaton, 1991) and schizophrenia (Gelber et al., 2004). Deficits in different reward processes (e.g., reward valuation, expectancy, and attainment) may result in the same anhedonic phenotype, but the neurobiological mechanisms underlying these phenomena are still largely unknown. Therefore, recent work has sought to quantify anhedonia and examine relationships between symptom severity and patterns of neural activity during reward processing. The Snaith-Hamilton Pleasure Scale (SHAPS) is one such

http://dx.doi.org/10.1016/j.jad.2016.11.042
Received 27 June 2016; Received in revised form 22 November 2016; Accepted 27 November 2016
Available online xxxx
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Please cite this article as: Bradley, K.A., Journal of Affective Disorders (2016), http://dx.doi.org/10.1016/j.jad.2016.11.042
commonly used measure of anhedonia severity and examines the capacity to experience pleasure (Snaith et al., 1995).

Functional magnetic resonance imaging (fMRI) has been widely utilized to assess reward processing (Richards et al., 2013; Urban et al., 2012). Several different task structures have been used, which may contribute to variations in fMRI findings (Richards et al., 2013). Passive reward tasks do not require active decision-making to receive probabilistically determined gains (Richards et al., 2013) and consequently may not be ideal to assess the motivation and expectancy components of reward processing. In contrast, instrumental-reward tasks do require simple action in response to a perceptual, cognitive, or motor task (Richards et al., 2013). The Monetary Incentive Delay (MID) Task is a common instrumental-reward task, in which participants respond to a simple two-choice task in order to win or lose (Knuston et al., 2000). However, reward outcomes in the MID Task are often predetermined probabilistically, and the ease of the two-choice task may not adequately impact motivation and thus performance. Building on prior work (Stern et al., 2011; Taylor et al., 2006), we developed the Reward Flanker Task (RFT) based on a combination of the common MID (Knuston et al., 2000) and Flanker (Eriksen and Eriksen, 1974) tasks, where monetary cues designate the reward value of correct responses to upcoming flanker stimuli containing a cognitive conflict component. Our approach of increasing task difficulty through the addition of a conflict component and eliminating probabilistically determined outcomes allows for the assessment of brain function during both motivation and reward receipt processes. Importantly, we also include an unknown cue condition in the design (7° cue instead of the monetary value) in order to allow us to additionally probe differences in neural processing of reward based on expectancy. Specifically, positive prediction error (PPE)—defined here as unexpected reward receipt—can be assessed. The study of PPE is important, as it is an interrelated facet of reward processing integral to reward learning.

In typical development, a common set of brain regions in the dopaminergic system has been associated with reward processing, including the ventral striatum (nucleus accumbens), orbitofrontal cortex (OFC), and anterior cingulate cortex (ACC) (Richards et al., 2013; Urban et al., 2012). Additional regions such as the thalamus, amygdala, insula, and inferior frontal gyrus (IFG), among others, have also been implicated in reward processing (Rademacher et al., 2010; Silverman et al., 2015). In healthy individuals, reward anticipation has been specifically associated with activity in the midbrain and ventral striatum (Knuston et al., 2001a, 2001b, 2005), whereas reward receipt has been associated with activity in the orbitofrontal cortex (Knuston et al., 2001a, 2001b). Reward receipt has also been associated with activity in the ventral striatum, but usually during early learning and initial feedback; activation of this region switches from the reward outcome phase to the anticipatory phase during reward learning (i.e., conditioning; Galvan et al., 2005). In patient populations, alterations in ventral striatal and mesial prefrontal cortex activity during reward processing are characteristic of adult (Arrondo et al., 2015; Zhang et al., 2013) and pediatric depression (Forbes et al., 2006, 2009, 2010; Forbes and Dahl, 2012), as well as adult schizophrenia (Arrondo et al., 2015) and obsessive-compulsive disorder (Figue & etal., 2011).

Given that striatal and mesial prefrontal cortex dysfunction during reward processing cut across psychiatric diagnostic categories, it is important to further investigate and isolate reward circuitry dysfunctions that may underlie alterations in specific phases of reward processing, including motivation, expectancy, and the experience of reward. It is particularly important to examine expectancy in reward processing because studies have shown that disruption in processing prediction errors could lead to anhedonia through disruptions in reward learning and the blunting of reward responses (Gradin et al., 2011; Greenberg et al., 2015; Kumar et al., 2008). Prediction errors occur when the expected reward outcome does not match the actual outcome, which is essential to reward learning. Gradin et al. (2011) found that both patients with depression and those with schizophrenia exhibited disruptions in neural activation in response to prediction errors; specifically, individuals with depression showed reduced activation in the striatum and midbrain that was correlated with increased anhedonia severity. In healthy individuals, but not depressed patients, there is evidence of an inverse relationship between reward expectancy and activation of the ventral striatum when processing prediction errors (Chase et al., 2013; Greenberg et al., 2015). Similarly, the recent EMBARC study found that greater anhedonia severity was associated with a reduction in this inverse relationship between reward expectancy and ventral striatal activity in response to prediction errors (Greenberg et al., 2015). Together, these studies suggest that dysfunctional prediction error processing is specifically associated with anhedonia.

Building upon the above investigations, the current study used a transdiagnostic RDoC approach to map the neurocircuitry of distinct reward processes. In this pilot investigation, we used the RFT, which allows for the discrimination of the core constructs of valuation and motivation (i.e., reward anticipation) and initial responsiveness to reward attainment (i.e. reward receipt). In addition, the RFT is able to examine brain function related to expectancy, specifically PPE. Consistent with RDoC principles, we piloted this reward task on youth with diverse mood and anxiety disorders, as well as healthy controls, in order to examine a wide range of anhedonia severity and thus reward dysfunction. We hypothesized that reward anticipation would be associated with activity in the ventral striatum, while reward attainment would evoke a broader network involving the orbitofrontal cortex and emotion-mediated limbic system. Furthermore, as PPE involves complex reward processes involved in reward learning, we expected that both anticipatory and consummatory networks would be engaged, including the ventral striatum (Chase et al., 2013; Greenberg et al., 2015). We also explored relationships between anhedonia severity as measured by the SHAPS and reward processing. We predicted that anhedonia severity would be inversely related to ventral striatal activation during reward anticipation and in response to positive prediction errors.

2. Methods

2.1. Participants

The sample consisted of 22 youth (M age=16.30, SD=2.32, range: 12–20 years; 10 females). Participants with diverse psychiatric symptoms (n=16), regardless of whether diagnostic criteria from the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) were met, were recruited, along with healthy controls (HC; n=6) with no significant presentation of psychiatric symptomatology or history of mental illness. Ten additional adolescents were scanned but excluded from all analyses: 3 for excessive head motion, 6 for poor/incomplete image acquisition, and 1 for an incidental finding on the MRI scan. Adolescents were recruited from the Mount Sinai Child and Adolescent Psychiatry Outpatient Clinic, physician referrals, and advertisements in the community. An Institutional Review Board (IRB) approved the study, and written informed consent was obtained from participants age 18 and older; those under age 18 provided signed assent, and a parent or legal guardian provided signed informed consent.

2.2. Inclusion and exclusion criteria

All participants were between the ages of 12 and 20 years old and did not present with any medical or neurological conditions. General exclusionary criteria included a low IQ (< 80) as assessed by the Kaufman Brief Intelligence Test [KBIT; (Kaufman and Kaufman, 1990)]. MRI contraindications, a positive drug toxicology test, and a positive pregnancy test in females.
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