Developmental Cognitive Neuroscience 11 (2015) 145–154

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn

Neural processing of reward in adolescent rodents

Nicholas W. Simon, Bita Moghaddam*

University of Pittsburgh, Department of Neuroscience, United States

ARTICLE INFO

Article history:
Received 9 June 2014
Received in revised form
11 November 2014
Accepted 13 November 2014
Available online 22 November 2014

Keywords:
Adolescent
Reward
Electrophysiology
Striatum
Dopamine
Rat

ABSTRACT

Immaturities in adolescent reward processing are thought to contribute to poor decision making and increased susceptibility to develop addictive and psychiatric disorders. Very little is known; however, about how the adolescent brain processes reward. The current mechanistic theories of reward processing are derived from adult models. Here we review recent research focused on understanding of how the adolescent brain responds to rewards and reward-associated events. A critical aspect of this work is that age-related differences are evident in neuronal processing of reward-related events across multiple brain regions even when adolescent rats demonstrate behavior similar to adults. These include differences in reward processing between adolescent and adult rats in orbitofrontal cortex and dorsal striatum. Surprisingly, minimal age related differences are observed in ventral striatum, which has been a focal point of developmental studies. We go on to discuss the implications of these differences for behavioral traits affected in adolescence, such as impulsivity, risk-taking, and behavioral flexibility. Collectively, this work suggests that reward-evoked neural activity differs as a function of age and that regions such as the dorsal striatum that are not traditionally associated with affective processing in adults may be critical for reward processing and psychiatric vulnerability in adolescents.

1. Introduction

Current research on psychiatric disorders has placed a strong emphasis on early detection and treatment. Many symptoms of schizophrenia, mood disorders and addiction first manifest during the adolescent period (Adriani and Laviola, 2004; Casey et al., 2008; Schramm-Sapyta et al., 2009; Mitchell and Potenza, 2014). Accordingly, it is critical to elucidate the biological and environmental risk factors that render adolescents highly vulnerable to these disorders. Such mechanistic knowledge is necessary for the development of interventions to prevent or attenuate the emergence of disease.

Previous preclinical research on brain development and disease has primarily assessed morphological changes or alterations at the receptor level. These studies have yielded critical information about adolescent biology and behavior. There is little known, however, about real-time dynamics of neuronal activity during behavior. This information is particularly relevant in light of recent theories positing that dysfunctional neuronal network activity is a critical contributor to the etiology of disease (Uhlhaas and Singer, 2012; Moghaddam and Wood, 2014). To fully understand how behaviorally relevant neuronal network activity is altered in vulnerable individuals, we must first understand how individual neurons and neural ensembles encode salient events in healthy adolescents and adults.

Changes in affect, motivation, and motivational processing during adolescence are among the first observed behaviors predictive of schizophrenia and other psychiatric illnesses in high risk individuals

* Corresponding author at: University of Pittsburgh, Department of Neuroscience, A210 Langley Hall, Pittsburgh, PA 15260, United States. Tel.: +1 412 624 2653; fax: +1 412 624 9198.
E-mail address: bita@pitt.edu (B. Moghaddam).

http://dx.doi.org/10.1016/j.dcn.2014.11.001

(Ernst et al., 2006; Gladwin et al., 2011; Juckel et al., 2012). To understand the development of symptoms during this vulnerable developmental period, it is essential to quantify the basic neural mechanisms underlying adolescent reward processing. Recent data accumulated in our lab using adolescence rats suggest substantial age-related differences in reward-induced neuronal activity. These differences are manifested even when (1) measurable behavior is equivalent between adolescent and adult subjects, and (2) baseline levels of neuronal activity are equivalent between age groups. Thus, reward-evoked neuronal activity may, in some instances, be more effective than behavioral measures of motivation or baseline activity as a marker of early vulnerability to disease. In this review, we summarize adolescent reward-processing data acquired from a rat model across multiple brain regions, and discuss the implications of these differences for adolescent behavior and disease vulnerability.

2. Adolescent reward processing differs from adults across multiple regions

The technique focused in this review is single-unit extracellular recording where neuronal activity of multiple neurons can be measured in real-time in behaving animals (Sturman and Moghaddam, 2011b). For this method, multiwire electrode arrays are implanted in specific brain regions and electrical signals are amplified and high pass filtered to isolate high frequency neuronal activity, such as action potentials or local field potential oscillations (Buzsaki, 2004; Sturman and Moghaddam, 2011b; Wood et al., 2012). Measuring neural activity in awake-behaving adolescent rats is a challenging endeavor, as the adolescent window only spans approximately between postnatal days 28–55 (Spear, 2000). After accounting for the required time for electrode implantation surgery, recovery and habituation, the brief remaining time window precludes the use of complex behavioral paradigms with electrophysiology. Therefore, behavioral tasks that do not require long training times must be used to measure reward processing in adolescent rats. Our lab utilizes a rewarded instrumental task in which rats learn to nose poke into a lit port to receive a single sugar pellet, while neural activity is recorded from electrode arrays implanted into specific brain regions (Fig. 1). Importantly, the task is simple enough that learning and performance of the primary components of the task are comparable between adults and adolescents (Sturman et al., 2010), thus any differences in neuronal activity are indicative of reward processing differences, rather than a product of behavioral asymmetry between groups. Each of these behavioral events can be synchronized with measures of neural activity with sub-second long temporal resolution, allowing assessment of neural activity associated with reward-related cues, goal-directed actions, and reward anticipation and delivery. Using variants of this task, we recorded from orbitofrontal cortex, dorsal and ventral striatum, and ventral tegmental area in adult and adolescent rats. We then discuss how these differences in reward-processing may be related to reward-related cognitive traits observed during adolescence, including impulsivity, risk taking and behavioral flexibility.

2.1. Prefrontal cortex

Prefrontal cortex (PFC) undergoes substantial development throughout adolescence, and this development has been implicated in adolescent behavioral tendencies, particularly the ability to regulate and inhibit motivated behaviors (Brenhouse et al., 2010; Geier et al., 2010; Sturman and Moghaddam, 2011a; Ernst, 2014). PFC is divided into multiple functionally distinct subregions with different implications for adolescent behavior and disease vulnerability. Orbitofrontal cortex (OFC) is a lateral prefrontal-cortical region that receives input from sensory regions and is extensively connected with limbic areas (Price, 2007; Rolls and Grabenhorst, 2008). Accordingly, OFC is ideally suited to integrate physical aspects of rewarding and aversive outcomes with emotional information, and then utilize this affective information to guide behavior. Neuronal activity in OFC has been associated with the representation of rewarding outcomes (van Duuren et al., 2007; Balleine et al., 2011; Schoenbaum et al., 2011), and has been implicated in multiple facets of impulsive behavior (Berlin et al., 2004; Winstanley et al., 2010; Zeeb et al., 2010), which is elevated in humans and rats during adolescence (Green et al., 1994; Adriani and Laviola, 2003; Burton and Fletcher, 2012; Doremus-Fitzwater et al., 2012; Mitchell and Potenza, 2014). Because OFC (along with other prefrontal regions) has been shown to be underdeveloped in human adolescents (Sowell et al., 1999; Galvan et al., 2006), OFC is a logical target for probing for age-related differences in reward processing.

Single unit extracellular recording was used to measure task-evoked activity in individual neurons. In adults, OFC population neuronal activity decreased during reward retrieval (Fig. 1B). In contrast, the adolescent OFC population activity was increased during retrieval (Sturman and Moghaddam, 2011b). This profound difference in activity occurred despite similar baseline firing rate between groups, and comparable neuronal inhibition during the performance phase of the instrumental action that lead to reward delivery. These data suggest that reward processing in OFC can be an effective biomarker of age-related differences, even when baseline neuronal activity and behavior are equivalent between groups.

Although baseline firing rate was similar between age groups, an alternate analysis of firing patterns revealed further distinctions. Adolescent OFC showed increased variability compared to adults in firing rate across multiple trials, as assessed by fano factor, which provides a measure of normalized variability and can be calculated as cross-trial variance divided by cross-trial mean (Churchland et al., 2010). This variability may be indicative of inefficient neural coding of reward-related events, as spike variability undermines effective inter-regional communication through spike-field coherence (Fries, 2005; Churchland et al., 2010). Importantly, this finding suggests that measures beyond simple firing rate may be necessary to detect functional differences in neural processing between age groups, and possibly between healthy controls and diseased or at-risk patients.