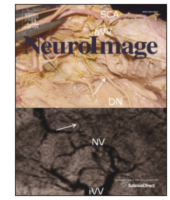
NeuroImage 118 (2015) 422–437

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



Normative development of ventral striatal resting state connectivity in humans

Dominic S. Fareri [a,b,*], Laurel Gabard-Durnam [a,c], Bonnie Goff [c], Jessica Flannery [d], Dylan G. Gee [e], Daniel S. Lumian [f], Christina Caldera [a], Nim Tottenham [a,c]

[a] *Department of Psychology, Columbia University, New York, NY 10027, USA*
[b] *Gordon F. Derner Institute of Advanced Psychological Studies, Adelphi University, Garden City, NY 11530, USA*
[c] *Department of Psychology, University of California-Los Angeles, Los Angeles, CA 90095, USA*
[d] *Department of Psychology, University of Oregon, Eugene, OR 97403, USA*
[e] *Sackler Institute for Developmental Psychobiology, Weill Cornell Medical College, New York, NY 10065, USA*
[f] *Department of Psychology, University of Denver, Denver, CO 80208, USA*

ARTICLE INFO

Article history:
Received 31 July 2014
Accepted 5 June 2015
Available online 16 June 2015

Keywords:
Ventral striatum
Development
Resting-state
Incentives
Valuation

ABSTRACT

Incentives play a crucial role in guiding behavior throughout our lives, but perhaps no more so than during the early years of life. The ventral striatum is a critical piece of an incentive-based learning circuit, sharing robust anatomical connections with subcortical (e.g., amygdala, hippocampus) and cortical structures (e.g., medial prefrontal cortex (mPFC), insula) that collectively support incentive valuation and learning. Resting-state functional connectivity (rsFC) is a powerful method that provides insight into the development of the functional architecture of these connections involved in incentive-based learning. We employed a seed-based correlation approach to investigate ventral striatal rsFC in a cross-sectional sample of typically developing individuals between the ages of 4.5 and 23-years old ($n = 66$). Ventral striatal rsFC with the mPFC showed regionally specific linear age-related changes in connectivity that were associated with age-related increases in circulating testosterone levels. Further, ventral striatal connectivity with the posterior hippocampus and posterior insula demonstrated quadratic age-related changes characterized by negative connectivity in adolescence. Finally, across this age range, the ventral striatum demonstrated positive coupling with the amygdala beginning during childhood and remaining consistently positive across age. In sum, our findings suggest that normative ventral striatal rsFC development is dynamic and characterized by early establishment of connectivity with medial prefrontal and limbic structures supporting incentive-based learning, as well as substantial functional reorganization with later developing regions during transitions into and out of adolescence.

Introduction

Incentives play a crucial role in our lives, providing opportunities to learn about and adapt to the environment. Pursuit (or avoidance) of incentives is a powerful motivator of behavior particularly during development (e.g., early life), when less is known about the world and the value of environmental stimuli is being learned rapidly. Research across species highlights the ventral striatum as a key neural structure supporting incentive-based valuation by coding for expected and experienced incentives of varying valence and magnitude to inform learning and decision-making (Alexander et al., 1990; Delgado, 2007; Haber and Knutson, 2010; Haber and McFarland, 1999; Hare et al., 2008a; O'Doherty, 2004; Plassmann et al., 2007; Robbins and Everitt, 1996; Robbins et al., 1989). This structure is extensively connected to both cortical and subcortical structures involved in valuation and learning, forming components of functional neural circuits supporting motivated behavior (Alexander et al., 1990; Haber and Knutson, 2010; Haber and McFarland, 1999; Pennartz et al., 2011). Because of its extensive connectivity, the ventral striatum is considered a hub of cognitive and affective integration (Cohen et al., 2009; Delgado et al., 2000; Di Martino et al., 2008; Haber and Knutson, 2010; Hare et al., 2008a; Knutson et al., 2001, 2005; Leotti and Delgado, 2011a,b; Li and Daw, 2011; Li et al., 2011; O'Doherty, 2004; Pennartz et al., 2011; Wimmer et al., 2012).

Ventral striatal function and connectivity patterns supporting incentive-based valuation and learning are well characterized in studies of adults (Cohen et al., 2009; Delgado et al., 2000; Di Martino et al., 2008; Hare et al., 2008a; Knutson et al., 2001, 2005; Leotti and Delgado, 2011a,b; Li et al., 2011; Li and Daw, 2011; O'Doherty, 2004; Wimmer et al., 2012), which show that ventral striatum lies at the vertex of an incentive-based learning circuit that includes the amygdala, hippocampus, medial prefrontal cortex, and insula. Each of these regions contributes uniquely to incentive-based learning. The amygdala

* Corresponding author at: Columbia University, Department of Psychology, 409A Schermerhorn Hall, New York, NY 10027, USA.
E-mail address: dsf2132@columbia.edu (D.S. Fareri).

http://dx.doi.org/10.1016/j.neuroimage.2015.06.022
1053-8119/© 2015 Published by Elsevier Inc.

is highly involved in rapid evaluation of potentially incentivizing stimuli and affective learning across species (Belova et al., 2007, 2008; Campeau and Davis, 1995; Paton et al., 2006; Phelps and LeDoux, 2005). Hippocampal contributions to incentive-based decision-making involve incorporating contextual information (e.g., past experiences) to bias future decisions (Barron et al., 2013; Wimmer and Shohamy, 2012) and constructing representations of incentive value for novel stimuli based on memories of related component stimuli (Barron et al., 2013). Regions of medial prefrontal cortex (e.g., orbitofrontal cortex (OFC), ventromedial PFC (vmPFC)) represent expected and experienced incentive value (Alexander and Brown, 2011; Behrens et al., 2007; Hare et al., 2008a; Kennerley et al., 2006; Kringelbach et al., 2003; O'Doherty et al., 2001; Rolls, 2000), and support representation of outcome history and action outcome predictions (Alexander and Brown, 2011; Bartra et al., 2013; Behrens et al., 2007; Kennerley et al., 2006; Phelps et al., 2014). Finally, the insula, while functionally diverse, is a key component of a valuation system (Bartra et al., 2013; Kuhnen and Knutson, 2005; Niv et al., 2012; Phelps et al., 2014; Preuschoff et al., 2008), important in evaluating risk (Kuhnen and Knutson, 2005; Niv et al., 2012; Pessiglione et al., 2006; Preuschoff et al., 2008; Seymour et al., 2004), learning from aversive incentives (Chang et al., 2013; Pessiglione et al., 2006; Preuschoff et al., 2008; Seymour et al., 2004), and integrating cognitive, affective and interoceptive information (Chang et al., 2013; Chein et al., 2011; Preuschoff et al., 2008).

Characterization of this system's development is an active area of investigation, with task-based functional magnetic resonance imaging (fMRI) studies largely focused on ventral striatal and prefrontal function within reward-seeking contexts (for reviews see Fareri et al., 2008; Galván, 2010; Richards et al., 2013; Somerville et al., 2010). A common thread within this body of work highlights large-scale functional changes occurring within the developing ventral striatum, such as heightened responses to monetary reward receipt and to reward anticipatory cues in adolescents compared to adults (Ernst et al., 2005; Somerville et al., 2011) and children (Somerville et al., 2011) (but see also (Bjork et al., 2004; 2010; Silvers et al., 2014)). More specifically, relative to children and adults, adolescents show enhanced sensitivity to larger versus smaller monetary rewards in the ventral striatum (Galván et al., 2006), enhanced learning-related signals (Niv and Schoenbaum, 2008) in the ventral striatum (Cohen et al., 2010), and stronger responses to positive affective cues (Somerville et al., 2011). Developmental differences in ventral striatal function during reward-seeking contexts are often observed in conjunction with differences in vmPFC and OFC recruitment, such as increased vmPFC activation in adolescents during high risk decisions (though see also Eshel et al., 2007; Van Leijenhorst et al., 2010a) and increased OFC activation in adults to omitted rewards (Van Leijenhorst et al., 2010b). A large region of vmPFC has also recently been implicated as showing a linear age-related increase in activation to the expected value associated with a decision (e.g., probability of receiving a reward ∗ amount of reward) (van Duijvenvoorde et al., 2015). The differential functional developmental trajectories of the ventral striatum and related prefrontal cortical regions may in part underlie observed increases in reward-seeking during this developmental period.

In addition to these developmental changes, the amygdala, hippocampus and insula each have their own developmental timelines. Findings suggest the amygdala to be a functionally early developing region (reviewed in Tottenham and Sheridan, 2009), showing robust reactivity during childhood and adolescence which attenuates with age (Gee et al., 2013; Guyer et al., 2008; Swartz et al., 2014; Tottenham et al., 2012; Vink et al., 2014; though see also Hare et al., 2008b), whereas hippocampal development tends to be more protracted (Gogtay et al., 2006; Payne et al., 2010; Tottenham and Sheridan, 2009) (but see also (Wierenga et al., 2014)). The insula, which shares connectivity with cortical and subcortical structures including the ventral striatum (Reynolds and Zahm, 2005) is one of the first cortical structures to develop, beginning to differentiate prenatally (Alcauter et al., 2013), though refinement of organization, function and connectivity likely continues into early adulthood (Alcauter et al., 2013; Scherf et al., 2006). Recent studies report an adolescent peak in insula recruitment related to computations of risk (van Duijvenvoorde et al., 2015) and social learning signals (Jones et al., 2014) as compared to childhood and adulthood.

Ventral striatal development has been most commonly studied in the context of its association with prefrontal cortical development, which continues into early adulthood. Many structural neuroimaging studies suggest protracted prefrontal development in comparison to striatal development (Giedd, 2004; though see also Raznahan et al., 2014; Sowell et al., 1999), often supported by differential functional developmental trajectories of these regions (Casey et al., 2010; Somerville and Casey, 2010). It is often suggested that differences in reward-seeking behavior across development may result from these differential developmental trajectories. In terms of task-based connectivity between the ventral striatum and prefrontal cortex, age-related linear increases in ventral striatal–mPFC functional connectivity have been reported between late childhood through early adulthood when receiving positive incentives (van den Bos et al., 2012). Other studies suggest differential ventral striatal–mPFC recruitment during incentive-based learning depending on age; for example, representation of incentive-based learning signals in ventral striatum, subgenual anterior cingulate cortex (sgACC) and ventrolateral PFC is more robust at younger ages, and negatively correlated with performance, whereas by adulthood, performance improves with more focal representation of such signals in vmPFC (Christakou et al., 2013). Thus while it is clear that age-related changes in ventral striatal functional connectivity manifest across childhood into adulthood, functional relationships with prefrontal cortex seem to differ as a function of specific task-based contexts (Richards et al., 2013). Further, recent work has begun to investigate development of connectivity between the ventral striatum and the insula during incentive-based processes, though noting similar patterns of connectivity between these regions in adolescents and adults, potentially due to task parameters (Cho et al., 2013). In light of these discrepancies, we sought to characterize stable functional changes in ventral striatal functional connectivity across this broad age range, from early childhood through young adulthood, in the absence of task-based demands.

One powerful approach to addressing the development of ventral striatal functional connectivity is the use of resting-state functional connectivity (rsFC), which has emerged as a non-invasive tool with which to investigate the stability of functional neural connections (Cole et al., 2010; Raichle, 2010; Raichle et al., 2001; Utevsky et al., 2014; Van Dijk et al., 2010). rsFC provides a means to characterize functional neural organization independently of differences in task demands and sensitivity to incentives (e.g., money) which may be confounded across development. rsFC is thought to reflect local oscillations of neuronal populations (Riedl et al., 2014) necessary for maintaining stable functional relationships between neural regions often involved in related processes (Buckner and Vincent, 2007). Successful implementations of rsFC have characterized the development of both functional neural networks (Fair et al., 2008, 2010; Pizoli et al., 2011) and connectivity of specific brain structures (Delmonte et al., 2013; Di Martino et al., 2011; Gabard-Durnam et al., 2014; Qin et al., 2012). In adulthood, striatal connectivity at rest shows widespread positive connectivity with mPFC, medial temporal lobe and posterior cortical structures (Di Martino et al., 2008), and network approaches have demonstrated connectivity between the ventral striatum and both association and limbic-related networks of regions (Choi et al., 2012). On the other hand, it has been demonstrated to date that children comparatively show less connectivity with medial prefrontal structures (Di Martino et al., 2011; Greene et al., 2014; but see also Porter et al., 2014). However, considering children and adults only makes it difficult to characterize the timing of neurodevelopmental changes in the construction and organization of ventral striatal functional connectivity. Delineating these changes