Developmental Cognitive Neuroscience 11 (2015) 83–95

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

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

# Age-related changes in the intrinsic functional connectivity of the human ventral vs. dorsal striatum from childhood to middle age

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ARTICLE INFO

*Article history:*
Received 10 April 2014
Received in revised form 22 July 2014
Accepted 21 August 2014
Available online 30 August 2014

*Keywords:*
Resting-state
Adolescence
Development
Functional-connectivity
Striatum
Prefrontal-cortex

ABSTRACT

The striatum codes motivated behavior. Delineating age-related differences within striatal circuitry can provide insights into neural mechanisms underlying ontogenic behavioral changes and vulnerabilities to mental disorders. To this end, a dual ventral/dorsal model of striatal function was examined using resting state intrinsic functional connectivity (iFC) imaging in 106 healthy individuals, ages 9–44. Broadly, the dorsal striatum (DS) is connected to prefrontal and parietal cortices and contributes to cognitive processes; the ventral striatum (VS) is connected to medial orbitofrontal and anterior cingulate cortices, and contributes to affective valuation and motivation. Findings revealed patterns of age-related changes that differed between VS and DS iFCs. We found an age-related increase in DS iFC with posterior cingulate cortex (pCC) that stabilized after the mid-twenties, but a decrease in VS iFC with anterior insula (aIns) and dorsal anterior cingulate cortex (dACC) that persisted into mid-adulthood. These distinct developmental trajectories of VS vs. DS iFC might underlie adolescents' unique behavioral patterns and vulnerabilities to psychopathology, and also speaks to changes in motivational networks that extend well past 25 years old.



## 1. Introduction

The basal ganglia, at the intersection of the midbrain and forebrain, are implicated in a wide range of motor, cognitive, and affective functions that are subserved by cortical–striatal–thalamic–cortical loops (Alexander et al., 1986; Haber, 2003; Selemon and Goldman-Rakic, 1985). Accordingly, the striatum, the major input component of the basal ganglia, receives connections from all cortical regions in a parallel, segregated fashion. Five parallel networks were originally proposed in the classic paper by Alexander et al. (1986); more recent accounts add the notion of a functional gradient within the striatum (Haber, 2003). Specifically, a ventral to dorsal schema has been linked with an affective/motivational to cognitive/motor

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http://dx.doi.org/10.1016/j.dcn.2014.08.011

gradient with relevance to various aspects of behaviors (e.g., learning, reward responses, goal-directed or habitual actions) (Fareri et al., 2008; Haber, 2003; Liljeholm and O'Doherty, 2012; O'Doherty et al., 2004; Voorn et al., 2004). Anatomically, the ventral striatum typically includes the nucleus accumbens (NAcc) and ventral regions of the caudate nucleus and putamen, and the dorsal striatum includes the dorsal regions of the putamen and caudate nucleus.

The striatal functional gradient is reminiscent of the dual neural systems model of adolescent behavior, which focuses on the interaction between cognitive and motivational neural systems that influence overt behavioral patterns (Casey et al., 2008; Hardin and Ernst, 2009; Luciana et al., 2012; Steinberg, 2010). Dual neural systems models have been formulated to account for risk-taking and sensation-seeking behaviors, which are particularly prominent and often worrisome in adolescence (Minino, 2010; Spear, 2000; Steinberg et al., 2008). These models theorize that different developmental trajectories of the cognitive and motivational networks are responsible for these behaviors (Casey et al., 2008; Galvan et al., 2006; Harden and Tucker-Drob, 2011; Luciana et al., 2012). Specifically, recent formulations suggest that a strong neural responsivity of the motivational system together with a progressively maturing cognitive system in adolescence sets up a dynamic state that leaves emotions and associated motivational drives insufficiently modulated by cognitive control (Ernst et al., 2006; Luciana et al., 2012; Steinberg, 2010). This dual-system model suggests that the transition from adolescence into adulthood might be marked by distinct ontogenic changes in ventral versus dorsal striatum.

A convincing literature from the fields of psychology and neuroimaging provides support for the dual-system theory, both at a behavioral (Harden and Tucker-Drob, 2011; Steinberg et al., 2008; Urosevic et al., 2012) and a neural level (Chein et al., 2011; Ernst et al., 2005; Galvan et al., 2006; Somerville et al., 2010; Van Leijenhorst et al., 2010; but see Bjork et al., 2004, 2010). For example, the ventral striatum, a key component of the motivational system, has been shown to be activated by reward contexts more strongly in adolescents than in adults (Chein et al., 2011; Ernst et al., 2005; Galvan et al., 2006; but see Bjork et al., 2004, 2010). In contrast, during decision-making (but not necessarily in other tasks, such as inhibitory control tasks, e.g., Ordaz et al., 2013), prefrontal cortical regions have been shown to be less activated in adolescents than in adults (Eshel et al., 2007; Galvan et al., 2006; Somerville et al., 2010). The greater activity of the ventral striatum together with the lower activity of the prefrontal cortex during reward-related decision-making in adolescence theoretically sets the stage for risk-taking behaviors. Moreover, from a behavioral standpoint, the transition from adolescence to adulthood witnesses a shift in this balance, characterized by decreasing motivational drives from an over-exuberant state and increasing cognitive control to reach maturation (Luciana and Collins, 2012; Luciana et al., 2005; Luna et al., 2004; Urosevic et al., 2012). However, existing studies only partly resonate with the neural systems framework, in the sense that they capture local age-related differences (regional activations), while failing to reveal how the networks themselves (i.e., collection of functionally connected nodes) work in concert to contribute to different patterns of information processing in adults vs. adolescents. In addition, neuroimaging studies of reward processes that have compared adolescents to adults have not shown clear distinctions between the contributions of ventral vs. dorsal striatum to age-related differences in reward processes (see review, Richards et al., 2013). We now have the methodology and analytic methods to examine and dissociate these networks using resting state intrinsic functional connectivity (iFC; Raichle et al., 2001).

The present study examines age-related differences in ventral striatal (VS) iFC and dorsal striatal (DS) iFC. This approach permits us to define and contrast the VS iFC and DS iFC networks, which are broadly linked to motivation and cognitive function, respectively (Haber, 2003), and to examine the influence of age on these systems. Resting-state iFC reflects phasic activity coupling between regions in an idle state. It is thought to provide a measure of both the history of use of a connection (more use may strengthen iFC; Buckner and Vincent, 2007) and the network's readiness to respond when challenged (Deco et al., 2011). Accordingly, we would expect generally a more strongly linked motivation network and a less strongly linked cognitive network in adolescents compared to adults.

In this study, we examined iFC of the VS and DS across the whole brain in a sample of 106 healthy individuals spanning the ages of 9–44 years. In keeping with the extant literature, we expected to observe a segregation of functional connections for each striatal region regardless of age, such that DS would be more strongly connected with higher cortical association areas in the frontal and parietal lobes, while VS would be more strongly connected with the ventral prefrontal cortex (PFC), the amygdala, midbrain, and anterior cingulate cortex (Choi et al., 2012; Di Martino et al., 2008). Based on a dual neural systems model (Luciana et al., 2012; Steinberg, 2010) and strong evidence of a decline in VS activation and associated behaviors from adolescence into adulthood (Urosevic et al., 2012), we expected decreasing VS iFC and increasing DS iFC in the transition from adolescence to adulthood. The age at which striatal connectivity changes stabilize is assumed to be in the mid-twenties, given recent structural findings as observed throughout the brain (Giedd et al., 1999; Giorgio et al., 2008; Lebel and Beaulieau, 2011), but no studies have yet reported on striatal iFC in the transition from adolescence to early adulthood and into mid-adulthood.

## 2. Methods

### 2.1. Participants

One hundred sixty-six healthy participants (75 males, 91 females; 8.5–44.8 years old) completed resting state fMRI scans (with identical parameters) within the context of multiple studies at the same research institution. Clinical assessments using psychiatric interviews (for minors: the Kiddie Schedule for Affective Disorders and Schizophrenia, KSADS; Kaufman et al., 1997; for adults: the Structured Clinical Interview for DSM-IV, SCID; First