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Research report

Fronto-striatal organization: Defining functional and microstructural substrates of behavioural flexibility

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ABSTRACT

Discrete yet overlapping frontal-striatal circuits mediate broadly dissociable cognitive and behavioural processes. Using a recently developed multi-echo resting-state functional MRI (magnetic resonance imaging) sequence with greatly enhanced signal compared to noise ratios, we map frontal cortical functional projections to the striatum and striatal projections through the direct and indirect basal ganglia circuit. We demonstrate distinct limbic (ventromedial prefrontal regions, ventral striatum – VS, ventral tegmental area – VTA), motor (supplementary motor areas – SMAs, putamen, substantia nigra) and cognitive (lateral prefrontal and caudate) functional connectivity. We confirm the functional nature of the cortico-striatal connections, demonstrating correlates of well-established goal-directed behaviour (involving medial orbitofrontal cortex – mOFC and VS), probabilistic reversal learning (lateral orbitofrontal cortex – lOFC and VS) and attentional shifting (dorsolateral prefrontal cortex – dlPFC and VS) while assessing habitual model-free (SMA and putamen) behaviours on an exploratory basis. We further use neurite orientation dispersion and density imaging (NODDI) to show that more goal-directed model-based learning (MB_c) is also associated with higher

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mOFC neurite density and habitual model-free learning (MF_c) implicates neurite complexity in the putamen. This data highlights similarities between a computational account of MF_c and conventional measures of habit learning. We highlight the intrinsic functional and structural architecture of parallel systems of behavioural control.

1. Introduction

Mapping the functional organization of cortico-basal ganglia-thalamo-cortical (CBGTC) circuit connectivity is crucial as it aids our understanding of behaviour, motor control and the emergence of neuropsychiatric disorders. Fronto-striatal circuitry can be broadly divided into motor, limbic and cognitive projections (Groenewegen, Wright, Beijer, & Voorn, 1999; Haber, 2003). In humans, resting state connectivity studies have used several methods to analyse fronto-striatal coupling including defining cortical projections from 6 striatal seeds (Di Martino et al., 2008) and striatal mapping using clustering algorithms of the entire cerebral cortex (Choi, Yeo, & Buckner, 2012; Jung et al., 2014). Here, we extend these studies by developing connectivity maps based on carefully defined prefrontal seed regions (based on function) and following striatal functional projections through the basal ganglia and thalamus. We use a novel multi-echo planar imaging sequence and independent components analysis (ME-ICA) that greatly enhances signal-to-noise ratios compared to single-echo sequences thus allowing higher spatial resolution of subcortical structures (Kundu, Inati, Evans, Luh, & Bandettini, 2012).

We further examine the functional relevance of these connections by assessing the behavioural correlates of fronto-striatal connectivity, focussing on goal-directed behaviours and attentional set shifting, with an exploratory focus on cognitive-behavioural flexibility in the form of reversal learning for both reward and loss and separately, habitual behaviour. The capacity to flexibly adapt behaviour is crucial to negotiating the vicissitudes of daily life. Behaviour is believed to be a product of parallel decisional systems. On the one hand, flexible goal-directed behaviour is guided by the assessment of a model of environmental contingencies and remains sensitive to outcome value, whereas habitual behaviour entails decisions that are made based on previously reinforced actions (Daw, Gershman, Seymour, Dayan, & Dolan, 2011). Although most of us seem to effortlessly blend or alternate between the two systems, several pathological disorders have been associated with their imbalance (Everitt & Robbins, 2005; Gillan et al., 2011; Sjoerds et al., 2013; Voon et al., 2014; de Wit et al., 2012). Recent computational theories describe two distinct forms of learning known as model-based and model-free reinforcement learning. These provide a computational framework which is hypothesized to underlie goal-directed and habitual behaviours, respectively (Dayan & Niv, 2008). We focus on mapping the intrinsic functional connections, as well as neural microstructure features, associated with model-based and MF_c in healthy volunteers.

Goal-directed behaviour has been explored using lesion studies in rodents and imaging studies in humans, particularly implicating the ventromedial prefrontal and orbitofrontal cortices (Balleine & O'Doherty, 2010; Yin, Ostlund, Knowlton, & Balleine, 2005). In contrast, to the ventromedial prefrontal cortex (vmPFC), which encodes action-outcome contingencies and action values to guide behaviour (Glascher, Hampton, & O'Doherty, 2009; Tanaka, Balleine, & O'Doherty, 2008; Wunderlich, Dayan, & Dolan, 2012; Yin et al., 2005), the orbitofrontal cortex (OFC) is involved in the computation and updating of outcome value in the context of changing internal motivational states or feedback (J. S. Morris & Dolan, 2001; O'doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001; Valentin, Dickinson, & O'Doherty, 2007). The OFC, ventral striatum (VS) and also amygdala respond not only to primary (food, drugs), but also to secondary rewards (money) (Haber & Knutson, 2010; Kringelbach & Rolls, 2003; Shin et al., 2013). Medial-lateral divisions within the OFC are apparent, with medial regions involved with reward and value monitoring and lateral regions becoming recruited when an action previously associated with reward must be suppressed (important for reversal learning) (Elliott, Friston, & Dolan, 2000; O'doherty et al., 2001). Anticipation and response to negative outcomes has been associated with the anterior insula (Seymour, Daw, Dayan, Singer, & Dolan, 2007), with activity within this region also predicting behavioural avoidance to losses (Kuhnen & Knutson, 2005; Samanez-Larkin, Hollon, Carstensen, & Knutson, 2008). The nucleus accumbens or VS, receives extensive anatomical connections from OFC(Groenewegen et al., 1999; Stefanacci & Amaral, 2002) and encodes anticipation and receipt of reward, tracking prediction error and linking motivationally-relevant reward properties with instrumental performance and response vigour (Corbit, Muir, & Balleine, 2001; Pessiglione, Seymour, Flandin, Dolan, & Frith, 2006; Schultz, Dayan, & Montague, 1997; Talmi, Seymour, Dayan, & Dolan, 2008). While a previous study implicated anatomical connectivity of the caudate nucleus in flexible goal-directed behaviour assessed via ‘slips of action’ (de Wit et al., 2012), ventral striatal activity has been linked to model-based valuation, as well as model-free reward prediction error (Daw et al., 2011). Furthermore, model-based behaviour has been associated with higher grey matter volume, particularly in the medial orbitofrontal cortex (mOFC) (Voon et al., 2014). Thus, the medial OFC and VS have been implicated in model-basedness and may act via linking outcome valuation-updating and reward-related motivation, vital for such behavioural adaptations.

During the course of affective learning, a gradient shift of information processing from ventromedial to dorsolateral striatum (equivalent to human posterior putamen) is believed