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Review

From ventral-medial to dorsal-lateral striatum: Neural correlates of reward-guided decision-making

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ABSTRACT

The striatum is critical for reward-guided and habitual behavior. Anatomical and interference studies suggest a functional heterogeneity within striatum. Medial regions, such as nucleus accumbens core and dorsal medial striatum play roles in goal-directed behavior, while dorsal lateral striatum is critical for control of habitual action. Subdivisions of striatum are topographically connected with different cortical and subcortical structures forming channels that carry information related to limbic, associative, and sensorimotor functions. Here, we describe data showing that as one progresses from ventral-medial to dorsal-lateral striatum, there is a shift from more prominent value encoding to activity more closely related to associative and motor aspects of decision-making. In addition, we will describe data suggesting that striatal circuits work in parallel to control behavior and that regions within striatum can compensate for each other when functions are disrupted.

1. Introduction

Decision-making is governed by goal-directed and stimulus–response (S–R) driven mechanisms, with the former being more closely associated with medial regions of striatum, including nucleus accumbens core (NAc) and dorsal medial striatum (DMS), and the latter with dorsal lateral striatum (DLS). During learning, the transition from goal-directed behavior to S–R driven habits is thought to depend on "spiraling" connectivity from ventral-medial regions in striatum to dopamine (DA) neurons, which then project to more dorsal lateral portions of striatum (Haber, Fudge, & McFarland, 2000; Houk, Adams, & Barto, 1995; Ikemoto, 2007; Joel, Niv, & Ruppin, 2002; Niv & Schoenbaum, 2008; Takahashi, Schoenbaum, & Niv, 2008; van der Meer & Redish, 2011). This network (Fig. 1) allows for feed-forward propagation of information from limbic networks to associative and sensorimotor networks (Haber, 2003; Haber & Knutson, 2010; Haber et al., 2000; Ikemoto, 2007).

Here, we review neural correlates from our labs related to reward-guided decision-making in NAc, DMS, and DLS (Fig. 1). We will specifically focus on neural correlates from studies where animals performed the same behavioral task, thus allowing for direct comparison. Along the way we will describe neural and behavioral changes that occur when these subdivisions are selectively interfered with, offering insight into how these networks guide decision-making. From these studies it appears that different regions in striatum can compensate for each other when function in one is disrupted, suggesting that these structures can work in parallel.

The review is broken down into three sections based on popular ways to subdivide striatum. The classic division has been to subdivide striatum along the dorsal–ventral axis. We will begin our discussion of neural correlates by focusing on neural selectivity from the extremes of this division, nucleus accumbens and dorsal lateral striatum (Fig. 1). Next, we will examine correlates from dorsal striatum along the medial–lateral axis. This work has focused on the finding that DMS and DLS function can be clearly dissociated using devaluation and contingency degradation paradigms showing their respective roles in goal-driven and habitual behaviors (Balleine & O'Doherty, 2010). Finally, we will discuss a synthesis of the dorsal–ventral and the medial–lateral distinction of striatum,

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namely, a ventromedial to dorsolateral functional organization based on connectivity (Haber & Knutson, 2010; Nakamura, Santos, Matsuzaki, & Nakahara, 2012; Voorn, Vanderschuren, Groenewegen, Robbins, & Pennartz, 2004). Afferents innervating striatum progress from limbic to associative to sensorimotor, moving from ventral-medial to central to dorsal-lateral striatum, respectively (Haber, 2003; Haber & Knutson, 2010; Haber et al., 2000; Voorn et al., 2004). In this section, we will describe primate data illustrating how reward, motor, and cognitive neural correlates progress across the diagonal of striatum (Fig. 5B). Collectively these studies suggest that as one progresses from ventral-medial to dorsal-lateral striatum, there is a shift from more prominent value encoding to encoding that better reflects associative and sensorimotor functions.

2. Nucleus accumbens core versus dorsal lateral striatum

Several studies have reported that neural activity in both NAc and DLS is correlated with the value of expected outcomes. We examined these correlates using an odor-guided decision-making task during which we manipulated anticipated value by independently varying reward size and the length of delay preceding reward delivery (Roesch, Singh, Brown, Mullins, & Schoenbaum, 2009). As illustrated in Fig. 2A, rats were trained to nose-poke in a central odor port where one of three different odors was presented. Odors predicted different stimulus–response associations, with one odor signaling the rat to respond to the left (forced-choice), another odor signaling the rat to respond to the right (forced-choice), and a third odor signaled that the rat was free to choose left or right (free-choice) to obtain a liquid sucrose reward. Odors were presented in a pseudo-random sequence such that the free-choice odor was presented on 7/20 trials and the left/right odors were presented in equal proportions for the remaining trials.

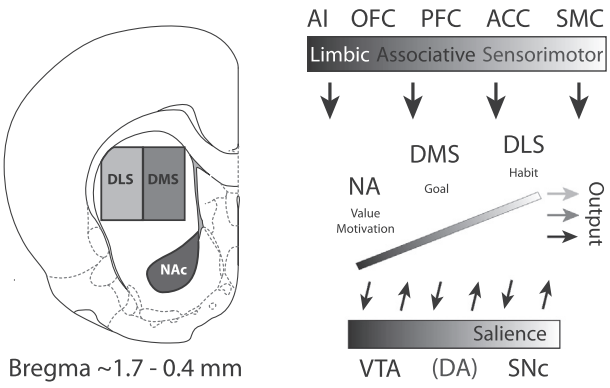

Fig. 1. Recording locations and connectivity of NAc, DMS and DLS. The boxes shown in the coronal section are approximations of recording sites from studies described in Figs. 2–4 (reprinted from Paxinos, G., Watson, C. (1997). *The rat brain, compact* (third ed., pp. 11–15). London: Academic Press. With permission from Elsevier). Recording sites for nucleus accumbens core (NAc) were ~1.6 mm anterior to bregma, 1.5 mm lateral to midline, and 4.5 mm ventral to brain surface taken from Roesch et al. (2009). Recording sites from dorsal medial striatum (DMS) were ~0.4 mm posterior to bregma, 2.6 mm lateral to midline, 3.5 mm ventral to brain surface (Stalnaker et al., 2010). Both NAc and DMS receive projections from medial prefrontal cortex (mPFC) and anterior cingulate cortex (ACC), however NAc is more heavily innervated by agranular insular cortex (AI). Recording sites for dorsal lateral striatum (DLS) were ~1.0 mm anterior to bregma, 3.2–3.6 mm lateral to midline, and 3.5 mm ventral to brain surface (Burton et al., 2014; Stalnaker et al., 2010). DLS receives predominantly sensorimotor-related information from sensorimotor cortex (SMC), as opposed to more ventromedial parts of striatum, which receives visceral information from AI. Striatal areas between NAc and DLS receive higher order associative information from mPFC and ACC. Functional differentiation can be recognized not only through cortical inputs, but also through afferents arising from amygdala, hippocampus and thalamus (Voorn et al., 2004). Amygdalostriatal projections are heaviest ventrally and progressively taper off in a dorsolateral gradient, with sensorimotor parts of striatum only sparsely innervated. The medial (A8) and lateral (A10) dopamine neurons project predominantly dorsolaterally and ventromedially in striatum, respectively, whereas dopamine neurons more centrally located (A9) project broadly to the intermediary striatal zone, with some dorsal dominance (Voorn et al., 2004). Progression from medial to lateral (VTA to SNc) reflects a shift from reward prediction error (RPE) encoding to salience encoding (Bromberg-Martin, Matsumoto, & Hikosaka, 2010). Abbreviations: AI, agranular insula; OFC, orbitofrontal cortex; PFC, prefrontal cortex; ACC, anterior cingulate cortex; SMC, sensorimotor cortex; NA, nucleus accumbens; DMS, dorsal medial striatum; DLS, dorsal lateral striatum; VTA, ventral tegmental area; SNc, substantia nigra pars compacta; DA, dopamine.

We manipulated value of response directions by changing the delay to and size of reward in a series of independent trial blocks (Fig. 2A). At the beginning of each recording session, one reward well was randomly designated as short (0.5 s delay to reward delivery) and the other as long (1–7 s delay to reward delivery). After ~60 trials, this response-outcome contingency switched (block two). In blocks three and four, we held the delay to reward delivery constant at 0.5 s and manipulated reward size. In the third block, the response direction that was previously associated with long delay now produced a big reward (2 boli), while the reward in the other fluid well remained small (1 bolus). Finally, in block four, response–outcome contingencies reversed one last time (Fig. 2A).

During performance of this task, rats switched their side preference after each block shift to obtain the better reward. Rats chose the higher value reward more often than the low value reward on free-choice trials (~60/40 over the entire trial block), and performed faster and more accurately for high value outcomes on forced-choice trials (reaction time: high value = 153 ms, low value = 172 ms; percent correct: high value = 84%, low value = 76%). After training, drivable electrodes were implanted in either NAc or DLS and recording commenced for several months. We found that both regions were significantly modulated by response direction and expected value.

In NAc, the majority of neurons fired significantly more strongly for odor cues that predicted high value outcomes for actions made into the neuron's response field (Roesch et al., 2009). This is illustrated in the population of cue-responsive NAc neurons in Fig. 2B–E for both delay and size blocks. Neural activity was significantly stronger during presentation of cues that predicted large reward and short delay, but only in the preferred direction (i.e., the direction that elicited the stronger response averaged over outcome manipulation). These data suggest that activity in NAc represents the motivational value associated with chosen actions and might be critical for translating cue-evoked value signals into motivated behavior (Catanese & van der Meer, 2013; McGinty, Lardeux, Taha, Kim, & Nicola, 2013). Consitent with this hypothesis, we and others have shown that firing in NAc is significantly correlated with reaction time (Bissonette et al., 2013; McGinty et al., 2013; Roesch et al., 2009).

In contrast to NAc, the majority of neurons in DLS did not fire more strongly for high value outcomes. This is illustrated in Fig. 2F and G, which plots the distributions of value indices computed by subtracting firing on low-value reward (i.e., long and small) from high-value reward (i.e., short and big) trials during cue sampling (odor onset to port exit) for both NAc and DLS after learning (i.e. last 10 trials in each block). For NAc, this distirubtion was signifcantly shifted in the positive direction, indicating a preponderance of cells that exhibited stronger firing for more valued outcomes (Fig. 2F; Wilcoxon, $p < 0.05$). In contrast to NAc, the distribution of value indices obtained from DLS was not significantly shifted from zero (Fig. 2G).

Importantly, this is not to say that activity in DLS was unaffected by they identity of expected outcomes. Over 40% of DLS neurons showed significant modulation by the outcome expected at the end of the trial, however the counts of neurons that showed maximal firing for each trial type were equally distributed across

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