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Working together: basal ganglia pathways in action selection

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Abstract

Jin, Tecuapetla, and Costa combined in vivo electrophysiology with optogenetic-identification to examine firing in multiple basal ganglia nuclei during rapid motor sequences. Their results support a model of basal ganglia function in which co-activation of the direct and indirect pathways facilitate appropriate, while inhibiting competing, motor programs.

The basal ganglia are a group of subcortical nuclei that regulate motor output. More specifically, the basal ganglia are suggested to mediate motor learning, in part by grouping individual movements into action sequences or behavioral “chunks” [1]. The newly published work of Jin and colleagues provides valuable insight into how basal ganglia direct and indirect pathways encode action sequences, and provide a first glimpse of a classic model of basal ganglia function in action.

The primary input nucleus of the basal ganglia is the striatum, which integrates information from cortical, thalamic, and mesolimbic inputs. There are two main projections from the striatum: one to the substantia nigra reticulata (SNr) comprised of direct pathway medium spiny neurons (dMSNs), and one to the external segment of the globus pallidus (GPe) made up of indirect pathway medium spiny neurons (iMSNs). Classic models of basal ganglia function suggest that dMSNs inhibit specific populations of neurons in the SNr, facilitating specific motor programs, whereas iMSNs inhibit neurons in the GPe, resulting in disinhibition of the subthalamic nucleus (STN) and SNr, thereby inhibiting competing motor programs (Figure 1a, b) [2-5].

Many electrophysiolgical studies have examined the relationship between activity in basal ganglia structures and movement. Historically it was impossible to distinguish striatal dMSNs from iMSNs using electrophysiological recordings alone; therefore most studies of the striatum have examined activity of the two populations together. Recordings during operant tasks suggest that the majority of striatal neurons are activated during the initiation or execution of goal-directed movements [6, 7]. Studies in non-reinforced paradigms or during spontaneous exploration also report that a majority of striatal neurons are activated

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during movement [8-10]. Finally, recent recordings from identified populations of dMSNs and iMSNs explicitly demonstrated that both pathways are co-activated during the initiation of movement [11, 12]. These findings are consistent with a model of basal ganglia function in which basal ganglia circuits come “online” prior to movement, at which point coordinated activity of dMSNs select appropriate motor programs, while iMSNs inhibit competing motor programs [5].

Several studies have also examined the effects of selectively ablating or optogenetically stimulating large populations of dMSNs or iMSNs. Selective ablation of iMSNs increased motor output [13, 14], consistent with the inhibitory actions of this pathway. Consistently, stimulation of iMSNs inhibited, whereas dMSNs facilitated, motor output [15]. The optogenetic and ablation results are consistent with the classic model of action selection, although in these manipulations essentially all motor programs were inhibited (via iMSN stimulation), disinhibited (via iMSN ablation), or facilitated (via dMSN stimulation) simultaneously (Figure 1c, d).

Despite the various approaches that have supported it, direct evidence of this model in action during natural behavior has been elusive. A recent paper by Jin and colleagues entitled Basal Ganglia subcircuits distinctly encode the parsing and concatenation of action sequences, provides a rare glimpse of this model in action by examining the activity of each pathway during learning and initiation of rapid motor sequences. Combining optogenetic identification with *in vivo* electrophysiological recordings, Jin and colleagues recorded from identified dMSNs and iMSNs, as well as other basal ganglia nuclei, as mice learned a rapid motor sequence. Similar percentages of dMSNs and iMSNs responded during the start or end of the sequence, confirming that these populations are co-activated during movement initiation and termination. However, while dMSNs responded similarly at the start and end of the sequence, iMSNs preferentially responded at the start of the sequence, presumably to inhibit competing motor programs. Additionally, dMSNs sustained firing, whereas iMSNs were preferentially inhibited, during the sequence itself. Consistent with the striatal recordings, SNr activity reflected that of dMSNs, while GPe activity reflected that of iMSNs. These results constitute the first direct evidence of differential activation of dMSN and iMSN during motor sequences. The authors also demonstrate that the majority of changes in MSN activity occurred during the start or end of the motor sequence and not during the sequence itself, supporting the idea that the basal ganglia controls sequences of behavior (chunking), rather than individual movements [1].

Although this study constitutes a large step in increasing our understanding of the striatal regulation of movement, several questions still remain. To date, studies examining the role of dMSNs and iMSNs in motor function have recorded activity of iMSNs and dMSNs in separate groups of animals. Future work using either the co-expression of distinct opsins for optogenetic identification of, or spectrally distinct calcium indicators for recording from, each population in the same animal would allow for more precise comparisons of the relationships between each pathway during movement. In addition, the majority of studies (including this one) examining striatal contributions to movement have used operant training to elicit behavior. While this has benefits for examining firing around temporally precise behavioral events, reward expectation can modulate movement-related striatal activity [6,

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12]. Therefore, future studies may examine pathway specific activity using behavioral paradigms that do not involve reinforcement. Overall, this new work of Jin, Tecuapetla, and Costa makes a great step forward in viewing the two basal ganglia pathways in action, and understanding how their coordinated activity supports the learning and selection of specific motor programs.

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References

1. Graybiel AM. The basal ganglia and chunking of action repertoires. Neurobiol Learn Mem. 1998; 70(1-2):119–36. [PubMed: 9753592]
2. Albin RL, Young AB, Penney JB. The functional anatomy of basal ganglia disorders. Trends Neurosci. 1989; 12(10):366–75. [PubMed: 2479133]
3. DeLong MR. Primate models of movement disorders of basal ganglia origin. Trends Neurosci. 1990; 13(7):281–5. [PubMed: 1695404]
4. Alexander GE, Crutcher MD, DeLong MR. Basal ganglia-thalamocortical circuits: parallel substrates for motor, oculomotor, “prefrontal” and “limbic” functions. Prog Brain Res. 1990; 85:119–46. [PubMed: 2094891]
5. Mink JW. The basal ganglia: Focused selection and inhibition of competing motor programs. Progress in Neurobiology. 1996; 50(4):381–425. [PubMed: 9004351]
6. Hollerman JR, Tremblay L, Schultz W. Influence of reward expectation on behavior-related neuronal activity in primate striatum. J Neurophysiol. 1998; 80(2):947–63. [PubMed: 9705481]
7. Kawagoe R, Takikawa Y, Hikosaka O. Expectation of reward modulates cognitive signals in the basal ganglia. Nat Neurosci. 1998; 1(5):411–6. [PubMed: 10196532]
8. DeLong MR. Activity of basal ganglia neurons during movement. Brain Res. 1972; 40(1):127–35. [PubMed: 4624486]
9. Costa RM, Cohen D, Nicolelis MA. Differential corticostriatal plasticity during fast and slow motor skill learning in mice. Curr Biol. 2004; 14(13):1124–34. [PubMed: 15242609]
10. Shi LH, et al. Neural responses in multiple basal ganglia regions during spontaneous and treadmill locomotion tasks in rats. Exp Brain Res. 2004; 157(3):303–14. [PubMed: 15067433]
11. Cui G, et al. Concurrent activation of striatal direct and indirect pathways during action initiation. Nature. 2013; 494(7436):238–42. [PubMed: 23354054]
12. Isomura Y, et al. Reward-modulated motor information in identified striatum neurons. J Neurosci. 2013; 33(25):10209–20. [PubMed: 23785137]
13. Sano H, et al. Conditional ablation of striatal neuronal types containing dopamine D2 receptor disturbs coordination of basal ganglia function. J Neurosci. 2003; 23(27):9078–88. [PubMed: 14534241]
14. Durieux PF, et al. D2R striatopallidal neurons inhibit both locomotor and drug reward processes. Nat Neurosci. 2009; 12(4):393–5. [PubMed: 19270687]
15. Kravitz AV, et al. Regulation of parkinsonian motor behaviours by optogenetic control of basal ganglia circuitry. Nature. 2010; 466(7306):622–6. [PubMed: 20613723]

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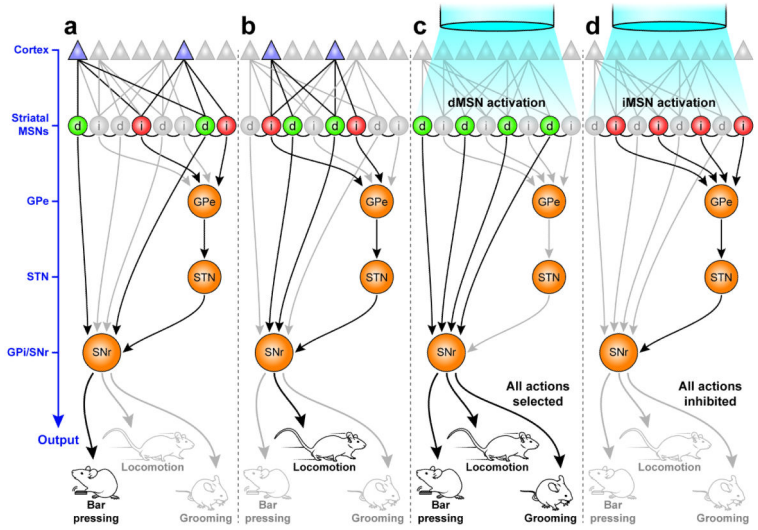

Figure 1.

Natural and optogenetically stimulated states of basal ganglia circuitry. (a, b) Schematics showing different populations of cortical neurons activating different populations of striatal dMSNs (d) and iMSNs (i), modulating downstream neurons in globus pallidus (GPe), subthalamic nucleus (STN), and substantial nigra pars reticulate (SNr), to select different actions. (c) Same circuitry during optogenetic activation of dMSNs, facilitating all actions. (d) Same circuitry during optogenetic activation of iMSNs, inhibiting all actions.