Journal Club

Editor's Note: These short reviews of recent *JNeurosci* articles, written exclusively by students or postdoctoral fellows, summarize the important findings of the paper and provide additional insight and commentary. If the authors of the highlighted article have written a response to the Journal Club, the response can be found by viewing the Journal Club at www.jneurosci.org. For more information on the format, review process, and purpose of Journal Club articles, please see <http://www.jneurosci.org/content/jneurosci-journal-club>.

Dorsal Striatum Dynamically Incorporates Velocity Adjustments during Locomotion

Brian S. Muntean

Department of Neuroscience, The Scripps Research Institute, Jupiter, Florida 33458

Review of Fobbs et al.

Decades of progress have established that basal ganglia-thalamo-cortical loops are essential for organizing locomotor processes. In this circuit, the striatum serves as the main input nucleus of the basal ganglia (Alexander and Crutcher, 1990), which are involved in action selection, initiation, and the learning required to perform refined movements (Penhune and Steele, 2012). However, it remains unclear how striatal neurons encode locomotor programs necessary to facilitate movement.

Recent findings have provided evidence for two models of the role of striatal activity in the control of locomotion. Some studies have shown that populations of striatal neurons exhibit increased firing rates precisely correlated with movement epochs. For example, bursts of striatal activity occur at the initiation and termination of specific action sequences during the execution of learned movements (Jin and Costa, 2010). These results are consistent with the burst-firing model, in which complex learned action sequences are performed by stringing individual movements into a single behavioral unit, generating a streamlined representation of action sequences, called “chunking” (Graybiel, 1998). In this burst-firing model, performing learned movements is simplified (e.g.,

performed habitually) because each individual component of the learned movement need not be separately encoded. Striatal burst-firing at the start and end of skilled tasks may therefore reflect activation of chunked behavioral units (Jin et al., 2014; Martiros et al., 2018).

In addition to flanking specific action sequences with discrete bursts of activity, striatal neurons have been observed to fire continuously during locomotor activity (Sales-Carbonell et al., 2018). These recent findings have inspired a second model suggesting that graded changes in striatal activity enable actions to be monitored and regulated in an ongoing fashion (Robbe, 2018). Continuous encoding may be necessary for adapting motor programs, such as adjusting the speed, during skilled behaviors (Rueda-Orozco and Robbe, 2015). In this way, striatal neurons could update motor programs to meet the demands of variable environmental conditions.

In a recent article in *The Journal of Neuroscience*, Fobbs et al. (2020) further investigated the connection between locomotion and activity of striatal neurons. First, mice were allowed to freely move in an open arena while the authors recorded electrophysiological activity in the dorso-medial striatum (DMS). Using this experimental setup, Fobbs et al. (2020) were able to investigate naturalistic movements that did not require prior training sessions, were not stimuli-dependent, and were not based on reward. With the aid of a machine learning-based behavioral classifier, the authors linked neuronal activity

with distinct actions. To assess neuronal firing patterns during locomotion, the authors aligned electrophysiological data from bins of high-speed movement (velocity exceeding 5 cm/s).

Consistent with previous work, the authors found that some striatal neurons marked the start and end of locomotion sessions with high-frequency bursts of activity. But a greater percentage of striatal neurons fired continuously during bouts of high-speed locomotion. These results provide evidence for both the burst-firing and the continuous-encoding models of motor encoding. To evaluate this data further, Fobbs et al. (2020) modeled the relationship between neuronal firing rates and animal velocity. This analysis revealed that striatal firing rate does not linearly scale with animal velocity (i.e., mice do not necessarily move faster during periods of high striatal activity). Rather, the peak firing rate of individual neurons and animal velocity data fit to a quadratic curve where the greatest percentage of peak firing rates occurred at lower speeds. This could be taken as evidence of firing that initiates chunked motor programs, thus supporting the burst-firing model. However, the observation that the remaining percentage of peak firing rates of individual neurons covered the entire velocity range demonstrates that striatal neurons are active throughout bouts of locomotion. This evidence supports the continuous encoding model in which activity in striatal neurons reflects updates to ongoing locomotor programs occurring on a moment-to-moment basis.

Received Apr. 17, 2020; revised July 16, 2020; accepted July 29, 2020.

The authors declare no competing financial interests.

Correspondence should be addressed to Brian S. Muntean at bmuntean@scripps.edu.

<https://doi.org/10.1523/JNEUROSCI.0905-20.2020>

Copyright © 2020 the authors

Fobbs et al. (2020) demonstrated continuous speed tuning of striatal neurons during volitional movements in unrestrained mice. However, others have demonstrated that discrete striatal neuron burst activity emerges most robustly when mice are restricted to generating a specific set of action sequences. Examples include pressing a lever or walking on a treadmill (Jin and Costa, 2010; Rueda-Orozco and Robbe, 2015; Martiros et al., 2018). This raises the question of whether the continuous encoding model is unique to the heterogeneous, uncued actions of unrestrained mice. To address this potential confound, Fobbs et al. (2020) performed multiarray *in vivo* electrophysiology in head-fixed mice on a wheel, thus limiting the number of available movement patterns. In this setup, speed-tuning profiles were similar to those in freely moving animals, thus reinforcing the role of striatal activity in encoding velocity during unrestrained movements. In addition, overall striatal activity was lower in head-fixed trials than when the same mice were removed from the wheel and placed in an open arena where choice of potential movement patterns was far greater. The higher activity of striatal neurons during unrestrained movements likely reflects additional nonvelocity parameters, which could include decision-making toward choice of motor program or unmonitored actions, such as head turns. Thus, by limiting movement choice, the authors provide more evidence that the neurons are indeed representing velocity adjustments. While the authors compared striatal activity with general locomotor velocity, there are also reports of continuous striatal activity during other motor tasks, including head movement (Kim et al., 2014), body turn angle (Klaus et al., 2017), and forelimb reaching (Panigrahi et al., 2015). Therefore, continuous encoding may describe striatal activity controlling a broad array of movements.

Striatal medium spiny neurons (MSNs) participate in one of two pathways having opposite effects on downstream structures. Whereas MSNs in the direct, striatonigral pathway (dMSNs) facilitate movement, MSNs in the indirect, striatopallidal pathway (iMSNs) have been proposed to suppress movement (Kravitz et al., 2010). However, both MSN populations are activated during locomotion (Cui et al., 2013). Because MSN subtypes cannot be distinguished by their firing characteristics (Gertler et al., 2008), electrophysiological recordings did not allow the authors to distinguish dMSNs and iMSNs in the previous experiments. To study circuit-

specific striatal activity, Fobbs et al. (2020) therefore used Cre driver lines to express the GCaMP6s calcium indicator in either dMSNs or iMSNs and then recorded calcium fluctuations with fiber photometry during locomotion. The results confirmed that both MSN populations were active during locomotion, and further revealed that similar nonlinear speed-tuning profiles were observed in dMSNs and iMSNs. This shows that striatal speed-tuning population codes are not driven by differences between MSN subtypes. The need for synchronized activity between MSN subtypes may be because of their opponent influence on behavior. Performing correct action sequences may require facilitating desired movements (dMSNs) with simultaneous restriction of competing motor programs (iMSNs) (Tecuapetla et al., 2016).

The electrophysiological recordings by Fobbs et al. (2020) indicated that not all dorsal striatal neurons exhibit speed tuning. This should not be surprising given the library of complex movements mice can execute, as well as the regulation of motor performance through the interplay between two dorsal striatal regions: dorsolateral (DLS) and dorsomedial (DMS) (Yin et al., 2009; Kawai et al., 2015; Rueda-Orozco and Robbe, 2015). This raises a question about whether spatially clustered neuronal ensembles within the DMS, where Fobbs et al. (2020) recorded, are differentially tuned to locomotor velocity. Imaging-based experiments have shown neuronal clusters broadly distributed throughout the dorsal striatum whose activity correlates with immobility and lower-speed ambulation (2 cm/s) (Barbera et al., 2016). Similar organization of striatal ensembles has also been reported in the DLS (Klaus et al., 2017). However, ensemble analysis has not been performed in the DMS during high-speed run experiments. Future work in this area may explain the diversity of speed tuning curves identified by Fobbs et al. (2020) to help further define the role of DMS during locomotion.

From a broader perspective, the burst-firing and continuous-encoding models might work together to guide movement. The long-standing hypothesized role of the dorsal striatal in action selection/initiation may be explained by the burst-firing model (Jin et al., 2014). Explicit evidence for this comes from a demonstration of striatal firing that brackets locomotion during a lever press task (Martiros et al., 2018). On the other hand, activity of striatal neurons during ongoing movements may be represented by the continuous-

encoding model. This is supported by evidence of speed-tuning curves during locomotion (Sales-Carbonell et al., 2018; Fobbs et al., 2020). Moreover, the dorsal striatum receives inputs from cortical and thalamic regions associated with motor function that may provide feedback, enabling striatal neurons to continuously adapt motor programs (Hintiryan et al., 2016; Hunnicutt et al., 2016; Robbe, 2018). Thus, burst-firing activity may play a role in action selection and initiation, whereas continuous firing could be involved in the mechanics of monitoring and adjusting ongoing locomotion.

In conclusion, the study by Fobbs et al. (2020) highlights speed tuning of striatal neurons during naturalistic movements. The findings provide evidence that the burst-firing and the continuous-firing models work in tandem, suggesting that encoding locomotor programs is more nuanced than previously recognized. Future experiments will continue to provide a more refined understanding of locomotor mechanisms and thus provide insight into the development of motor pathologies.

References

- Alexander GE, Crutcher MD (1990) Functional architecture of basal ganglia circuits: neural substrates of parallel processing. *Trends Neurosci* 13:266–271.
- Barbera G, Liang B, Zhang L, Gerfen CR, Culurciello E, Chen R, Li Y, Lin DT (2016) Spatially compact neural clusters in the dorsal striatum encode locomotion relevant information. *Neuron* 92:202–213.
- Cui G, Jun SB, Jin X, Pham MD, Vogel SS, Lovinger DM, Costa RM (2013) Concurrent activation of striatal direct and indirect pathways during action initiation. *Nature* 494:238–242.
- Fobbs WC, Bariselli S, Licholai JA, Miyazaki NL, Matikainen-Ankney BA, Creed MC, Kravitz AV (2020) Continuous representations of speed by striatal medium spiny neurons. *J Neurosci* 40:1679–1688.
- Gertler TS, Chan CS, Surmeier DJ (2008) Dichotomous anatomical properties of adult striatal medium spiny neurons. *J Neurosci* 28:10814–10824.
- Graybiel AM (1998) The basal ganglia and chunking of action repertoires. *Neurobiol Learn Mem* 70:119–136.
- Hintiryan H, Foster NN, Bowman I, Bay M, Song MY, Gou L, Yamashita S, Bienkowski MS, Zingg B, Zhu M, Yang XW, Shih JC, Toga AW, Dong HW (2016) The mouse cortico-striatal projectome. *Nat Neurosci* 19:1100–1114.
- Hunnicutt BJ, Jongbloets BC, Birdsong WT, Gertz KJ, Zhong H, Mao T (2016) A comprehensive excitatory input map of the striatum reveals novel functional organization. *Elife* 5:e19103.
- Jin X, Costa RM (2010) Start/stop signals emerge in nigrostriatal circuits during sequence learning. *Nature* 466:457–462.

- Jin X, Tecuapetla F, Costa RM (2014) Basal ganglia subcircuits distinctively encode the parsing and concatenation of action sequences. *Nat Neurosci* 17:423–430.
- Kawai R, Markman T, Poddar R, Ko R, Fantana AL, Dhawale AK, Kampff AR, Olveczky BP (2015) Motor cortex is required for learning but not for executing a motor skill. *Neuron* 86:800–812.
- Kim N, Barter JW, Sukharnikova T, Yin HH (2014) Striatal firing rate reflects head movement velocity. *Eur J Neurosci* 40:3481–3490.
- Klaus A, Martins GJ, Paixao VB, Zhou P, Paninski L, Costa RM (2017) The spatiotemporal organization of the striatum encodes action space. *Neuron* 95:1171–1180.e1177.
- Kravitz AV, Freeze BS, Parker PR, Kay K, Thwin MT, Deisseroth K, Kreitzer AC (2010) Regulation of parkinsonian motor behaviours by optogenetic control of basal ganglia circuitry. *Nature* 466:622–626.
- Martiros N, Burgess AA, Graybiel AM (2018) Inversely active striatal projection neurons and interneurons selectively delimit useful behavioral sequences. *Curr Biol* 28:560–573.e565.
- Panigrahi B, Martin KA, Li Y, Graves AR, Vollmer A, Olson L, Mensh BD, Karpova AY, Dudman JT (2015) Dopamine is required for the neural representation and control of movement vigor. *Cell* 162:1418–1430.
- Penhune VB, Steele CJ (2012) Parallel contributions of cerebellar, striatal and M1 mechanisms to motor sequence learning. *Behav Brain Res* 226:579–591.
- Robbe D (2018) To move or to sense? Incorporating somatosensory representation into striatal functions. *Curr Opin Neurobiol* 52:123–130.
- Rueda-Orozco PE, Robbe D (2015) The striatum multiplexes contextual and kinematic information to constrain motor habits execution. *Nat Neurosci* 18:453–460.
- Sales-Carbonell C, Taouali W, Khalki L, Pasquet MO, Petit LF, Moreau T, Rueda-Orozco PE, Robbe D (2018) No discrete start/stop signals in the dorsal striatum of mice performing a learned action. *Curr Biol* 28:3044–3055.e3045.
- Tecuapetla F, Jin X, Lima SQ, Costa RM (2016) Complementary contributions of striatal projection pathways to action initiation and execution. *Cell* 166:703–715.
- Yin HH, Mulcare SP, Hilario MR, Clouse E, Holloway T, Davis MI, Hansson AC, Lovinger DM, Costa RM (2009) Dynamic reorganization of striatal circuits during the acquisition and consolidation of a skill. *Nat Neurosci* 12:333–341.