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SUPPLEMENTARY INFORMATION

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Diametric neural ensemble dynamics in parkinsonian and dyskinetic states

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Supplementary Note

§1. How do manipulations of dopaminergic signaling affect SPN activity in behaving mice?

Although *in vitro* studies have suggested that activation of D1 dopamine receptors (D1Rs) elevates dSPN excitability, and that activation of D2 dopamine receptors (D2Rs) reduces iSPN excitability[1], it has been unknown how systemic administration of dopamine receptor agonists and antagonists modulates dSPN and iSPN activity in live animals. One cannot simply extrapolate the *in vitro* results, because D1Rs and D2Rs are widely expressed throughout the brain, implying that systemic administration of dopamine receptor agonists and antagonists are likely to have more complex effects than those observed in brain slices.

In the striatum alone, cholinergic and GABAergic interneurons have dopamine receptors, as do the pre-synaptic terminals of nigrostriatal dopamine, corticostriatal glutamate and pallidostriatal GABA neurons[2-9]. Further, any manipulation of striatal excitability is likely to have complex effects on feedback loops involving the basal ganglia, thalamus and cortex, making it hard to predict the effects of dopamine receptor agonists or antagonists on SPN activity in behaving animals.

Highlighting this difficulty, predictions based on SPN-autonomous dopamine receptor signaling do not fully explain several of the pharmacological effects that we observed. For instance, before 6-OHDA lesion, D1R agonism, D2R agonism and D2R antagonism all suppressed dSPN activity (**Extended Data Fig. 7d–f**). However, the vast majority (>95%) of dSPNs do not express D2Rs[10,11], and D1R agonism enhances dSPN excitability *in vitro*[1], implying that for all three of these drugs the straightforward predictions fail. Thus, what might explain these observations?

In **§2–4** below, we consider how systemic, dopaminergic manipulations may exert their effects on SPN activity based on the striatum's microcircuitry and the more extended circuitry of the basal ganglia. The discussion has three parts: (**§2**) Pharmacological effects in healthy animals;

(**§3)** Effects of dopamine depletion; and (**§4**) Pharmacological effects in hemi-parkinsonian mice.

§2. Pharmacological effects in healthy animals.

Before dopamine depletion, we systemically administered D1R- and D2R-selective agonists and antagonists to a subset of our mice (**Fig. 1a, Extended Data Fig. 7**). Strikingly, though most dSPNs do not express D2Rs[10,11], D2R agonism and antagonism both suppressed dSPN activity (**Extended Data Fig. 7d, f**). Further, D1R agonism suppressed activity in both dSPNs and iSPNs (**Extended Data Fig. 7d–f**), which was surprising since D1R activation enhances dSPN excitability *in vitro*[1], and almost all iSPNs lack D1Rs[10,11].

A straightforward explanation for the suppression of dSPN activity by D2R agonism is that D2R agonists inhibit dopamine neurons[5], which could thereby reduce the level of D1R signaling through endogenous dopamine release. Consistent with this proposal, D2R agonism did not inhibit dSPNs after the lesion of dopamine neurons (**Fig. 4d–f**).

By comparison, a variety of mechanisms might account for the suppression of dSPN activity by D2R antagonism. One possibility is that D2R antagonism facilitates the collateral inhibition of dSPNs by iSPNs[12]. Another possibility is that the antagonism of D2Rs on cholinergic interneurons and GABAergic pallidostriatal terminals might also have contributed to the decline of dSPN activity[3,8,9,13,14].

The finding that systemic D1R agonism suppressed both dSPNs and iSPNs is more perplexing. Given that the agonist we used, SKF81297, also binds to D5-dopamine receptors, this finding could result from D5R agonism in fast-spiking interneurons[4]. Higher doses of a D1R agonist might overcome this type of inhibitory effect, although we did not test this idea in healthy, non-lesioned mice.

§3. Effects of dopamine depletion.

Dopamine depletion via 6-OHDA lesion suppressed dSPN activity (**Fig. 3d–f**), which is consistent with the *in vitro* finding that D1R signaling enhances the excitability of these cells[1]. Thus, the loss of D1R-mediated signaling after dopamine depletion provides a straightforward explanation for the resulting persistent decline in dSPN activity, but other adaptations could also play a role. For example, a reduction in dSPN dendritic arborization after 6-OHDA lesion could further diminish the excitatory drive to dSPNs[15] and is consistent with the decline in striatal neuropil fluorescence in D1-Cre mice after dopamine depletion (**Extended Data Fig. 5d**). The loss of dopamine could also suppress dSPNs by augmenting cholinergic interneuron activity[13,16], enhancing pallido-striatal GABA transmission[8,9,14], reducing thalamo-striatal or cortico-striatal input via circuit-mediated feedback, or through decreases in thalamo-striatal innervation[17].

iSPNs were initially hyperactive after 6-OHDA lesion, but this effect was reduced by two weeks after dopamine deletion, when iSPN activity was uncoupled from movement and decorrelated in space and time (**Fig. 3d–j**). The initial hyperactivity of iSPNs is consistent with a decline in D2R-mediated signaling, which *in vitro* normally reduces iSPN excitability[1]. However, reduced collateral SPN connectivity[12] or reduced pallido-striatal feedback inhibition[55,56,58] could also contribute to iSPN hyperactivity. As a caveat, although mice that received saline infusions did not exhibit the same locomotor deficits as mice that received 6-OHDA (**Extended Data Fig. 5c**), in principle there could be inflammatory or other post-operative responses specific to 6-OHDA infusion that somehow influenced striatal dynamics one day after the infusion.

Although iSPN activity rates remained persistently elevated in resting mice after dopamine depletion, there are several possible compelling explanations for why iSPN activity rates during movement re-normalized in the days after the 6-OHDA lesion. After dopamine depletion, iSPNs undergo many cellular-level changes not seen in dSPNs to the same extent. iSPNs lose dendritic

spines and cortico-striatal inputs[15,18,19], GABAergic connections onto iSPNs from fast-spiking interneurons are selectively increased after 6-OHDA lesions[20], and excitatory thalamo-cortical inputs are reduced[9,17]. Importantly, by diminishing cortico-striatal coupling these changes in connectivity and structural plasticity may also cause iSPN activity to become uncoupled from movement and to lose their spatiotemporal coordination (**Fig. 3g–j**).

§4. Pharmacological effects after unilateral lesion of SNc dopamine neurons.

After unilateral loss of dopamine neurons, both D1R and D2R agonists elevated dSPN activity (**Fig. 4**). Although this effect of D1R agonism is predicted by the rate-model, as discussed above (**§2**) this was not the case before dopamine depletion (**Extended Data Fig. 7d, f**). One possible explanation for this difference is increased D1R sensitivity in dSPNs after 6-OHDA lesion[10,21].

A likely explanation for the different effect of the D2R agonist on dSPN activity after dopamine depletion is the absence of dopamine neuron autoreceptor engagement[5], which in normal mice may have led to a drop in D1R signaling in dSPNs (**Extended Data Fig. 7d, f**). Without this autoreceptor engagement, multiple other D2R-dependent effects might emerge that further elevate dSPN activity. For example, D2R agonists might disinhibit dSPNs by suppressing cholinergic interneurons[13,16] or diminishing collateral inhibition from iSPNs, although this collateral inhibition generally declines after 6-OHDA lesion[12].

Another notable difference in the pharmacological results attained before versus after dopamine depletion was that after 6-OHDA lesion, D2R agonism substantially enhanced spatiotemporal coordination in both dSPNs and iSPNs (**Fig. 4h**). In iSPNs, this might have resulted from autonomous D2R activation, which would be similar to the presumed means by which the dopamine derived from L-DOPA activates D2Rs in iSPNs[22]. Notably, like D2R agonism, L-DOPA also increased the proximal co-activity of iSPNs in lesioned mice (**Fig. 4h**).

It is less clear why D2R agonism enhanced the spatiotemporal coordination of dSPN activity (**Fig. 4h**), but this could result from an attenuation of cholinergic input or of GABAergic pallido-striatal feedback transmission[8,9,13,14,16]. Notably, D2R agonism elevates dSPN activity without reducing the spatiotemporal coordination of these cells, which might partly explain why D2R agonists have a lower propensity than L-DOPA to cause dyskinesia in PD patients[23]. As a caveat to all of our studies in parkinsonian mice, given the system route of drug administration and the unilateral loss of dopamine neurons in our model, drug effects in the contralateral striatum or even outside of striatum cannot be ruled out as possible explanations for the phenomena we report. Nonetheless, the greatest density of dopamine receptors in the brain is in striatum[24], so it is safe to assume that effects on dopamine receptor signaling in striatum played a major role in the dynamics we observed.

The effects of a dyskinesiogenic dose of L-DOPA on dSPN and iSPN activity rates were consistent with the idea that dopamine respectively increases and decreases the excitability of these two cell types (**Fig. 5c–e**). However, such a high dose of L-DOPA also de-correlated dSPN activity and uncoupled it from movement (**Fig. 5f, g**). Strikingly, these changes paralleled those of iSPNs after dopamine depletion (**Figs. 4i, 5h**).

The parallel nature of these findings may reflect common mechanisms by which SPN activity can become spatiotemporally de-correlated. Specifically, 6-OHDA lesions induce a selective loss of dendritic spines in iSPNs; L-DOPA induced dyskinesia (LID) reverses this spine deficit, but also causes a selective loss of spines in dSPNs[15]. If these congruent structural changes contribute to the de-correlation of SPN activity, and if this de-correlation contributes to motor symptoms, then the molecular pathways controlling SPN structural plasticity may represent novel therapeutic targets for treating PD and LID.

Supplementary Methods

***In vitro* electrophysiological and Ca^{2+} imaging studies in striatal tissue slices.** Using standard techniques[25], we made oblique horizontal brain slices (300-μm thickness) containing the dorsal striatum from D1-Cre and A2A-Cre mice >3 weeks after viral injection. In brief, we anesthetized mice with isofluorane before decapitation. We then immersed the brain in chilled artificial cerebrospinal fluid (ACSF) containing 125 mM NaCl, 2.5 mM KCl, 2 mM $CaCl_2$, 1.25 mM NaH_2PO_4, 1 mM $MgCl_2$, 25 mM $NaHCO_3$ and 15 mM D-glucose (300–305 mOsm). We prepared brain slices with a vibrating microtome (Leica VT1200 S), allowed them to equilibrate in ACSF at 34 °C for 30 min and then at room temperature (20–22 °C) for at least another 30 min, and then transferred the slices to a recording chamber. We completed all slice experiments within 5 h of brain extraction. We saturated all solutions with 95% O_2 and 5% CO_2.

The recording chamber for holding an individual brain slice during the dual optical and electrophysiological studies was mounted on an upright microscope (Olympus BX-51). While continuously perfusing the slice with ACSF (2–4 mL/min; 30–31°C), we visually identified GCaMP6m-expressing striatal SPNs via infrared differential interference contrast (DIC) and epi-fluorescence imaging using a water-immersion objective lens (40× magnification; 0.8 numerical aperture; Olympus).

To attain the same numerical aperture (NA) as that of the miniature microscope used in freely behaving mice, we mounted an adjustable iris at the back aperture of the objective and reduced the effective NA to 0.5. We used a broad-spectrum light source (Lambda XL, Sutter), and filter sets with excitation (470–490 nm) and emission (515–550 nm) pass bands suitable for imaging GCaMP6m. We imaged striatal Ca^{2+} transients at a frame acquisition rate of 20 Hz, using a scientific-grade CMOS camera (ORCA-Flash 4.0 LT, Hamamatsu Photonics) and Micro-Manager software (NIH)[26].

We obtained whole-cell current-clamp recordings of GCaMP6m-expressing SPNs using a patch pipette (3–5 MΩ) filled with a solution containing 135 mM KCH_3SO_3, 5 mM KCl, 10 mM HEPES, 8 mM Na_2-Phosphocreatine, 0.3 mM Na_2GTP, and 4 mM MgATP (pH 7.2–7.3, 285–290 mOsm). We measured each cell's series resistance by injecting hyperpolarizing pulses (−5 mV, 100 ms). All series resistances were <20 MΩ. In current clamp recording mode, we applied bridge balance to compensate series resistance. We adjusted the resting membrane potential to between -65 and –60 mV to mimic the resting membrane potential of SPNs *in vivo*[25] and to facilitate action potential generation upon injection of current pulses (1 nA, 1 ms pulses; 1 to 10 pulses delivered at 5, 10, 20, 50 or 100 Hz). We obtained recordings using a Multiclamp 700B (Molecular Devices, USA) patch clamp amplifier. We filtered the signals at 2.2 kHz and digitized them at 10 kHz with a data acquisition card (NI PCI-6221, National Instruments). We recorded and monitored the data using WinWCP software (Strathclyde Electrophysiology Software), and then analyzed it offline using Clampfit 10.0 (Molecular Devices).

Two-photon Ca^{2+} imaging in behaving mice. We used mice expressing the red fluorophore tdTomato in dSPNs and GCaMP6m in both SPN types (see **Mice** in **Methods**) after implantation of an optical guide tube and GRIN microendoscope in the dorsomedial striatum (see **Surgeries** in **Methods**). We head-fixed the mice via their implanted head bar beneath the microscope objective lens carrier of a custom-built two-photon microscope[27]. While head-restrained, the mice were free to walk or run on a plastic running wheel (13.6 cm diameter; Innowheel, Innovive). A rotary encoder (HB5M-500-236-NE-S-D, US Digital) provided a readout of the wheel revolutions and hence of the mouse's running velocity. We recorded the encoder signals along with the timing pulses from the microscope's frame clock using a digital data acquisition system (Logic 8, Saleae).

The two-photon microscope was equipped with a resonant galvanometer laser-scanning mirror (CRS 8K, Cambridge Technologies), allowing a 30-Hz frame acquisition rate (512 × 512

pixels) under the control of ScanImage 5.2 software[28] (Vidrio Technologies). A wavelength-tunable Ti:sapphire laser (Mai Tai BB, Spectra Physics) provided ultrashort-pulsed illumination with a center wavelength of 920 nm. We adjusted the laser illumination power entering the microscope so that ~50 mW reached the specimen. We optically aligned a 1.0 NA, 20× water-immersion objective lens (XLUMPlanFL N, Olympus) to the GRIN microendoscope implanted within the mouse. We detected fluorescence signals using a GaAsP photomultiplier tube (H10770PA-40, Hamamatsu) and band-pass fluorescence emission filters (FF01-520/60 for GCaMP, FF01-590/36 for tdTomato; Semrock).

To acquire volumetric imaging data from four different axial planes in the brain with near simultaneity, we mounted the microscope objective lens on a piezo-electric objective scanner (P-725.4CD, Physik Instrumente). We used the ScanImage software to generate a 6-Hz sawtooth voltage wave for the axial movement of the objective lens, leading to a volume acquisition rate of 6 Hz. The four image planes in each volume were offset by 15 μm. Ca^{2+} imaging sessions lasted 18–25 min. To distinguish dSPNs from iSPNs in the analyses of Ca^{2+} activity, we acquired 100 volume scans of the red fluorescence from the tdTomato-expressing dSPNs, at the same four image planes and using the same scanning parameters as for Ca^{2+} imaging.

Similarities of the neural ensembles activated on movements of different types. To evaluate statistically the relative similarity in the neural ensembles activated on movement bouts of either the same or different types, or during baseline periods, we used the Jaccard similarity index (**Extended Data Figs. 3d, e, 8d–g**). This is the same statistical index used to characterize cells' pairwise co-activity levels (see **Determinations of cells' pairwise co-activity levels** in **Methods**), and as above we chose it for its insensitivity to cells' instances of inactivity.

We computed the mean value of the Jaccard index, averaged across all possible pairs of movement bouts drawn from the two different movement types, based on the identities of the

specific cells activated on each bout. Cells were defined as active if they had at least one Ca^{2+} event during the interval [–1 s, 2 s] relative to movement onset. For comparisons to baseline periods, cells were defined as active during baseline if they had at least one Ca^{2+} event during the interval [–4 s, –1 s] relative to movement onset.

Using these same time intervals to classify a cell as active or not, we determined the weighted average distance, D_{km}, between cells on different movement types k and m as:

$$\frac{\sum_{i=1}^{N}\sum_{j=1}^{N} f_i^k f_j^m d_{ij}}{\sum_{i=1}^{N}\sum_{j=1}^{N} f_i^k f_j^m}$$

where f_i^k is the mean activity rate for cell i in movement type k, N is the total number of cells, and d_{ij} is the distance between cells i and j. We then compared the mean weighted distance between the cells that were active during two different types of movement to the same quantity determined under the null hypothesis that the spatial separations of the active cells were independent of movement type. For the latter determination, we created shuffled datasets in which we randomly permuted each cell's firing rate between the two movement types, and we averaged the results over twenty-five different shuffled datasets. We normalized each distance value (**Extended Data Figs. 3f** and **8h–k**) by taking the actual mean value, subtracting the mean value determined under the null hypothesis, and then dividing this difference by the standard deviation of the distance across the twenty-five shuffled datasets.

Computational simulations of SPN activity traces. To examine the temporal accuracy with which we could use Ca^{2+} events in SPNs to determine the times of the accompanying action potentials, we created artificial datasets based on the fluorescence responses to action potentials observed in our dual electrical-optical recordings *in vitro* and on basic facets of the fluorescence recordings *in vivo*.

We computationally generated 100 artificial sets of dual electrical-optical recordings (30-

min duration; 1-kHz sampling rate) of SPN spiking and intracellular Ca^{2+} activity (as transduced by GCaMP6m). We set the mean spike rate in the simulations to that of the mean Ca^{2+} event rate observed *in vivo* (**Extended Data Fig. 1l**). The simulated Ca^{2+} transient waveforms had amplitudes (5% $\Delta F/F$) approximately equal to the mean amplitude observed *in vivo* (**Extended Data Fig. 1m**). The time-constants governing the rise and fall of the simulated Ca^{2+} transients were approximately those observed *in vitro* for single action potentials: τ_{on} = 80 ms and τ_{off} = 500 ms (**Extended Data Fig. 1g, h**).

To match the properties of the simulated Ca^{2+} traces to those acquired using the miniature microscope, we down-sampled the simulated traces to 5 Hz by linear interpolation. We then added Gaussian random noise (σ = 0.1% $\Delta F/F$) so that the Ca^{2+} transients had approximately the same event detection fidelity value (d' ~20) as those in the real data (**Extended Data Fig. 5f–h**). We applied the same procedures for detecting Ca^{2+} events and assigning their occurrence times as used for the real data (see **Detection of Ca^{2+} transients** in **Methods**). We found the time differences between the simulated spikes and those determined for the corresponding Ca^{2+} events using our event detection algorithm. This comparison revealed that the times assigned to Ca^{2+} events were 23 ± 4 ms (s.e.m.) after the real spike times, which was statistically indistinguishable from zero (P = 0.6 compared to zero offset; sign test; N = 5823 simulated spikes), indicating the absence of systematic bias. The spike timing error was ±305 ms (s.d.).

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Supplementary Table 1 | Summary of statistical results associated with the figures and extended data figures.

Figure	Comparison	Test	p-value	N-value	Num. cells	Num. Mice
2a	dSPN event rate (moving vs. resting)	Sign	1.52E-05	17 (mice)	5312	17
	iSPN event rate (moving vs. resting)	Sign	9.54E-07	21 (mice)	5509	21
2c	dSPN event rate change (moving vs. resting)	Wilcoxon sign-rank	1.50E-199	2899 (movement bouts)	5312	17
	iSPN event rate change (moving vs. resting)	Wilcoxon sign-rank	2.75E-217	3559 (movement bouts)	5509	21
	dSPN spatiotemporal coordination change (moving vs. resting)	Wilcoxon sign-rank	3.48E-13	2282 (movement bouts)	5312	17
	iSPN spatiotemporal coordination change (moving vs. resting)	Wilcoxon sign-rank	3.90E-14	2587 (movement bouts)	5509	21
2d	dSPN-dSPN Jaccard index, relative to temporally shuffled comparisons (as a function of pairwise cell distance)	n/a	n/a	n/a	1.02E+06 (cell pairs)	17
	iSPN-iSPN Jaccard index, relative to temporally shuffled comparisons (as a function of pairwise cell distance)	n/a	n/a	n/a	848025 (cell pairs)	21
2e	Resting proximal dSPN-dSPN Jaccard index (actual vs. temporally shuffled)	Wilcoxon signed-rank	2.93E-04	17 (mice)	4.50E+05 (proximal cell pairs)	17
	Resting proximal iSPN-iSPN Jaccard index (actual vs. temporally shuffled)	Wilcoxon signed-rank	5.96E-05	21 (mice)	3.62E+05 (proximal cell pairs)	21
	Moving proximal dSPN-dSPN Jaccard index (actual vs. temporally shuffled)	Wilcoxon signed-rank	2.93E-04	17 (mice)	4.50E+05 (proximal cell pairs)	17
	Moving proximal iSPN-iSPN Jaccard index (actual vs. temporally shuffled)	Wilcoxon signed-rank	5.96E-05	21 (mice)	3.62E+05 (proximal cell pairs)	21

Figure	Comparison	Test	p-value	N-value	Num. Mice
3c	Distance traveled (Post 1-d vs. Pre-lesion)	Wilcoxon signed-rank	1.00E-04	25 (mice)	25
	Distance traveled (Post 14-d vs. Pre-lesion)	Wilcoxon signed-rank	2.10E-03	25 (mice)	25
	Distance traveled (Post 14-d vs. Post 1-d)	Wilcoxon signed-rank	1.28E-02	25 (mice)	25
3f	Resting dSPN event rate (Post 1d vs. Pre-lesion)	Wilcoxon signed-rank	3.39E-29	14 speed bins per mouse	12
	Resting dSPN event rate (Post 14-d vs. Pre-lesion)	Wilcoxon signed-rank	5.12E-29	14 speed bins per mouse	12
	Resting iSPN event rate (Post 1d vs. Pre-lesion)	Wilcoxon signed-rank	4.98E-29	14 speed bins per mouse	13
	Resting iSPN event rate (Post 14-d vs. Pre-lesion)	Wilcoxon signed-rank	3.22E-17	14 speed bins per mouse	13
	Moving dSPN event rate (Post 1d vs. Pre-lesion)	Wilcoxon signed-rank	1.04E-43	24 speed bins per mouse	12
	Moving dSPN event rate (Post 14-d vs. Pre-lesion)	Wilcoxon signed-rank	1.03E-44	24 speed bins per mouse	12
	Moving iSPN event rate (Post 1d vs. Pre-lesion)	Wilcoxon signed-rank	3.39E-36	24 speed bins per mouse	13
	Moving iSPN event rate (Post 14-d vs. Pre-lesion)	Wilcoxon signed-rank	1.40E-01	24 speed bins per mouse	13
3g	dSPN event rate change (moving vs. resting; Post 14-d)	Wilcoxon signed-rank	5.02E-56	2848 (movement bouts)	12
	dSPN event rate change at movement (Post 14-d vs Pre-lesion)	Wilcoxon rank-sum	9.78E-62	1905 Pre-lesion and 2848 Post 14-d (movement bouts)	12
	iSPN event rate change (moving vs. resting; Post 14-d)	Wilcoxon signed-rank	4.29E-22	3110 (movement bouts)	13
	iSPN event rate change at movement (Post 14-d vs Pre-lesion)	Wilcoxon rank-sum	1.08E-111	2331 Pre-lesion and 3110 Post 14-d (movement bouts	13
	dSPN spatiotemporal coordination change (moving vs. resting; Post 14-d)	Wilcoxon signed-rank	5.81E-09	1326 (movement bouts)	12
	dSPN spatiotemporal coordination change at movement (Post 14-d vs Pre-lesion)	Wilcoxon rank-sum	3.91E-01	1494 Pre-lesion and 1326 Post 14-d (movement bouts)	12
	iSPN spatiotemporal coordination change (moving vs. resting; Post 14-d)	Wilcoxon signed-rank	2.98E-01	2957 (movement bouts)	13
	iSPN spatiotemporal coordination change at movement (Post 14-d vs. Pre-lesion)	Wilcoxon rank-sum	1.29E-09	1778 Pre-lesion and 2957 Post 14-d (movement bouts	13

Figure	Comparison	Test	p-value	N-value	Num. Mice
3h	D1-Cre event-triggered average speed (event vs. baseline; Post 14-d)	Wilcoxon signed-rank	3.16E-303 11 ± 1% (effect size; mean ± s.e.m)	5323 (cells)	12
	A2A-Cre event-triggered average speed (event vs. baseline; Post 14-d)	Wilcoxon signed-rank	2.00E-03 0.8 ± 0.3% (effect size; mean ± s.e.m)	5529 (cells)	13
3i	dSPN event rate change at movement (Post 1-d vs. Pre-lesion)	Wilcoxon rank-sum	2.85E-02	12 (mice)	12
	dSPN event rate change at movement (Post 14-d vs Pre-lesion)	Wilcoxon rank-sum	7.65E-02	12 (mice)	12
	iSPN event rate change at movement (Post 1-d vs. Pre-lesion)	Wilcoxon rank-sum	7.95E-02	13 (mice)	13
	iSPN event rate change at movement (Post 14-d vs. Pre-lesion)	Wilcoxon rank-sum	8.90E-07	13 (mice)	13
3j	Moving proximal dSPN-dSPN Jaccard index relative to temporally shuffled (Post 1-d vs. Pre-lesion)	Wilcoxon rank-sum	1.04E-04	96 Pre-lesion and 96 Post 1-d (co-activity values)	12
	Moving proximal dSPN-dSPN Jaccard index relative to temporally shuffled (Post 14-d vs. Pre-lesion)	Wilcoxon rank-sum	1.76E-04	96 Pre-lesion and 384 Post 14-d (co-activity values)	12
	Moving proximal iSPN-iSPN Jaccard index relative to temporally shuffled (Post 1-d vs. Pre-lesion)	Wilcoxon rank-sum	3.42E-12	104 Pre-lesion and 104 Post 1-d (co-activity values)	13
	Moving proximal iSPN-iSPN Jaccard index relative to temporally shuffled (Post 14-d vs. Pre-lesion)	Wilcoxon rank-sum	5.16E-38	104 Pre-lesion and 416 Post 14-d (co-activity values)	13

Figure	Comparison		Test		p-value	N compared	Num. Mice
4a	Contralateral Bias during 40 min locomotion after drug or vehicle injection		Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons		see values below for pairwise comparisons	7 D1-Cre and 6 A2A-Cre (mice)	13
		Saline	Quinpirole 1 mg/kg	Quinpirole 6 mg/kg	SKF 1 mg/kg	SKF 6 mg/kg	L-DOPA 1 mg/kg
	Pre-lesion	2.40E-03					
	Quinpirole 1 mg/kg	1.70E-03					
	Quinpirole 6 mg/kg	2.40E-03	2.10E-02				
	SKF 1 mg/kg	2.00E-04	8.10E-03	2.73E-01			
	SKF 6 mg/kg	2.00E-04	2.00E-04	2.00E-04	1.20E-03		
	L-DOPA 1 mg/kg	5.00E-04	3.27E-02	4.70E-01	6.85E-01	1.70E-03	
	L-DOPA 6 mg/kg	7.00E-04	2.40E-03	1.20E-03	1.10E-01	1.50E-03	1.05E-02

Figure	Comparison		Test			p-value		N-value			Num. Mice	
4e	Calcium event rates during periods of rest Pre-lesion, or after drug injection Post-lesion (vs. saline)		Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons			see values below for pairwise comparisons		7 D1-Cre and 6 A2A-Cre mice (14 speed bins per mouse)			7 D1-Cre and 6 A2A-Cre	
			dSPNs					iSPNs				
		Saline	Quinpirole 1 mg/kg	SKF 1 mg/kg	L-DOPA 1 mg/kg		Saline	Quinpirole 1 mg/kg	SKF 1 mg/kg	L-DOPA 1 mg/kg		
	Pre-lesion	8.33E-18				Pre-lesion	5.36E-07					
	Quinpirole 1 mg/kg	1.77E-16				Quinpirole 1 mg/kg	9.36E-04					
	Quinpirole 6 mg/kg	1.17E-17	6.81E-01			Quinpirole 6 mg/kg	5.18E-13	4.97E-14				
	SKF 1 mg/kg	8.86E-18				SKF 1 mg/kg	2.30E-01					
	SKF 6 mg/kg	1.39E-16		2.27E-01		SKF 6 mg/kg	1.20E-02		3.70E-04			
	L-DOPA 1 mg/kg	3.73E-12				L-DOPA 1 mg/kg	2.78E-12					
	L-DOPA 6 mg/kg	8.33E-18			4.83E-07	L-DOPA 6 mg/kg	1.28E-09			8.17E-17		

Figure	Comparison		Test			p-value		N-value			Num. Mice	
4f	Calcium event rates during periods of movement Pre-lesion, or after drug injection Post-lesion (vs. saline)		Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons			see values below for pairwise comparisons		7 D1-Cre and 6 A2A-Cre mice (24 speed bins per mouse)			7 D1-Cre and 6 A2A-Cre	
			dSPNs					iSPNs				
		Saline	Quinpirole 1 mg/kg	SKF 1 mg/kg	L-DOPA 1 mg/kg		Saline	Quinpirole 1 mg/kg	SKF 1 mg/kg	L-DOPA 1 mg/kg		
	Pre-lesion	2.55E-29				Pre-lesion	4.14E-01					
	Quinpirole 1 mg/kg	7.47E-12				Quinpirole 1 mg/kg	5.43E-03					
	Quinpirole 6 mg/kg	7.44E-21	2.42E-02			Quinpirole 6 mg/kg	9.42E-13	1.61E-16				
	SKF 1 mg/kg	2.01E-28				SKF 1 mg/kg	5.36E-04					
	SKF 6 mg/kg	5.16E-19		8.29E-01		SKF 6 mg/kg	1.23E-01		4.10E-03			
	L-DOPA 1 mg/kg	7.90E-24				L-DOPA 1 mg/kg	5.52E-23					
	L-DOPA 6 mg/kg	1.81E-28			4.79E-02	L-DOPA 6 mg/kg	1.70E-06			4.47E-21		

Figure	Comparison		Test			p-value		N-value			Num. Mice	
4g	Calcium event rate change at motion onset Pre-lesion, or after drug injection Post-lesion (vs. saline)		Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons			see values below for pairwise comparisons		11 time bins per mouse per treatment			7 D1-Cre and 6 A2A-Cre mice	
			dSPNs					iSPNs				
		Saline	Quinpirole 1 mg/kg	SKF 1 mg/kg	L-DOPA 1 mg/kg		Saline	Quinpirole 1 mg/kg	SKF 1 mg/kg	L-DOPA 1 mg/kg		
	Pre-lesion	8.77E-05				Pre-lesion	1.72E-12					
	Quinpirole 1 mg/kg	1.06E-03				Quinpirole 1 mg/kg	5.17E-01					
	Quinpirole 6 mg/kg	3.05E-02	9.06E-01			Quinpirole 6 mg/kg	5.17E-01	2.44E-01				
	SKF 1 mg/kg	7.61E-01				SKF 1 mg/kg	7.84E-02					
	SKF 6 mg/kg	4.89E-03		8.86E-03		SKF 6 mg/kg	7.27E-07		8.84E-04			
	L-DOPA 1 mg/kg	2.05E-02				L-DOPA 1 mg/kg	6.81E-07					
	L-DOPA 6 mg/kg	6.17E-05			7.69E-04	L-DOPA 6 mg/kg	5.43E-10			9.85E-09		

Figure	Comparison		Test			p-value		N-value			Num. Mice	
4h	Proximal pairwise Jaccard index during movement relative to temporally shuffled Pre-lesion, or after drug injection Post-lesion (vs. saline)		Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons			see values below for pairwise comparisons		8 bins of cell-cell separation per mouse			7 D1-Cre and 6 A2A-Cre mice	
			dSPNs					iSPNs				
		Saline	Quinpirole 1 mg/kg	SKF 1 mg/kg	L-DOPA 1 mg/kg		Saline	Quinpirole 1 mg/kg	SKF 1 mg/kg	L-DOPA 1 mg/kg		
	Pre-lesion	7.69E-07				Pre-lesion	1.63E-09					
	Quinpirole 1 mg/kg	1.38E-02				Quinpirole 1 mg/kg	4.51E-07					
	Quinpirole 6 mg/kg	5.03E-05	5.68E-01			Quinpirole 6 mg/kg	6.43E-09	8.49E-02				
	SKF 1 mg/kg	1.31E-03				SKF 1 mg/kg	1.95E-03					
	SKF 6 mg/kg	1.47E-03		7.27E-02		SKF 6 mg/kg	8.30E-02		5.80E-01			
	L-DOPA 1 mg/kg	1.61E-02				L-DOPA 1 mg/kg	4.73E-01					
	L-DOPA 6 mg/kg	6.64E-09			2.95E-06	L-DOPA 6 mg/kg	8.56E-05			3.31E-04		

Figure	Comparison	Test	p-value	N-value
5a	Contralateral Bias during first 40 min after drug or vehicle injection	Wilcoxon signed-rank	see values below for pairwise comparison	13 mice
		Saline	L-DOPA 1 mg/kg	L-DOPA 6 mg/kg
	L-DOPA 1 mg/kg	5.00E-04		
	L-DOPA 6 mg/kg	7.00E-04	1.05E-02	
	L-DOPA 10 mg/kg	2.00E-04	5.00E-04	3.27E-02
	Comparison	**Test**	**p-value**	**N-value**
	AIMS total during first 40 min after drug or vehicle injection	see below	see values below for pairwise comparison	13 (L-DOPA) and 5 (saline) mice
		Wilcoxon rank-sum	Wilcoxon signed-rank	
		Saline	L-DOPA 1 mg/kg	L-DOPA 6 mg/kg
	L-DOPA 1 mg/kg	0.1218		
	L-DOPA 6 mg/kg	0.0107	0.002	
	L-DOPA 10 mg/kg	0.0001	0.0002	0.0132

Figure	Comparison		Test	p-value	N-value
5b	AIMS during first 40 min after drug or vehicle injection (L-DOPA vs. saline)		Wilcoxon rank-sum	see values below for pairwise comparison	13 (L-DOPA) and 5 (saline) mice
		Saline			
		Limb	Axial	Orofacial	Total
	L-DOPA 1 mg/kg	0.5752	0.2778	0.3203	0.1218
	L-DOPA 6 mg/kg	0.2778	0.0121	0.0449	0.0107
	L-DOPA 10 mg/kg	0.0359	0.0007	0.0001	0.0001

Figure	Comparison	Test	p-value	N-value
5d	dSPN event rates during periods of rest. Pre-lesion or after drug injection Post-lesion (vs. saline)	Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons	8.33E-18 (Pre-lesion) 8.33E-18 (L-DOPA)	14 speed bins <0.5 cm/sec for 7 D1-Cre mice
5d	iSPN event rates during periods of rest, Pre-lesion or after drug injection Post-lesion (vs. saline)	Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons	5.35E-07 (Pre-lesion) 1.71E-15 (L-DOPA)	14 speed bins <0.5 cm/sec for 6 A2A-Cre mice
5e	dSPN event rates during periods of movement, Pre-lesion or after drug injection Post-lesion (vs. saline)	Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons	2.55E-29 (Pre-lesion) 2.55E-29 (L-DOPA)	24 speed bins >0.5 cm/sec for 7 D1-Cre mice
5e	iSPN event rates during periods of movement, Pre-lesion or after drug injection Post-lesion (vs. saline)	Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons	4.14E-01 (Pre-lesion) 2.39E-18 (L-DOPA)	24 speed bins >0.5 cm/sec for 6 A2A-Cre mice
5f	dSPN event rate change at motion onset, Pre-lesion or after drug injection Post-lesion (vs. saline)	Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons	8.77E-05 (Pre-lesion) 1.69E-11 (L-DOPA)	11 time bins per mouse per treatment for 7 D1-Cre mice
5f	iSPN event rate change at motion onset, Pre-lesion or after drug injection Post-lesion (vs. saline)	Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons	1.72E-12 (Pre-lesion) 1.19E-11 (L-DOPA)	11 time bins per mouse per treatment for 6 A2A-Cre mice
5g	Proximal Jaccard index during movement in dSPN pairs, relative to temporally shuffled Pre-lesion or after drug injection Post-lesion (vs. saline)	Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons	7.69E-07 (Pre-lesion) 7.55E-11 (L-DOPA)	8 bins of cell-cell separation per mouse for 7 D1-Cre mice
5g	Proximal Jaccard index during movement in iSPN pairs, relative to temporally shuffled Pre-lesion or after drug injection Post-lesion (vs. saline)	Wilcoxon signed-rank, Dunn-Sidak correction for multiple comparisons	1.63E-09 (Pre-lesion) 4.78E-02 (L-DOPA)	8 bins of cell-cell separation per mouse for 6 A2A-Cre mice

Figure	Comparison	Test	Number of APs	p-value	N-value
Extended Data 1e	Ca^{2+} transient waveform amplitudes evoked by different stimulus intensities	Two-way repeated measures ANOVA (mixed-design)	1	4.92E-01	9 dSPNs and 8 iSPNs
			2	5.02E-01	
			3	4.85E-01	
			4	4.57E-01	
			5	7.39E-01	
			6	5.05E-01	
			7	5.41E-01	
			8	3.78E-01	
			9	5.13E-01	
			10	4.62E-01	
Extended Data 1f	Area under the Ca^{2+} transient waveform (AUC) evoked by different stimulus intensities	Two-way repeated measures ANOVA (mixed-design)	1	2.24E-01	9 dSPNs and 8 iSPNs
			2	3.73E-01	
			3	8.05E-01	
			4	1.84E-01	
			5	3.59E-01	
			6	5.51E-02	
			7	4.75E-01	
			8	5.22E-01	
			9	4.15E-01	
			10	2.49E-01	
Extended Data 1i	Ca^{2+} transient waveform AUC evoked by different stimulus intensities (SKF vs. vehicle)	Two-way repeated measures ANOVA	2	5.89E-01	6 dSPNs
			6	7.68E-01	
			10	7.90E-01	
	Ca^{2+} transient waveform AUC evoked by different stimulus intensities (quinpirole vs. vehicle)	Two-way repeated measures ANOVA	2	9.39E-01	6 iSPNs
			6	8.85E-01	
			10	9.73E-01	

Figure	Comparison	Test	Integration time (s)	p-value	N-value	Num. Mice
Extended Data 2e	dSPN event-triggered average maximum speed offset (vs. zero offset)	Wilcoxon signed-rank	0.2	2.61E-02	37 cross-correlations	16
			0.6	1.68E-02		
			1	4.09E-02		
			1.4	4.24E-02		
			1.8	6.24E-02		
	iSPN event-triggered average maximum speed offset (vs. zero offset)	Wilcoxon signed-rank	0.2	1.10E-04	52 cross-correlations	21
			0.6	1.02E-04		
			1	6.45E-04		
			1.4	2.76E-04		
			1.8	2.73E-03		
Extended Data 2e	Event-triggered average speed (D1-Cre vs. A2A-Cre)	Wilcoxon rank-sum	0.2	1.20E-01	37 (D1-Cre) and 52 (A2A-Cre) cross-correlations	16 (D1-Cre) and 21(A2A-Cre)
			0.6	3.60E-01		
			1	4.40E-01		
			1.4	2.70E-01		
			1.8	3.70E-01		

Figure	Comparison	Test	p-value		N-value (bouts)		Num. Mice
Extended Data 3b	Fraction of dSPN population activated (movement type vs. baseline)	Wilcoxon signed-rank	Forward	1.63E-09	Forward	492	17
			Right	2.24E-09	Right	657	
			Left	1.63E-09	Left	810	
			Groom	4.64E-03	Groom	732	
			Rear	4.70E-04	Rear	204	
	Fraction of iSPN population activated (movement type vs. baseline)	Wilcoxon signed-rank	Forward	1.89E-11	Forward	790	21
			Right	6.65E-12	Right	785	
			Left	2.90E-12	Left	1015	
			Groom	2.94E-01	Groom	792	
			Rear	6.62E-05	Rear	164	
Extended Data 3c	dSPN event rate change at movement (moving vs. resting)	Wilcoxon signed-rank	Forward	1.74E-40	Forward	492	17
			Right	1.50E-42	Right	657	
			Left	3.29E-67	Left	810	
			Groom	4.32E-11	Groom	732	
			Rear	8.78E-07	Rear	204	
	iSPN event rate change at movement (moving vs. resting)	Wilcoxon signed-rank	Forward	3.50E-65	Forward	790	21
			Right	3.23E-45	Right	785	
			Left	3.14E-87	Left	1015	
			Groom	6.22E-16	Groom	792	
			Rear	2.15E-09	Rear	164	
Extended Data 3e	dSPN ensemble similarity distribution for movement types (same vs. different)	Kolmogorov-Smirnov	1.37E-03		102 (same) and 255 (different) movement type bouts		17
	iSPN ensemble similarity distribution for movement types (same vs. different)	Kolmogorov-Smirnov	6.75E-03		126 (same) and 315 (different) movement type bouts		21

Figure	Comparison	Test	p-value		N-value	Num. Mice
Extended Data 4h	Mean time at which movement-evoked dSPN vs iSPN population activity exceeded their respective baseline values by ≥ 3 s.d.	Wilcoxon rank-sum	9.15E-01		5 (mice)	5
Extended Data 4k	Proximal SPN Jaccard index during running (actual vs. temporally shuffled)	Wilcoxon rank-sum	dSPN-dSPN	1.59E-02	5 (mice)	5
			iSPN-iSPN	3.17E-02		
			dSPN-iSPN	1.59E-02		
	Mean ratio of actual and temporally shuffled proximal SPN Jaccard indices during running (compared between different cell-type pairs)	Wilcoxon rank-sum	dSPN-dSPN vs. iSPN-iSPN	0.22	5 (mice)	5
			dSPN-dSPN vs. dSPN-iSPN	0.15		
			iSPN-iSPN vs. dSPN-iSPN	0.69		

Figure	Comparison	Test	p-value		N-value		Num. Mice
Extended Data 5d	Mean fluorescence in D1-Cre mice (before vs. after lesion)	Wilcoxon rank-sum	1.80E-09		5 (mice)		5
	Mean fluorescence in A2A-Cre mice (before vs. after lesion)	Wilcoxon rank-sum	5.03E-08		7 (mice)		7
	Mean fluorescence in D1-Cre mice (after lesion)	Spearman's correlation	3.50E-01		5 (mice)		5
	Mean fluorescence in A2A-Cre mice (after lesion)	Spearman's correlation	8.33E-02		7 (mice)		7
Extended Data 5e	Number of active dSPNs over time	Friedman ANOVA	5.06E-02		5 (mice)		5
	Number of active iSPNs over time	Friedman ANOVA	2.16E-02		7 (mice)		7
Extended Data 5f	dSPN Δ*F/F* (Pre-lesion vs. Post 14-d)	Wilcoxon rank-sum	<2.22E-308		3492 cells (Pre-lesion) 3734 cells (Post 14-d)		12
	iSPN Δ*F/F* (Pre-lesion vs. Post 14-d)	Wilcoxon rank-sum	2.27E-47		3711 cells (Pre-lesion) 3332 cells (Post 14-d)		13
Extended Data 5g	dSPN event *d'* (Pre-lesion vs. Post 14-d)	Wilcoxon rank-sum	<2.22E-308		3492 cells (Pre-lesion) 3734 cells (Post 14-d)		12
	dSPN event *d'* (Pre-lesion vs. Post 14-d)	Wilcoxon rank-sum	3.10E-107		3711 cells (Pre-lesion) 3332 cells (Post 14-d)		13
Extended Data 5h	Mean dSPN event d' (vs. Post 14-d)	Wilcoxon rank-sum	Pre-lesion	1.33E-314	Pre-lesion	2027 (dSPNs)	5
			Post 14-d	n/a	Post 14-d	1968 (dSPNs)	
			L-DOPA	3.22E-155	L-DOPA	2010 (dSPNs)	
			Quinpirole	1.44E-91	Quinpirole	1875 (dSPNs)	
			SKF	1.42E-94	SKF	1770 (dSPNs)	
	Mean iSPN event d' (vs. Post 14-d)	Wilcoxon rank-sum	Pre-lesion	2.47E-75	Pre-lesion	1943 (iSPNs)	7
			Post 14-d	n/a	Post 14-d	2334 (iSPNs)	
			L-DOPA	6.49E-74	L-DOPA	2393 (iSPNs)	
			Quinpirole	8.50E-182	Quinpirole	2074 (iSPNs)	
			SKF	9.25E-85	SKF	1719 (iSPNs)	

Figure	Comparison	Test	p-value		N-value	Num. Mice
Extended Data 6a	dSPN event rates during periods of rest Post 1-d or Post 14-d compared to Pre-lesion	Wilcoxon rank-sum	Post 1-d	6.44E-310	3732 (Pre-lesion) 2554 (Post 1-d) 3472(Post 14-d) cells	12
			Post 14-d	1.00E-314		
	iSPN event rates during periods of rest Post 1-d or Post 14-d compared to Pre-lesion	Wilcoxon rank-sum	Post 1-d	2.09E-165	3325 (Pre-lesion) 3818 (Post 1-d) 3702 (Post 14-d) cells	13
			Post 14-d	1.07E-109		
Extended Data 6b	dSPN event rates during periods of movement Post 1-d or Post 14-d compared to Pre-lesion	Wilcoxon rank-sum	Post 1-d	1.37E-158	3718 (Pre-lesion) 2554 (Post 1-d) 3351(Post 14-d) cells	12
			Post 14-d	5.99E-246		
	iSPN event rates during periods of movement Post 1-d or Post 14-d compared to Pre-lesion	Wilcoxon rank-sum	Post 1-d	1.03E-52	3209 (Pre-lesion) 3533 (Post 1-d) 3523 (Post 14-d) cells	13
			Post 14-d	2.40E-10		
Extended Data 6c,d	dSPN event rates during rotarod performance Post 1-d or Post 14-d compared to Pre-lesion	Wilcoxon rank-sum	Post 1-d	9.41E-54	1930 (Pre-lesion) 712 (Post 1-d) 1672(Post 14-d) cells	5 (Pre-lesion) 2 (Post 1-d) 5 (Post 14-d)
			Post 14-d	6.33E-73		
	iSPN event rates during rotarod performance Post 1-d or Post 14-d compared to Pre-lesion	Wilcoxon rank-sum	Post 1-d	1.50E-15	1731(Pre-lesion) 853 (Post 1-d) 1607 (Post 14-d) cells	7 (Pre-lesion) 3 (Post 1-d) 7 (Post 14-d)
			Post 14-d	4.99E-03		
Extended Data 6e	Mean proximal dSPN-dSPN Jaccard index, normalized to temporally shuffled comparisons during rotarod perfomance (Post 1-d vs. Pre-lesion)	Wilcoxon rank-sum	8.66E-02		16 bins (8 per mouse)	2 (Pre-lesion) 2 (Post 1-d)
	Mean proximal dSPN-dSPN Jaccard index, normalized to temporally shuffled comparisons during rotarod perfomance (Post 14-d vs. Pre-lesion)	Wilcoxon rank-sum	6.10E-01		40 bins (8 per mouse)	5 (Pre-lesion) 5 (Post 14-d)
	Mean proximal iSPN-iSPN Jaccard index, normalized to temporally shuffled comparisons during rotarod perfomance (Post 1-d vs. Pre-lesion)	Wilcoxon rank-sum	4.40E-01		24 bins (8 per mouse)	2 (Pre-lesion) 2 (Post 1-d)
	Mean proximal iSPN-iSPN Jaccard index, normalized to temporally shuffled comparisons during rotarod perfomance (Post 14-d vs. Pre-lesion)	Wilcoxon rank-sum	1.73E-17		56 bins (8 per mouse)	7 (Pre-lesion) 7 (Post 14-d)

Figure	Comparison	Test	p-value		N-value	Num. Mice
Extended Data 7f	dSPN event rate at rest (drug vs. saline)	Wilcoxon signed-rank	SCH	2.69E-17	14 speed bins per mouse	7 D1-Cre
			Raclopride	3.42E-06		
	dSPN event rate during movement (drug vs. saline)	Wilcoxon signed-rank	SCH	5.62E-18	24 speed bins per mouse	7 D1-Cre
			Raclopride	1.10E-01		
	iSPN event rate at rest (drug vs. saline)	Wilcoxon signed-rank	SCH	4.48E-02	14 speed bins per mouse	11 A2A-Cre
			Raclopride	1.80E-03		
	iSPN event rate during movement (drug vs. saline)	Wilcoxon signed-rank	SCH	1.77E-01	24 speed bins per mouse	11 A2A-Cre
			Raclopride	1.56E-05		
	dSPN event rate at rest (drug vs. saline)	Wilcoxon signed-rank	SKF	8.86E-18	14 speed bins per mouse	7 D1-Cre
			Quinpirole	2.18E-10		
	dSPN event rate during movement (drug vs. saline)	Wilcoxon signed-rank	SKF	1.65E-25	24 speed bins per mouse	7 D1-Cre
			Quinpirole	1.08E-08		
	iSPN event rate at rest (drug vs. saline)	Wilcoxon signed-rank	SKF	7.50E-24	14 speed bins per mouse	11 A2A-Cre
			Quinpirole	2.14E-12		
	iSPN event rate during movement (drug vs. saline)	Wilcoxon signed-rank	SKF	4.27E-37	24 speed bins per mouse	11 A2A-Cre
			Quinpirole	5.31E-10		
Extended Data 7i, j	Shuffle-subtracted dSPN proximal co-activtiy (drug vs. saline)	Wilcoxon signed-rank	SCH	1.66E-09	8 spatial bins per mouse	7 D1-Cre
			Raclopride	1.42E-03		
	Shuffle-subtracted iSPN proximal co-activtiy (drug vs. saline)	Wilcoxon signed-rank	SCH	1.69E-02	8 spatial bins per mouse	11 A2A-Cre
			Raclopride	1.59E-03		
	Shuffle-subtracted dSPN proximal co-activtiy (drug vs. saline)	Wilcoxon signed-rank	SKF	1.94E-03	8 spatial bins per mouse	7 D1-Cre
			Quinpirole	5.59E-05		
	Shuffle-subtracted iSPN proximal co-activtiy (drug vs. saline)	Wilcoxon signed-rank	SKF	6.12E-02	8 spatial bins per mouse	11 A2A-Cre
			Quinpirole	7.21E-07		

Figure	Comparison	Test	p-value		N-value (bouts)		Num. Mice
Extended Data 8b	Fraction of dSPN population activated (movement type vs. baseline)	Wilcoxon signed-rank	Forward	7.48E-03	Forward	206	12
			Right	1.40E-03	Right	200	
			Left	3.52E-04	Left	290	
			Groom	7.59E-02	Groom	314	
	Fraction of iSPN population activated (movement type vs. baseline)	Wilcoxon signed-rank	Forward	2.20E-03	Forward	331	13
			Right	1.32E-03	Right	295	
			Left	2.54E-04	Left	194	
			Groom	7.65E-01	Groom	339	
Extended Data 8c	dSPN event rate change at movement (moving vs. resting)	Wilcoxon signed-rank	Forward	1.88E-11	Forward	206	12
			Right	4.83E-08	Right	200	
			Left	8.03E-17	Left	290	
			Groom	1.00E-03	Groom	314	
	iSPN event rate change at movement (moving vs. resting)	Wilcoxon signed-rank	Forward	1.21E-07	Forward	331	13
			Right	2.41E-04	Right	295	
			Left	1.08E-10	Left	194	
			Groom	3.94E-03	Groom	339	
Extended Data 8f	dSPN ensemble similarity distribution for different movement type comparisons (Post 14-d vs. Pre-lesion)	Kolmogorov-Smirnov, Benjamini-Hochberg correction for multiple comparisons	1.72E-08		255 (Pre-lesion) and 180 (Post 14-d) comparisons of different movement bout types		17 (Pre-lesion) 12 (Post 14-d)
	iSPN ensemble similarity distribution for different movement type comparisons (Post 14-d vs. Pre-lesion)	Kolmogorov-Smirnov, Benjamini-Hochberg correction for multiple comparisons	1.16E-10		315 (Pre-lesion) and 195 (Post 14-d) comparisons of different movement bout types		21 (Pre-lesion) 13 (Post 14-d)
Extended Data 8h	Distance between dSPNs activated on bouts of different movement types (Post 14-d vs. Pre-lesion)	Kolmogorov-Smirnov, Benjamini-Hochberg correction for multiple comparisons	2.38E-01		255 (Pre-lesion) and 156 (Post 14-d) comparisons of different movement bout types		17 (Pre-lesion) 12 (Post 14-d)
	Distance between dSPNs activated on bouts of different movement types (Post 14-d vs. Pre-lesion)	Kolmogorov-Smirnov, Benjamini-Hochberg correction for multiple comparisons	1.92E-02		305 (Pre-lesion) and 173 (Post 14-d) comparisons of different movement bout types		21 (Pre-lesion) 13 (Post 14-d)

Figure	Comparison	Test	N-value	
Extended Data 9a-c	Contralateral bias (drug vs saline)	Two-way repeated measures ANOVA	13 mice, 9 time bins of 20 min each	
	p-values			
		Dose	Time	Dose x Time
	Quinpirole	2.48E-01	3.90E-03	3.20E-03
	SKF	1.20E-03	<1.00E-4	<1.00E-4
	L-DOPA	<1.00E-4	<1.00E-4	<1.00E-4

Figure	Comparison	Test	N-value	
Extended Data 9e	Contralateral bias during 40 min after drug or vehicle injection	Wilcoxon signed-rank	13 mice	
	p-values			
		Saline	Quipirole 6 mg/kg	SKF 1 mg/kg
	Quinpirole 6 mg/kg	2.40E-03		
	SKF 1 mg/kg	2.00E-04	2.73E-01	
	L-DOPA 1 mg/kg	5.00E-04	4.70E-01	6.85E-01

Figure	Comparison	Test	N-value	
Extended Data 9f-i	AIMS (drug vs saline)	Two-way repeated measures ANOVA	13 (drug-injected) 5 (saline-injected) mice 9 time bins of 20 min each	
	p-values			
		Dose	Time	Dose x Time
	Axial	<1.00E-4	<1.00E-4	<1.00E-4
	Orofacial	<1.00E-4	<1.00E-4	<1.00E-4
	Limb	3.74E-02	<1.00E-4	1.08E-02
	Total	<1.00E-4	<1.00E-4	<1.00E-4

Figure	Comparison	Test	N-value
Extended Data 9j	AIMS	Wilcoxon signed-rank	13 mice
	p-values		
		L-DOPA 1 mg/kg	L-DOPA 6 mg/kg
	L-DOPA 6 mg/kg	2.00E-03	
	L-DOPA 10 mg/kg	2.00E-04	1.32E-02