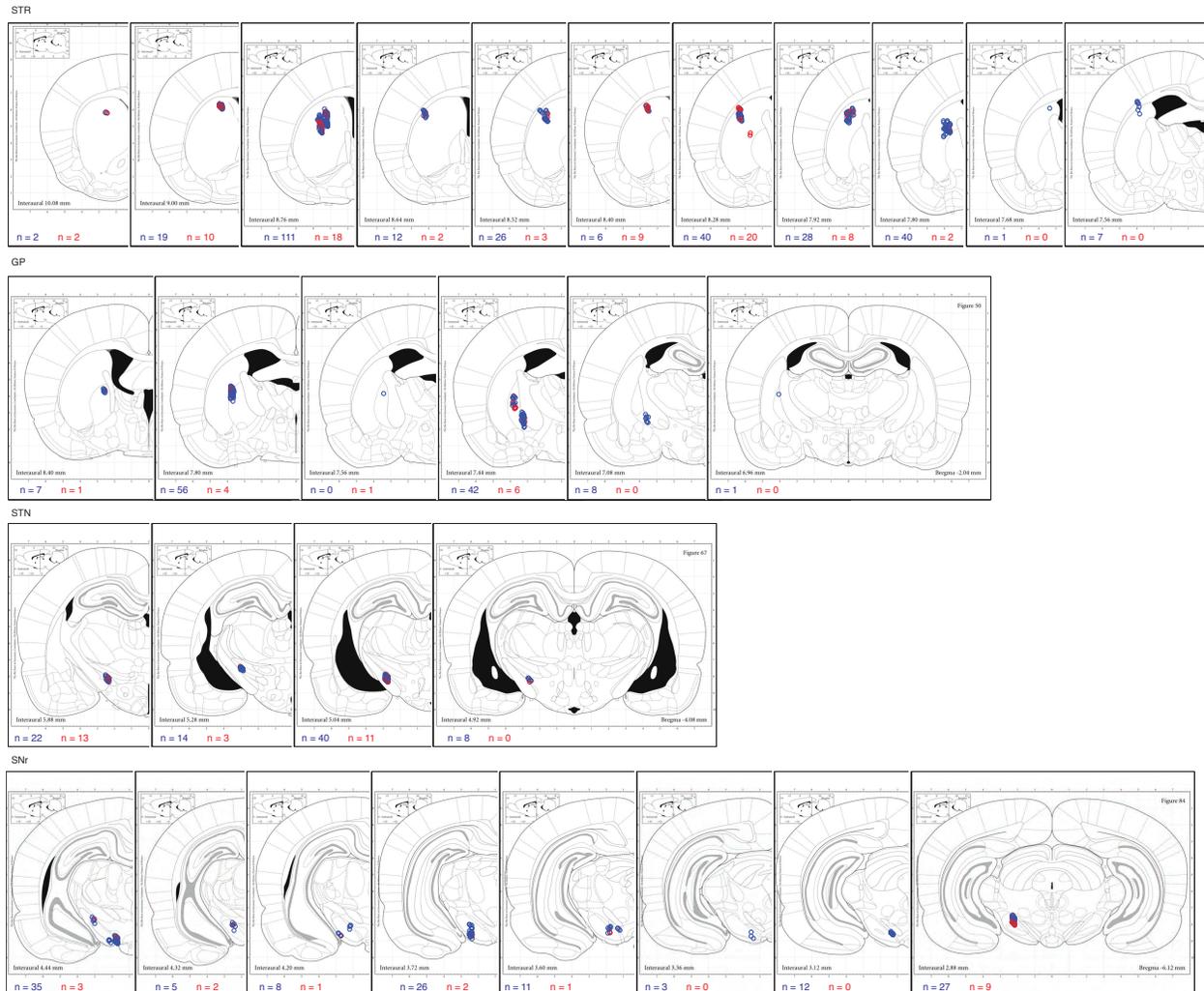


## Supplemental Material

### Canceling actions involves a race between basal ganglia pathways

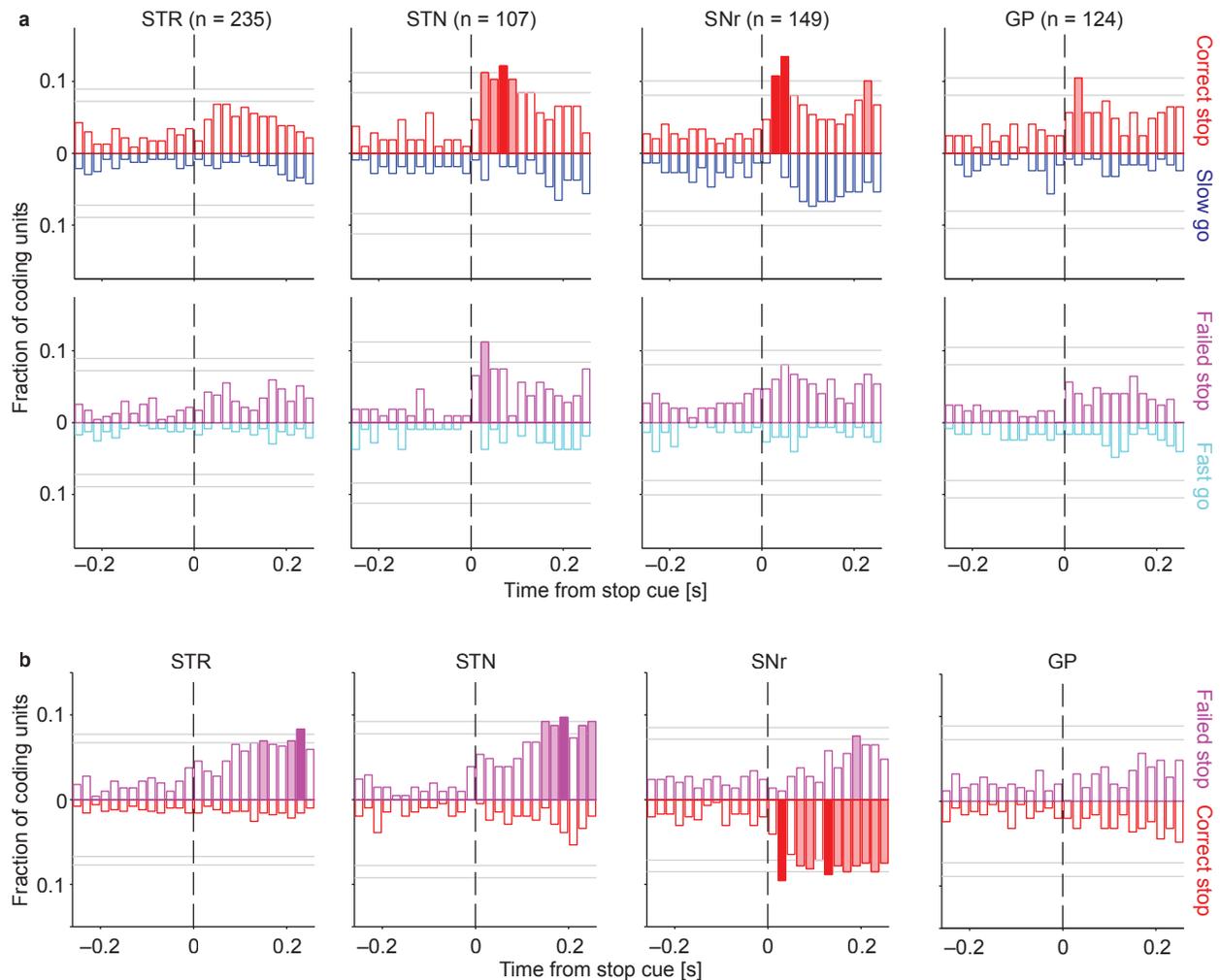
Robert Schmidt, Daniel K. Leventhal, Nicolas Mallet, Fujun Chen and Joshua D. Berke

#### Supplemental Fig. 1:



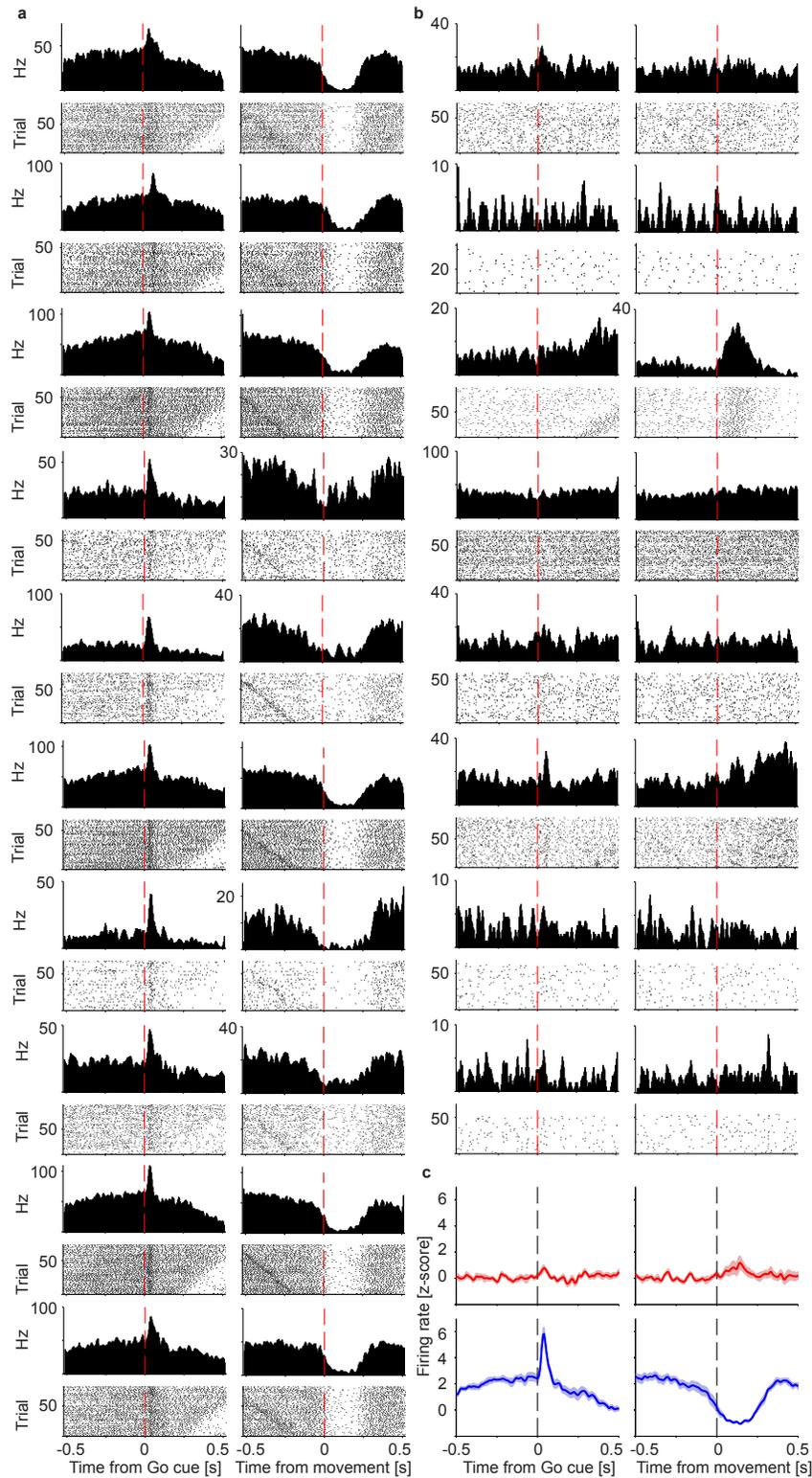
**Figure S1.** Recording sites of single units within basal ganglia structures. Shown are all units from the multi-site recordings in Experiment 1 (see **Tab. S1**). Units in red are the subsets included in **Figs. 3, 5, and S8**. All recording sites were histologically verified to be within the boundaries of the stated structures; in a few cases marker circles are shown slightly outside due to variability of individual rat anatomy compared to these images from the reference atlas<sup>51</sup>.

## Supplemental Fig. 2:



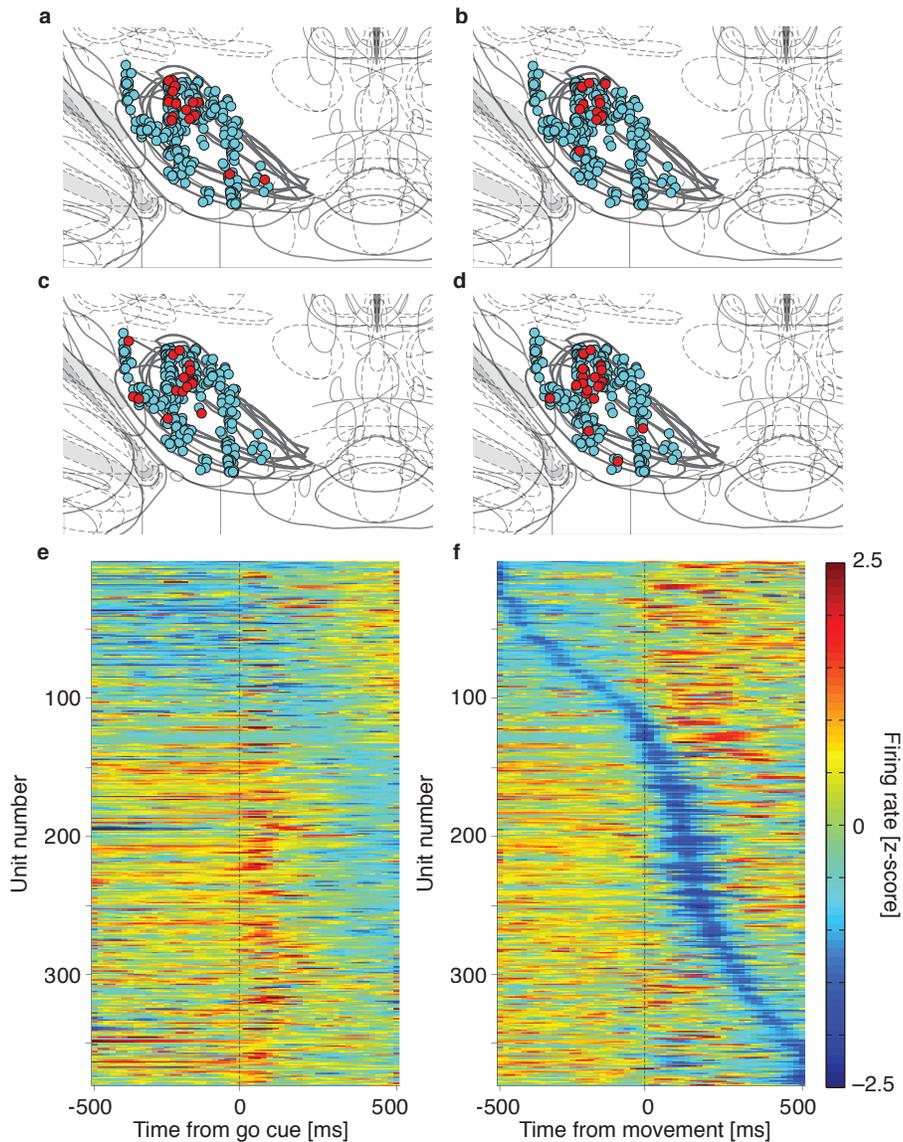
**Figure S2 (a)** Stop cue processing on ipsilateral trials. Same analysis as in **Fig. 2** but for trials in which the Go cue indicated movement to the direction ipsilateral of the recording site. Fast Stop cue responses were also visible in these trials. **(b)** Direct comparison of Correct and Failed Stop trials. Same analysis method as **Fig. 3**, combining ipsi- and contralateral trials. Note that only SNr shows a significant difference between Correct and Failed Stop trials briefly after the Stop cue (red bar). Movement-related activity in STR and STN is seen in Failed Stop trials (filled purple bars).

**Supplemental Fig. 3:**



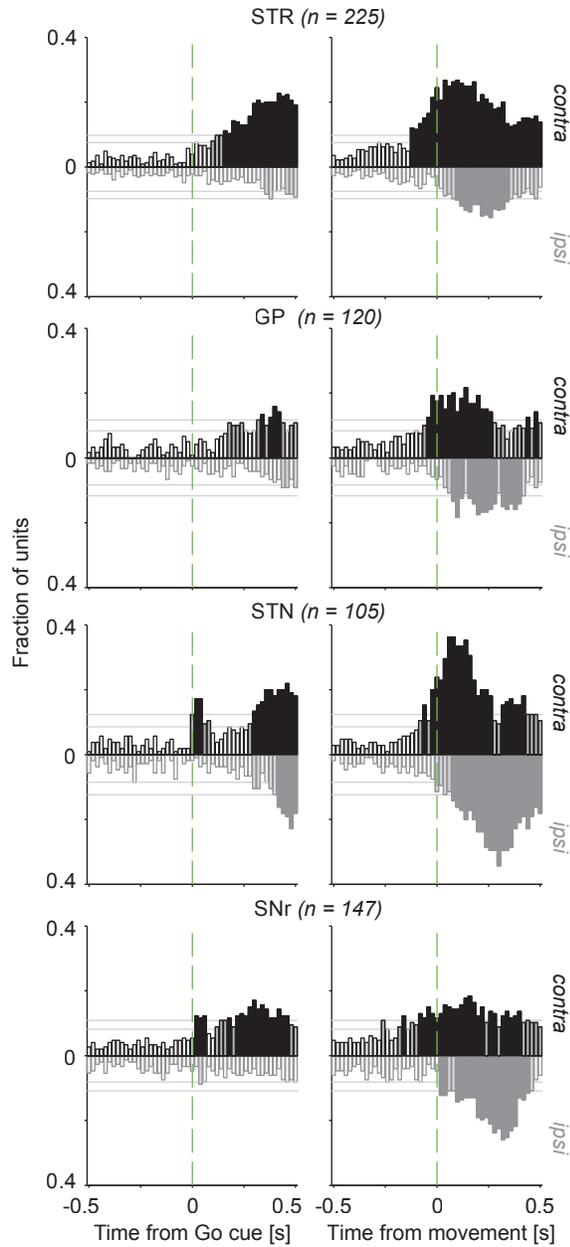
**Figure S3** Activity patterns for individual Stop-related SNr units during Go trials. **(a)** Most SNr units with Stop responses (10/18) also respond to the Go cue (left column) and decrease activity during movement initiation (right column). Upper panels shows peri-event firing rate histograms, lower panels show spike raster plots, sorted by reaction time. **(b)** Remaining SNr units do not show consistent response patterns. **(c)** Mean firing rate histograms of the units from (a) and (b), in blue and red respectively.

**Supplemental Fig. 4:**



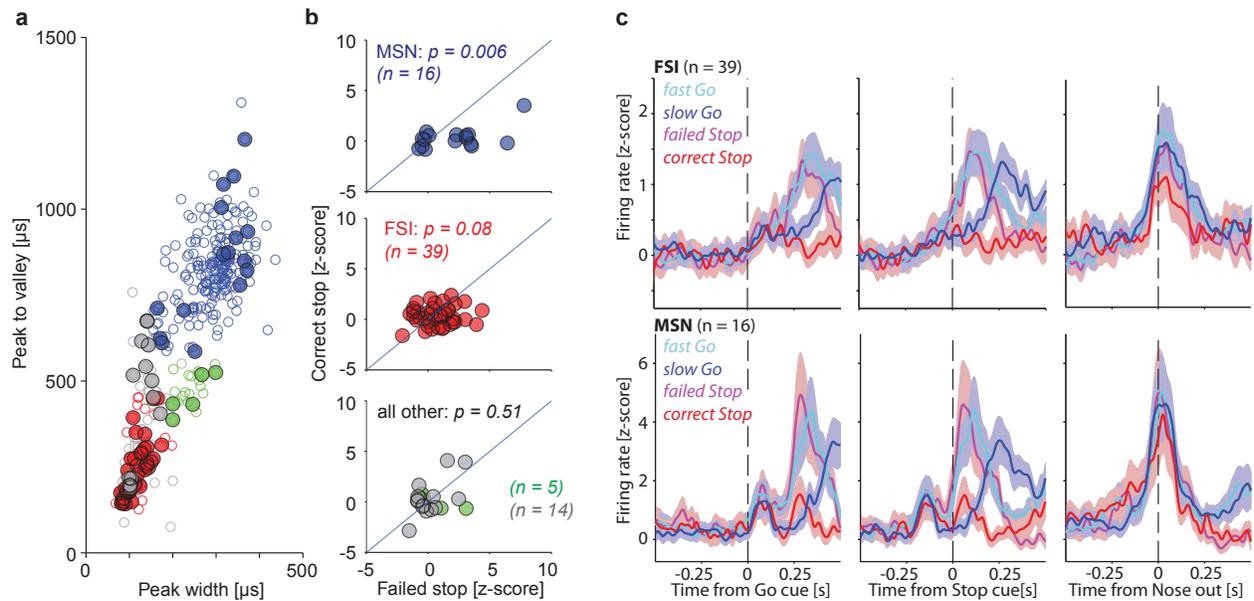
**Figure S4** Stop-related units cluster in the dorsolateral part of SNr. (a,b) Units in red distinguish Failed Stop and Correct Stop trials briefly after the Stop cue in (a) contralateral and (b) ipsilateral trials. Data are combined from Experiments 1 and 2. Latency-matched comparisons between Slow Go and Correct Stop trials in (c) contralateral and (d) ipsilateral trials confirm that the dorsolateral cluster of red units is selective to stopping rather than just movement. (e,f) Activity patterns in the entire SNr population for correct contralateral Go trials, aligned to presentation of the Go cue (e) and movement onset (f). The units are ordered by the time of minimum activity in the right panel. Note the different subsets of units that increase activity during movement (~first third from top) and decrease activity during movement (~second third). This latter subset is also marked by Go cue responses (e).

### Supplemental Fig. 5:



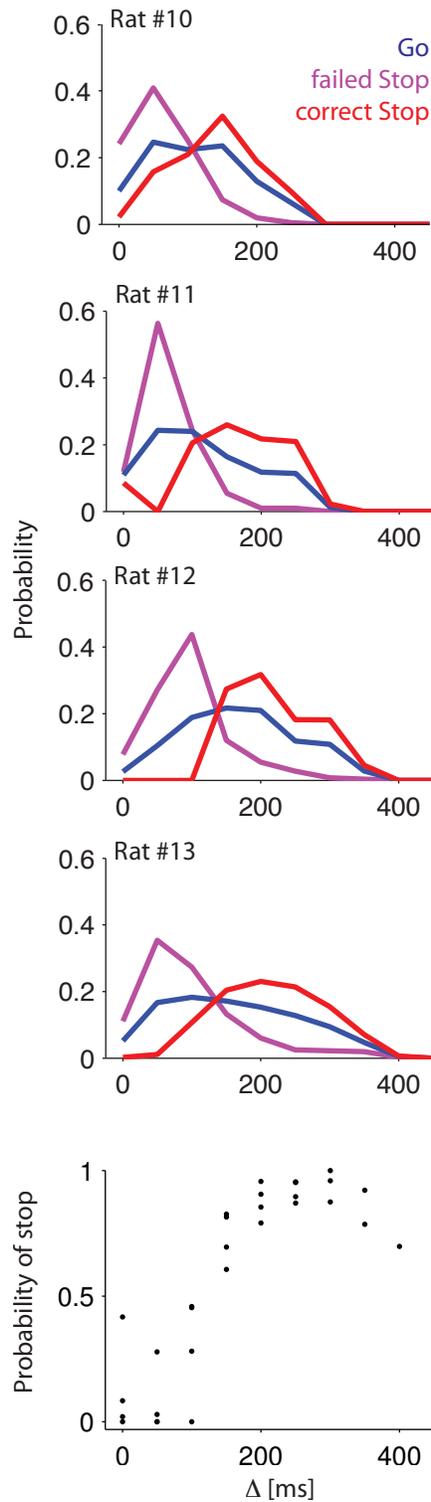
**Figure S5** Coding of movement direction in basal ganglia subregions. Same as **Fig. 5a**, but showing all basal ganglia regions. Note that neurons tend to preferentially fire on contralateral trials, especially around movement onset. In addition, significant numbers of STN and SNr cells show fast responses to contralateral-instructing Go cues.

**Supplemental Fig. 6:**



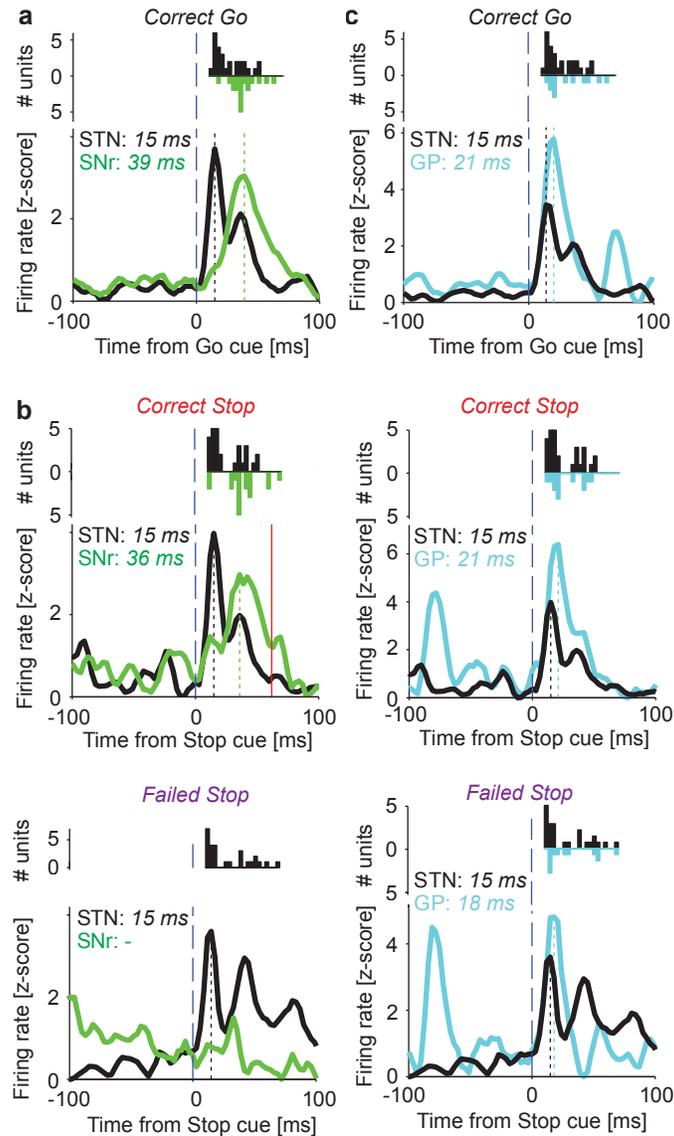
**Figure S6** Activity of individual striatal units at Stop cue onset. (a) Waveform classification of all striatal units (following same criteria as ref. 20). Presumed medium spiny neurons (MSNs) are marked in blue, presumed fast-spiking interneurons (FSIs) in red, “O” cells in green<sup>53</sup>, and unclassified in grey. The 74 neurons included in the analyses of **Fig. 5b,c** are marked with filled circles. While we are not able to distinguish direct and indirect pathway MSNs here, a recent study suggests that both subtypes become concurrently activity during movement initiation<sup>49</sup>. (b) Instantaneous z-score at Stop-cue onset for these 74 cells, comparing Correct and Failed Stop trials. Presumed MSNs were significantly more active on Failed than on Correct Stop trials (p-value from shuffle test). Note that the high number of FSIs in this subset ( $n = 39/74$ ) is consistent with a coherent pulse of increased FSI activity around choice execution<sup>20</sup>. (c) Mean ( $\pm$  s.e.m.) firing rate z-score for FSIs and MSNs.

### Supplemental Fig. 7:



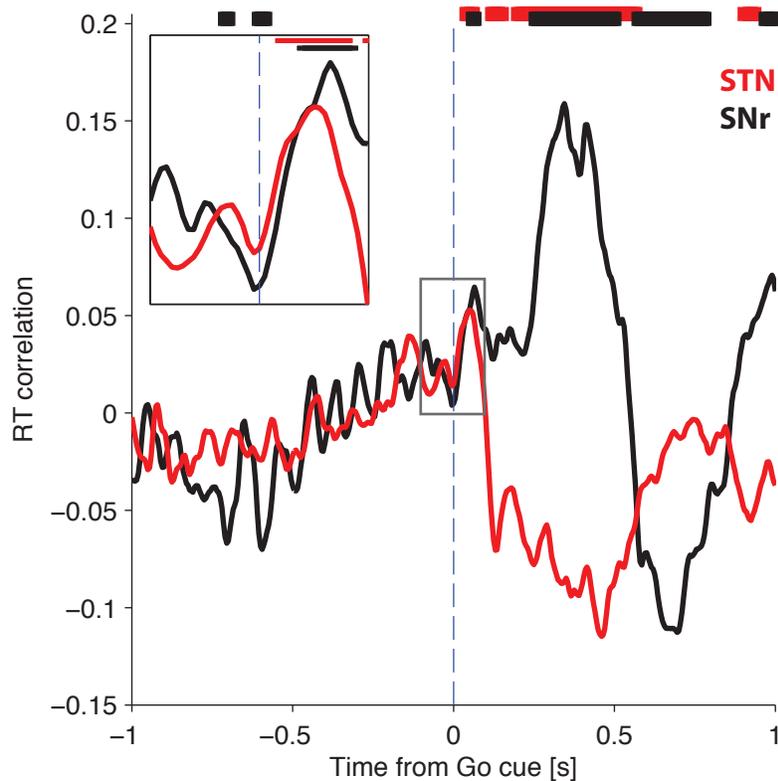
**Figure S7.** Connecting the integrate-and-fire model of SNr with behavioral rat data. The top four panels show reaction time (RT) histograms for each individual rat in Experiment 1. Only reaction times of up to 500ms are included. Note that here RTs are expressed relative to the onset of the Stop cue (i.e. as the parameter  $\Delta$ ). For Go trials (blue), RTs are relative to the time the Stop cue would have occurred (since SSDs are fixed within a session). Go and Failed Stop trial RT distributions are directly measured, while Correct Stop RTs are inferred from those distributions (see Methods). The resulting distributions of  $\Delta$  are used to generate model responses for Correct and Failed Stop trials (**Fig. 6d**). From these behavioral data we derived a probability of Correct Stop for a given RT (bottom panel). Interestingly, there seems to be a switch from low to high probabilities of stopping around 150ms, a good match with estimated SSRTs (**Tab. S1**).

**Supplemental Fig. 8:**



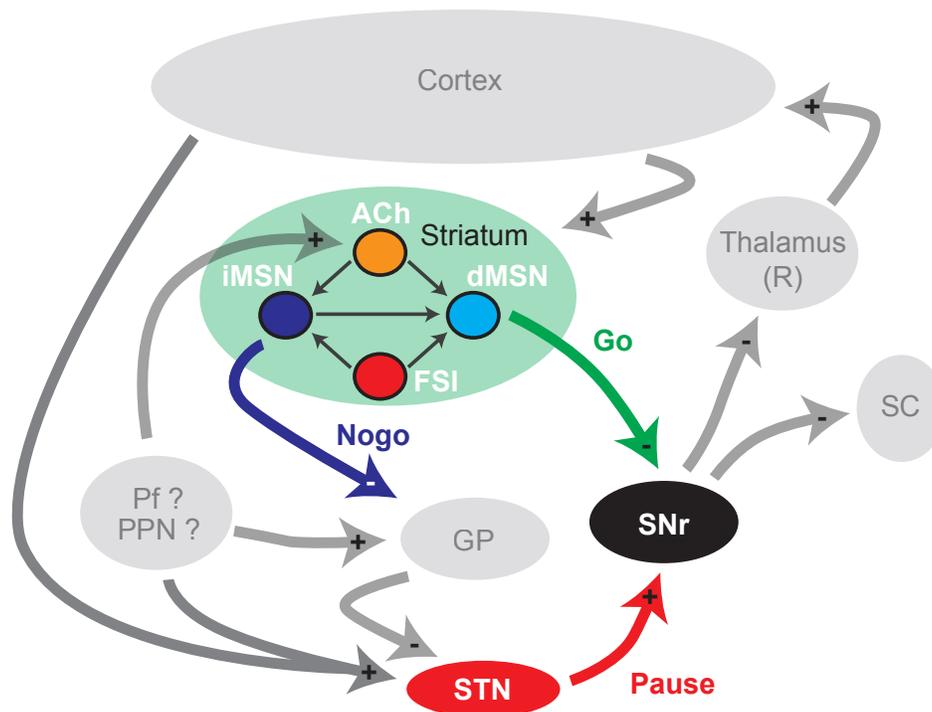
**Figure S8** STN, GP and SNr responses to Go and Stop cues. **(a)** Comparison of STN and SNr response latencies to the Go cue, in correct Go trials. Analysis procedures are identical to **Fig. 3b**, but using the contralateral Go cue instead of the Stop cue. **(b)** For comparison of response latencies, Correct and Failed Stop trial responses to the Stop cue are shown again. **(c)** Corresponding comparisons of STN with GP Go and Stop cue latencies. GP latency distributions were not significantly different from STN (for Correct Stop:  $p = 0.91$ , Kolmogorov-Smirnov test).

**Supplemental Fig. 9:**



**Figure S9** Reaction times are longer on trials with greater STN and SNr responses to the Go cue. Correlation coefficients between normalized activity of Stop-related STN and SNr subsets (same units as in **Fig. 3**) and trial-by-trial reaction times were determined with a sliding window (width: 50 ms) around the Go cue in correct Go trials. The inset shows the same results on a shorter timescale ( $\pm 100$  ms; marked by grey box in main figure). Black and red horizontal bars at top indicate significant correlation coefficients ( $p < 0.05$ , corrected for multiple comparisons). Briefly after the Go cue, trials with increased STN and SNr activity have longer reaction times, consistent with a delaying action of the STN-SNr pathway. Potentially, these responses may help prevent premature movement initiation, i.e. movement initiation with very short reaction times. The stronger correlations  $>100$  ms after the Go cue reflect movement-related activity (mostly increases in STN and decreases in SNr; see also **Fig. 3**).

**Supplemental Fig. 10:**



**Figure S10.** Proposed scheme of coordinated pathways in action cancellation. Circuits through the basal ganglia with complementary dynamics contribute to distinct aspects of cancellation. The SNr serves as a gateway that normally prevents movement initiation, via tonic inhibition of structures such as superior colliculus (SC) and thalamic relay nuclei. The relative timing of “Go”, “NoGo” and “Pause” inputs determines whether this gate opens or not. The parafascicular thalamus (Pf) and/or pedunculopontine nucleus (PPN) drives the STN-SNr Stop pathway quickly - before the stop-signal reaction time - allowing rapid arrest of actions that are very close to execution. Responses in this pathway are very fast, yet transient, and are not specific to Stop cues. Engagement of this pathway alone would slow reaction times, but not prevent movement execution (as is seen when “Continue” cues are substituted for “Stop” cues<sup>36</sup>). In parallel, projections to striatum can lead to a slower reset of actions that are under preparation. Pf projections to cholinergic interneurons (ACh) are likely to be particularly important in this switching of striatum-based plans<sup>40,44,46</sup>, which may involve both suppression of direct pathway Go neurons (dMSN) and enhancement of indirect pathway NoGo neurons (iMSN). This striatum-based action cancellation process (which may be considered an “interactive” race - see ref. 4) is slower due to both the intrinsic dynamics of striatal microcircuitry, and the need to determine whether a salient cue should lead to action termination, or not (as with “Continue” cues). Together, the faster STN-SNr pathway and slower striatum-based signaling can produce action cancellation that is both swift and selective.

## Supplemental Table 1:

Experiment 1: Basal ganglia multisite recordings

Rat	STN	STR	GP	SNr	Go acc [%]	Go RT $\pm$ std [ms]	Go MT $\pm$ std [ms]	# Sessions	# Completed Go trials / session $\pm$ sem	# Stop trials / session $\pm$ sem	Stop acc	Failed stop RT $\pm$ std [ms]	SSD $\pm$ std [ms]	SSRT $\pm$ std [ms]	LH [ms]	MH [ms]
Rat 10 (IM-164) L	51	93	9	76	87	419 $\pm$ 39	322 $\pm$ 13	15	166 $\pm$ 10	58 $\pm$ 4	71	366 $\pm$ 106	272 $\pm$ 36	114 $\pm$ 27	800-1000	600
Rat 11 (IM-166) L	60	56	8	16	91	331 $\pm$ 32	303 $\pm$ 21	9	160 $\pm$ 18	51 $\pm$ 6	45	295 $\pm$ 14	225 $\pm$ 13	174 $\pm$ 60	800	600
Rat 12 (IM-174) L	0	78	60	24	86	332 $\pm$ 25	254 $\pm$ 16	10	147 $\pm$ 8	63 $\pm$ 5	48	267 $\pm$ 46	150 $\pm$ 0	205 $\pm$ 26	800	500
Rat 13 (IM-225) L	0	139	49	34	81	305 $\pm$ 49	305 $\pm$ 17	16	171 $\pm$ 12	61 $\pm$ 4	54	286 $\pm$ 87	147 $\pm$ 12	194 $\pm$ 33	700	550

Experiment 2: Functional mapping of SNr

Rat	STN	STR	GP	SNr	Go acc [%]	Go RT $\pm$ std [ms]	Go MT $\pm$ std [ms]	# Sessions	# Completed Go trials / session $\pm$ sem	# Stop trials / session $\pm$ sem	Stop acc	Failed stop RT $\pm$ std [ms]	SSD $\pm$ std [ms]	SSRT $\pm$ std [ms]	LH [ms]	MH [ms]
Rat 14 (IM-310) R	0	0	0	73	86	351 $\pm$ 41	304 $\pm$ 17	12	176 $\pm$ 18	95 $\pm$ 8	48	287 $\pm$ 14	187 $\pm$ 9	243 $\pm$ 46	800	600
Rat 15 (IM-336) R	0	0	0	77	81	412 $\pm$ 45	270 $\pm$ 13	21	145 $\pm$ 9	62 $\pm$ 4	68	382 $\pm$ 23	316 $\pm$ 19	142 $\pm$ 41	650-700	600
Rat 16* (IM-361) R	0	0	0	38	90	195	233	1	213	97	41	160	90	163	600	450
Rat 17* (IM-364) R	0	0	0	24	95	241	242	1	189	68	32	189	110	200	600	450
Rat 18* (IM-368) L	0	0	0	20	92	231	202	1	301	135	49	153	75	162	600	450

**Table S1.** Summary of behavioral and electrophysiological data in each rat. Columns show Rat ID (“L” and “R” indicate recording sites were in the left or right hemisphere); the number of recorded units in the indicated subregions; the percentage of correct performance on completed Go trials; the mean of session median correct Go reaction time; the mean of session median correct Go movement time; the number of included recording sessions for each rat; the mean number of completed Go trials per session; the mean number of completed Stop trials per session; the percentage of correctly performed Stop trials; the mean session-by-session median reaction time on Stop-failure trials; the mean SSD across sessions; the mean SSRT across sessions; and the range of limited hold (LH) and movement hold (MH) values for each rat. Rats marked with an asterisk in Experiment 2 received silicon probe implants, all other animals had 21-tetrode implants.