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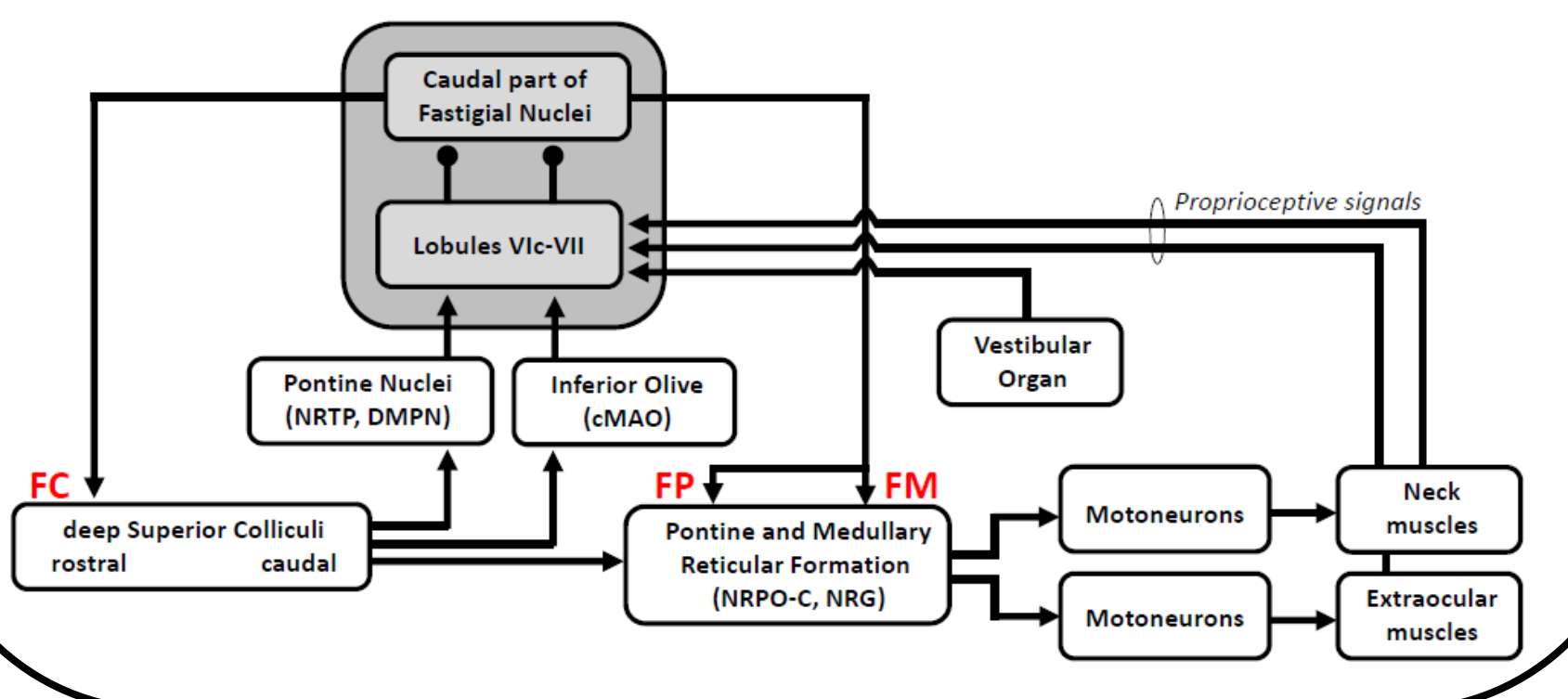
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Cerebellar control of visually-guided eye movements by the bilateral mass of activity in the caudal fastigial nuclei

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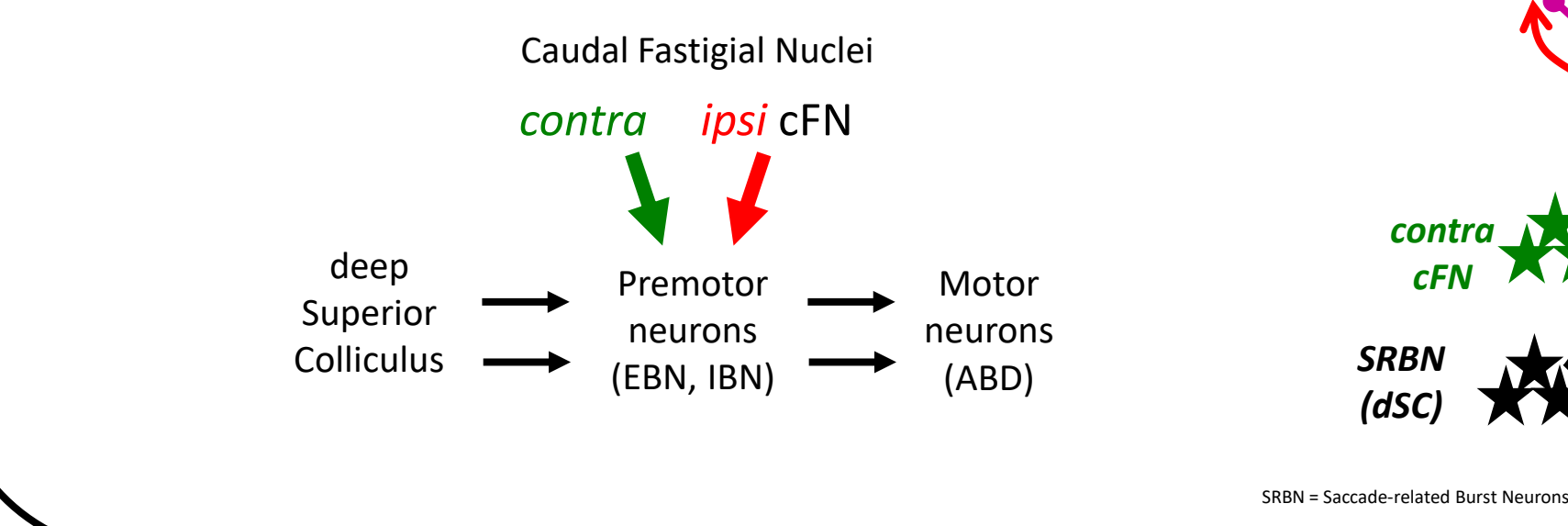
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The caudal part of both fastigial nuclei (cFN) plays a crucial role in the ability to foveate a static or moving visual target. In the monkey, an unilateral inactivation of cFN by local injection of muscimol impairs the horizontal component of saccadic eye movements. An ipsilesional gaze offset is also observed while a target is being fixated or pursued. In the head-unrestrained monkey (and cat), the head exhibits an ipsilesional deviation relative to the trunk (cervical dystonia).

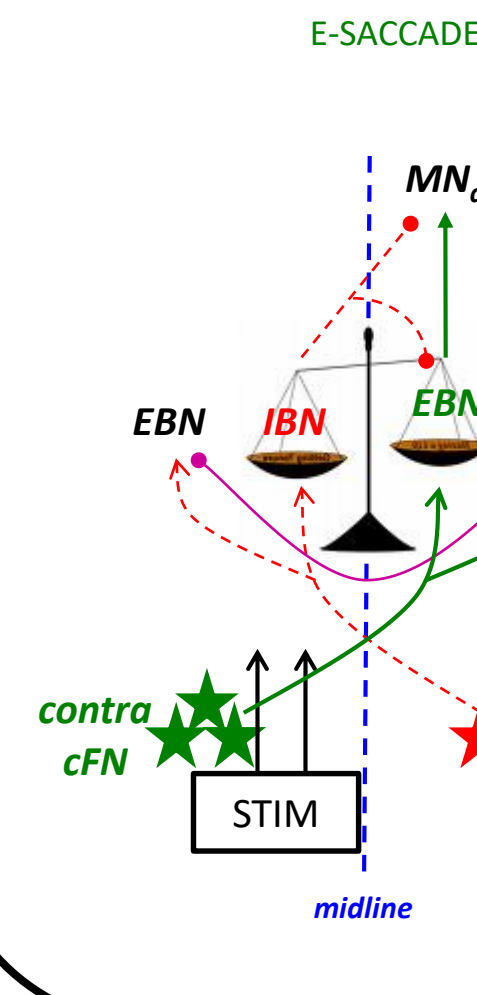


BILATERAL HYPOTHESIS

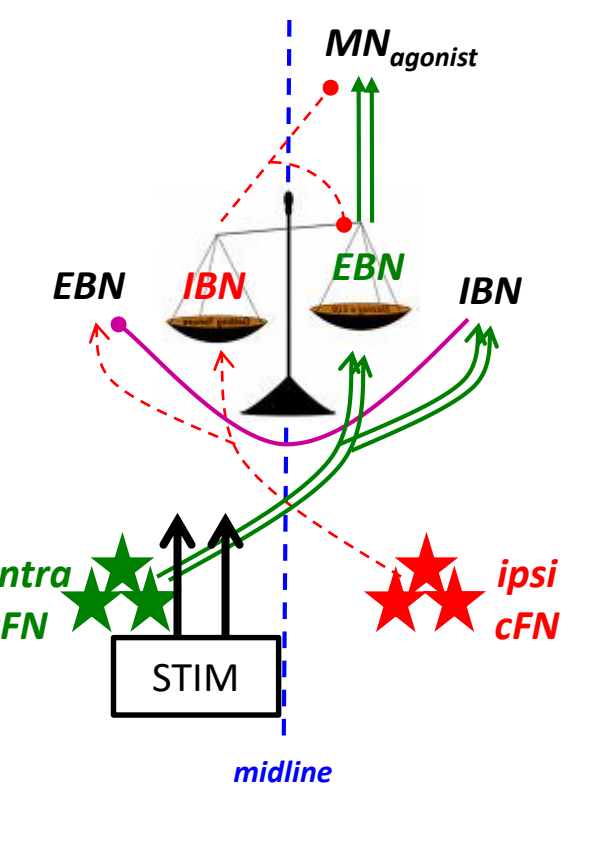
For every saccade (horizontal, oblique or vertical), the left and right cFN regulate the balance of activity between the excitatory and inhibitory input (from EBNs and IBNs) to the motor and internuclear neurons in the abducens nucleus.



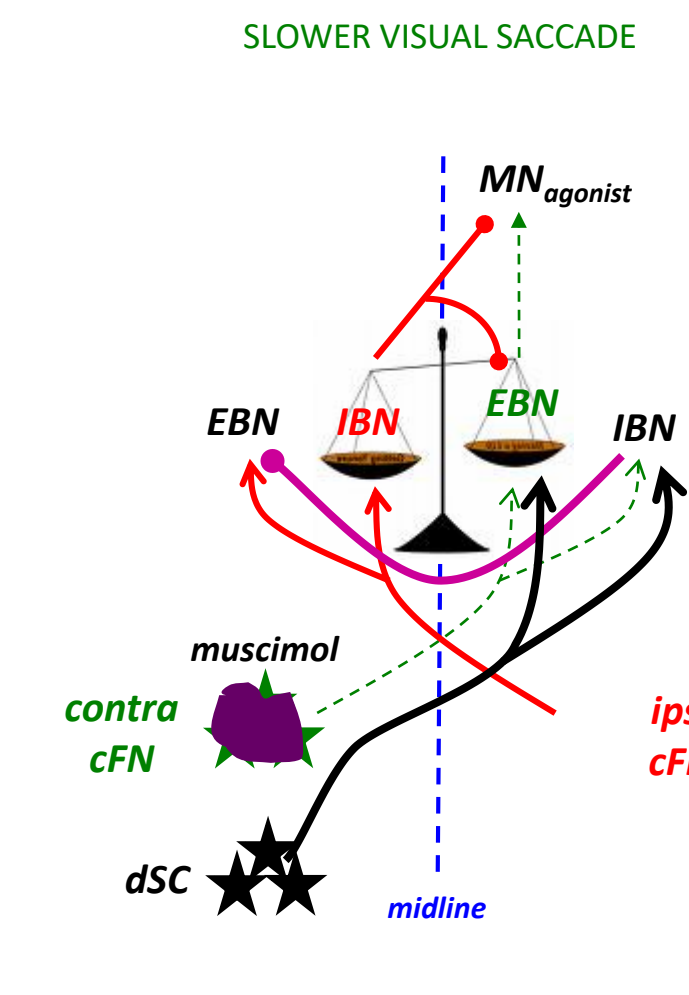
ELECTRICAL MICROSTIMULATION



FASTER E-SACCADE



INACTIVATION



ELEMENTS FOR A CONTROVERSY

In a computational study, Eggert, Robinson & Straube (2016) reported more variability in saccade endpoints after cFN inactivation than before., and interpreted this effect as altered putative "noises" in brain activity: planning noise and/or signal dependent motor noise. Unfortunately, they did not consider the fact that after cFN inactivation, the monkeys have difficulties to foveate a visual target. The variability in saccade endpoints can indeed result from the fact that saccades did not start from the same starting positions (Table 1 and Fig. 1). Moreover, when we look at the literature, we do not find any particular increase in the variability of amplitudes. However, we find differences between experiments: the amount of dysmetria varies between the experiments (Fig. 2).

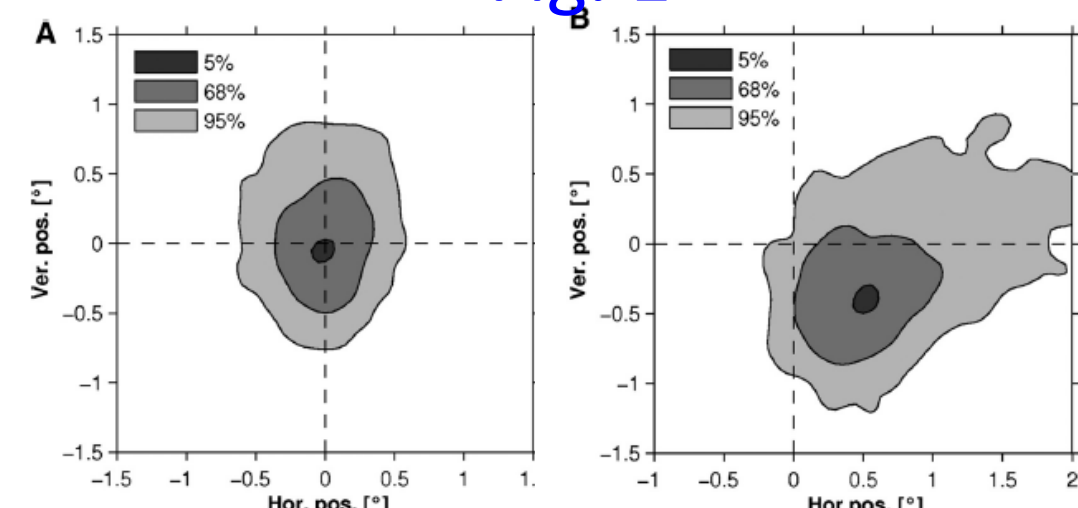
Table 1

Experiment	Injection	Session	n	Horizontal Eye Position			Vertical Eye Position		
				Mean	Range	Difference	Mean	Range	Difference
Q1	Left cFN (0.4 µl)	Control	378	-0.5 ± 0.6	[-1.9; 1.3]	-1.2*	0.0 ± 0.6	[-1.5; 1.8]	0.4*
		Muscimol	614	-1.7 ± 1.0	[-6.9; 2.4]		0.4 ± 0.6	[-1.6; 3.0]	
Q2	Left cFN (0.4 µl)	Control	665	0.6 ± 0.6	[-1.1; 2.4]	-2.4*	0.2 ± 0.7	[-2.2; 3.3]	-0.1 NS
		Muscimol	502	-1.8 ± 1.6	[-6.6; 4.0]		0.1 ± 1.6	[-6.0; 6.1]	
Q3	Left cFN (0.4 µl)	Control	782	0.0 ± 0.7	[-3.2; 3.3]	-1.2*	0.1 ± 0.7	[-2.5; 3.4]	-0.3*
		Muscimol	1071	-1.2 ± 1.2	[-7.2; 2.7]		-0.2 ± 0.6	[-3.0; 2.4]	
Q4	Right cFN (0.6 µl)	Control	690	-0.2 ± 1.0	[-5.2; 3.3]	2.0*	0.3 ± 0.9	[-3.0; 3.1]	0.1 NS
		Muscimol	962	1.8 ± 1.3	[-3.5; 6.4]		0.1 ± 0.8	[-3.1; 3.3]	
S1	Left cFN (1.0 µl)	Control	335	0.0 ± 0.6	[-3.2; 3.3]	-1.4*	-0.7 ± 0.3	[-1.7; 1.2]	
		Muscimol	341	-1.4 ± 1.1	[-6.4; 1.4]		-0.6 ± 0.6	[-2.2; 2.0]	0.1 NS
S2	Left cFN (0.6 µl)	Control	488	0.0 ± 0.8	[-3.4; 3.6]	-1.3*	-0.5 ± 0.4	[-1.7; 0.9]	
		Muscimol	378	-1.2 ± 0.8	[-6.4; 1.4]		-0.9 ± 0.4	[-2.4; 0.9]	
S3	Right cFN (0.6 µl)	Control	490	-0.4 ± 0.7	[-2.8; 3.8]	-0.4*	0.0 ± 0.5	[-1.2; 1.9]	
		Muscimol	488	0.0 ± 0.8	[-3.4; 3.6]		-0.6 ± 0.6	[-2.2; 2.0]	
S4	Right cFN (0.8 µl)	Control	396	0.1 ± 0.6	[-2.4; 1.7]	0.8*	0.0 ± 0.4	[-1.2; 1.7]	-1.0*
		Muscimol	422	0.0 ± 0.7	[-2.5; 3.3]		-1.0 ± 0.4	[-2.2; 0.7]	
S5	Left cFN (0.8 µl)	Control	471	0.0 ± 0.8	[-2.8; 3.2]	-0.3*	0.0 ± 0.5	[-1.6; 2.1]	-0.1*
		Muscimol	609	-0.3 ± 0.8	[-3.2; 3.3]		-0.1 ± 0.5	[-1.6; 1.6]	
I1	Right cFN (1.2 µl)	Control	88	0.3 ± 0.8	[-2.0; 2.5]	0.3*	-0.1 ± 0.4	[-1.2; 1.2]	0.2*
		Muscimol	154	0.6 ± 1.0	[-1.6; 3.8]		0.1 ± 0.8	[-1.4; 2.5]	

Difference was tested with a Student's t-test for independent samples. NS: no statistically significant difference; *P < 0.05. LED, light-emitting diode; cFN, caudal fastigial nucleus.

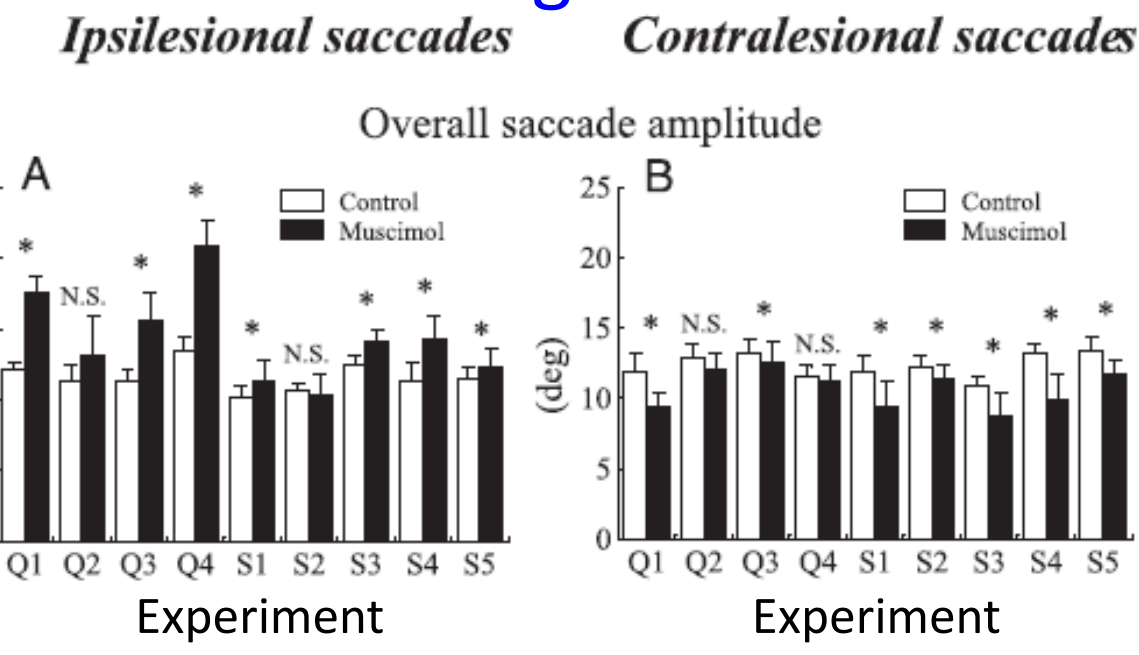
from Goffart, Chen & Sparks *Journal of Neurophysiology* (2004)

Fig. 1



from Guerrasio, Quinet, Büttner & Goffart *J Neurophysiol* (2010)

Fig. 2



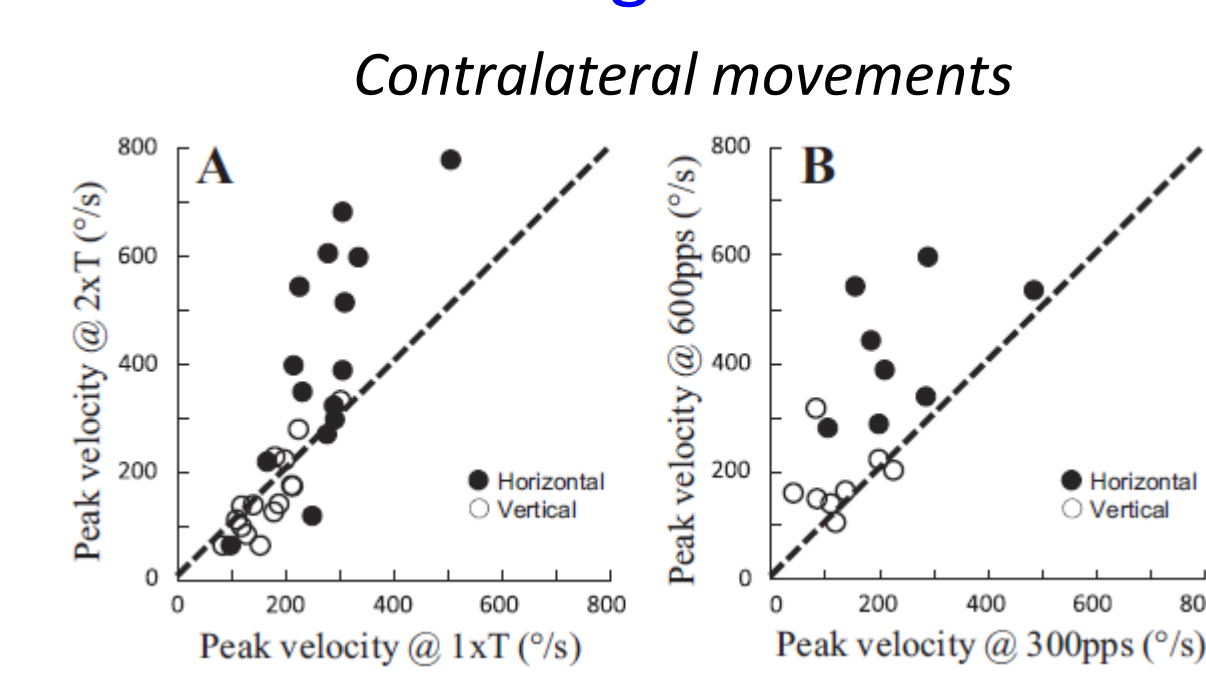
Mean amplitude of horizontal (ipsilesional (A) and contralateral (B) saccades recorded before (□) and after (■) muscimol injection in the cFN. Saccades were initiated from the central fixation LED and aimed at a 12° eccentric target LED. The error bars represent the SDs. N.S.: no statistically significant difference; *P < 0.05 (Mann-Whitney U test).

from Goffart, Chen & Sparks *J Neurophysiol* (2004)

NEURONAL RECRUITMENT HYPOTHESIS

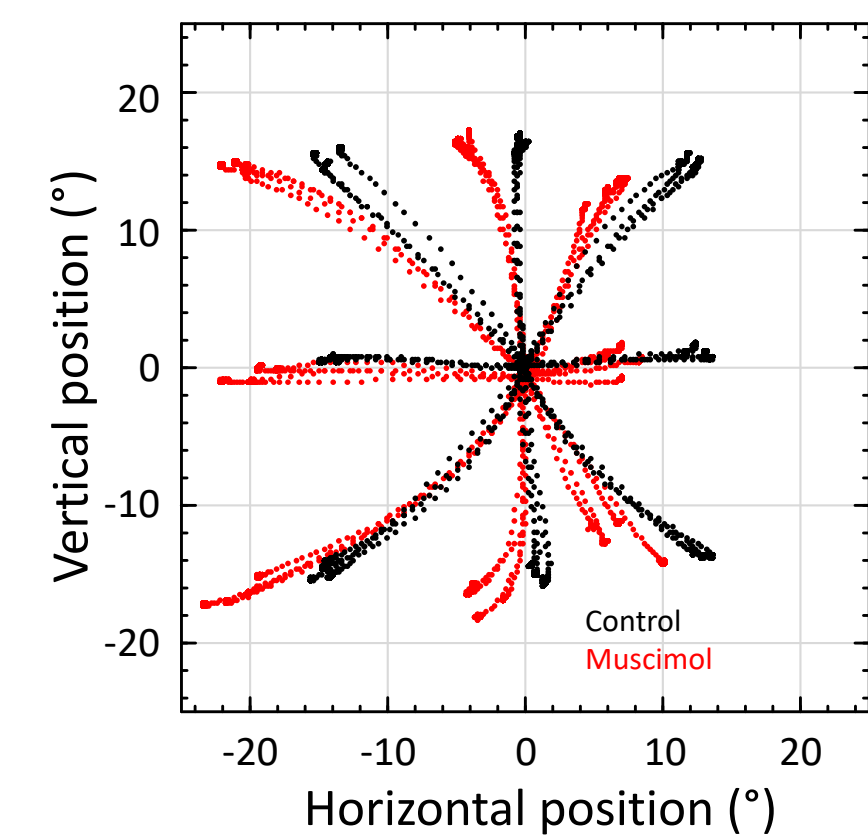
From the demonstration that larger current enhances the size and velocity of saccades evoked by electrical cFN microstimulation (Fig. 3), we propose that the variability of saccade endpoints reflects the variable size of the active population of cFN neurons contributing to the movement generation. Indeed, if during the pharmacological experiments, the perturbation is not exactly centered in cFN, the number of inactivated neurons should increase as the muscimol diffuses, resulting in a dysmetria that increases with time.

Fig. 3

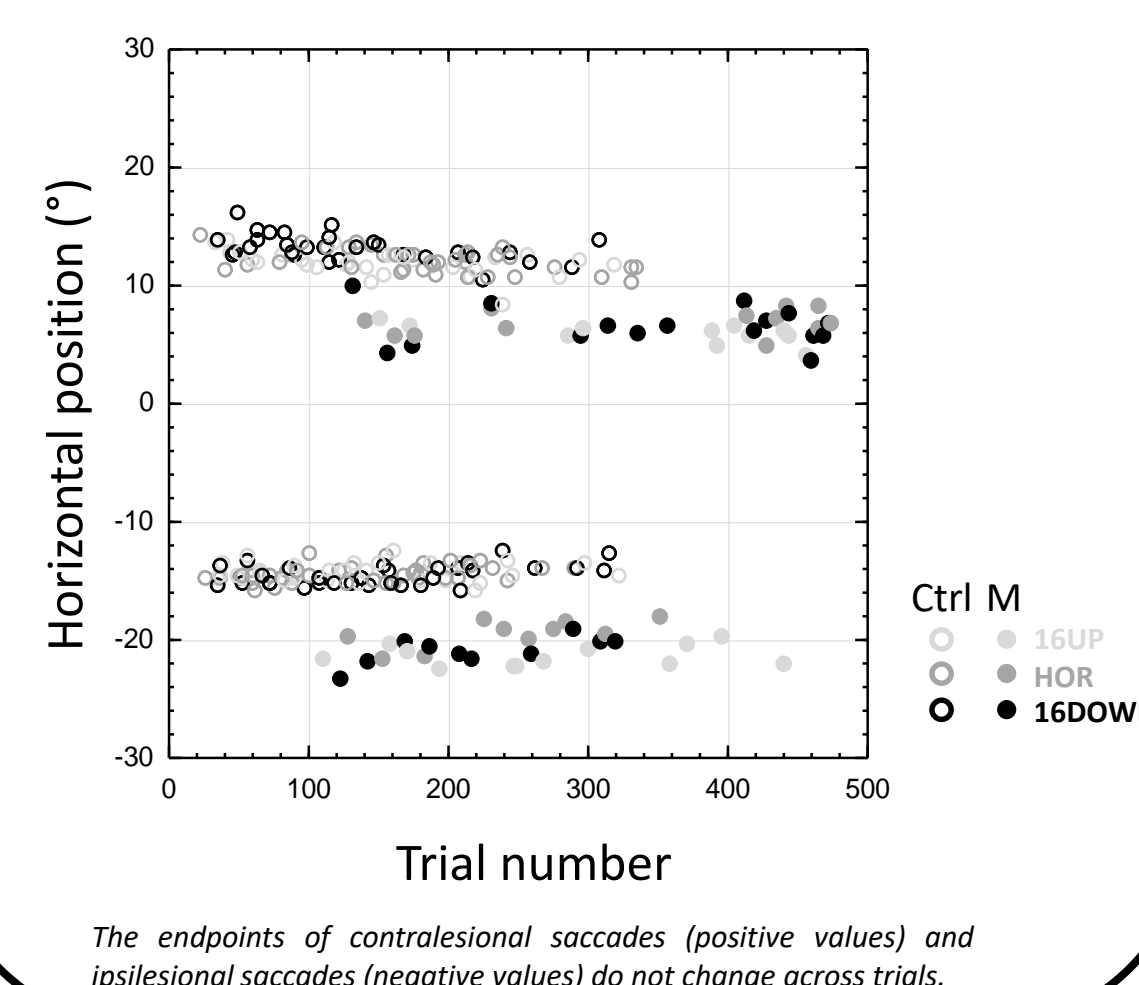


from Quinet & Goffart *J Neurophysiol* (2015)

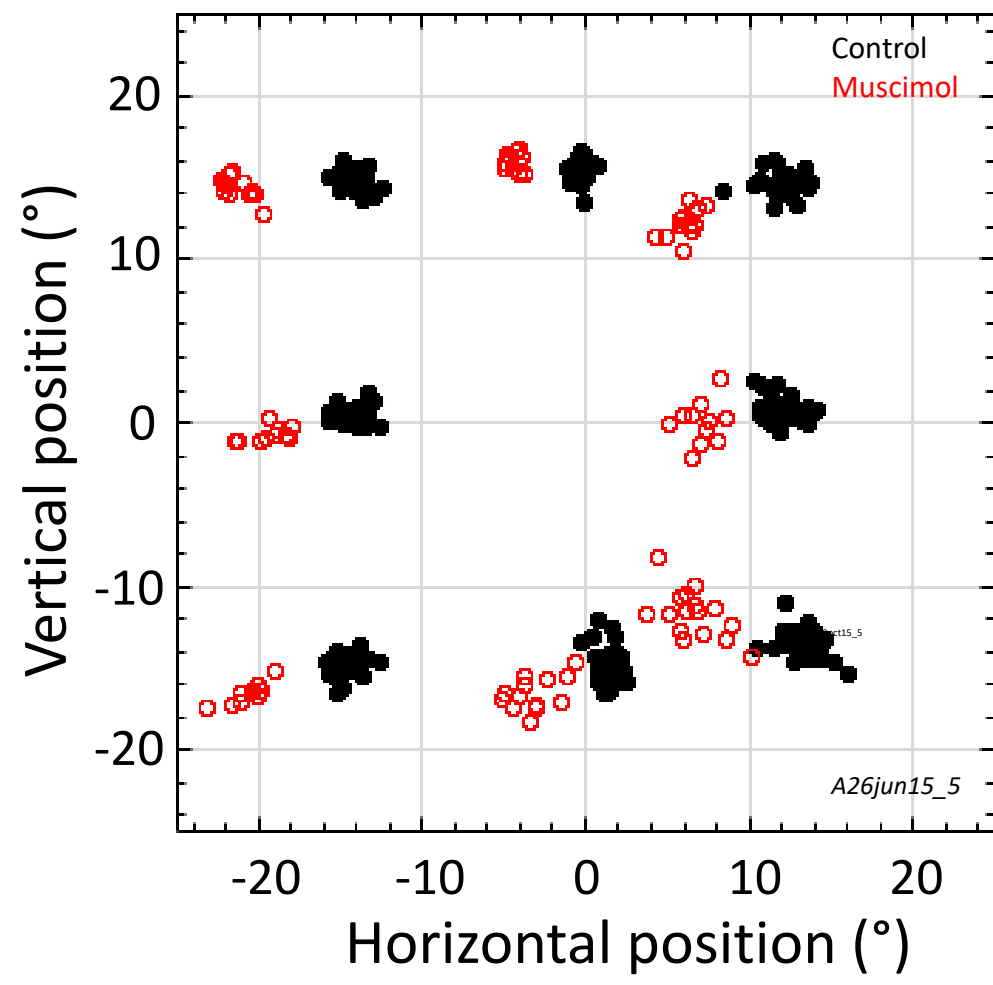
TYPICAL EXPERIMENT



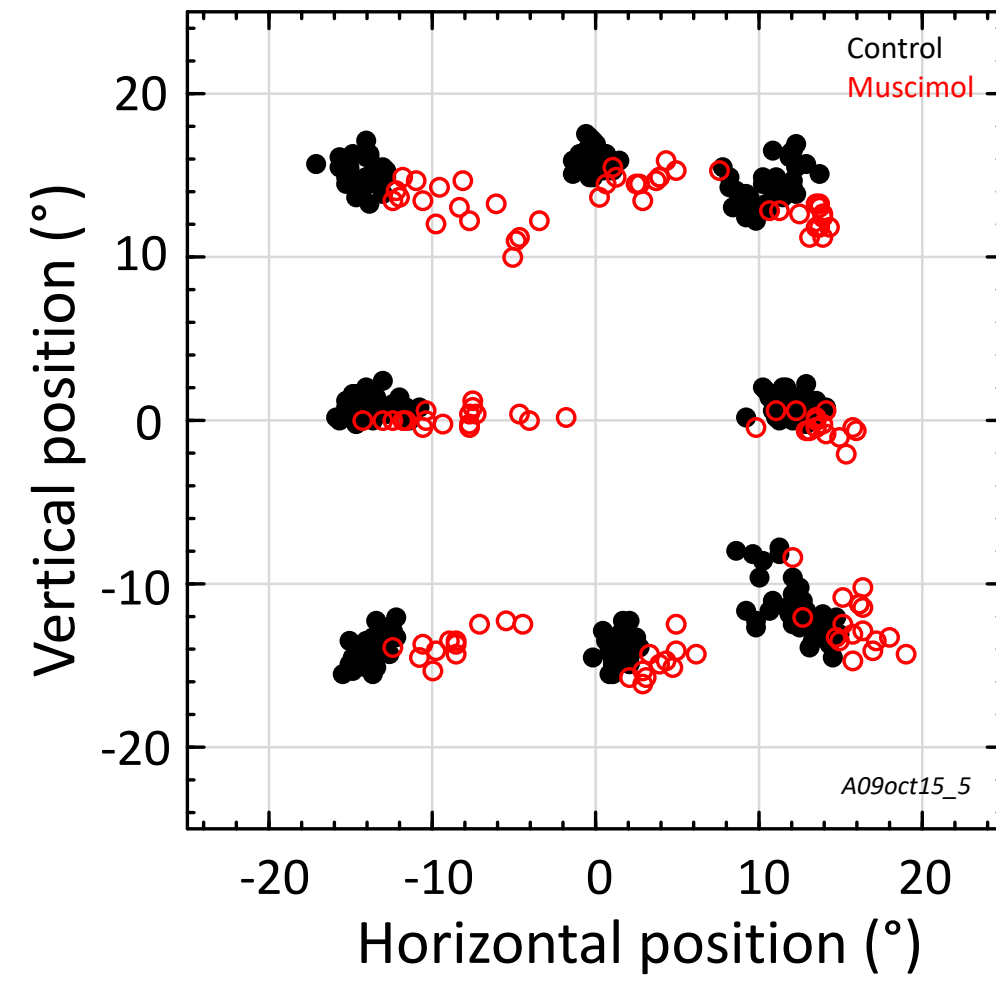
After muscimol injection in the left caudal fastigial nucleus, the horizontal component is hypermetric for ipsilateral (leftward) saccades and hypometric for contralateral (rightward) saccades. Vertical saccades also exhibit a leftward deflection in their trajectory.



Injection in left cFN

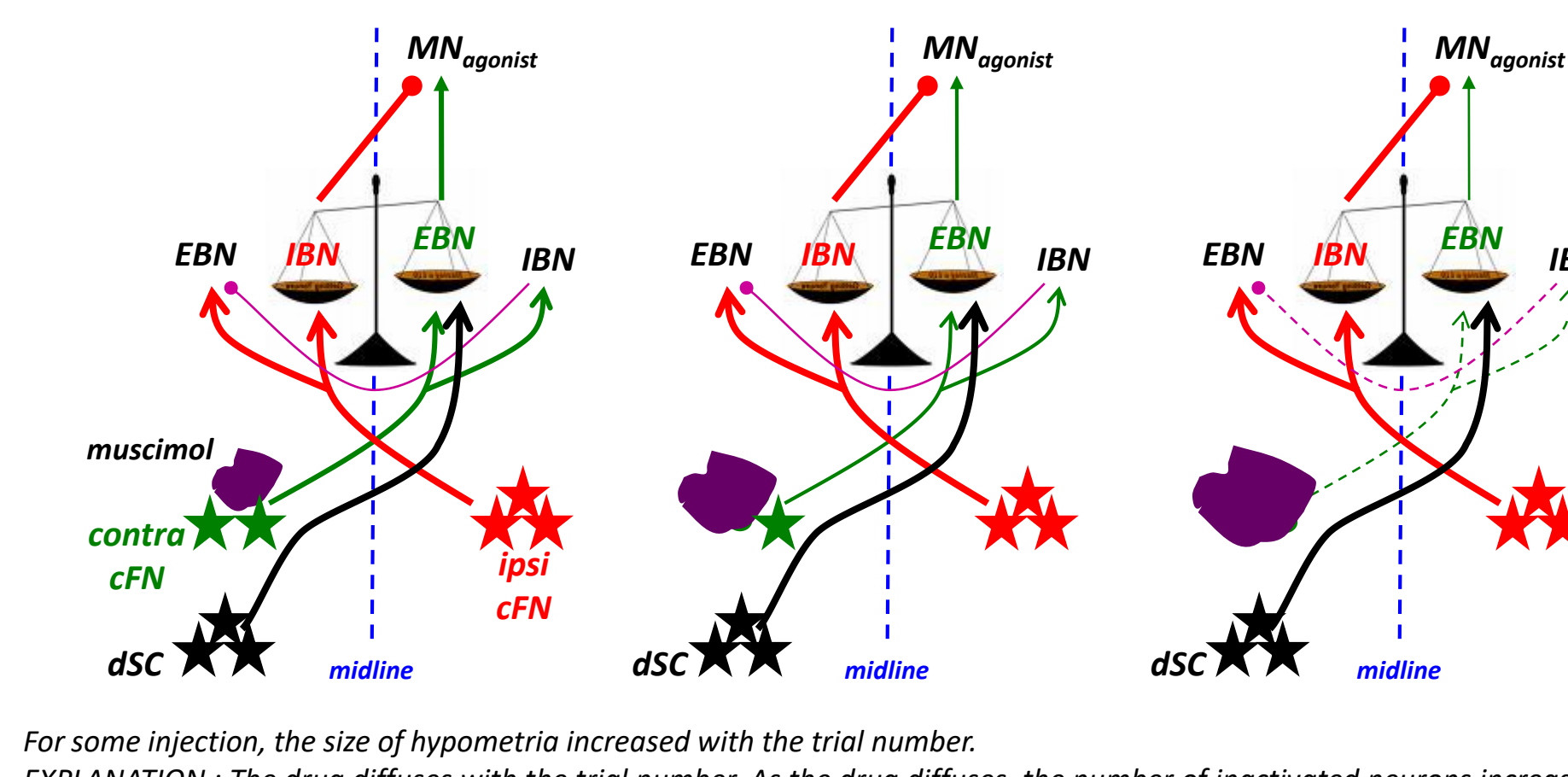
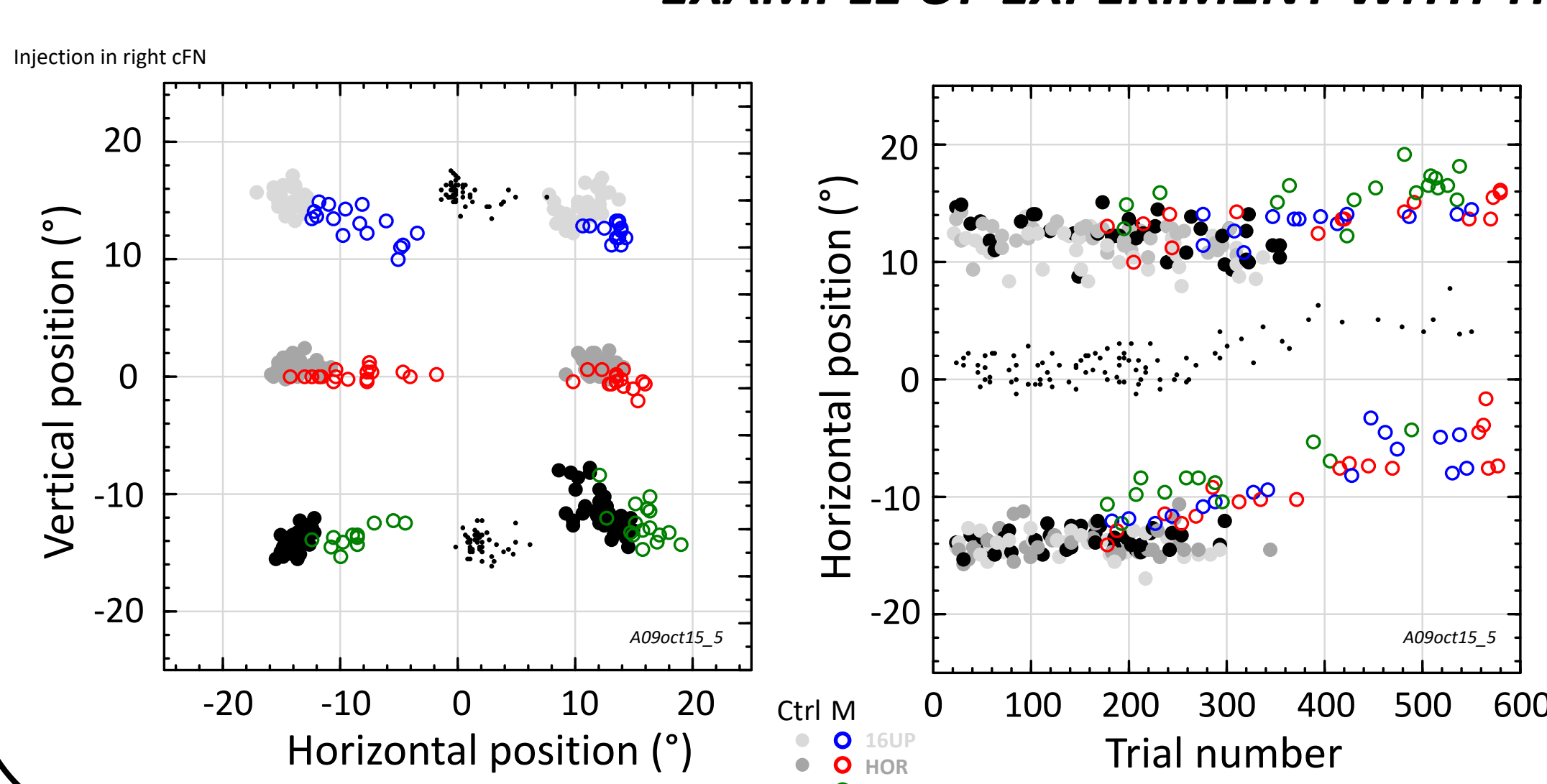


Injection in right cFN



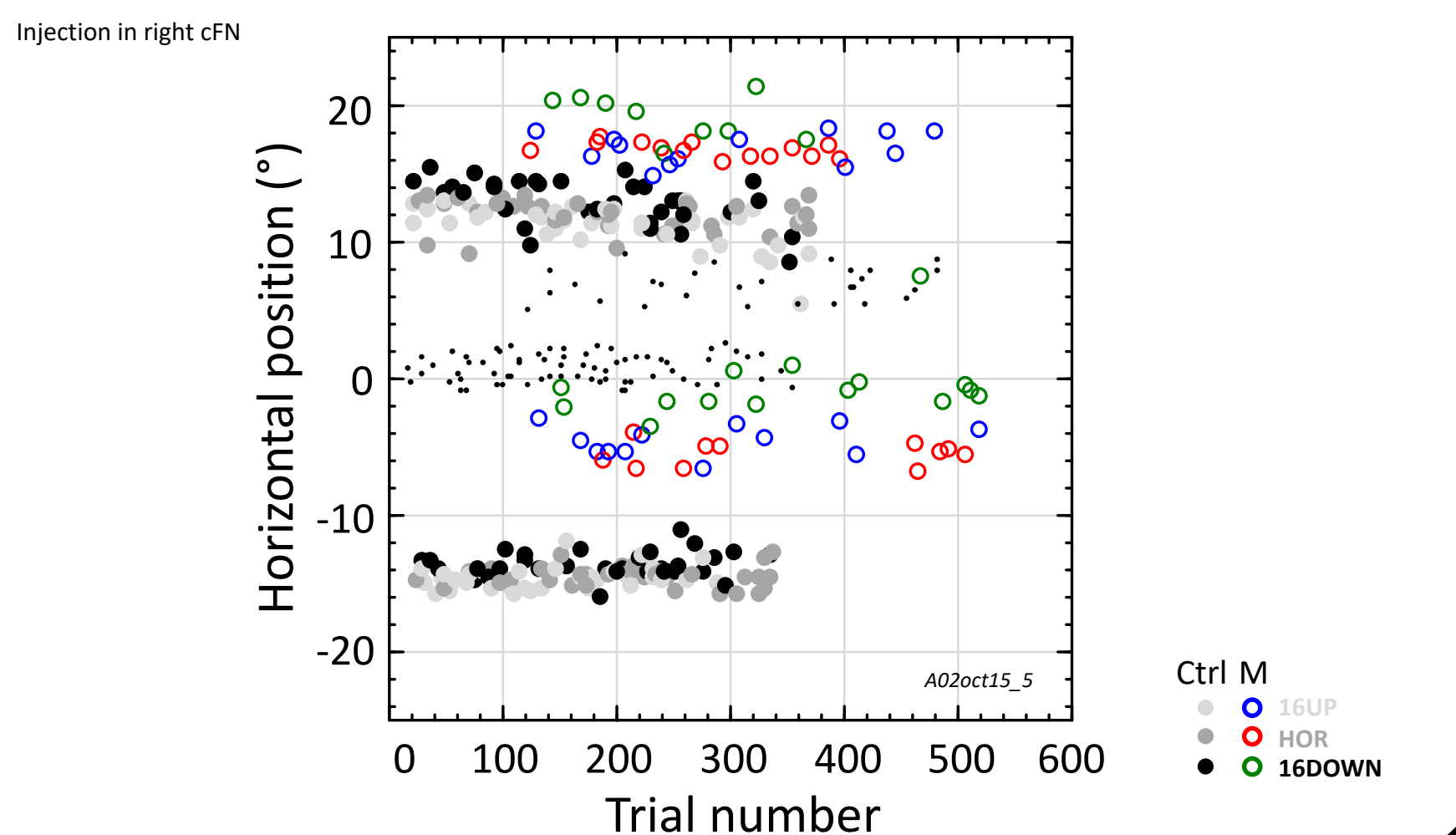
Endpoints of saccades before (●) and after muscimol injection in the left (same injection as in the previous panel) or in the right cFN (○) of the same monkey. The next panel to the right show that the hypometria of contralateral saccades increased during the experiment (top).

EXAMPLE OF EXPERIMENT WITH TIME-DEPENDENT HYPOMETRIA

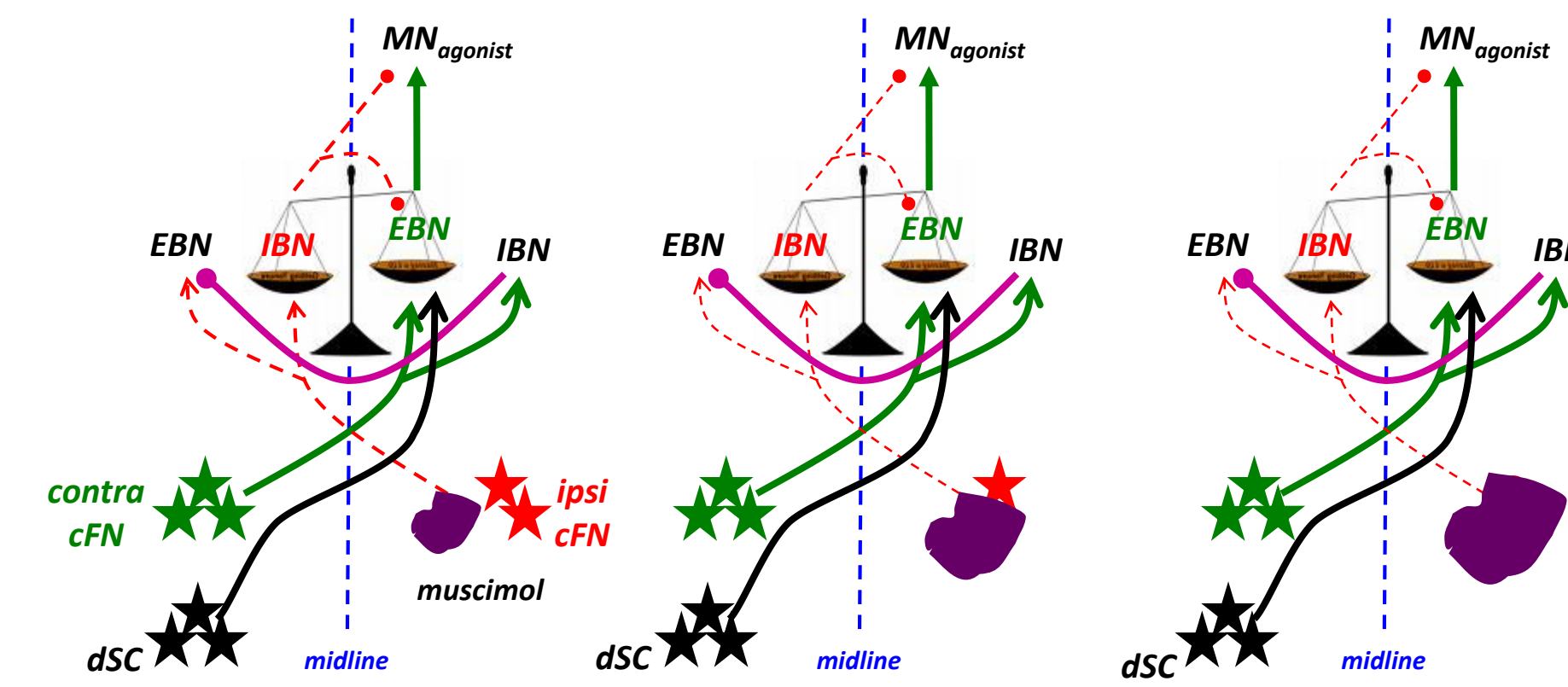
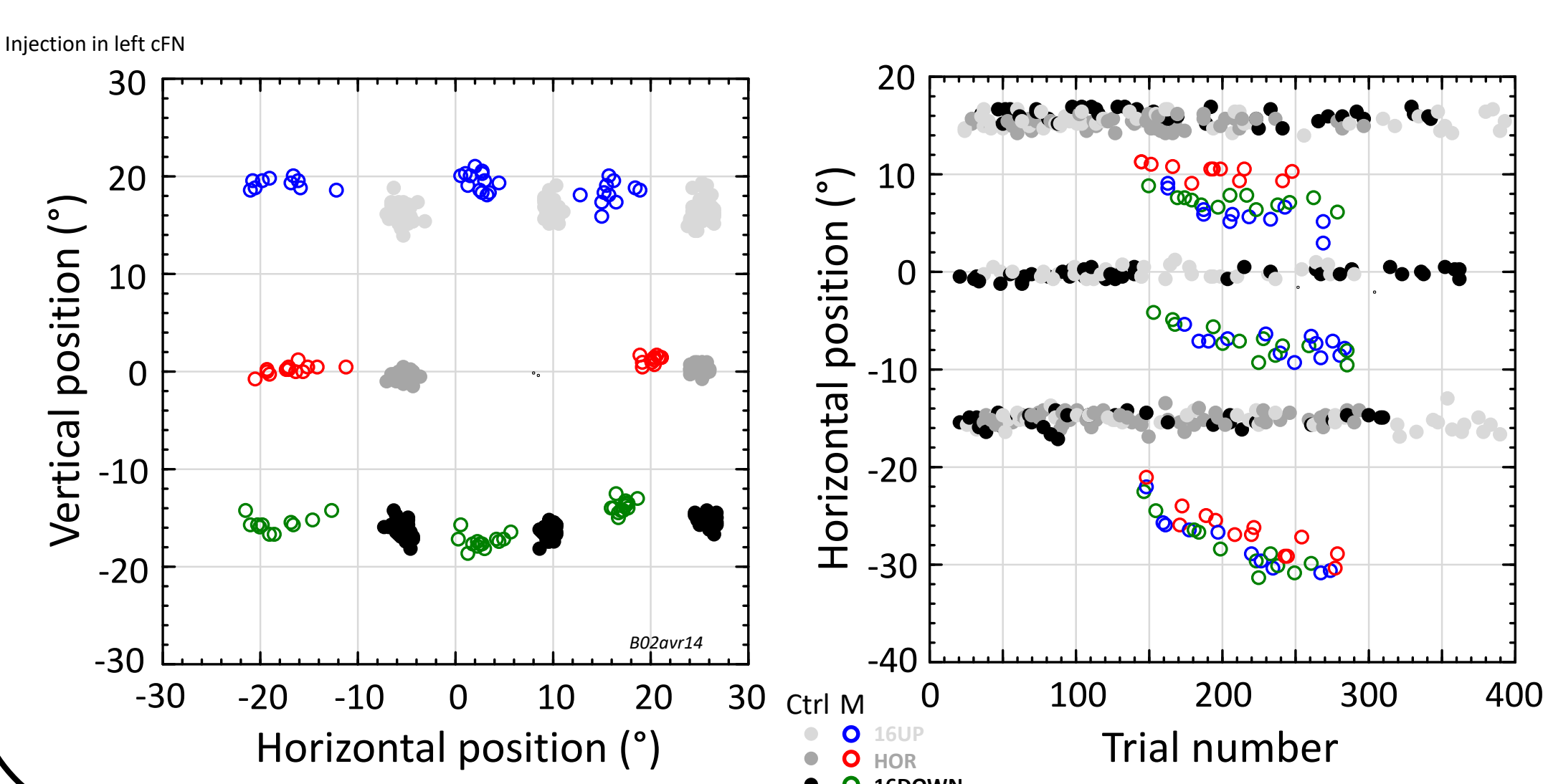


For some injection, the size of hypometria increased with the trial number. EXPLANATION: The drug diffuses with the trial number. As the drug diffuses, the number of inactivated neurons increases (= the number of active neurons diminishes). The reduced number of active neurons diminishes the peak velocity without compensatory increase in saccade duration, leading to hypometric saccades.

ANOTHER EXAMPLE OF EXPERIMENT WITH STABLE DYSMETRIA



EXAMPLE OF EXPERIMENT WITH TIME-DEPENDENT HYPERMETRIA



For some injection, the magnitude of hypermetria increased with the trial number. EXPLANATION: The drug diffuses with the trial number. As the drug diffuses, the number of inactivated neurons increases (= the number of active neurons diminishes). The reduced number of active neurons removes the drive that cFN neurons exert upon neurons (IBNs) inhibiting the agonist motoneurons. This disinhibiting effect increases the peak velocity and/or does not prevent the excitatory EBN input from continuing to drive the motor neurons, leading to hypermetric saccades.

CONCLUSION

There is no need to appeal to various kinds of noise in the brain to explain the variability of saccades after cFN inactivation.

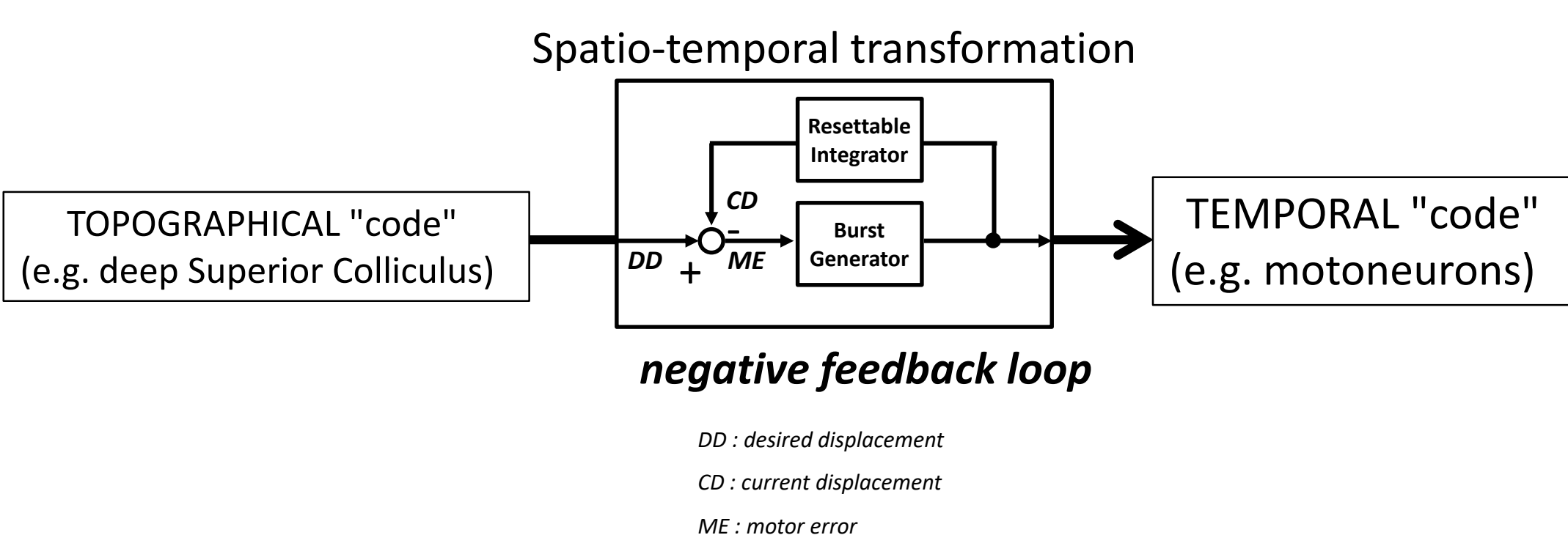
The number of active neurons contributes to the dynamics of saccades

The different evolutions of ipsilesional and contralateral dysmetria suggest that these two deficits are unrelated

Between the topographical and temporal "codes", instead of appealing to a negative feedback loop that reduces a mismatch between internal signals encoding kinematic parameters (desired versus current displacement as estimated from the integration of velocity commandes), we propose that a saccade is the outcome of a process that restores symmetry of activities between commands exerting opposite movement tendencies.

The orienting movement is saccadic for no teleological purpose; it is saccadic merely because the flow of activity from the retinal to the motor neurons involves neurons whose pattern of firing is bursting and also because of fast-twitch properties of extraocular muscles.

CURRENT FRAMEWORK



ALTERNATIVE FRAMEWORK

