

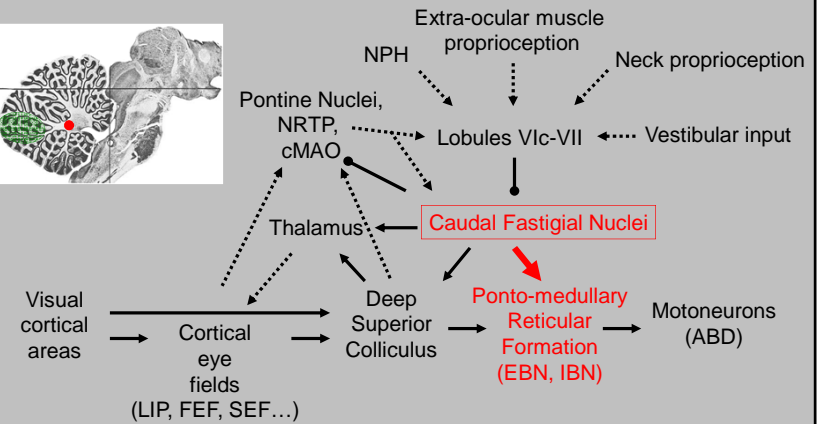
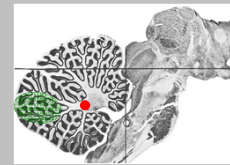
A meeting honoring our memory of late David A. Robinson
 May 26-27, 2017
 Baltimore, USA

Cerebellar control of saccades by the size of the active population in the caudal fastigial nucleus

Laurent Goffart, PhD

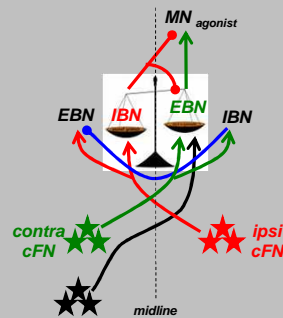
CNRS
 INT, Marseille, France

Fastigio-reticular projections and the cerebellar control of visual saccades



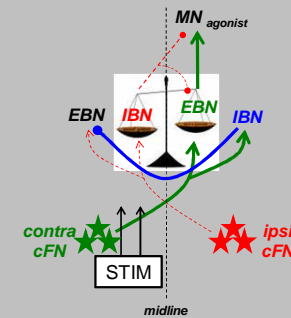
Bilateral hypothesis

For every saccade (horizontal, oblique or vertical), the left and right cFN regulate the dynamic balance of activity between the excitatory and inhibitory input (from EBNs and IBNs) to the motor and internuclear neurons in the abducens nucleus. (Goffart, Chen & Sparks *Journal of Neurophysiology* 2004)



Electrical microstimulation evokes a contralateral saccade

Cogdell B, Hassul M & Kimm J. *Archives of Otolaryngology* 1977
 Noda H, Murakami S, Yamada J, Tamada J, Tamaki Y & Aso T. *Journal of Neurophysiology* 1988
 Quinet J & Goffart L. *Journal of Neurophysiology* 2009 (head free monkey)
 Quinet J & Goffart L. *Journal of Neurophysiology* 2015 (head fixed monkey)



J Neurophysiol 113: 3323–3336, 2015.
 First published March 5, 2015; doi:10.1152/jn.01021.2014.

Cerebellar control of saccade dynamics: contribution of the fastigial oculomotor region

Julie Quinet and Laurent Goffart
 Institut de Neurosciences de la Timone, UMR 7289, Centre National de la Recherche Scientifique, Aix-Marseille Université, Marseille, France
 Submitted 17 December 2014; accepted in final form 26 February 2015

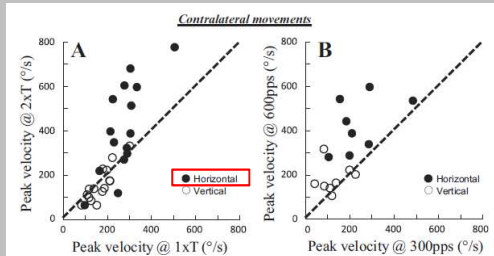
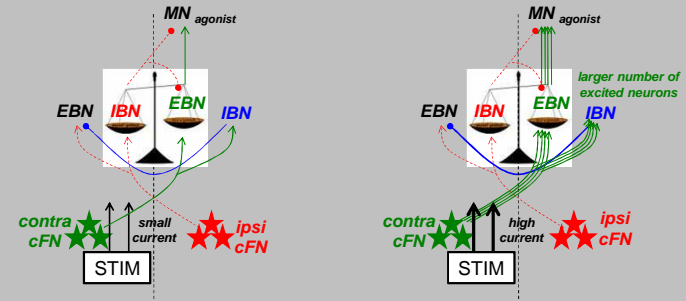


Fig. 6. Effect of increased fastigial activity on peak velocity of contralateral saccades. The effects of doubling the stimulation current (A) and frequency (B) on the average horizontal (filled circles) and vertical peak velocities (open circles) are shown. In A, the stimulation current was increased from 1T to 2T (15 tested sites), whereas in B, the stimulation frequency was increased from 300 to 600 pps (8 sites).

J Neurophysiol 113: 3323–3336, 2015.
 First published March 5, 2015; doi:10.1152/jn.01021.2014.

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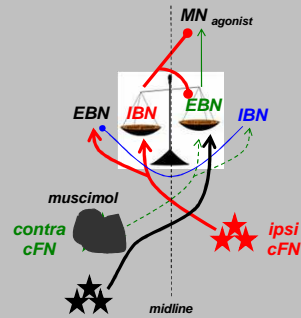
Julie Quinet and Laurent Goffart
 Institut de Neurosciences de la Timone, UMR 7289, Centre National de la Recherche Scientifique, Aix-Marseille Université, Marseille, France
 Submitted 17 December 2014; accepted in final form 26 February 2015



WORKING HYPOTHESIS :
 the cerebellar control of saccade dynamics consists of
 regulating the size of the population of active premotor burst neurons

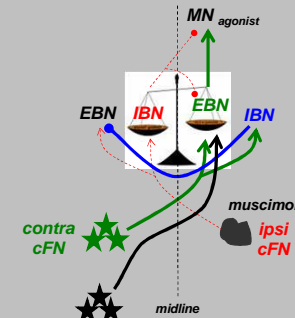
cFN inactivation does not suppress contralateral saccades, but reduces their horizontal velocity and amplitude

Robinson FR, Straube A & Fuchs AF *Journal of Neurophysiology* 1993
 Ohtsuka K, Sato H & Noda H. *Journal of Neurophysiology* 1994
 Goffart L & Pélisson D. *Journal of Neurophysiology* 1994, 1998 (*head free* cat)
 Goffart L, Chen LL & Sparks DL. *Journal of Neurophysiology* 2004
 Quinet J & Goffart L. *Journal of Neurophysiology* 2005, 2007 (*head free* monkey)



cFN inactivation also affects ipsilateral saccades, making their horizontal amplitude hypermetric

Robinson FR, Straube A & Fuchs AF *Journal of Neurophysiology* 1993
 Ohtsuka K, Sato H & Noda H. *Journal of Neurophysiology* 1994
 Goffart L & Pélisson D. *Journal of Neurophysiology* 1994, 1998 (*head free* cat)
 Goffart L, Chen LL & Sparks DL. *Journal of Neurophysiology* 2004
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RESEARCH ARTICLE
Modeling Inter-trial Variability of Saccade Trajectories: Effects of Lesions of the Oculomotor Part of the Fastigial Nucleus
 Thomas Egger^{1*}, Farrel R. Robinson², Andreas Straube¹
¹ Department of Neurology, Ludwig-Maximilians University, Munich, Germany, ² Department of Biological Structure, University of Washington, Seattle, Washington, United States of America

PLOS Computational Biology | DOI:10.1371/journal.pcbi.1004866 June 28, 2016

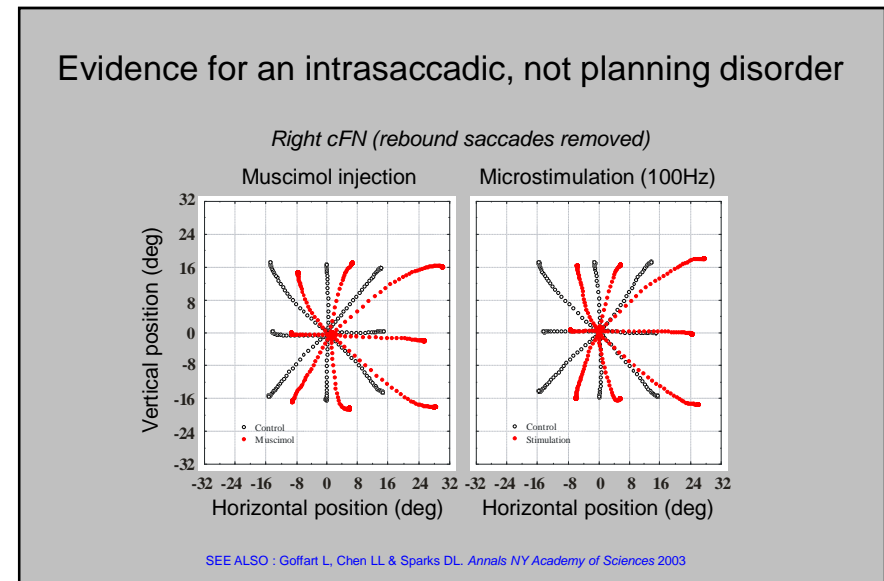
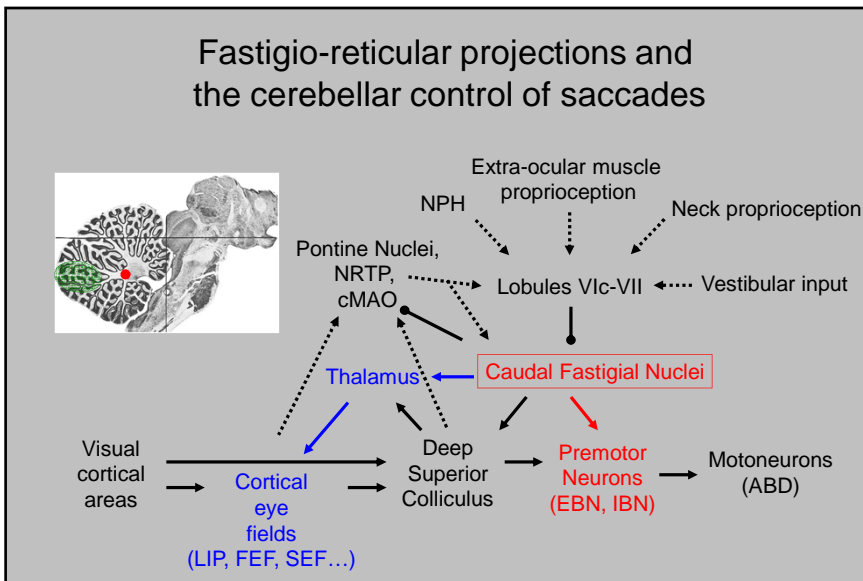
This study investigates the inter-trial variability of saccade trajectories observed in five rhesus macaques (*Macaca mulatta*). For each time point during a saccade, the inter-trial variance of eye position and its covariance with eye end position were evaluated. Data were modeled by a superposition of three noise components due to 1) planning noise, 2) signal-dependent motor noise, and 3) signal-dependent premotor noise entering within an internal feedback loop. Both planning noise and signal-dependent motor noise (together called accumulating noise) predict a simple S-shaped variance increase during saccades, which was not sufficient to explain the data. Adding noise within an internal feedback loop enabled the model to mimic variance/covariance structure in each monkey, and to estimate the noise amplitudes and the feedback gain. Feedback noise had little effect on end point noise, which was dominated by accumulating noise. This analysis was further extended to saccades executed during inactivation of the caudal fastigial nucleus (cFN) on one side of the cerebellum. Saccades ipsiversive to an inactivated cFN showed more end point variance than did normal saccades. During cFN inactivation, eye position during saccades was statistically more strongly coupled to eye position at saccade end. The proposed model could fit the variance/covariance structure of ipsiversive and contraversive saccades. Inactivation effects on saccade noise are explained by a decrease of the feedback gain and an increase of planning and/or signal-dependent motor noise. The decrease of the fitted feedback gain is consistent with previous studies suggesting a role for the cerebellum in an internal feedback mechanism. Increased end point variance did not result from impaired feedback but from the increase of accumulating noise. The effects of cFN inactivation on saccade noise indicate that the effects on motor noise cannot be explained entirely with the cFN's direct connections to the saccade-related premotor centers in the brainstem.

"planning noise" = "all noise sources that contribute to the variability of the planned saccade amplitude" (page 3)
 i.e.,
 "non-motor noise affecting sensory processing, target selection, and cortical representations of the initial motor error" (page 3)

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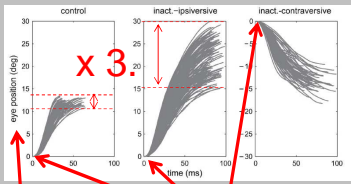


Is the endpoint variance increased for ipsilesional saccades ?

RESEARCH ARTICLE
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PLOS Computational Biology | DOI:10.1371/journal.pcbi.1004866 June 28, 2016



Not position but amplitude !
 NOT EXACT

J Neurophysiol 102: 3351–3367, 2004. First published June 30, 2004; doi:10.1152/jn.01199.2003.
Deficits in Saccades and Fixation During Muscimol Inactivation of the Caudal Fastigial Nucleus in the Rhesus Monkey

Laurent Goffart,^{1,2,3} Longfang L. Chen,² and David L. Sparks^{1,2}
¹Department of Psychology, University of Pennsylvania, Philadelphia, Pennsylvania 19104, ²Department of Neuroscience, Baylor College of Medicine, Houston, Texas 77030, and ³Service Dynamique de la Vision et de l'Action, Institut de Neurosciences Cognitives de la Méditerranée, UMR 5186 de Recherche CNRS Centre National de la Recherche Scientifique—Université de la Méditerranée, 13402 Marseille, France

TABLE 1. Comparison of the horizontal and vertical position of the eye prior to the saccade toward the target LED before and after muscimol injection in the cFN

Experiments	Injection	Session	n	Horizontal Eye Position			Vertical Eye Position		
				Mean	Range	Difference	Mean	Range	Difference
G1	Left cFN (0.8 μM)	Control	378	-0.5 ± 0.6	-1.8–1.31	-1.2*	0.6 ± 0.6	-1.5–1.81	0.4*
	Muscimol	614	-1.7 ± 1.0	-6.95–2.01		0.4 ± 0.6	-1.6–3.08		
G2	Left cFN (0.8 μM)	Control	605	0.6 ± 0.6	-1.1–2.43	-2.4*	0.2 ± 0.7	-2.2–3.71	-0.1 NS
	Muscimol	522	-1.8 ± 1.5	-6.84–0.61		0.1 ± 0.7	-0.6–0.61		
G3	Left cFN (0.8 μM)	Control	782	0.6 ± 0.5	-1.8–2.31	-1.2*	0.1 ± 0.7	-2.5–2.46	-0.3*
	Muscimol	1071	-1.2 ± 1.2	-5.25–2.71		-0.2 ± 0.6	-3.0–2.46		
G4	Right cFN (0.6 μM)	Control	680	-0.2 ± 1.0	-5.53–2.31	2.8*	0.2 ± 0.9	-3.0–3.11	-0.2*
	Muscimol	962	1.8 ± 1.3	-5.53–0.61		0.1 ± 0.8	-1.1–3.31		
J1	Left cFN (1.0 μM)	Control	333	0.0 ± 0.6	-1.53–2.31	-1.4*	0.1 ± 0.8	-1.1–3.31	0.1 NS
	Muscimol	341	-1.4 ± 1.1	-6.43–0.61		-0.4 ± 0.6	-2.2–2.08		
J2	Right cFN (0.6 μM)	Control	190	0.1 ± 0.7	-1.13–0.91	-1.3*	-0.2 ± 0.4	-1.73–0.91	-0.4*
	Muscimol	376	-1.2 ± 0.8	-3.43–0.61	-0.4*	-0.9 ± 0.4	-2.4–0.91		
J4	Right cFN (0.8 μM)	Control	470	-0.4 ± 0.7	-2.4–3.31	0.8*	-0.2 ± 0.4	-1.4–1.31	-0.2*
	Muscimol	396	0.1 ± 0.6	-2.4–3.31		0.0 ± 0.4	-1.23–1.91		
J5	Left cFN (0.8 μM)	Control	422	0.9 ± 0.7	-0.33–2.31	-1.0*	-1.0 ± 0.4	-2.2–0.71	-0.1*
	Muscimol	471	0.0 ± 0.8	-2.4–2.21	-0.3*	0.0 ± 0.5	-1.6–2.11		
J7	Right cFN (1.2 μM)	Control	609	-0.3 ± 0.8	-5.2–2.31	0.3*	-0.1 ± 0.5	-1.6–1.61	0.2*
	Muscimol	38	0.3 ± 0.8	-2.0–3.31		0.1 ± 0.8	-1.4–2.31		

Differences were 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.

Increased variability of starting positions

Is the endpoint variance increased for ipsilesional saccades ?

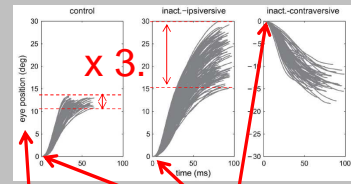
RESEARCH ARTICLE
Modeling Inter-trial Variability of Saccade Trajectories: Effects of Lesions of the Oculomotor Part of the Fastigial Nucleus

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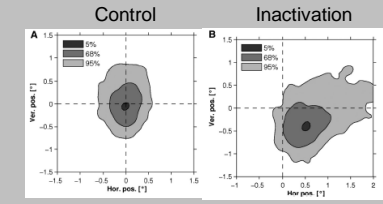
PLOS Computational Biology | DOI:10.1371/journal.pcbi.1004866 June 28, 2016

J Neurophysiol 101: 1088–1091, 2009. First published February 3, 2009; doi:10.1152/jn.00771.2009.
Fastigial Oculomotor Region and the Control of Foveation During Fixation

Lorenzo Guerrato,¹ Julie Quintet,² Ulrich Rüttner,³ and Laurent Goffart¹
¹Department of Neurology, Klinikum Großhadern, LMU, Munich, Germany; ²Unité 534, Institut National de la Santé et de la Recherche Médicale/Université Claude Bernard Lyon 1, FFR; ³Institut Fédératif des Neurosciences de Evry, Evry, France; and ⁴Unité de Neurosciences Cognitives de la Méditerranée, Unité Mixte Recherche 6193, Centre National de la Recherche Scientifique, Aix-Marseille Université, Marseille, France

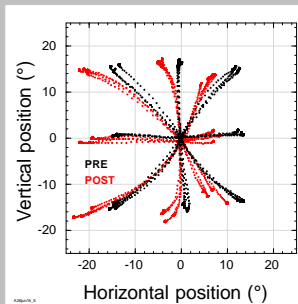


Not position but amplitude !
 NOT EXACT

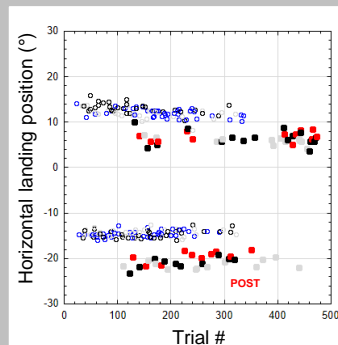


Increased variability of starting positions due to :
 - shifted centroid of positions **AND**
 - horizontal dysmetria of fixational saccades

No increase of endpoint variance for ipsilesional saccades

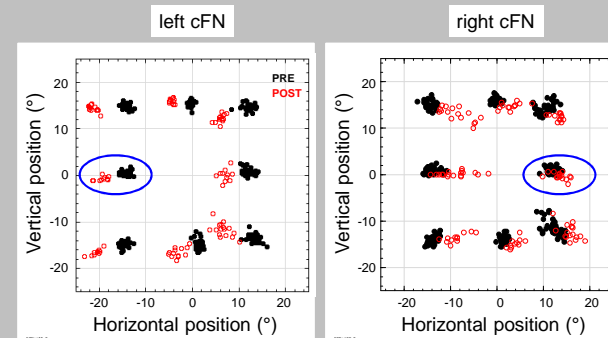


flashed target (100 ms)
 gap = 200 ms
 Other possible target locations
 (+/-8,0); (0,+/-8); (+/-8,+/-8)



PRE POST
 ○ ● 16UP
 ○ ● HOR
 ○ ● 16DOWN

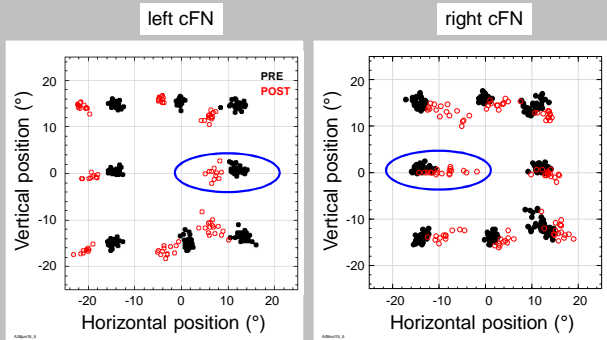
Searching for symmetry



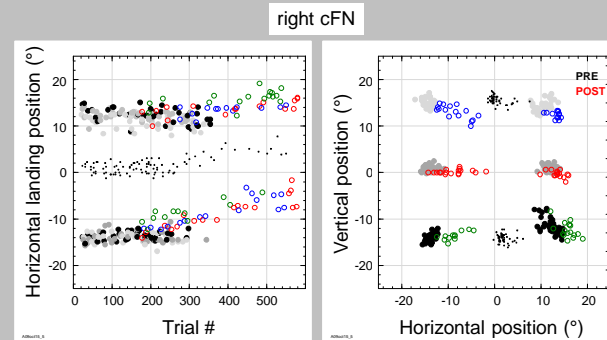
Larger hypermetria

Smaller hypermetria

Searching for symmetry

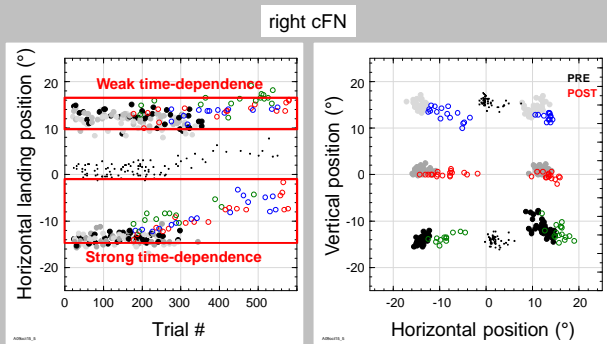


Increased endpoint variability for contralesional saccades !!!



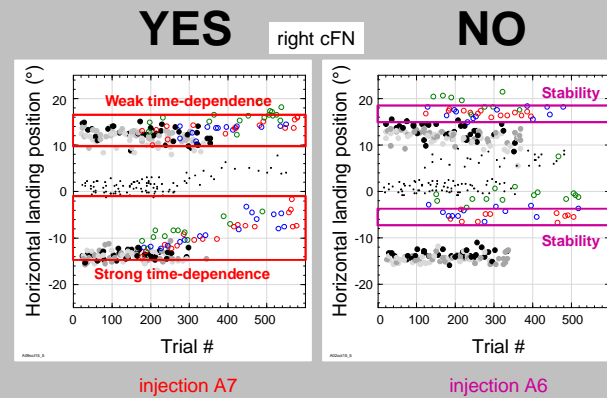
Other possible target locations (+/-8,0); (0,+/-8); (+/-8,+/-8)

Time-dependent endpoint variability for contralesional saccades



Other possible target locations (+/-8,0); (0,+/-8); (+/-8,+/-8)

Time-dependent endpoint variability for contralesional saccades depends upon the experiment



For some injection, the magnitude of hypometria increases with the trial number.

The drug diffuses with the trial number.

As the drug diffuses, the number of inactivated neurons increases = the number of active neurons diminishes

Reduced number of active neurons → reduced peak velocity → enhanced hypometria
insufficient duration

Time-dependent endpoint variability also possible for only ipsilesional saccades

As the drug diffuses, the number of active neurons diminishes

Reduced number of active neurons → enhanced duration
unchanged peak velocity } enhanced hypermetria
enhanced

Enhanced duration is due to : - desinhibited residual input from descending commands
- due to prolonged inhibition of OPN by the agonist drive

Saccade duration and the local feedback control

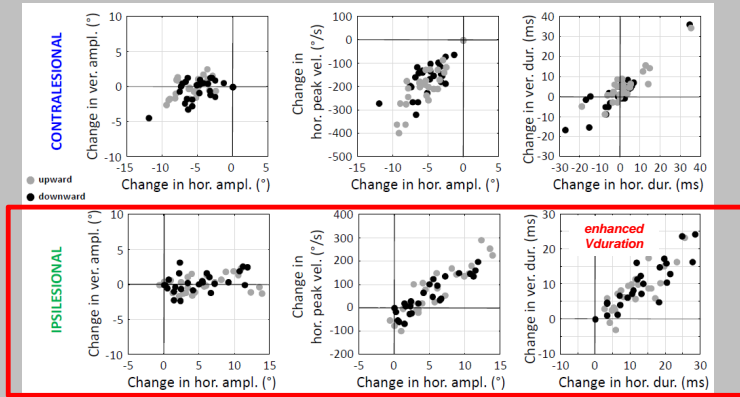
Coupling between the Horizontal and Vertical Saccade
Generators after Inactivation of the Caudal Fastigial Nucleus
in the Monkey

Goffart, Koene & Quinet *SFN abstr.* 2005
Goffart, Koene & Quinet 2005 *rejected*

reduced feedback gain during ipsilesional saccades → longer H duration → longer V duration

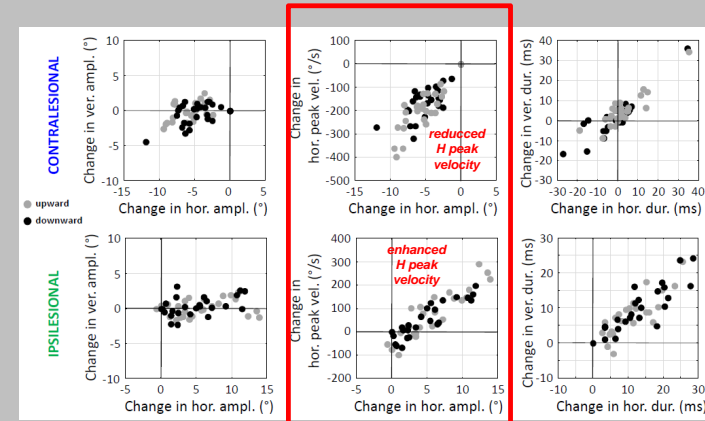
Oblique saccades

25 muscimol injections in the cFN of 4 monkeys



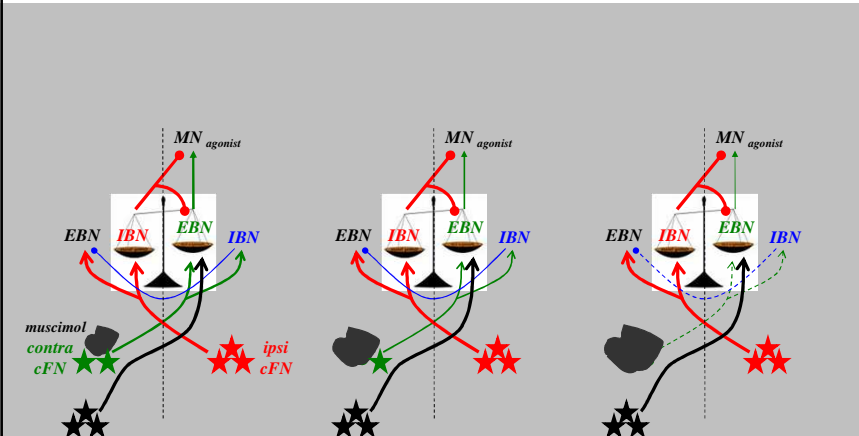
CONCLUSION

1. **BOTH** cFN contribute to accelerate **AND** decelerate the horizontal component of any saccade



CONCLUSION : the bilateral mass hypothesis

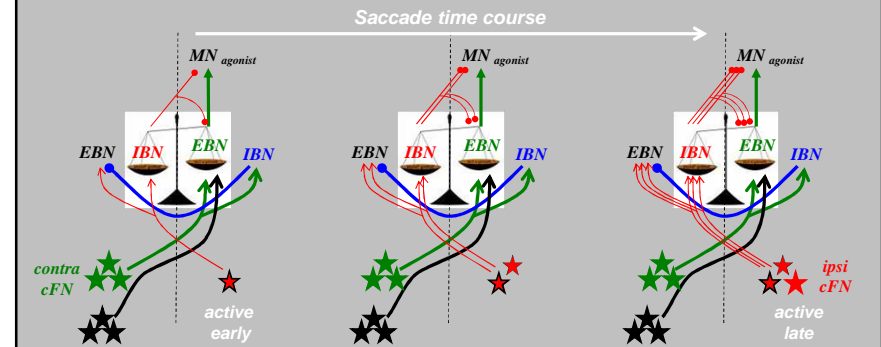
1. **BOTH** cFN contribute to accelerate **AND** decelerate the horizontal component of any saccade
2. The **NUMBER** of active neurons in **BOTH** cFN matters in the specification of saccade dynamics



CONCLUSION : the bilateral mass hypothesis

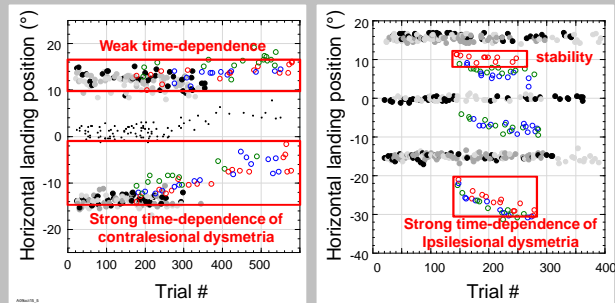
1. **BOTH** cFN contribute to accelerate **AND** decelerate the horizontal component of any saccade
2. The **NUMBER** of active neurons in **BOTH** cFN matters in the specification of saccade dynamics
3. The late burst of some neurons in the ipsilateral cFN is the signature of a **RECRUITMENT**

Ohtsuka K & Noda H. *Journal of Neurophysiology* 1991
 Fuchs AF, Robinson FR & Straube A. *Journal of Neurophysiology* 1993
 Kleine JF, Guan Y & Büttner U. *Journal of Neurophysiology* 2003



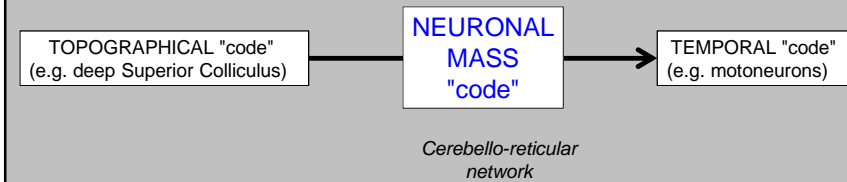
CONCLUSION : the bilateral mass hypothesis

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4. Different evolutions of ipsi/contra-lesional dysmetria suggest **DISTINCT ROUTES** to EBN/IBNs



CONCLUSION : the bilateral mass hypothesis

1. **BOTH** cFN contribute to accelerate **AND** decelerate the horizontal component of any saccade
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3. The late burst of some neurons in the ipsilateral cFN is the signature of a **RECRUITMENT**
4. Different evolutions of ipsi/contra-lesional dysmetria suggest **DISTINCT ROUTES** to EBN/IBNs
5. Between the topographical and temporal "codes", the **NEURONAL MASS** "code"



neuronal mass = the **number of active neurons** contributing to the agonist burst

Gratefulness and thanks for their support



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Lorenzo GUERRASIO

Ulrich BÜTTNER

Julie QUINET

Clara BOURRELLY

Patrick CAVANAGH

Human Frontier Science Program



POSITION (P. Cavanagh)



The past is neither behind nor can it be erased ; it is below, moving the present upward ...