


Marseille, Laboratoire de Neurosciences Intégratives et Adaptatives
 2010 January 14th

Structure and function : in search for the (neuro)biological foundations of visuomotor space

Laurent Goffart

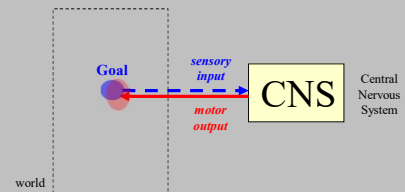
CNRS

Institut de Neurosciences Cognitives de la Méditerranée
Marseille, France

Neural representations of target location : sensory and motor

In most goal-directed movements, there is a spatial congruence between :

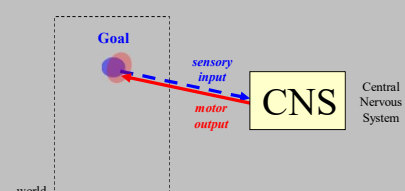
- the source of sensory stimuli and
- the endpoint of movements directed toward this source



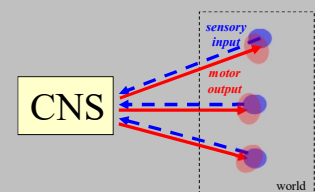
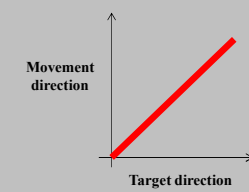
Neural representations of target location : sensory and motor

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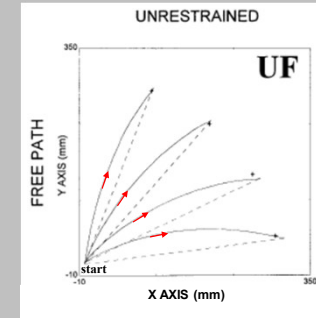
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- the endpoint of movements directed toward this source



Sensorimotor mapping with one-to-one correspondence (\pm variability)

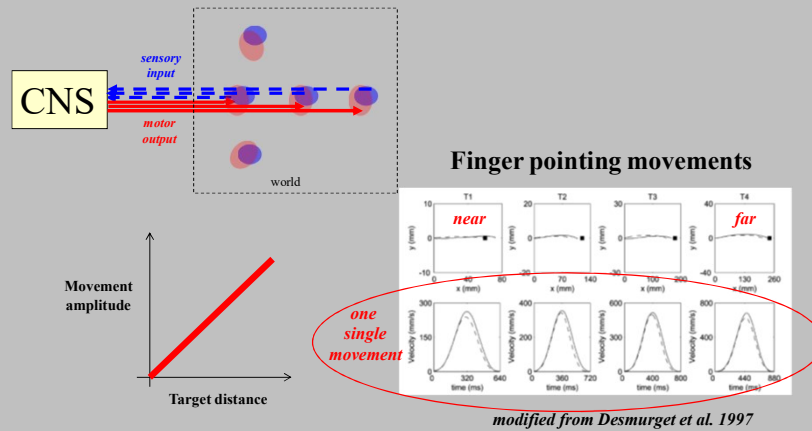



Finger pointing movements

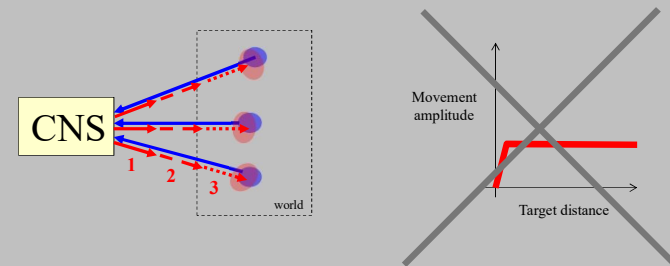


modified from Desmurget et al. 1997

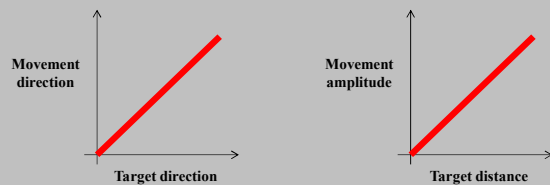
Sensorimotor mapping with one-to-one correspondence



In normal conditions, simple goal-directed movements **are not** performed by appending elementary movement units



Goal-directed movements follow some spatial rules.



How are these rules implemented in the brain ?

How are they determined ?

Neck and eye proprioception contribute to the spatial control of pointing movements

NECK MUSCLE VIBRATION MODIFIES THE REPRESENTATION OF VISUAL MOTION AND DIRECTION IN MAN

by B. BIGUER,¹ I. M. L. DONALDSON,² A. HEIN³ and M. JEANNEROD¹
 (From the ¹Laboratoire de Neuropsychologie Expérimentale, INSERM Unité 94, Bron, France, ²Department of Pharmacology, University of Edinburgh, Edinburgh, UK, and ³Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA)

Brain 1988

The Role of Ocular Muscle Proprioception in Visual Localization of Targets

GABRIEL M. GAUTHIER, DANIELLE NOMMAY, JEAN-LOUIS VERCHER

Science 1989

Eye and neck proprioceptive messages contribute to the spatial coding of retinal input in visually oriented activities

R. Roll, J.L. Velay, and J.P. Roll
 Laboratoire de Neurobiologie Humaine - URA CNRS 372, Université de Provence, Avenue Escadillon Normande Niemen, F-13397 Marseille Cedex 13, France

Exp Brain Res 1991

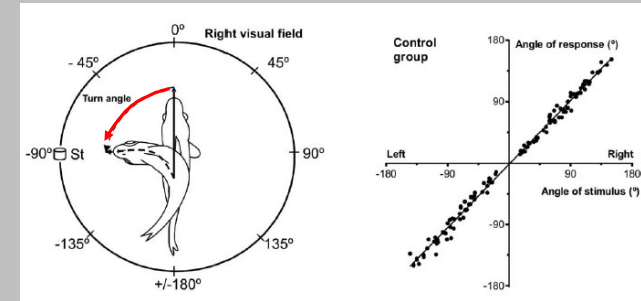
Neck and eye proprioception contribute to the spatial control of pointing movements

But

Orienting movements of the eyes, of the head and of the body also follow spatial rules.

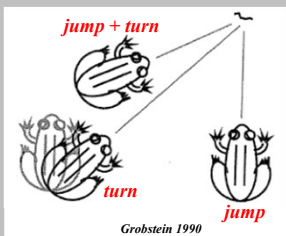
The spatial properties of pointing/reaching movements could originate from the gaze orienting system (see misreaching with prismatic spectacles)

Orienting movement of the mouth in the goldfish



Torres et al. Brain Res. Bull. 2005

Orienting movement of the body in the frog



Grobstein 1990

Result of first reaction : orient the field of sensorimotor interactions toward the target

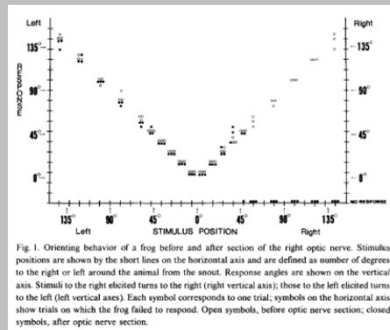


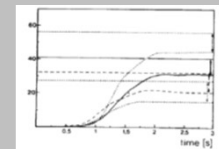
Fig. 1. Orienting behavior of a frog before and after section of the right optic nerve. Stimulus positions are shown by the short lines on the horizontal axis and are defined as number of degrees to the right or left around the animal from the snout. Response angles are shown on the vertical axis. Stimuli to the right elicited turns to the right (right vertical axis); those to the left elicited turns to the left (left vertical axis). Each symbol corresponds to one trial; symbols on the horizontal axis show trials on which the frog failed to respond. Open symbols, before optic nerve section; closed symbols, after optic nerve section.

Kostyk & Grobstein 1982

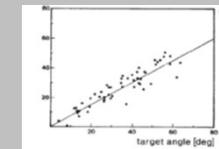
Orienting movement of the head in the salamander



Schülert & Dicke J. Exp Biol 2002

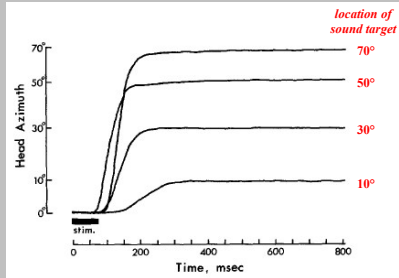


avec distracteur



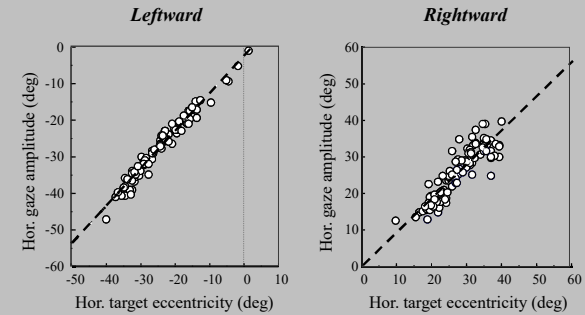
Werner & Himstedt Zool. Jb. Physiol. 1985

Orienting movement of the head in the barn owl



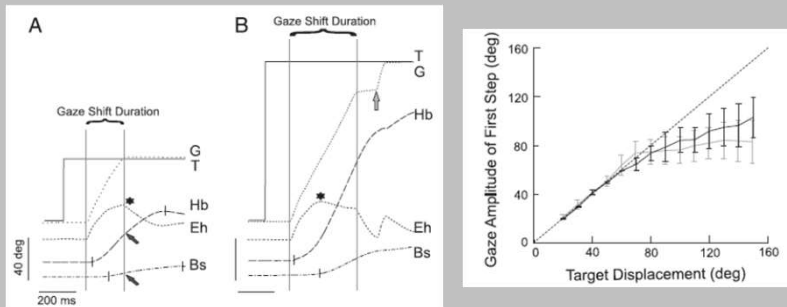
Knudsen, Blasdel & Konishi JCP 1979

Orienting gaze shifts in the cat (head free, open loop)



modified from Goffart & Pélisson JNP 1994

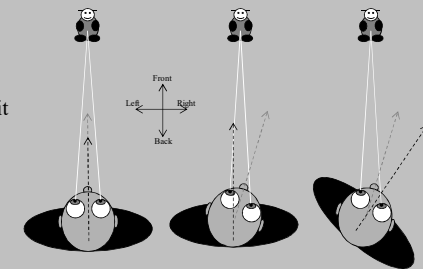
Orienting gaze shifts in the monkey (head free)



McCluskey & Cullen JNP 2007

Gaze = field of visuomotor interactions

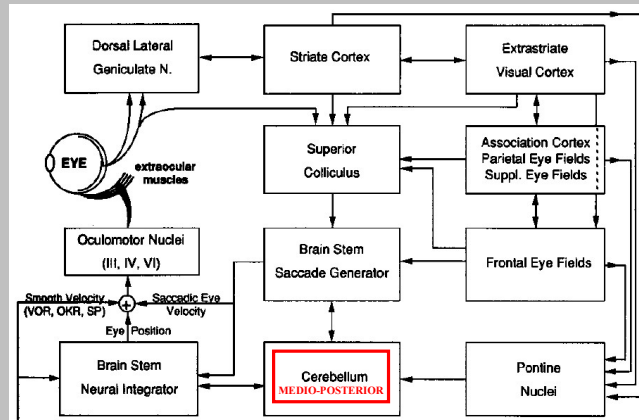
Gaze orientation
 =
 Orientation of the eyes in the orbit
 +
 Orientation of the head / trunk
 +
 Orientation of the trunk / hip



Depending on the context, orienting gaze shifts are ensured by :

- a movement of both eyes (eye saccade)
- a combined movement of the eyes and the head
- a movement involving the eyes, the head and the trunk

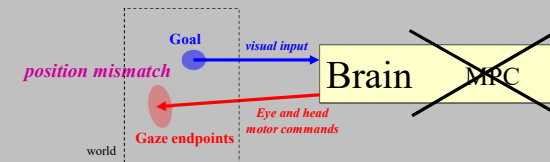
Several brain regions between the retinal activation and the contraction of extra-ocular muscles (in less than 300 ms)



The medio-posterior cerebellum (MPC) and the control of orienting gaze shifts

Dysfunction of MPC leads to gaze **dysmetria** i.e. it alters the spatial congruence between :

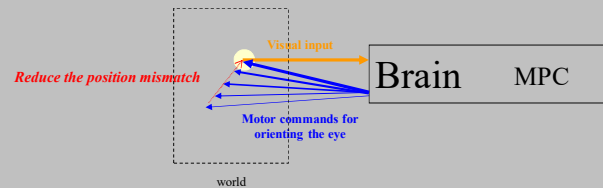
- the location of a visual event
- the endpoint of gaze shifts towards it



How does the cerebellum help us to reach a goal ?

Adaptive control of saccade accuracy

The function of the MPC is to build or re-establish the spatial congruence (visuo-motor calibration) that could be disrupted: from eye muscle weakening, from intrasaccadic target step (in the laboratory), from some brain injury ...



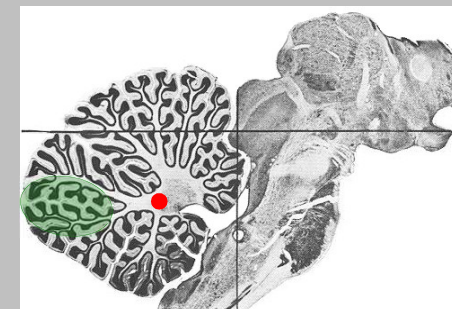
The medio-posterior cerebellum

Lobules VIc-VII

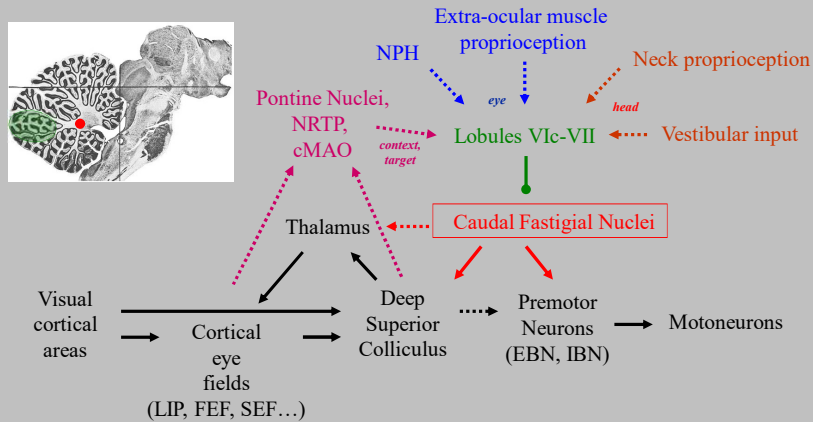


caudal Fastigial Nuclei
(Fastigial Oculomotor Regions)

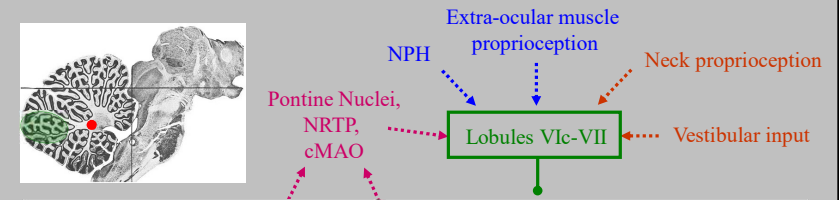
Saccade-related activity
Pursuit-related activity



The medio-posterior cerebellum



MPC : a space-time metric tensor for orienting gaze ?



SPACE-TIME REPRESENTATION IN THE BRAIN.
THE CEREBELLUM AS A PREDICTIVE
SPACE-TIME METRIC TENSOR

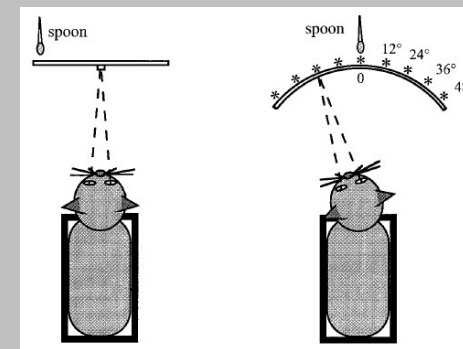
A. PELLIONISZ and R. LLINÁS
Department of Physiology and Biophysics, New York University Medical Center,
550 First Avenue, New York, NY 10016, U.S.A.

Neuroscience 1982

Part #1

Effects of unilateral inactivation of
the caudal fastigial nucleus (cFN) on
orienting gaze shifts
in the head unrestrained cat

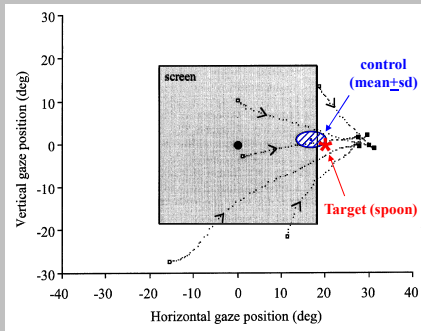
Testing conditions



Gaze and head movements recorded with the search coil technique (Eye = Gaze - Head) before and after injecting a small amount of muscimol in the caudal Fastigial Nucleus (0.3µl, 1µg/µl)

Ipsilesional gaze shifts

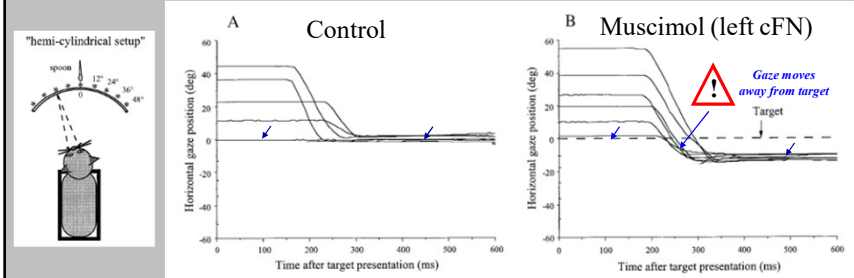
Muscimol injection in the right cFN (0.3 μ l; 1 μ g/ μ l; cat F)



modified from Goffart & Pélisson JNP 1998

Ipsilesional gaze shifts

Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat I)

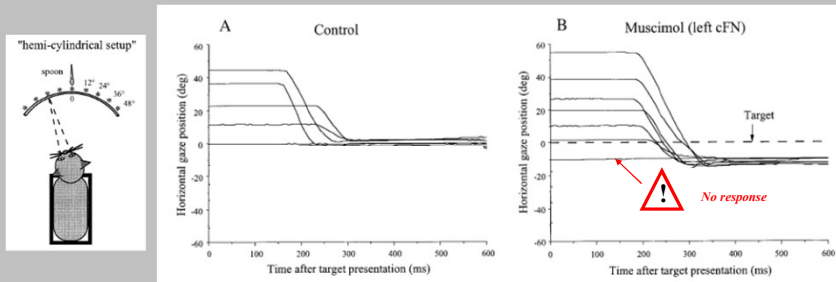


modified from Goffart & Pélisson JNP 1998

Ipsilesional gaze shifts

Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat I)

Muscimol injection in the left cFN (0.3 μ g)

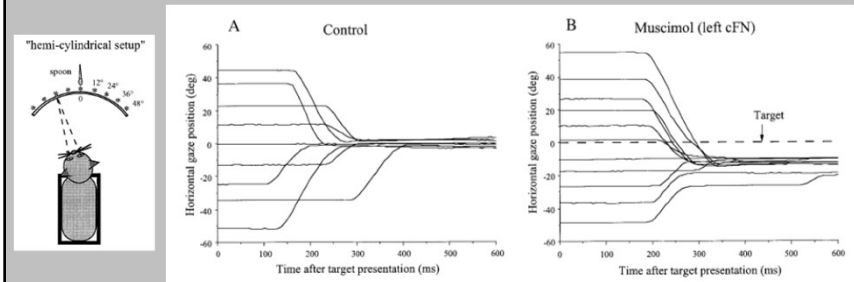


modified from Goffart & Pélisson JNP 1998

Ipsilesional and contralesional gaze shifts

Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat I)

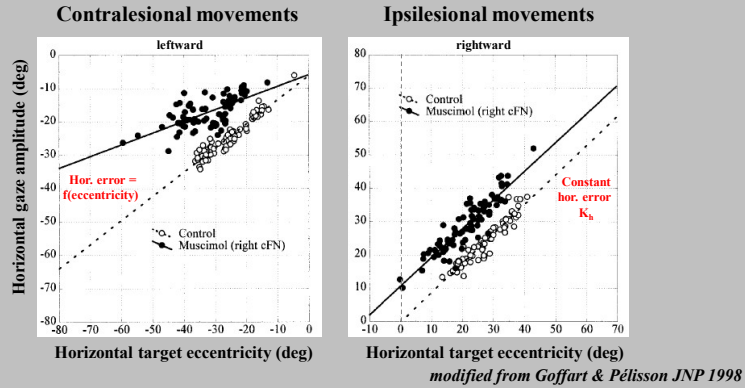
Muscimol injection in the left cFN (0.3 μ g)



modified from Goffart & Pélisson JNP 1998

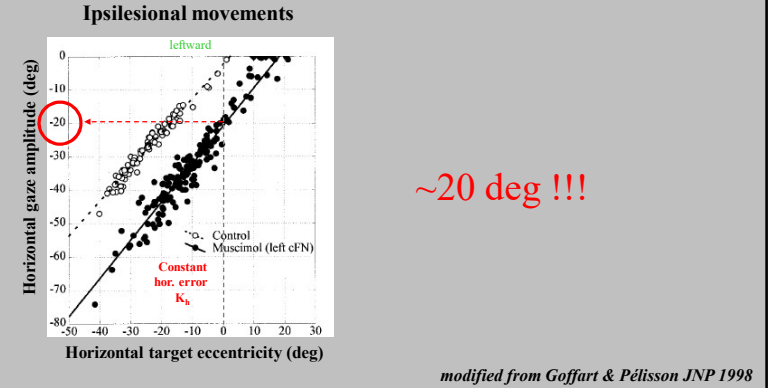
Gaze dysmetria

Muscimol injection in the right cFN (0.3 μ l; 1 μ g/ μ l, cat F)



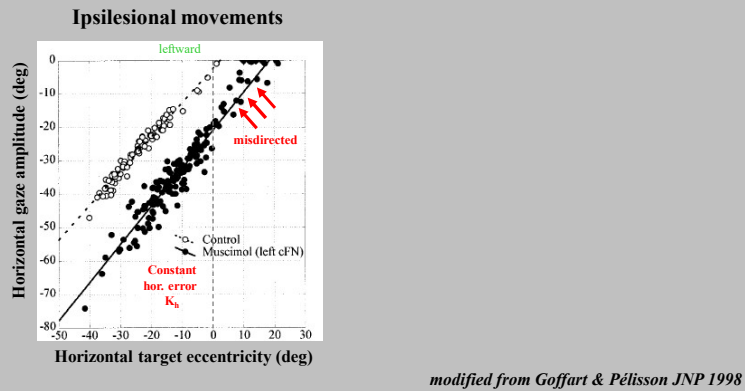
Gaze dysmetria

Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat G)



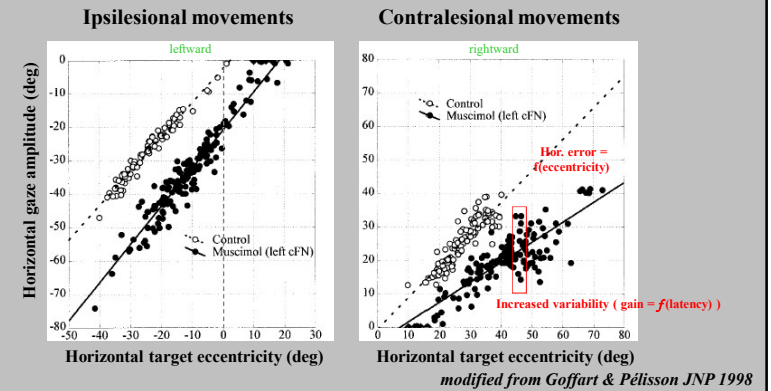
Gaze dysmetria

Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat G)



Gaze dysmetria

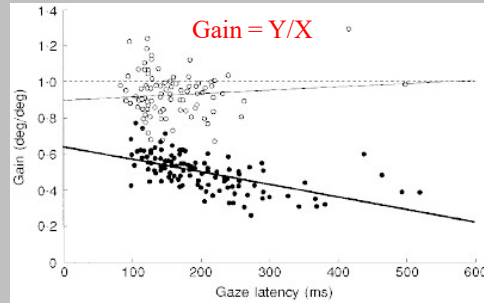
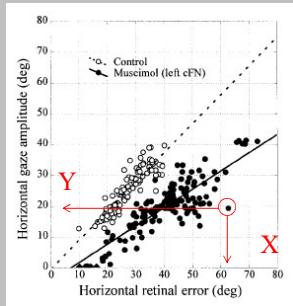
Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat G)



Relationship dysmetria - latency

Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat G)

Contralesional movements



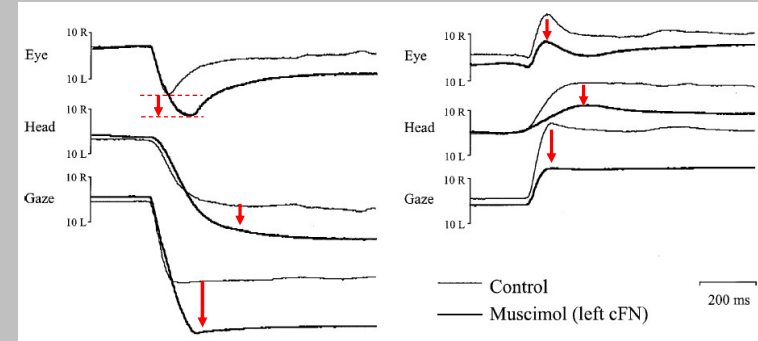
modified from Goffart & Pélisson JPhysiol 1997

Dysmetria affects both eye and head movements

Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat G)

Ipsilesional HYPERmetria

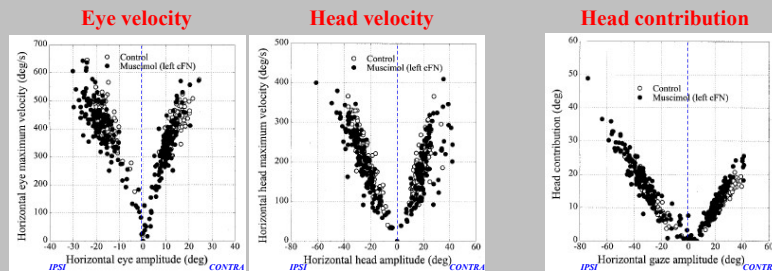
Contralesional HYPOmetria



modified from Goffart, Pélisson & Guillaume. JNP 1998

No sign of movement execution disorder

Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat G)



modified from Goffart, Pélisson & Guillaume. JNP 1998

Conclusion (1)

cFN inactivation in the head unrestrained cat

Ipsilesional gaze hypermetria

Contralesional gaze hypometria

- Dysmetria affects both eye and head components \rightarrow **GAZE DEFICIT**

- No sign of execution disorder (no change in eye or head velocity, no change in eye-head coupling)

\rightarrow **DEFICIT BEFORE MOVEMENT ONSET**

- Final hor. error = K

- misdirected movements

- Final hor. error = f (target eccentricity, latency)

\rightarrow **DEFICIT IN THE SPATIAL SPECIFICATION OF THE GOAL**

Control (pre-injection)



Deficit in the spatial specification of the goal ?

Muscimol (right cFN)



Conclusion

Head unrestrained cat

Impairment **before movement onset** in the spatial specification of the **goal for gaze**

Goffart & Pélisson *JNP* 1994,1998
Goffart et al. *JNP* 1998a,b
Goffart & Pélisson *JP* 1997

Head restrained monkey

Impairment in **accelerating driving** (contralateral) and **braking decelerating** (ipsilateral) saccades **choking**

Ohtsuka & Noda, *JNP* 1991,1995
Robinson & Fuchs *Annu. Rev. Neurosc.* 2001
Kleine & Büttner *JNP* 2004
Quaia, Lefèvre & Optican 1999

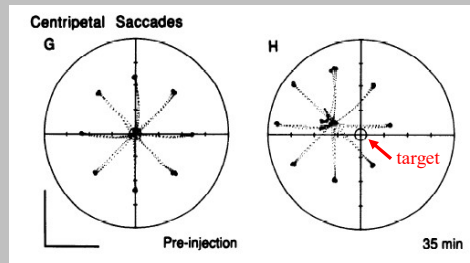
JOURNAL OF NEUROPHYSIOLOGY
Vol. 71, No. 5, May 1994, Printed in U.S.A.

RAPID PUBLICATION

Saccadic Burst Neurons in the Fastigial Nucleus Are Not Involved in Compensating for Orbital Nonlinearities

KENJI OHTSUKA, HITOSHI SATO, AND HIROHARU NODA*

Department of Ophthalmology, Sapporo Medical College, Sapporo, Hokkaido 060, Japan; and Visual Science Department, School of Optometry, Indiana University, Bloomington Indiana 47405



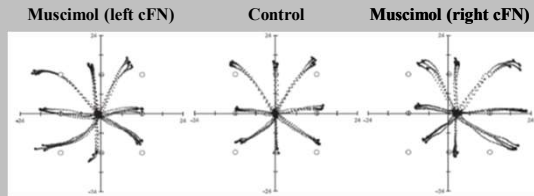
Part #2

Effects of unilateral inactivation of the caudal fastigial nucleus (cFN) on orienting gaze shifts in the head restrained monkey

Inactivation of caudal Fastigial Nucleus

Head restrained monkey

target LEDs @ 145 cm : 0.25° visual angle, mesopic conditions, 0.4 μl (1 μg/μl)



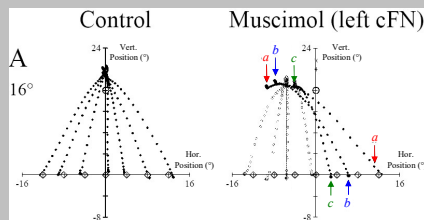
Goffart, Chen & Sparks, JNP 2004

Ipsilesional saccades : horizontal component is **hypermetric** (too large)

Contralateral saccades : horizontal component is **hypometric** (too small)

Horizontal error is not constant

Head restrained monkey

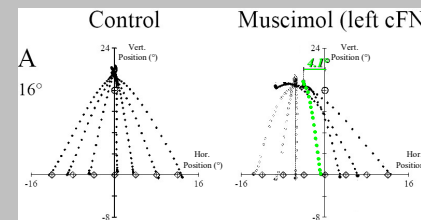


modified from Goffart, Chen & Sparks JNP 2004

Hor. Error **saccade a** > Hor. Error **saccade b** > Hor. Error **saccade c**

Horizontal error is not constant

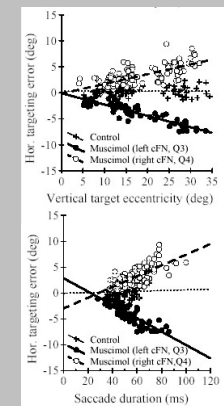
Head restrained monkey



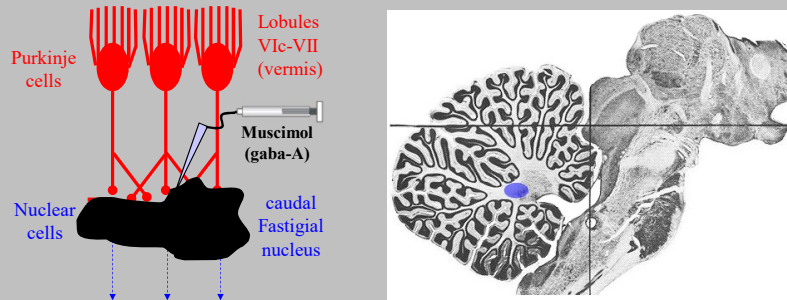
modified from Goffart, Chen & Sparks JNP 2004

Hor. error. = $f(\text{target eccentricity})$
 $f(\text{saccade duration})$

Vertical saccades



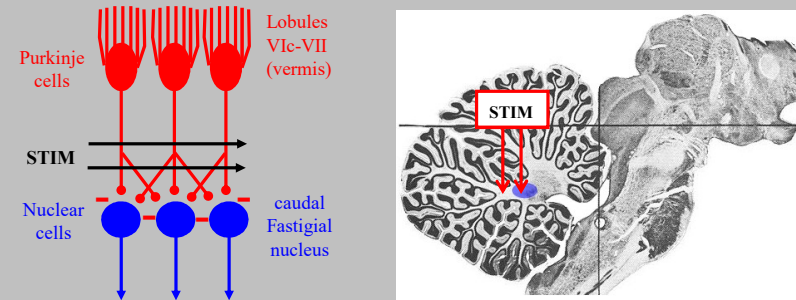
Impaired planning or execution ?



Duration of inactivation ~ 2-3 hours :

This long-lasting perturbation does not allow deficits that are presaccadic to be distinguished from those occurring during saccade execution

Inhibition of cFN activity with electrical microstimulation

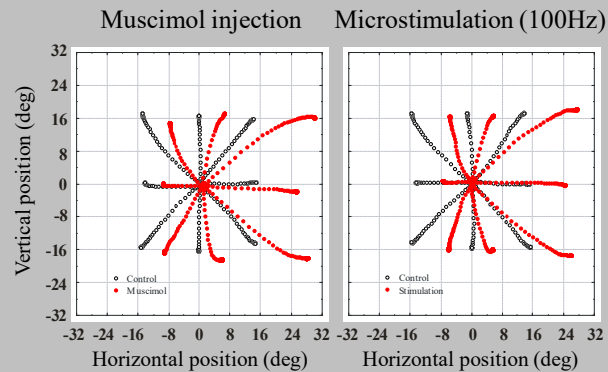


Purkinje cells inhibit cFN neurons with Gaba-A as a neurotransmitter.

By stimulating their axons, one should be able to mimics, with a microstimulation train, the effects of muscimol on saccade accuracy.

Inhibition of cFN

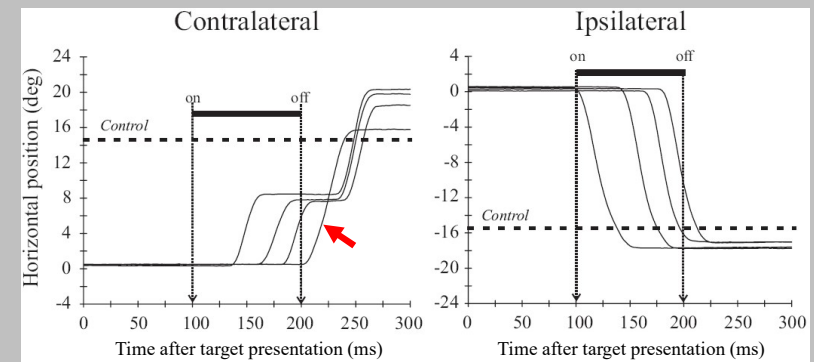
Right cFN (rebound saccades removed)



Goffart & Quinet unpubl. obs.
See also Goffart et al. ANYAS 2003

Time window of the perturbation

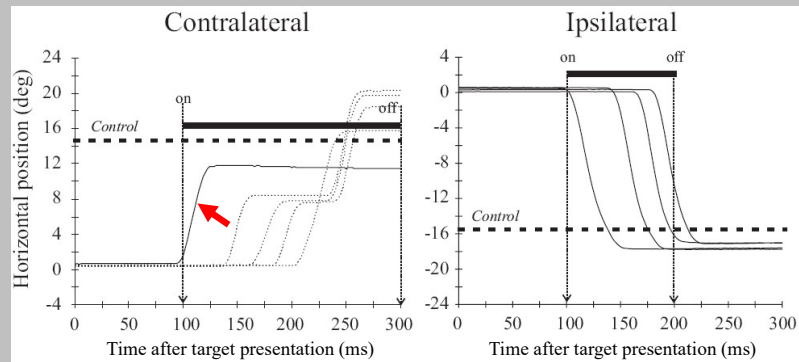
Horizontal saccades



Goffart & Quinet unpubl. obs.

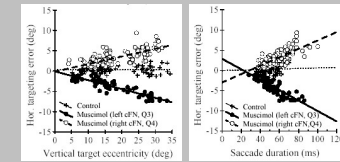
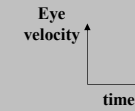
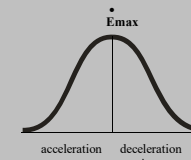
Time window of the perturbation

Horizontal saccades



How does cFN activity influence saccade amplitude ?

« push-pull » hypothesis

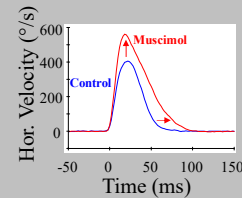
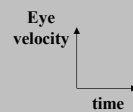
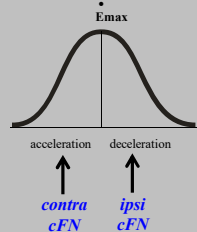


This hypothesis does not explain the ipsipulsion of vertical saccades (ipsipulsion increases with target eccentricity).

Robinson, Straube & Fuchs *Journal of Neurophysiology* 1993
Robinson & Fuchs *Annual Review of Neuroscience* 2001

How does cFN activity influence saccade amplitude ?

« push-pull » hypothesis



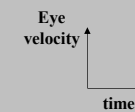
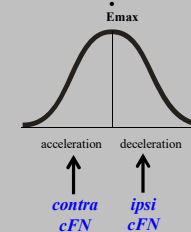
This hypothesis does not explain the ipsipulsion of vertical saccades (ipsipulsion increases with target eccentricity).

Moreover, perturbing the cFN can affect the « acceleration » of ipsilesional saccades or the « deceleration » of contralesional ones.

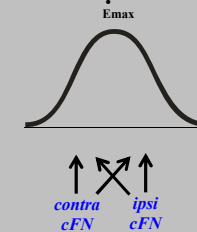
Robinson, Straube & Fuchs *Journal of Neurophysiology* 1993
Robinson & Fuchs *Annual Review of Neuroscience* 2001

How does cFN activity influence saccade amplitude ?

« push-pull » hypothesis



« bilateral » hypothesis

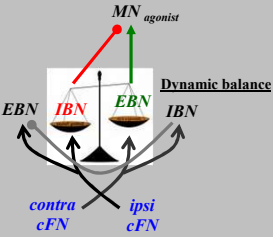
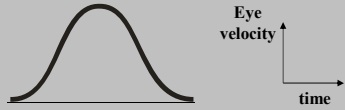


Robinson, Straube & Fuchs *Journal of Neurophysiology* 1993
Robinson & Fuchs *Annual Review of Neuroscience* 2001

Goffart, Chen & Sparks *Journal of Neurophysiology* 2004

« Bilateral » hypothesis

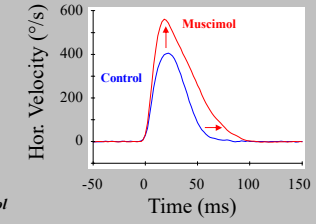
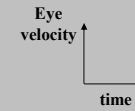
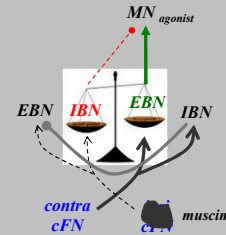
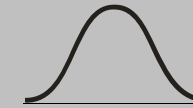
For every saccade (horizontal, oblique or vertical),
the bilateral cFN activity regulates the balance of activity
between excitatory input (EBNs) and inhibitory input (IBNs) to the motoneurons
(van Gisbergen et al. JNP 1981)



1. Contralateral EBNs are silent during off-direction saccades,
2. no evidence for co-contraction.

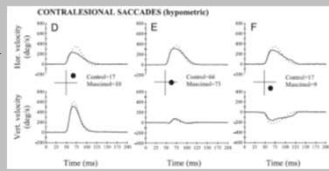
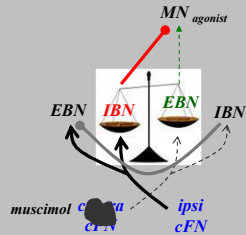
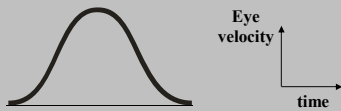
« Bilateral » hypothesis

Ipsilesional hypermetria



« Bilateral » hypothesis

Contralesional hypometria

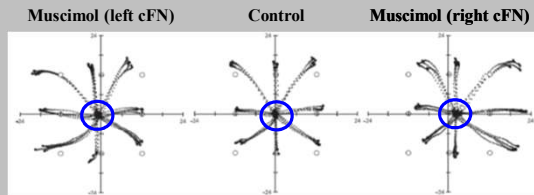


modified from Goffart, Chen & Sparks JNP 2004

Ipsilesional fixation offset

Head restrained monkey

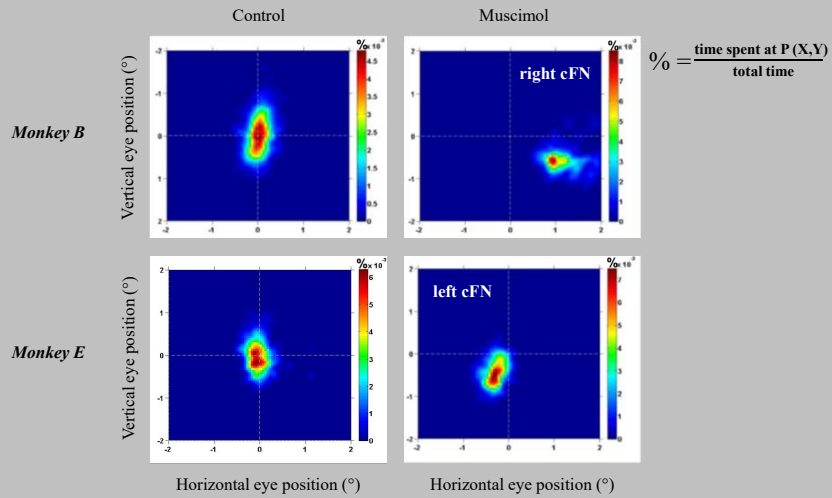
target LEDs @ 145 cm : 0.25° visual angle, mesopic conditions



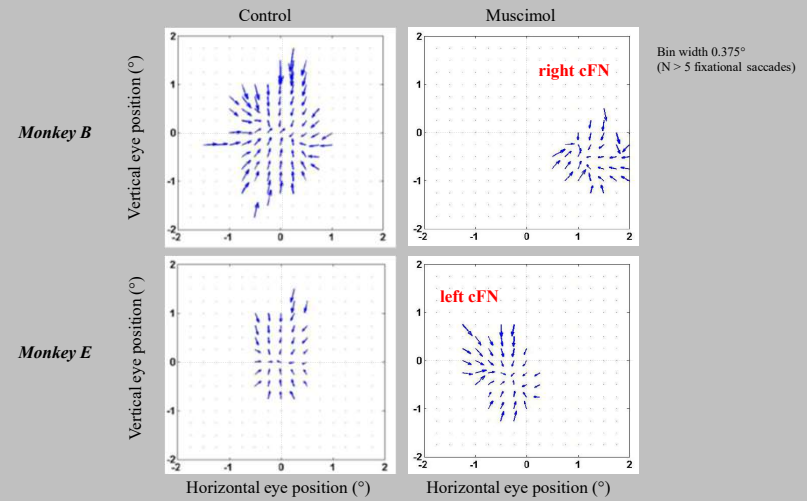
Goffart, Chen & Sparks, JNP 2004

Fixation offset : ipsilesional shift in the scatter of eye position during fixation

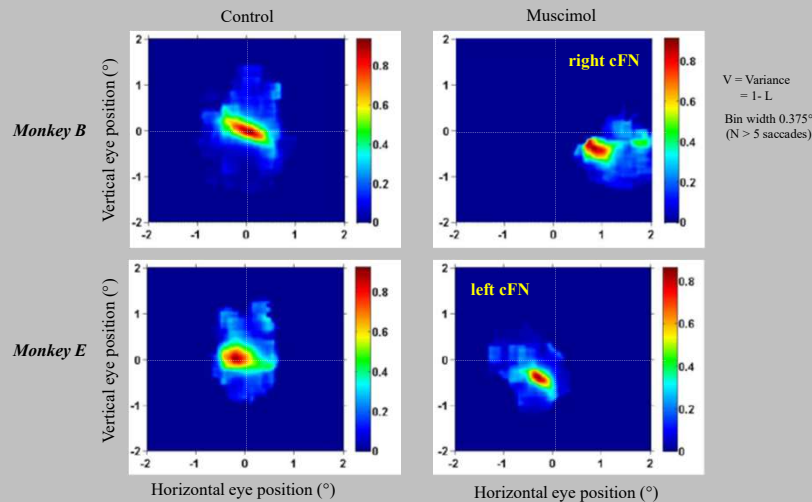
Fixation offset : spatio-temporal map



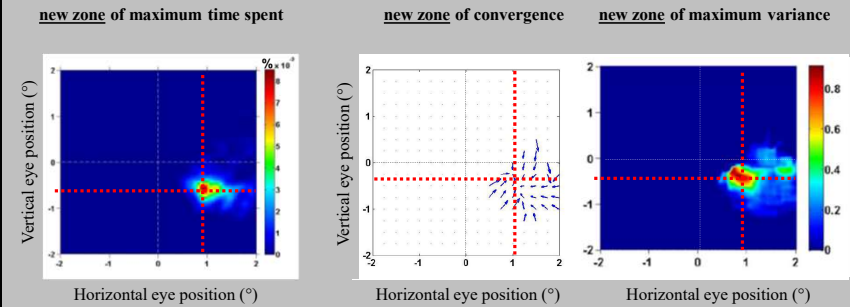
Directional field of fixational saccades



Directional field : zone of maximum variance



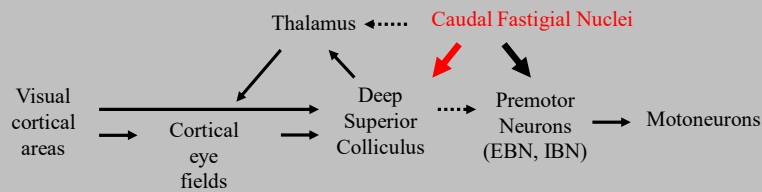
Fixational saccades become inaccurate BUT



→ a new oculomotor encoding of the foveal target ?
(Guerrasio, Quinet, Büttner & Goffart JNP 2010)

Fastigio-tectal projections could participate in the oculomotor encoding of foveal targets

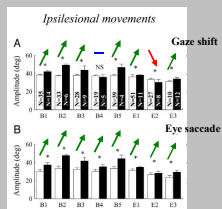
1. *May, Hartwich-Young, Nelson, Sparks & Porter Neuroscience 1990*
The **fastigiotectal pathway** is derived from cells in the caudal fastigial nucleus and projects bilaterally to the **rostral end of the intermediate gray layer**.
2. *Quinet & Goffart JNP 2005*
Magnitude of fixation offset ($\sim 1^\circ$) is similar between the **head restrained** and **head unrestrained** conditions \rightarrow **gaze fixation offset**
3. *Hafed, Goffart & Krauzlis JN 2008*
Muscimol injection in the rostral Superior Colliculus leads to a **fixation offset**



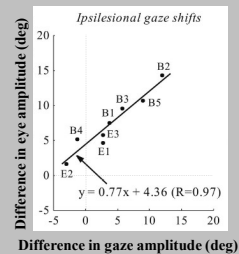
Part #3

Effects of unilateral inactivation of the caudal fastigial nucleus (cFN) on orienting gaze shifts in the head unrestrained monkey

Ipsilesional gaze shifts : average results from 2 monkeys

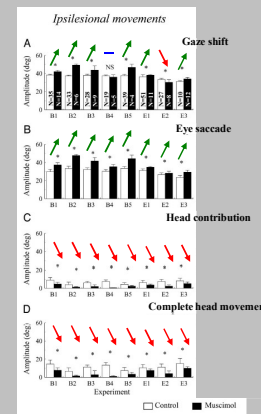


Increase in gaze amplitude : 6/8 experiments
Increase in eye amplitude : ALL



modified from Quinet & Goffart JNP 2005

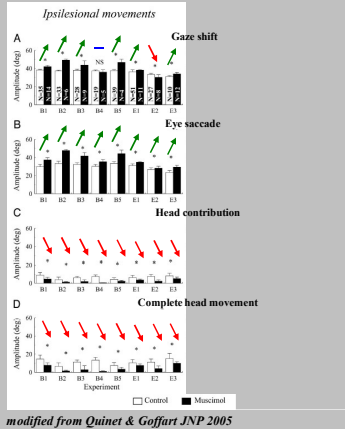
Ipsilesional gaze shifts



Increase in gaze amplitude : 6/8 experiments
Increase in eye amplitude : ALL
Decrease in head contribution : ALL
Decrease in ampl. of complete head movement : ALL

modified from Quinet & Goffart JNP 2005

Ipsilesional gaze shifts



Increase in gaze amplitude : 6/8 experiments
 Increase in eye amplitude : ALL
 Decrease in head contribution : ALL
 Decrease in ampl. of complete head movement : ALL

The decrease in the amplitude of head movements contrasts with the observations made in the head free cat.

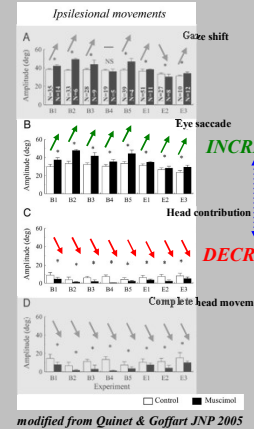
In the monkey :

- hypermetric eye
- hypometric head

In the cat :

- hypermetric eye
- hypermetric head

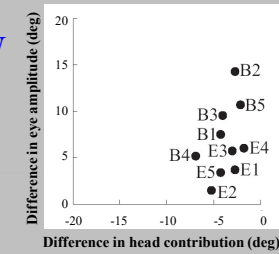
Ipsilesional gaze shifts



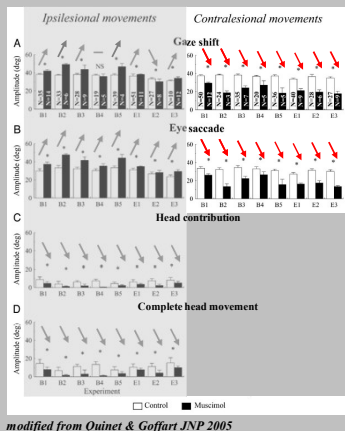
The changes in head ampl. are independent of the changes in eye amplitude.

The head does not try to compensate for the eye saccade hypermetria.

INCREASE
 NO CORRELATION
 DECREASE

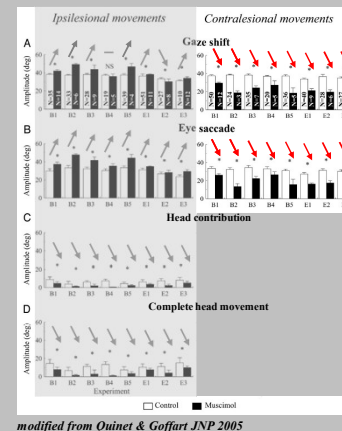


Contralesional gaze shifts

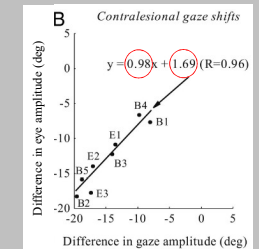


Decrease in gaze amplitude : ALL
 Decrease in eye amplitude : ALL

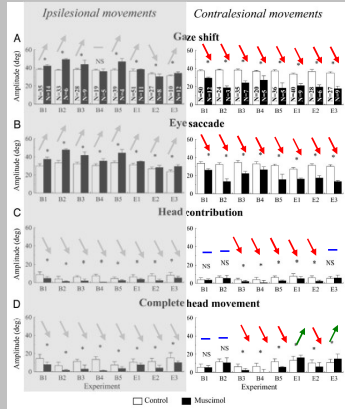
Contralesional gaze shifts



Decrease in gaze amplitude : ALL
 Decrease in eye amplitude : ALL

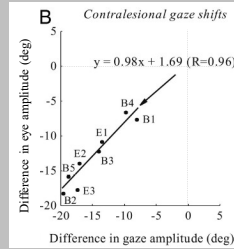


Contralesional gaze shifts



Decrease in gaze amplitude : ALL
 Decrease in eye amplitude : ALL
 Decrease in head contribution : 5/8 experiments
 Decrease in ampl. of complete head movement : 4/8

NOTE : The head contribution does not increase in amplitude to compensate for the eye saccade hypometria



modified from Quinet & Goffart JNP 2005

cFN inactivation in the head unrestrained monkey

Ipsilesional gaze shifts become hypermetric because :

- the horizontal eye component is hypermetric and
- the head does not compensate for this increase in eye amplitude

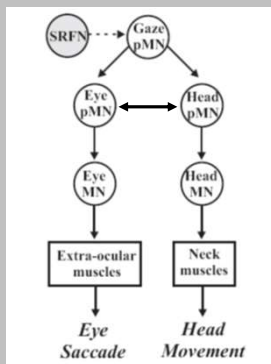
Contralesional gaze shifts become hypometric because :

- the horizontal eye component is hypometric and
- the head does not compensate for this decrease in eye amplitude

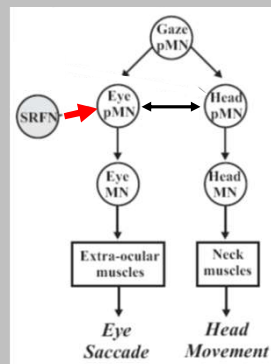
Vertical gaze shifts are deviated toward the injected side :

- the eye component has an ipsilesional deviation
- the head does not compensate for this horizontal deviation of the eyes

Cat



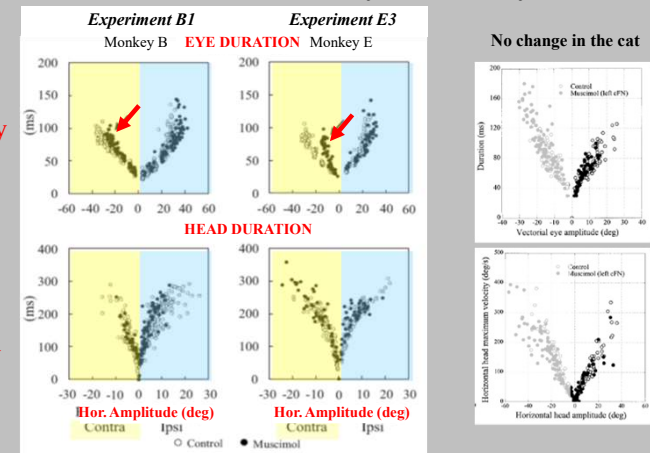
Monkey



Additional evidence for an oculomotor disorder after cFN inactivation : eye velocity

Change in EYE velocity (contra)

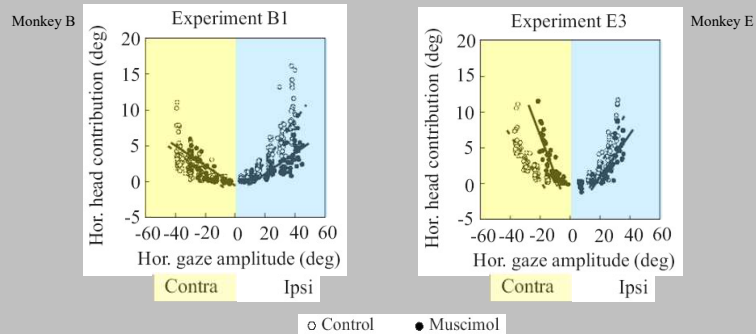
NO change in HEAD velocity



Eye-head coupling is altered by cFN inactivation

Ipsi : head contributes less

Contra : head contributes more



Summary

The Fastigial Oculomotor Region (FOR) ensures the spatial congruence between :

- the location of a stationary visual target (peripheral or foveal locus of activity) and
- the endpoint of a saccade toward this location (oculomotor commands).

The FOR is mostly involved in the control of the horizontal component of gaze shifts

The control is exerted during fixation and during saccades by the equilibrium of activity between the left and right FOR.

During saccadic gaze shifts, the control concerns eye and head movements in the cat. In primates, it seems restricted to the oculomotor system. Further experiments are required in other vertebrate species (fish, reptile, rodent, bird) to see whether non-oculomotor deficits are possible.

The lack of change in eye-head synergy after cFN inactivation in the cat suggests that mechanisms coupling the eye saccades with head movements and/or body movements are located outside the cerebellum (gaze orienting as a model for *synergetics*).

The two FOR influence the accuracy of saccades by their projections toward the EBN/IBN region. They participate to the oculomotor encoding of foveal targets by their projections toward the rostral SC.

Perturbation of the rostral SC does not affect the accuracy of saccades to peripheral targets but leads to a fixation offset which is similar to that observed after cFN inactivation.

Summary

Pharmacological inactivation

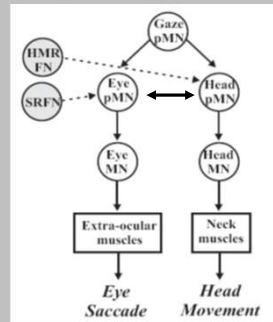
Quinet & Goffart JNP 2005, 2007

Electrical microstimulation

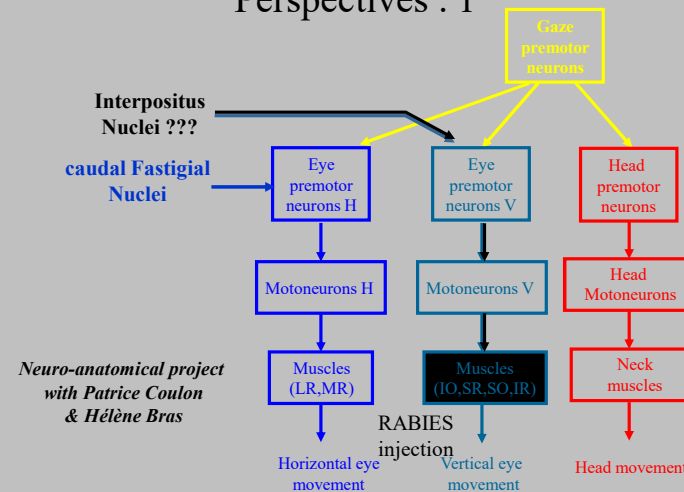
Quinet & Goffart JNP 2009

Anatomical studies

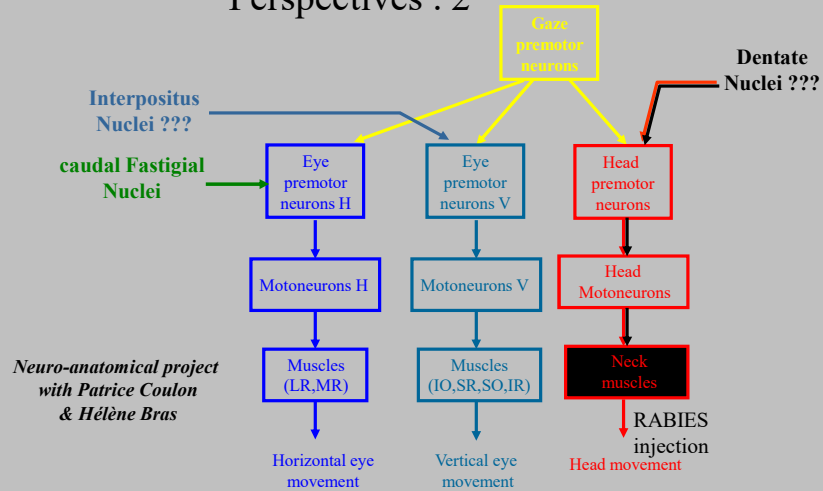
Robinson, Phillips & Fuchs JCN 1994



Perspectives : 1



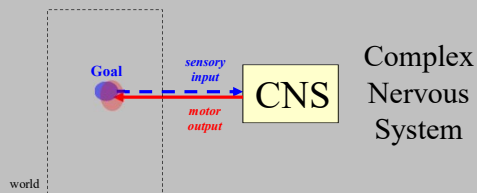
Perspectives : 2



Perspectives

Neural representations of target location : sensory and motor

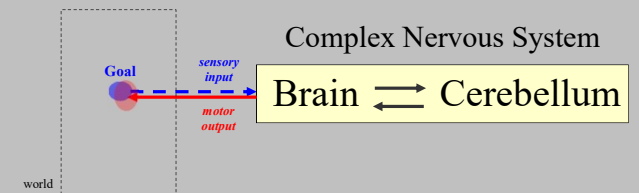
- A **complex nervous system** ensures the spatial congruence between
- the source of a sensory stimulus and
 - the endpoint of movements directed toward this source.



Neural representations of target location : sensory and motor

- A **complex nervous system** ensures the spatial congruence between
- the source of a sensory stimulus and
 - the endpoint of movements directed toward this source.

The cerebellum plays a major role in this visuomotor mapping. More experiments (in **rodents, amphibians** and **fishes**) are required to test **whether this cerebellar influence depends upon the species**.



The medio-posterior cerebellum : a space-time metric tensor for orienting gaze ?

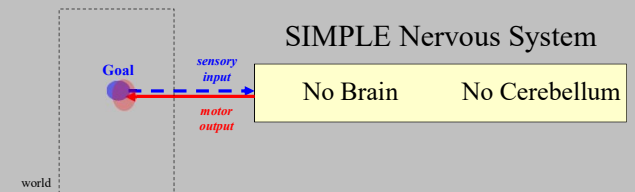
SPACE-TIME REPRESENTATION IN THE BRAIN. THE CEREBELLUM AS A PREDICTIVE SPACE-TIME METRIC TENSOR

A. PELLIONISZ and R. LLINÁS

Department of Physiology and Biophysics, New York University Medical Center,
550 First Avenue, New York, NY 10016, U.S.A.

Neural representations of target location : sensory and motor

Simpler nervous systems, with a few ganglia, are able to achieve the spatial congruence,
even for foveating a moving target (accuracy in space-time).



Orienting movement of the head in an insect (praying mantis)

20 deg rightward target



50 deg rightward target

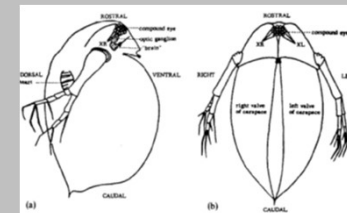


Sampled with 400 images/sec

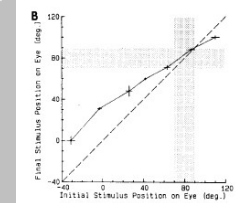
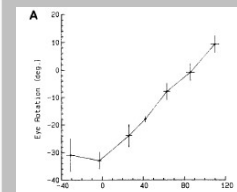
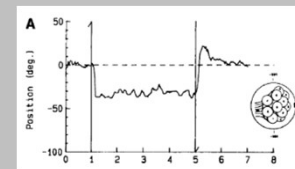
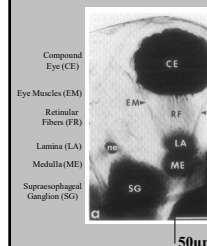
Goffart & Yamawaki, unpublished results

Orienting movement in a small crustacean (*Daphnia magna*)

Body Size :
approx. 2-3 mm

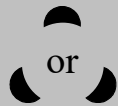


Saccades of the compound eye



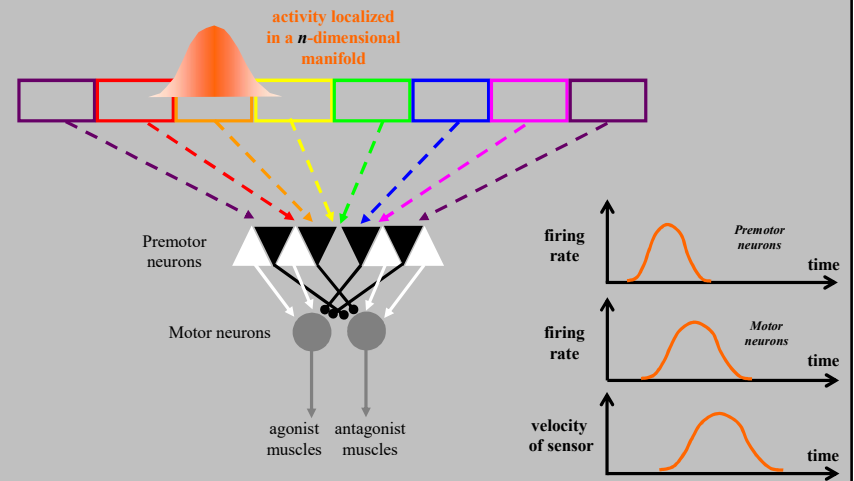
Genetic determinism and/or morphogenesis ?

Is the visuomotor spatial congruence the result of common genes from Daphnia to Primates ?
Is there a genetic representation of the spatial organization of the environment ?

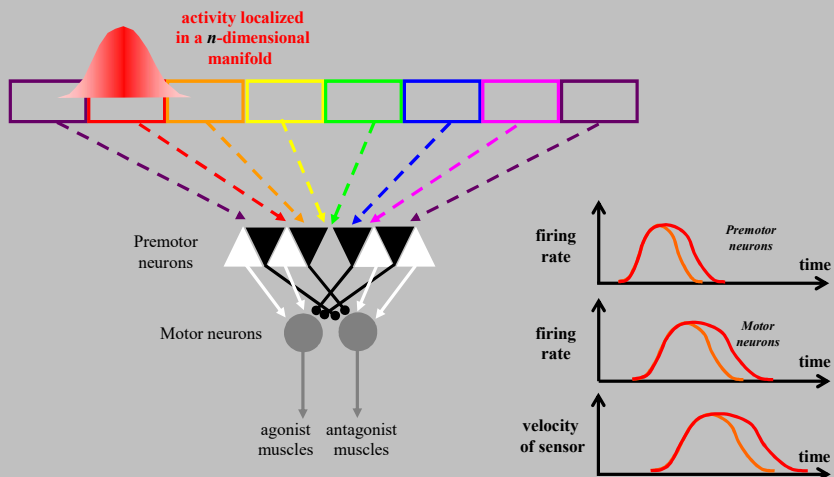


Is the spatial congruence due to the fact that all these animals live in the same environment and that they are endowed with learning abilities which permit to align their motor and sensory spaces ?

Spatio-temporal transformation



Spatio-temporal transformation

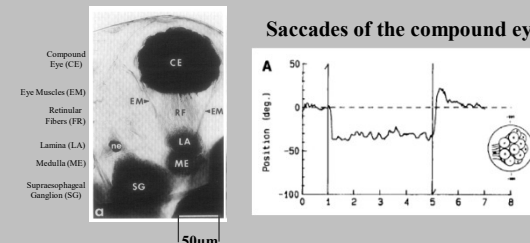


Molecular mechanisms for the spatio-temporal transformation

Is it possible to generate saccades in vitro ?

What determines the duration of firing rate in premotor and motor neurons ?

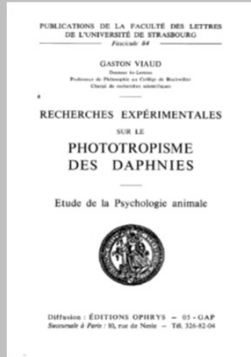
What is the best biological model ? Vertebrate ? Invertebrate ? *Daphnia magna* ?



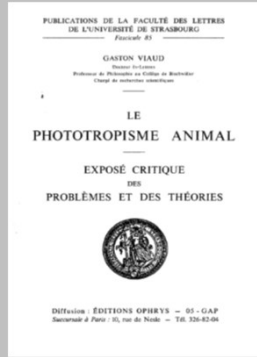
From orienting behavior to animal phototropism

Gaston Viaud

1938



1938



Acknowledgements

Experiments in the head-restrained monkey

David L. Sparks, PhD

Longtang L. Chen, PhD



Experiments in the head-restrained and -unrestrained monkey

Julie Quinet, PhD

Sandrine Hugues, PhD

Lorenzo Guerrasio, MSc

Ulrich Büttner, MD PhD



Experiments in the praying mantis

Yoshifumi Yamawaki, PhD

Samuel Rossel, PhD



Experiments in the cat

Denis Pélisson, PhD

Alain Guillaume, PhD



*“L’expérience ne nous donne qu’un certain nombre de points isolés ;
il faut les réunir par un trait continu”* Henri Poincaré