Bron, Institut des Sciences Cognitives
2010 March 1st

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

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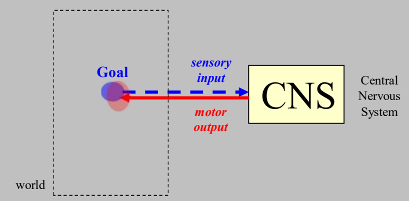
Marseille, France

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



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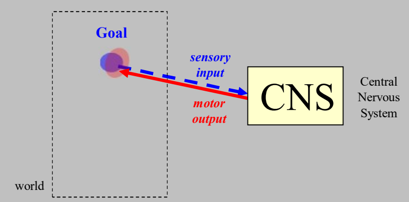
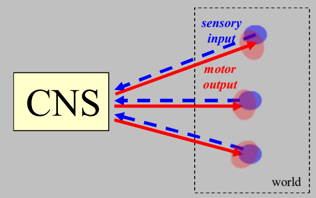
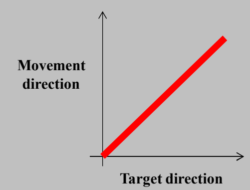
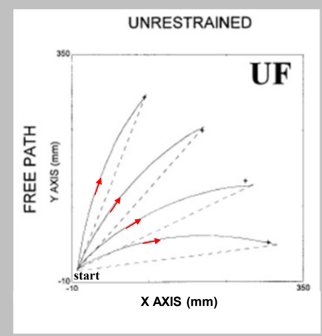


Sensorimotor mapping with one-to-one correspondence (± variability)



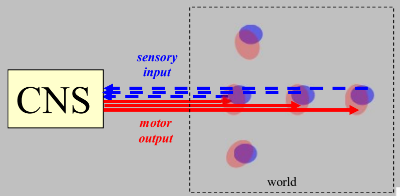


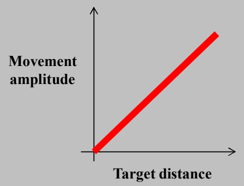
Finger pointing movements

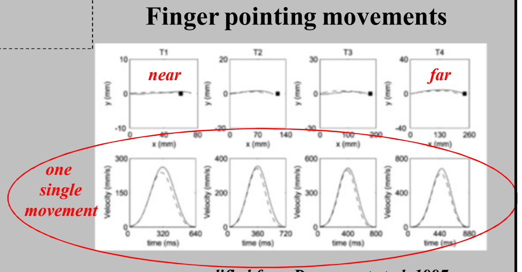


modified from Desmurget et al. 1997

Sensorimotor mapping with one-to-one correspondence

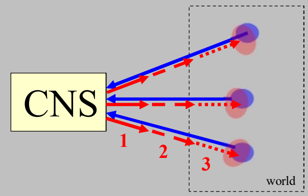


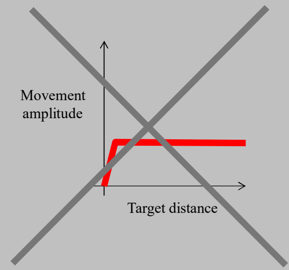




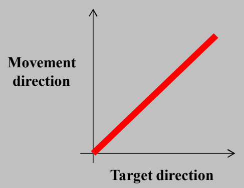
modified from Desmurget et al. 1997

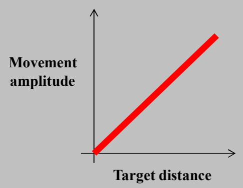
In normal conditions, simple goal-directed movements **are not** performed by appending elementary movement units





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. HEIN[3] and M. JEANNEROD[1]

(From the [1]Laboratoire de Neuropsychologie Expérimentale, INSERM Unité 94, Bron, France, [2]Department of Pharmacology, University of Edinburgh, Edinburgh, UK, and [3]Department 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 Escadrille Normandie Niemen, F-13397 Marseille Cedex 13, France

Exp Brain Res 1991

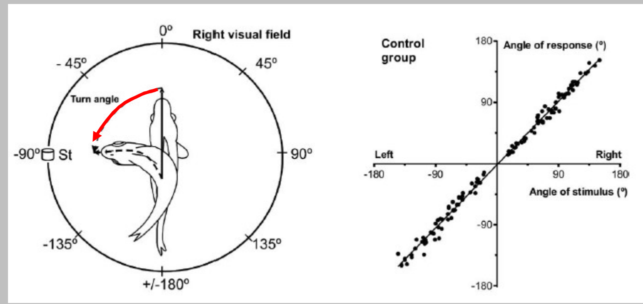
Neck and eye proprioception contribute to the spatial control of pointing movements

But

<u>Orienting</u> movements
of the eyes, of the head and of the body
also follow spatial rules.

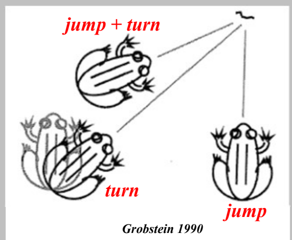
The spatial properties of pointing/reaching movements
could originate from the gaze orienting system
(e.g., see misreaching with prismatic spectacles)

Orienting movement of the body in the goldfish



Torres et al. Brain Res. Bull. 2005

Orienting movement of the body in the frog



Result of first reaction :
orient the
<u>field of sensorimotor interactions</u>
toward the target

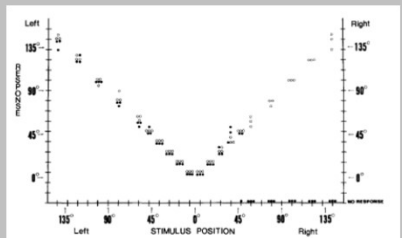
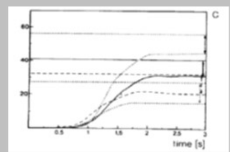


Fig. 1. Orienting behavior of a frog before and after section of the right optic nerve. Stimulus positions are shown by the short lines on the horizontal axis and are defined as number of degrees to the right or left around the animal from the snout. Response angles are shown on the vertical axis. Stimuli to the right elicited turns to the right (right vertical axis); those to the left elicited turns to the left (left vertical axes). 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.

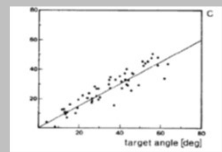
Kostyk & Grobstein 1982

Orienting movement of the head in the salamander

Schülert & Dicke J. Exp Biol 2002

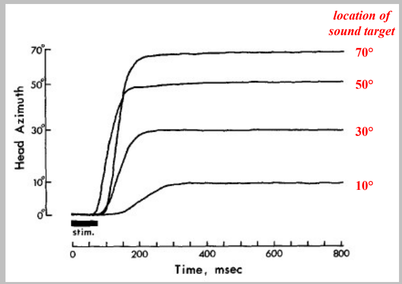


avec distracteur



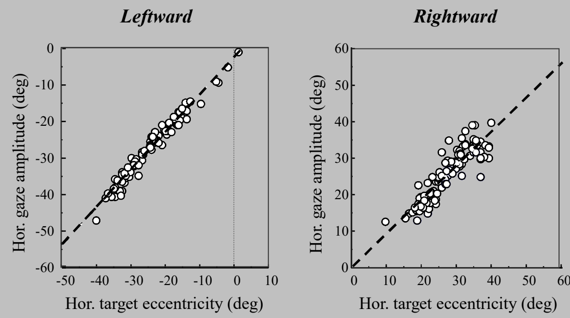
Werner & Himstedt Zool. Jb. Physiol. 1985

Orienting movement of the head in the barn owl



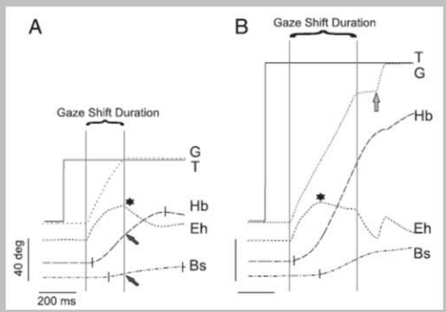
Knudsen, Blasdel & Konishi JCP 1979

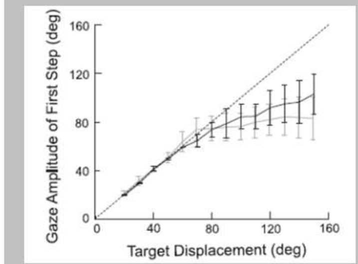
Orienting gaze shifts in the cat (head free, open loop)



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

=

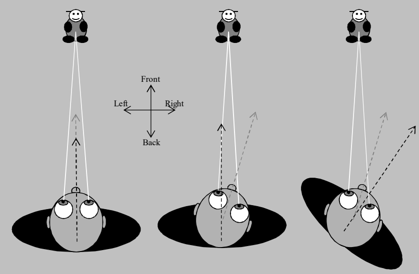
Orientation of the eyes in the orbit

+

Orientation of the head / trunk

+

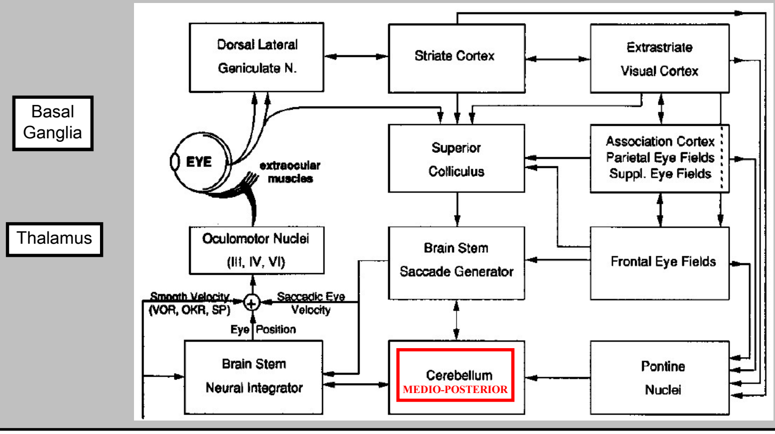
Orientation of the trunk / hip



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 (<u>in less than 300 ms)</u>

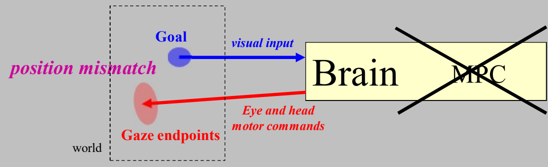


The medio-posterior cerebellum (MPC) and the control of orienting gaze shifts

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

- the location of a visual event

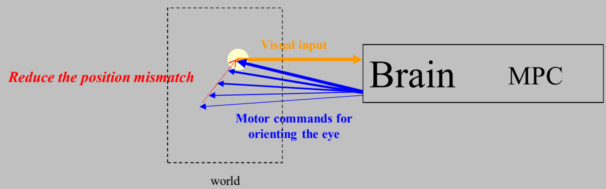
- the endpoint of gaze shifts towards it



<u>How does the cerebellum help us to reach a goal ?</u>

Adaptive control of saccade accuracy

The function of the MPC is to <u>build</u> or <u>re-establish</u> 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 ...



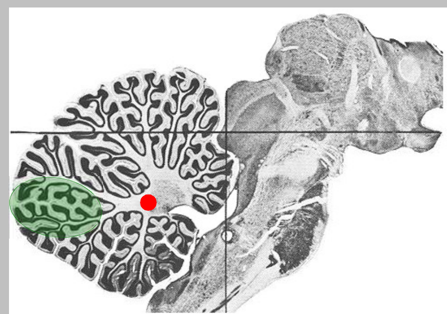
The medio-posterior cerebellum

Lobules VIc-VII

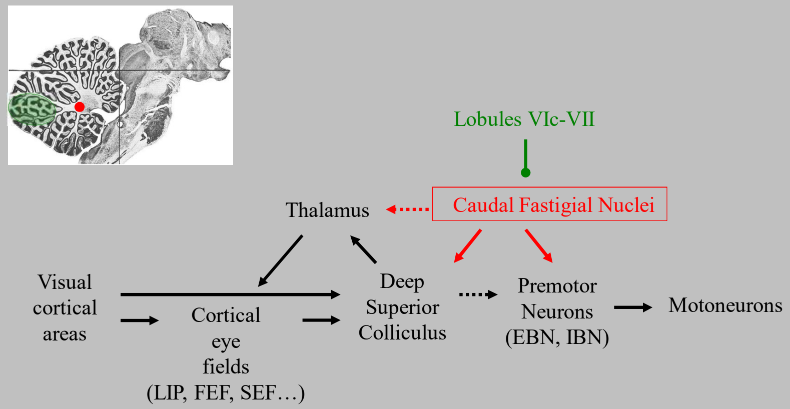
caudal Fastigial Nuclei
(Fastigial Oculomotor Regions)

Saccade-related activity

Pursuit-related activity

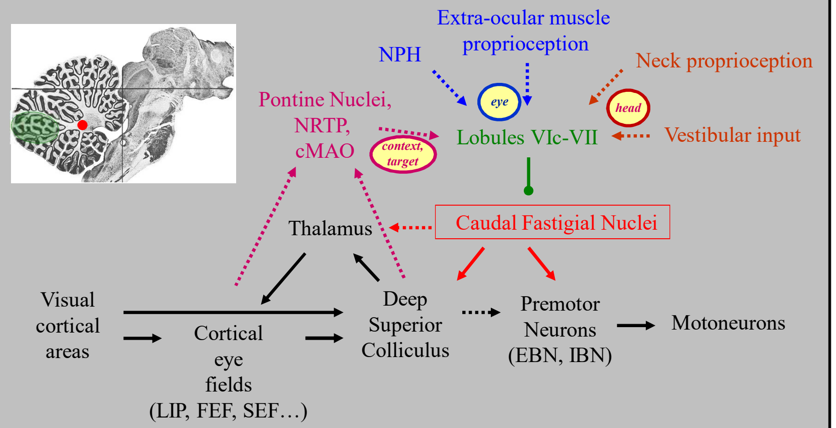


The medio-posterior cerebellum

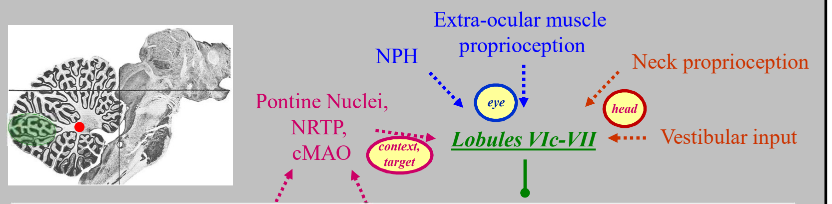


Cerebellar inputs with different dynamics

(different delays, temporal patterns etc…)



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

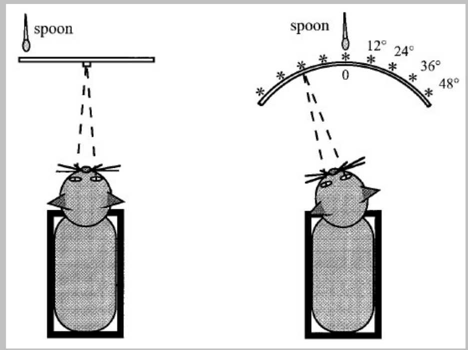
Department of Physiology and Biophysics, New York University Medical Center, 550 First Avenue, New York, NY 10016, U.S.A.

Neuroscience 1982

Part #1

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

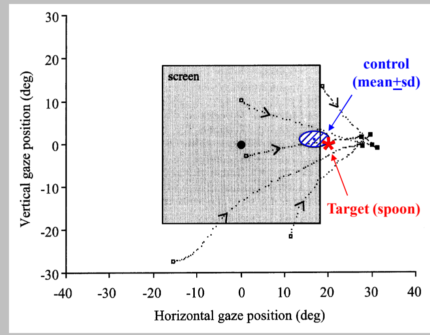
Testing conditions



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

Ipsilesional gaze shifts

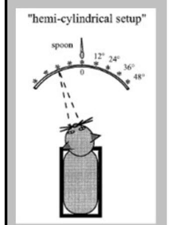
Muscimol injection in the right cFN (0.3 µl; 1µg/µl; cat F)

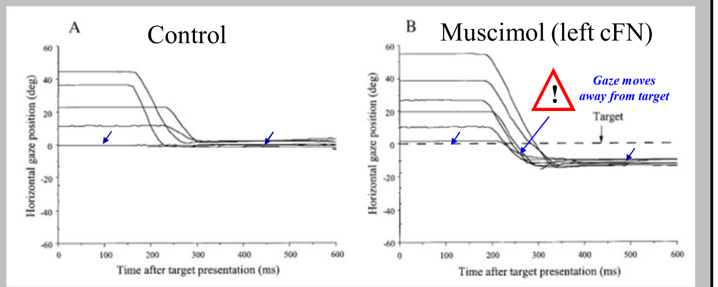


modified from Goffart & Pélisson JNP 1998

Ipsilesional gaze shifts

Muscimol injection in the left cFN (0.3 µl; 1µg/µl, cat I)



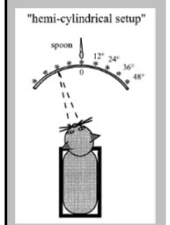


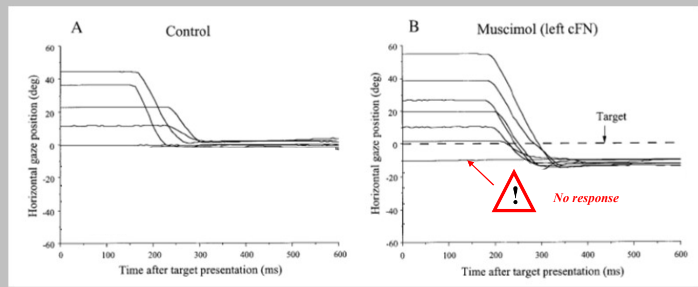
modified from Goffart & Pélisson JNP 1998

Ipsilesional gaze shifts

Muscimol injection in the left cFN (0.3 µl; 1µg/µl, cat I)

Muscimol injection in the left cFN (0.3 µg)



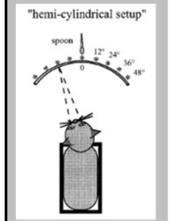


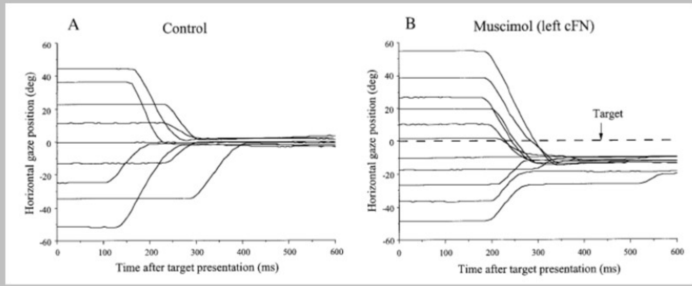
modified from Goffart & Pélisson JNP 1998

Ipsilesional and contralesional gaze shifts

Muscimol injection in the left cFN (0.3 µl; 1µg/µl, cat I)

Muscimol injection in the left cFN (0.3 µg)



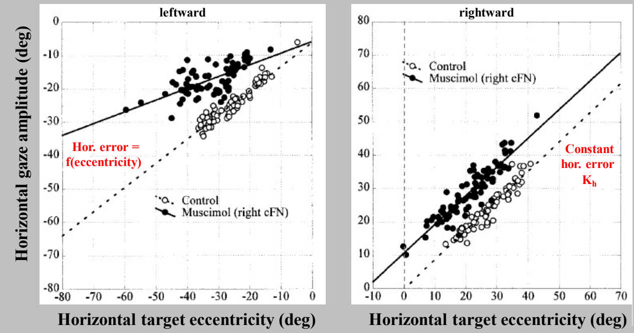


modified from Goffart & Pélisson JNP 1998

Gaze dysmetria

Muscimol injection in the right cFN (0.3 µl; 1µg/µl, cat F)

Contralesional movements **Ipsilesional movements**

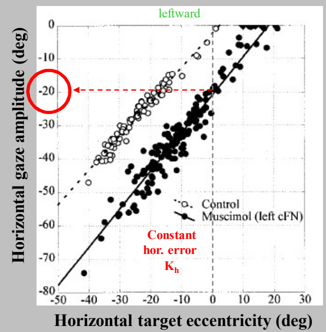


modified from Goffart & Pélisson JNP 1998

Gaze dysmetria

Muscimol injection in the left cFN (0.3 µl; 1µg/µl, cat G)

Ipsilesional movements



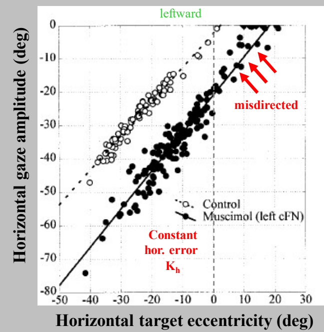
~20 deg !!!

modified from Goffart & Pélisson JNP 1998

Gaze dysmetria

Muscimol injection in the left cFN (0.3 µl; 1µg/µl, cat G)

Ipsilesional movements

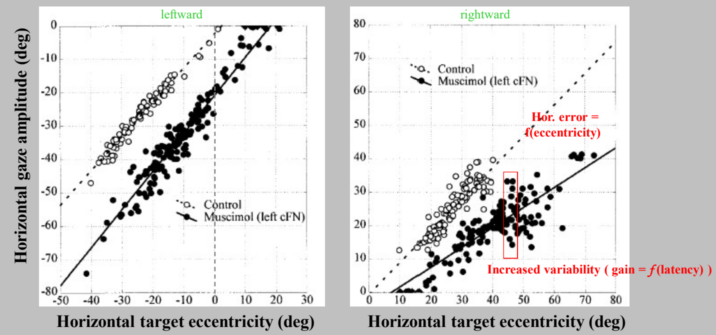


modified from Goffart & Pélisson JNP 1998

Gaze dysmetria

Muscimol injection in the left cFN (0.3 µl; 1µg/µl, cat G)

Ipsilesional movements **Contralesional movements**

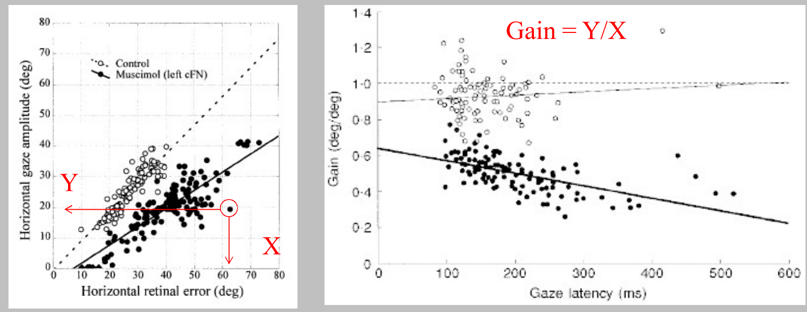


modified from Goffart & Pélisson JNP 1998

Relationship dysmetria - latency

Muscimol injection in the left cFN (0.3 µl; 1µg/µl, cat G)

Contralesional movements

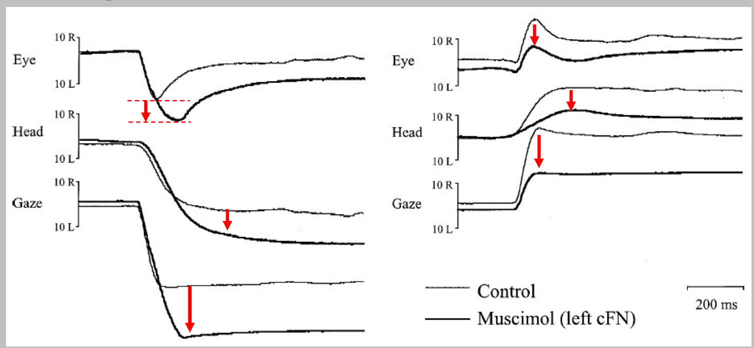


modified from Goffart & Pélisson JPhysiol 1997

Dysmetria affects both eye and head movements

Muscimol injection in the left cFN (0.3 µl; 1µg/µl, cat G)

Ipsilesional HYPERmetria **Contralesional HYPOmetria**

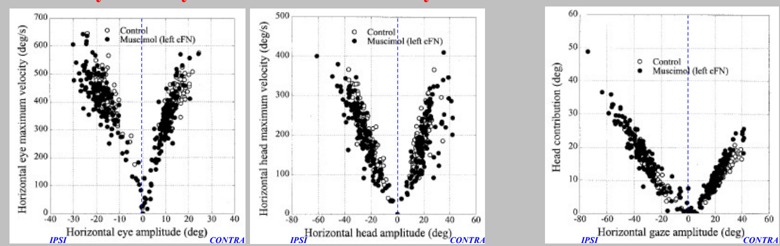


modified from Goffart, Pélisson & Guillaume JNP 1998

No sign of movement execution disorder

Muscimol injection in the left cFN (0.3 µl; 1µg/µl, cat G)

Eye velocity **Head velocity** **Head contribution**



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 ⟶ **GAZE DEFICIT**

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

⟶ **DEFICIT BEFORE MOVEMENT ONSET**

- Final hor. error = K
- misdirected movements

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

⟶ **DEFICIT IN THE SPATIAL SPECIFICATION OF THE GOAL**

Control (pre-injection)

Deficit in the spatial specification of the goal ?

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 / choking (ipsilateral) saccades

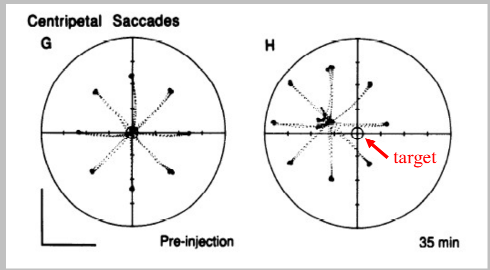
Ohtsuka & Noda, *JNP* 1991,1995
Robinson & Fuchs *Annu. Rev. Neurosc*. 2001
Kleine & Büttner *JNP* 2004
Quaia, Lefèvre & Optican *JNP* 1999

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

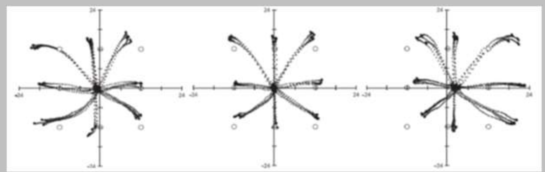
Effects of unilateral inactivation of the caudal fastigial nucleus (cFN) on orienting gaze shifts in the head restrained monkey

Inactivation of caudal Fastigial Nucleus

Head restrained monkey

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

Muscimol (left cFN) **Control** **Muscimol (right cFN)**



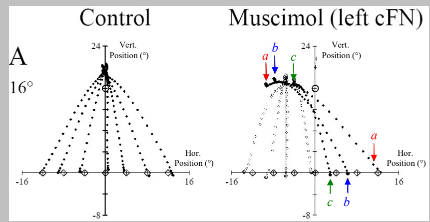
Goffart, Chen & Sparks, JNP 2004

Ipsilesional saccades : horizontal component is **hyper**metric (too large)

Contralesional saccades : horizontal component is **hypo**metric (too small)

Horizontal error is not constant

Head restrained monkey

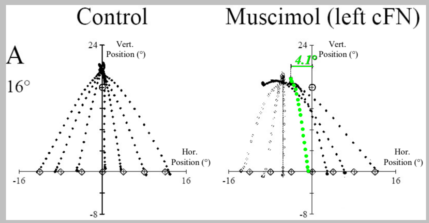


modified from Goffart, Chen & Sparks JNP 2004

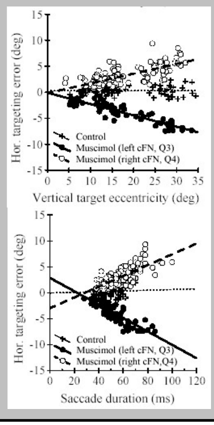
Hor. Error $_{saccade\ a}$ > **Hor. Error** $_{saccade\ b}$ > **Hor. Error** $_{saccade\ c}$

Horizontal error is not constant

Head restrained monkey



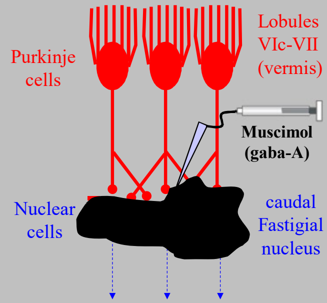
modified from Goffart, Chen & Sparks JNP 2004

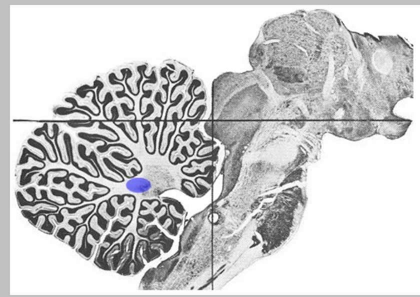


Hor. error. = *f*(target eccentricity)
f(saccade duration)

Impaired planning or execution ?

(pre- or intra-saccadic disorder ?)

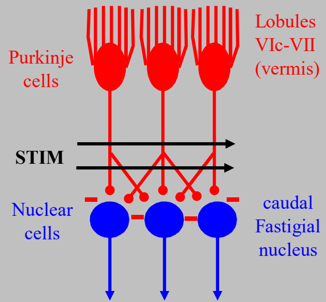


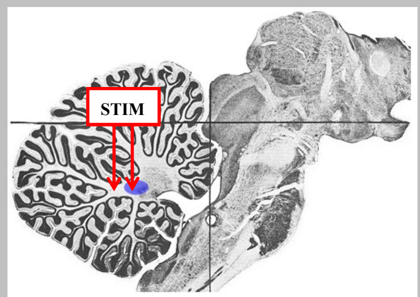


Duration of inactivation ~ 2-3 hours :

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



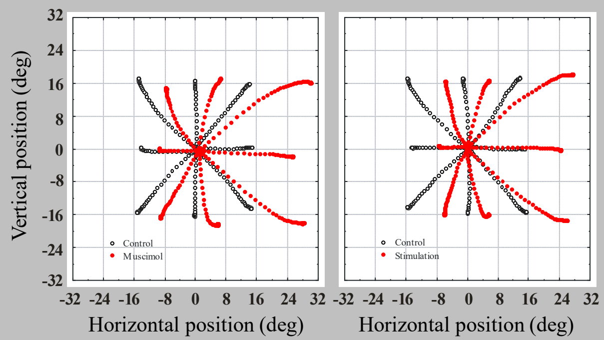


Purkinje cells inhibit cFN neurons with Gaba-A as a neurotransmitter.

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

Inhibition of cFN

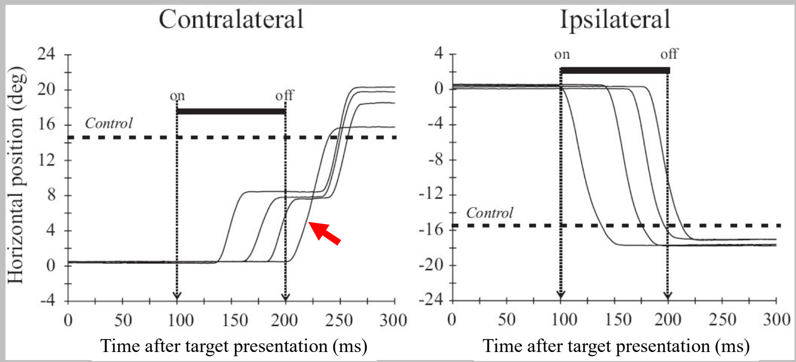
Right cFN (rebound saccades removed)



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

Time window of the perturbation

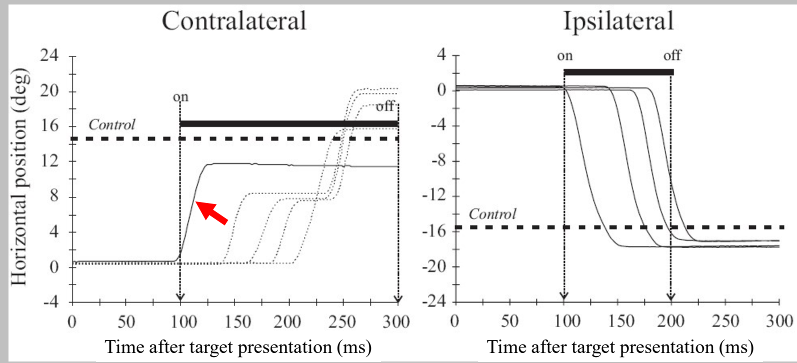
Horizontal saccades



Goffart & Quinet unpubl. obs.

Time window of the perturbation

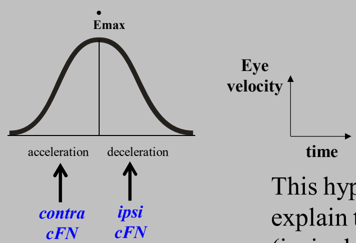
Horizontal saccades

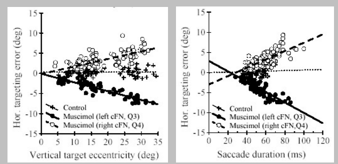


Goffart & Quinet unpubl. obs.

How does cFN activity influence saccade amplitude ?

« push-pull » hypothesis



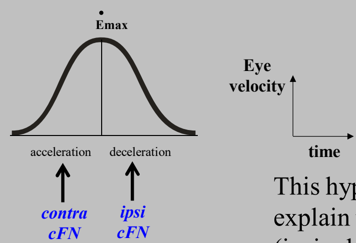


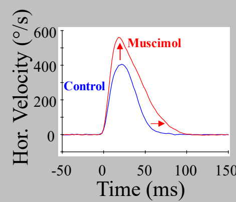
This hypothesis does not
explain the ipsipulsion of vertical saccades
(ipsipulsion increases with target eccentricity).

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

How does cFN activity influence saccade amplitude ?

« push-pull » hypothesis

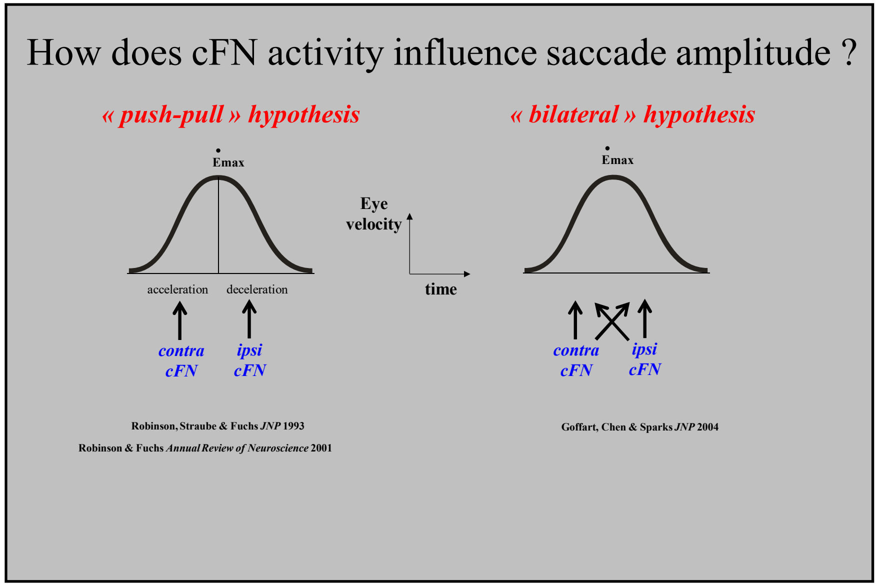


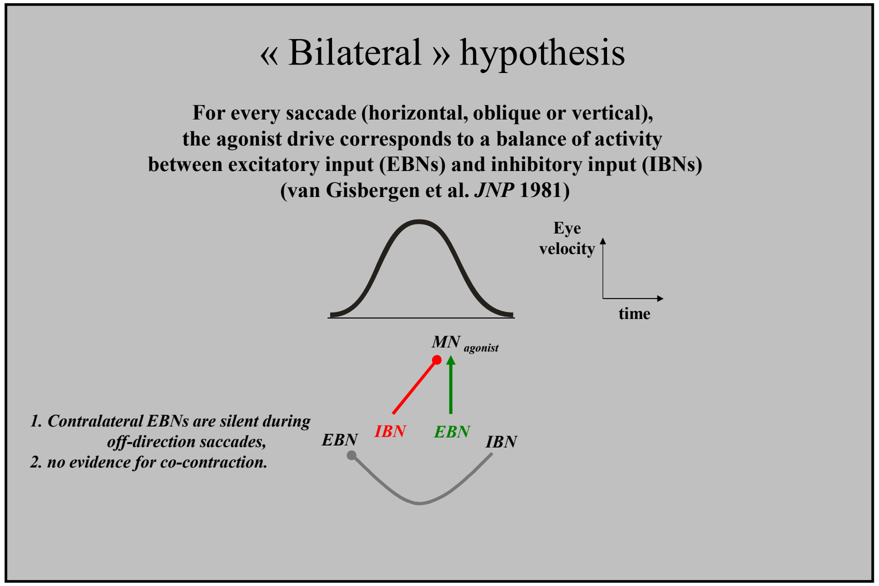


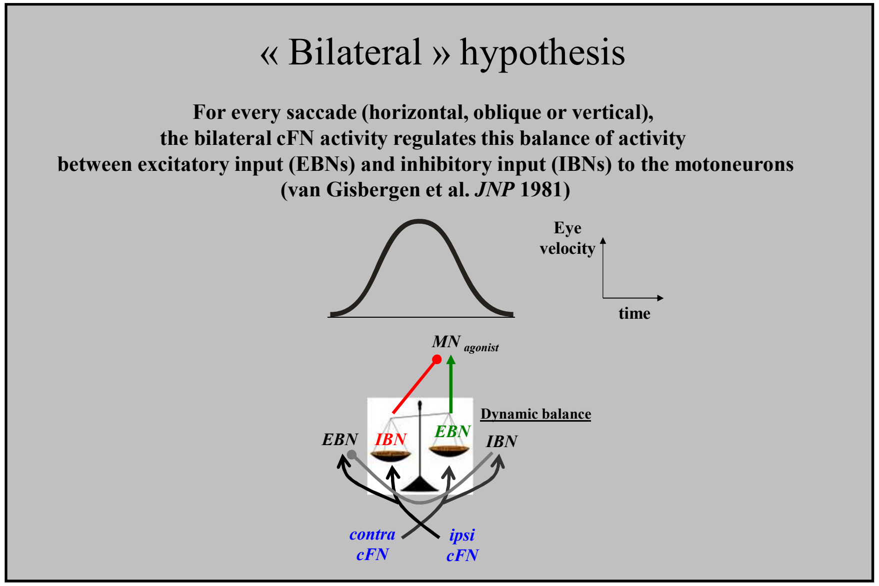
This hypothesis does not
explain the ipsipulsion of vertical saccades
(ipsipulsion increases with target eccentricity).

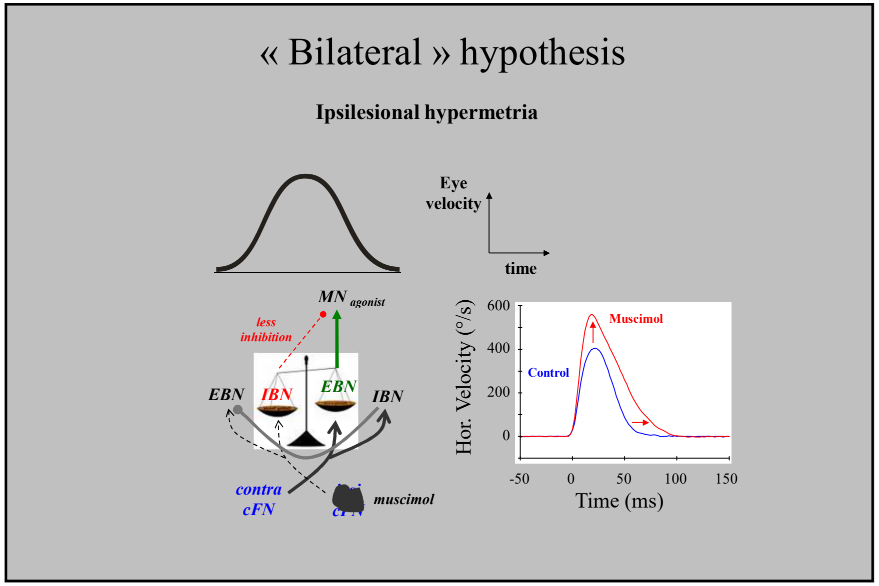
Moreover, perturbing the cFN can affect
the « acceleration » of ipsilesional saccades
or the « deceleration » of contralesional ones.

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


How does cFN activity influence saccade amplitude ?
« push-pull » hypothesis
« bilateral » hypothesis
Emax
acceleration
deceleration
contra cFN
ipsi cFN
Eye velocity
time
Emax
contra cFN
ipsi cFN
Robinson, Straube & Fuchs JNP 1993
Robinson & Fuchs Annual Review of Neuroscience 2001
Goffart, Chen & Sparks JNP 2004

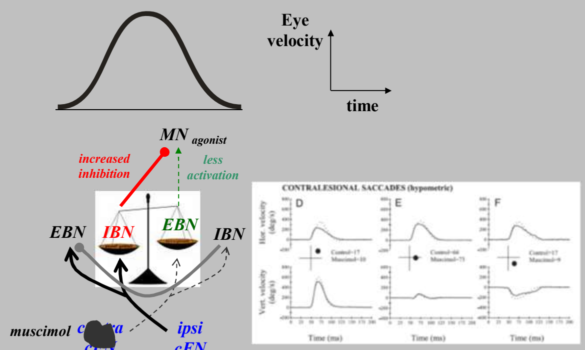

« Bilateral » hypothesis
For every saccade (horizontal, oblique or vertical),
the agonist drive corresponds to a balance of activity
between excitatory input (EBNs) and inhibitory input (IBNs)
(van Gisbergen et al. JNP 1981)
Eye velocity
time
MN agonist
1. Contralateral EBNs are silent during off-direction saccades,
2. no evidence for co-contraction.
EBN
IBN
EBN
IBN


« Bilateral » hypothesis
For every saccade (horizontal, oblique or vertical),
the bilateral cFN activity regulates this balance of activity
between excitatory input (EBNs) and inhibitory input (IBNs) to the motoneurons
(van Gisbergen et al. JNP 1981)
Eye velocity
time
MN agonist
Dynamic balance
EBN
IBN
EBN
IBN
contra cFN
ipsi cFN


« Bilateral » hypothesis
Ipsilesional hypermetria
Eye velocity
time
MN agonist
less inhibition
EBN
IBN
EBN
IBN
contra cFN
muscimol
Hor. Velocity (°/s)
600
400
200
0
Muscimol
Control
-50
0
50
100
150
Time (ms)

« Bilateral » hypothesis

Contralesional hypometria



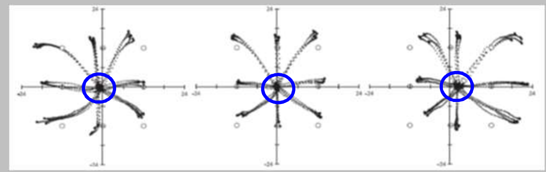
modified from Goffart, Chen & Sparks JNP 2004

Ipsilesional fixation offset

Head restrained monkey

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

Muscimol (left cFN) **Control** **Muscimol (right cFN)**

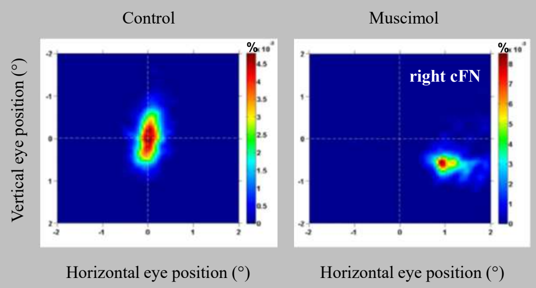


Goffart, Chen & Sparks, JNP 2004

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

Fixation offset : spatio-temporal map

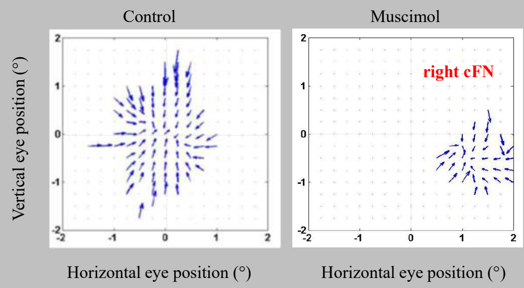
Monkey B



$\% = \dfrac{\textbf{time spent at P (X,Y)}}{\textbf{total time}}$

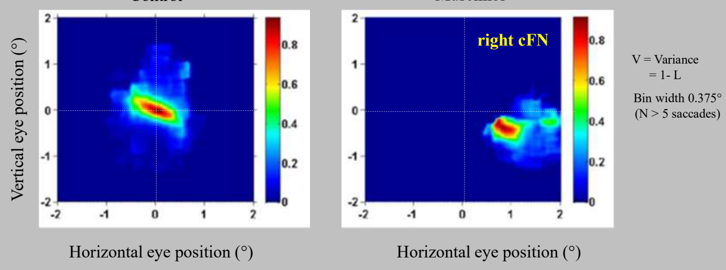
Directional field of fixational saccades

Monkey B

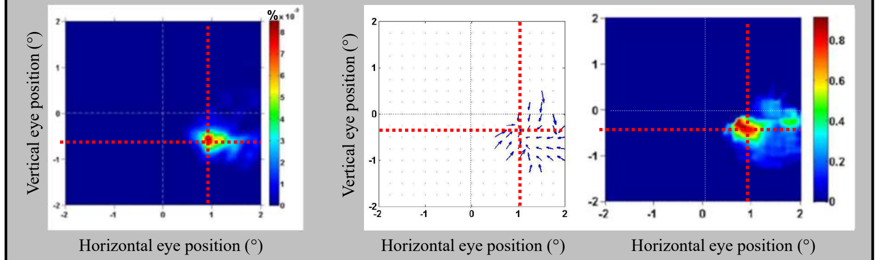


Bin width 0.375°
(N > 5 fixational saccades)

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 <u>rostral end of the intermediate gray layer.</u>

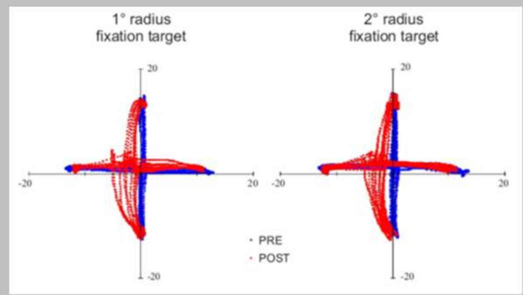
2. ***Quinet & Goffart JNP 2005***
   Magnitude of fixation offset (~1°) is similar between the head restrained and head unrestrained conditions → <u>gaze fixation offset</u>

3. ***Hafed, Goffart & Krauzlis JN 2008***
   Muscimol injection in the rostral Superior Colliculus leads to a <u>fixation offset</u>

Thalamus ⇠ Caudal Fastigial Nuclei

Visual cortical areas → Cortical eye fields → Deep Superior Colliculus ⇢ Premotor Neurons (EBN, IBN) → Motoneurons

Fixation offset after muscimol injection in the rostral SC



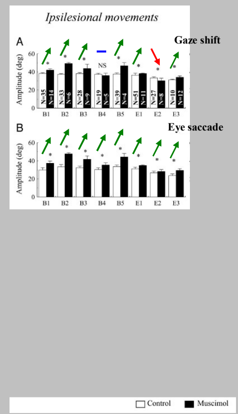
Saccades to peripheral targets are accurate

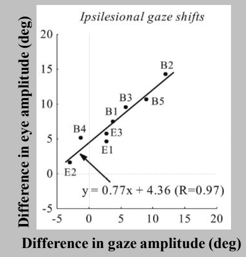
Part #3

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

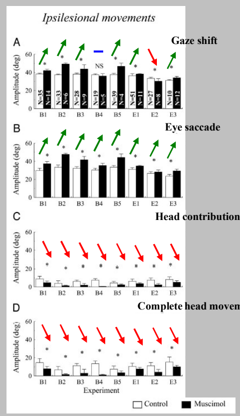
Increase in gaze amplitude : 6/8 experiments
Increase in eye amplitude : ALL





modified from Quinet & Goffart JNP 2005

Ipsilesional gaze shifts



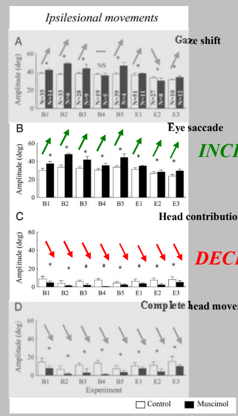
modified from Quinet & Goffart JNP 2005

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

In the monkey :
- hypermetric eye
- hypometric head

In the cat :
- hypermetric eye
- hypermetric head

Ipsilesional gaze shifts



INCREASE

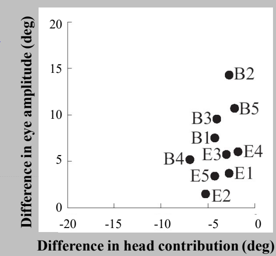
NO CORRELATION

DECREASE

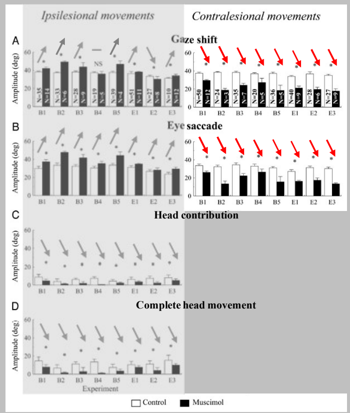
modified from Quinet & Goffart JNP 2005

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

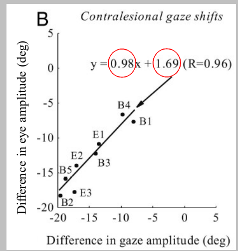
The head does not try to compensate for the eye saccade hypermetria.



Contralesional gaze shifts

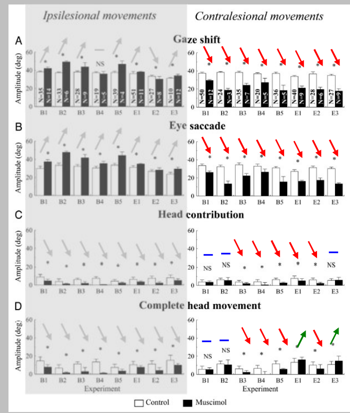


Decrease in gaze amplitude : ALL
Decrease in eye amplitude : ALL

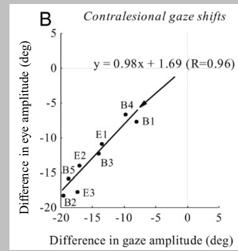


modified from Quinet & Goffart JNP 2005

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



modified from Quinet & Goffart JNP 2005

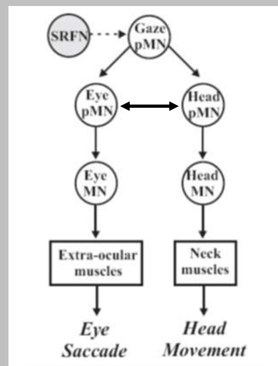
cFN inactivation in the head unrestrained monkey

Ipsilesional gaze shifts become hypermetric because :
- the horizontal eye component is hypermetric and
- the head does not compensate for this increase in eye amplitude

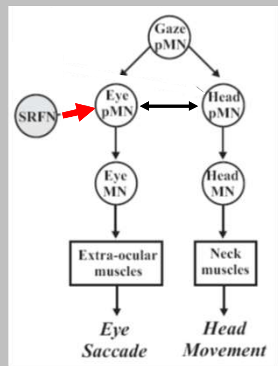
Contralesional gaze shifts become hypometric because :
- the horizontal eye component is hypometric and
- the head does not compensate for this decrease in eye amplitude

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



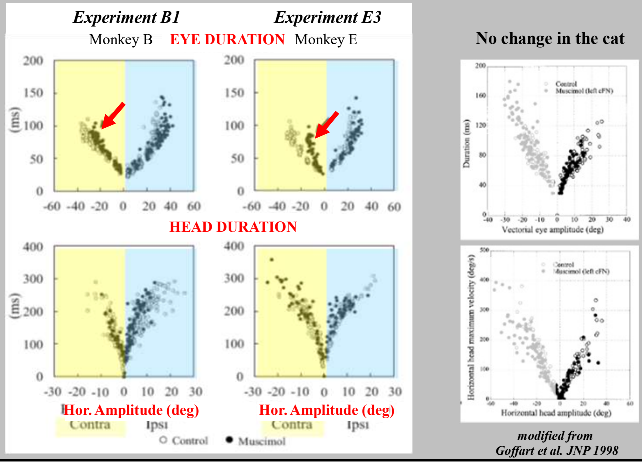
Monkey



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

Change in EYE velocity (contra)

NO change in HEAD velocity



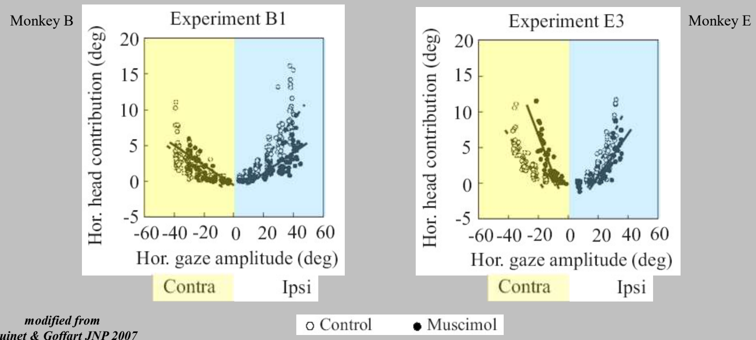
modified from Quinet & Goffart JNP 2007

modified from Goffart et al. JNP 1998

Eye-head coupling is altered by cFN inactivation

Ipsi : head contributes less

Contra : head contributes more



modified from Quinet & Goffart JNP 2007

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 amplitude 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.

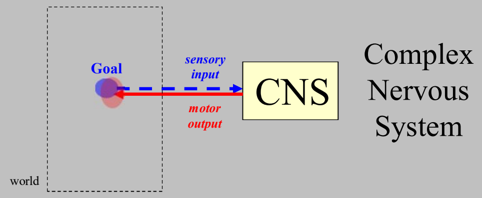
The two FOR influence the accuracy of saccades by their projections toward the EBN/IBN region.
They participate to the oculomotor encoding of foveal targets by their projections toward the rostral SC.

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.

Perspectives

Neural representations of target location : sensory and motor

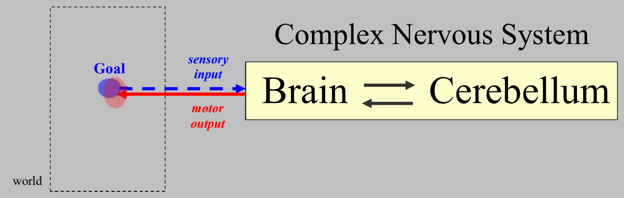
A **complex** nervous system ensures the spatial congruence between
- the source of a sensory stimulus and
- the endpoint of movements directed toward this source.



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.



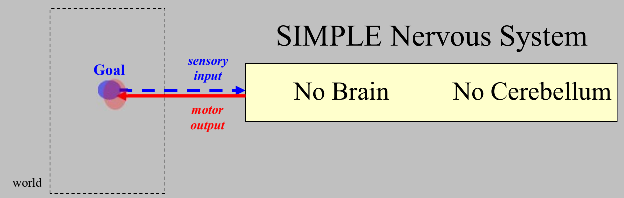
The medio-posterior cerebellum : a space-time metric tensor for orienting gaze ?

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 ganglions, are able to achieve the spatial congruence, <u>even for foveating a moving target</u> (accuracy in space-time).



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

20 deg rightward target

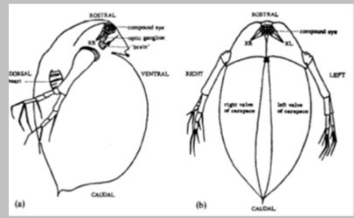
50 deg rightward target

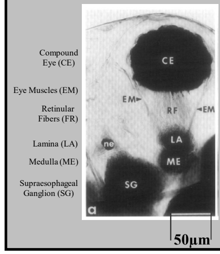
Sampled with 400 images/sec

Goffart & Yamawaki, unpublished results

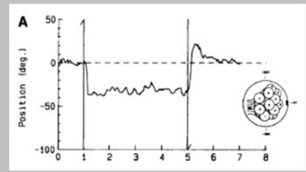
Orienting movement in a small crustacean (*Daphnia magna*)

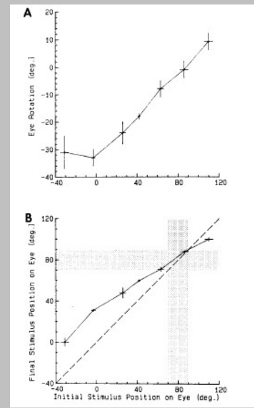
Body Size : approx. 2-3 mm





Saccades of the compound eye





Genetic determinism and/or morphogenesis ?

Is the neurobiological visuomotor space the result of common genes from Daphnia to Primates (see e.g., *eyeless* mutants) ? Is there a genetic representation of the spatial extent of the environment, considering that topographical signals must be transformed in temporal commands ?

Is it the consequence of 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 ?
In vertebrates, the MP cerebellum is well suited to compensate for the various and diverse forms of visual organs and motor designs but …

Acknowledgements

Experiments in the head-restrained monkey

David L. Sparks, PhD
Longtang L. Chen, PhD

Human Frontier Science Program

Experiments in the head-restrained and -unrestrained monkey

Julie Quinet, PhD
Sandrine Hugues, PhD
Lorenzo Guerrasio, MSc
Ulrich Büttner, MD PhD

Inserm

Experiments in the praying mantis

Yoshifumi Yamawaki, PhD
Samuel Rossel, PhD

Experiments in the cat

Denis Pélisson, PhD
Alain Guillaume, PhD

Inserm

"L'expérience ne nous donne qu'un certain nombre de points isolés ; il faut les réunir par un trait continu" Henri Poincaré