

Workshop « Cerebellum and eye movements »
 Paris, ICM, 11 juin 2013

Cerebellar mechanisms for orienting toward the location where a target is : *lessons from perturbing the output of the midline cerebellum*

Laurent Goffart, PhD

CNRS

Institut de Neurosciences de la Timone
 Marseille, France

Orienting reaction

A set of coordinated and organized muscle contractions / relaxations that lead to orient **rapidly** one (several) sensory organ(s) **toward** the location of a detected object, regardless of whether the object is moving or not.

→ *in foveate animals : orient the fovea toward the right place at the right time.*

Morphological diversity & Functional invariants

Across the vertebrates, many morphological differences are observed in the :

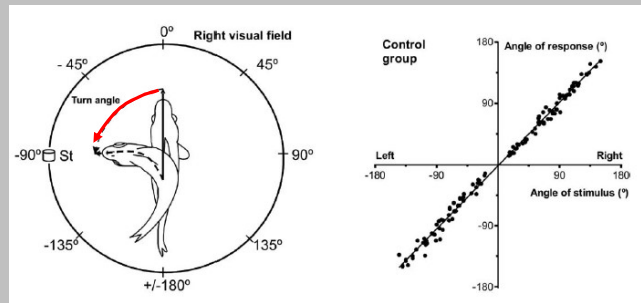
- sensory organs (retina, cochlea, olfactory bulb, etc.),
- motor plants (extra-ocular and neck muscles, morphology, architecture etc.),
- nervous system connecting them.

In spite of this diversity, some *invariants* (within and between species) appear in the temporal and spatial structure of the orienting action.

Temporal invariant : the orienting reaction is always extremely rapid (step-like), regardless of the motor plant (eye, head, body).

Spatial invariant : the spatial properties of the orienting reaction fit with the spatial extent of the environment with a relatively restricted variability.

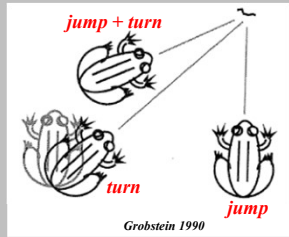
Orienting movement of the body in the goldfish



The diagram on the left shows a goldfish's visual field with angles from 0° to -180°. A stimulus (St) is located at -90°. A red arrow indicates the turn angle towards the stimulus. The diagram on the right is a scatter plot for a control group showing a strong positive correlation between the angle of stimulus (°) on the x-axis and the angle of response (°) on the y-axis, both ranging from -180 to 180.

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

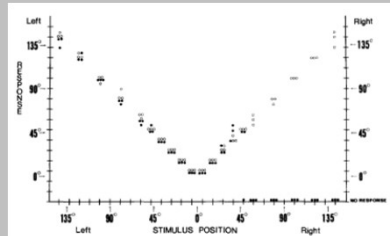
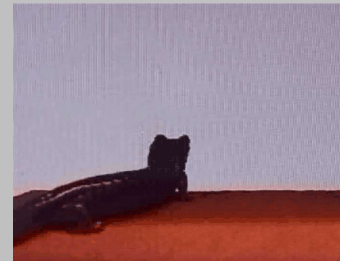


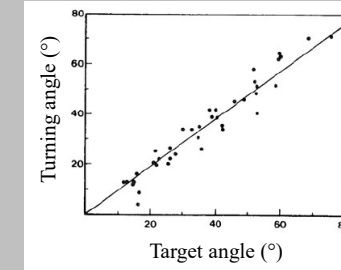
Fig. 1. Orienting behavior of a frog before and after section of the right optic nerve. Stimulus positions are shown by the short lines on the horizontal axis and are defined as number of degrees to the right or left around the animal from the snout. Response angles are shown on the vertical axis. Stimuli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

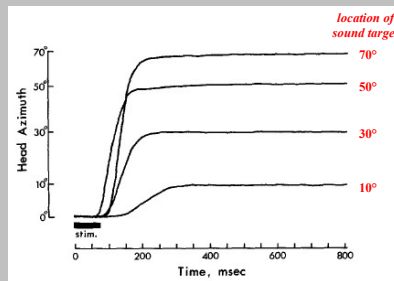


Schülert & Dicke J. Exp Biol 2002



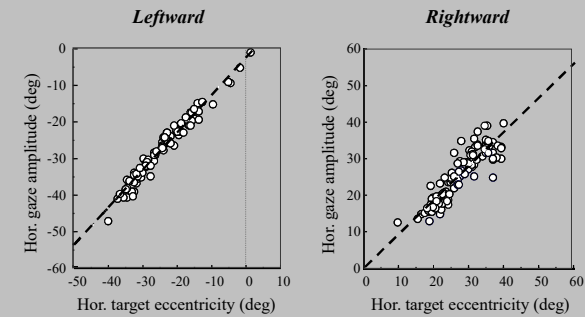
Werner & Himstedt Zool. Jb. Physiol. 1985

Orienting movement of the head in the barn owl



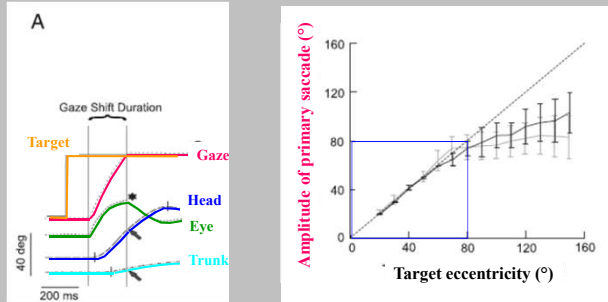
Knudsen, Blasdel & Konishi JCP 1979

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



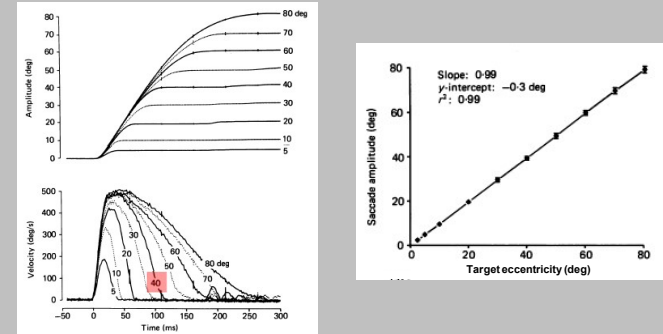
modified from Goffart & Pélisson JNP 1994

Orienting gaze shifts in the monkey (head free)



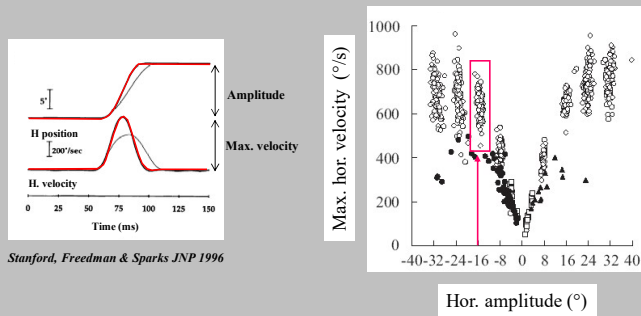
McCluskey & Cullen JNP 2007

Eye saccades in the human subject



Collewijn et al JP 1988

Variability in movement execution

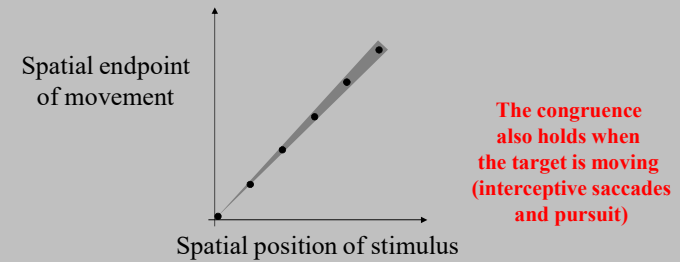


Stanford, Freedman & Sparks JNP 1996

Quinet & Goffart JNP 2009

Spatial invariant

In spite of the diversity of sensory organs, motor devices and nervous systems and variable execution (velocity, eye-head-body coupling)



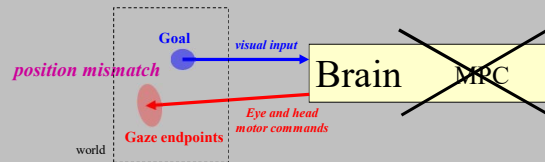
What are the (neuro)biological foundations of this relationship ?

The medio-posterior cerebellum (MPC) and the control of spatial congruence

Dysfunction of MPC leads to gaze **dysmetria** :
the spatial congruence between :

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

is altered.

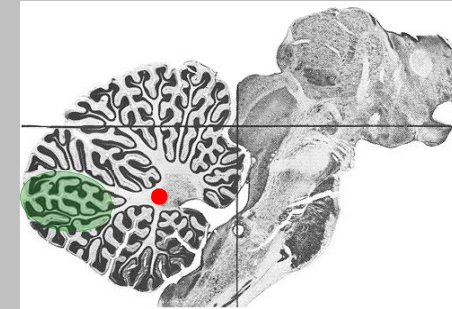


The medio-posterior cerebellum

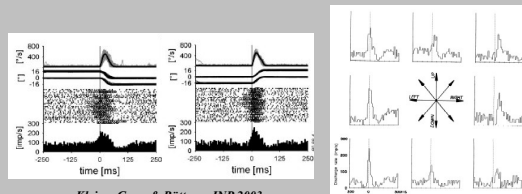
Lobules VIc-VII

caudal Fastigial Nuclei
(Fastigial Oculomotor Regions)

Saccade-related activity
Pursuit-related activity



Saccade-related activity in the caudal fastigial nucleus (head-restrained monkey)

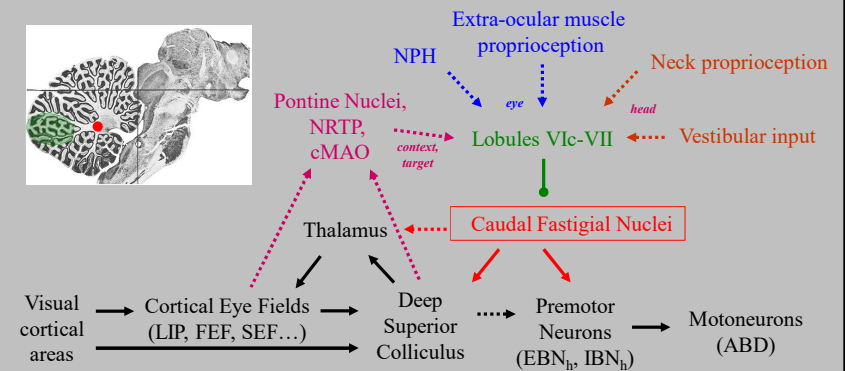
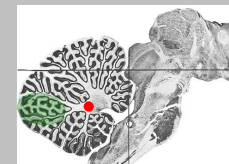


Kleine, Guan & Büttner JNP 2003

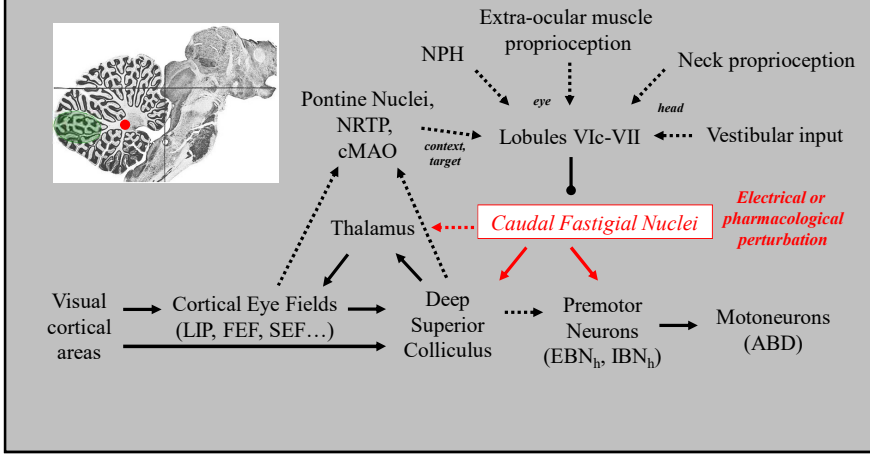
Ohtsuka & Noda JNP 1991

1. Burst of action potentials for all saccades regardless of the amplitude and direction
2. Sustained firing rate during intersaccadic intervals

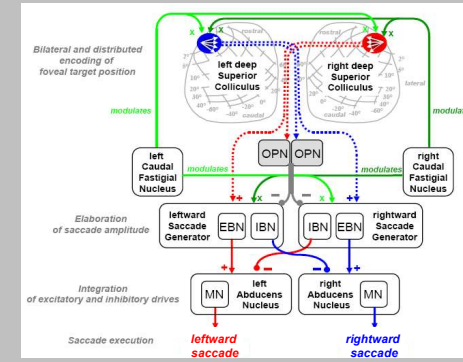
The medio-posterior cerebellum



Methodological approach : perturbation

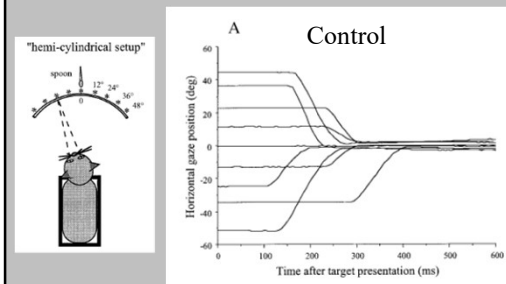


Take-home message : the MPC regulates (at least) two balances



Dysmetric gaze shifts in the cat

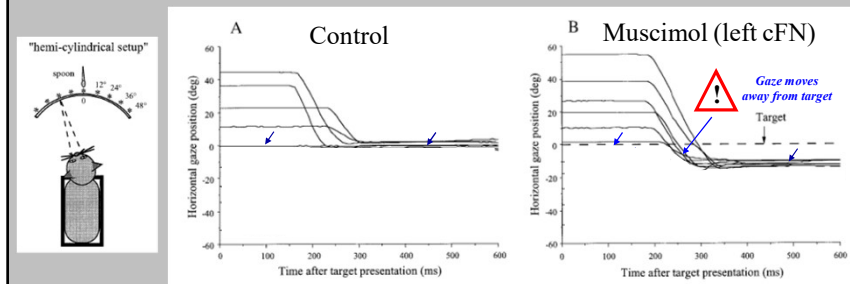
Muscimol injection in the left cFN (0.3 μl; 1 μg/μl, cat 1)



modified from Goffart & Pétilson JNP 1998

Dysmetric gaze shifts in the cat

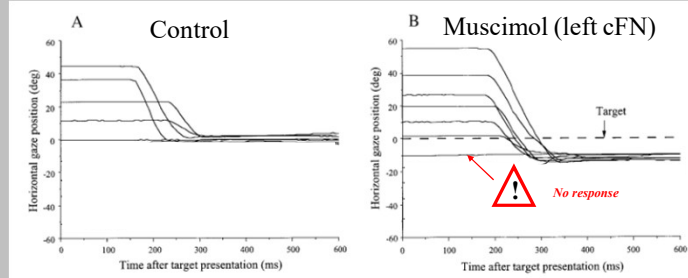
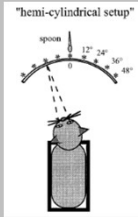
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Dysmetric gaze shifts in the cat

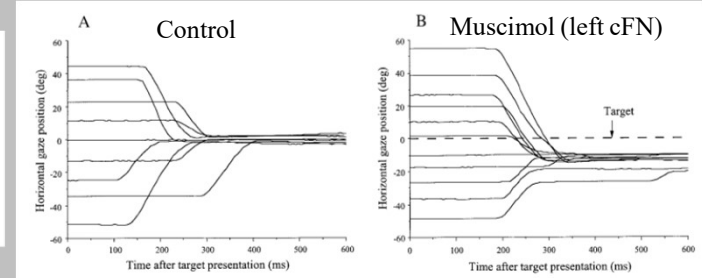
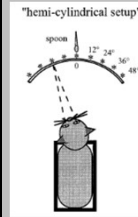
Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat I)



modified from Goffart & Pélisson JNP 1998

Dysmetric gaze shifts in the cat

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

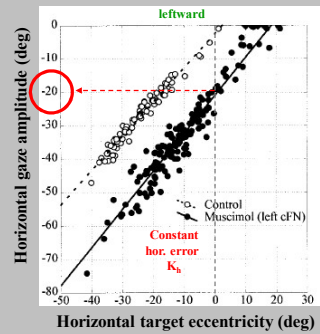


modified from Goffart & Pélisson JNP 1998

Gaze dysmetria

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

Ipsilesional movements

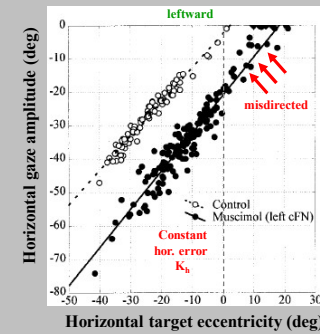


modified from Goffart & Pélisson JNP 1998
(see also Goffart & Pélisson JNP 1994 ; JP 1997)

Gaze dysmetria

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

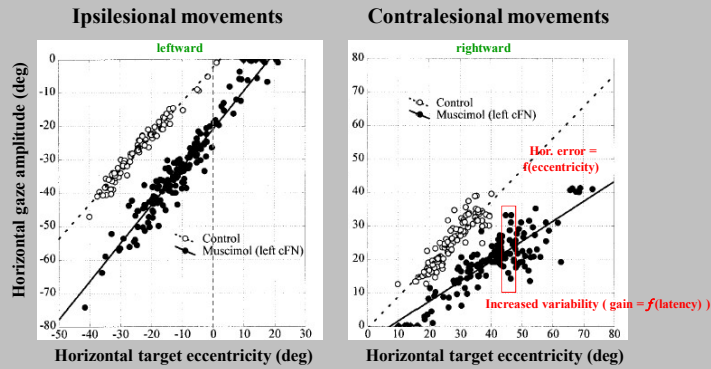
Ipsilesional movements



modified from Goffart & Pélisson JNP 1998
(see also Goffart & Pélisson JNP 1994 ; JP 1997)

Gaze dysmetria

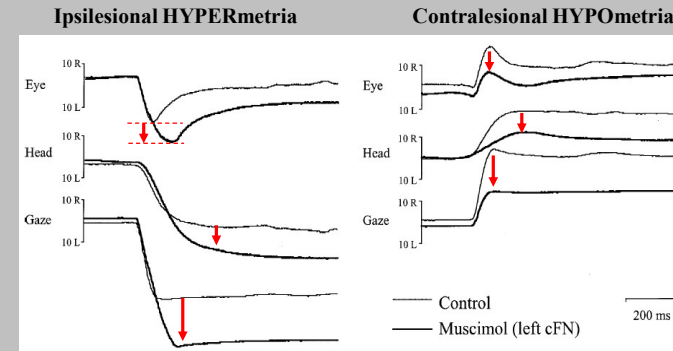
Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat G)



modified from Goffart & Pélisson JNP 1998
(see also Goffart & Pélisson JNP 1994 ; JP 1997)

Dysmetria affects both eye and head movements

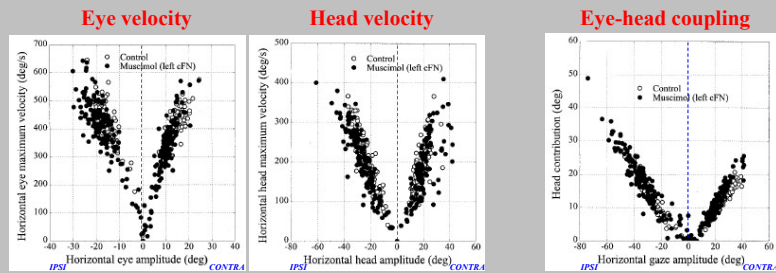
Muscimol injection in the left cFN (0.3 μ l; 1 μ g/ μ l, cat G)



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

Control (pre-injection)

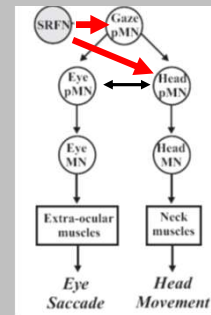


Deficit in head orientation

Muscimol (right cFN)



Cat

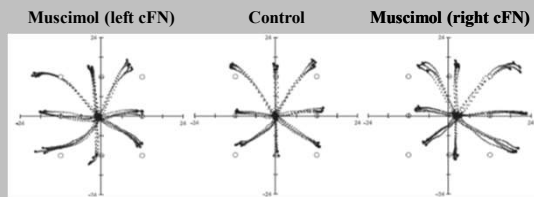


- Gaze dysmetria due to dysmetric eye + head
- Eye/head velocity **unchanged**
- Eye/head coupling **unchanged**

Goffart et al JNP 1998

Observations in the monkey

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



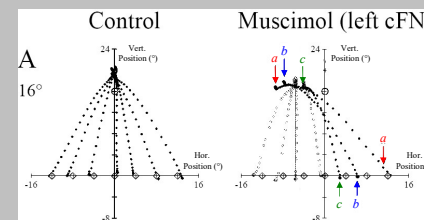
Goffart, Chen & Sparks JNP 2004

- Ipsilesional saccades : horizontal component is **hyper**metric (too large)
- Contralesional saccades : horizontal component is **hypo**metric (too small)

like in the head-unrestrained cat

Horizontal error is not constant

unlike in the head-unrestrained cat

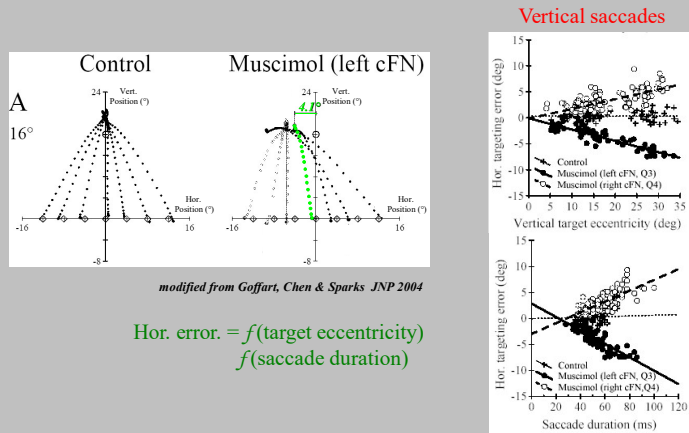


modified from Goffart, Chen & Sparks JNP 2004

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

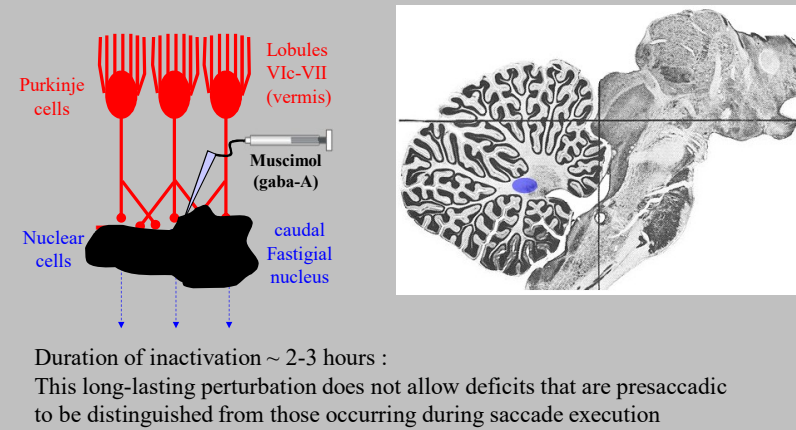
Horizontal error is not constant

unlike in the head-unrestrained cat

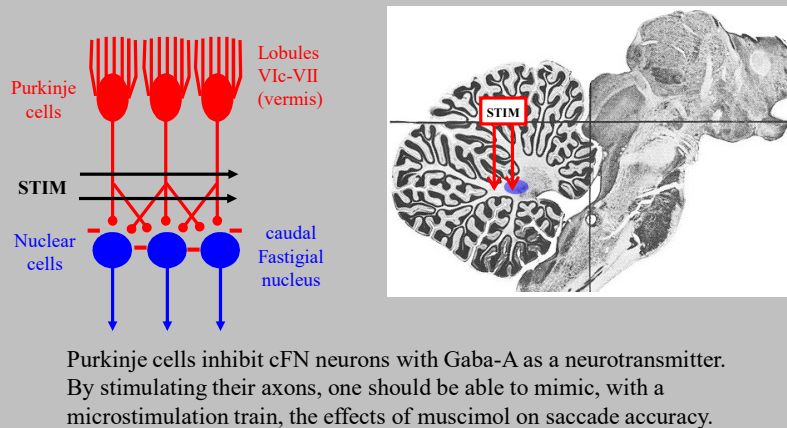


Impaired planning or execution ?

(pre- or intra-saccadic disorder ?)

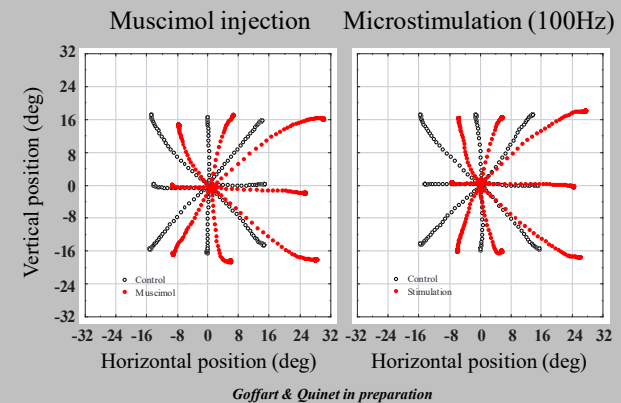


Inhibition of cFN activity with electrical microstimulation



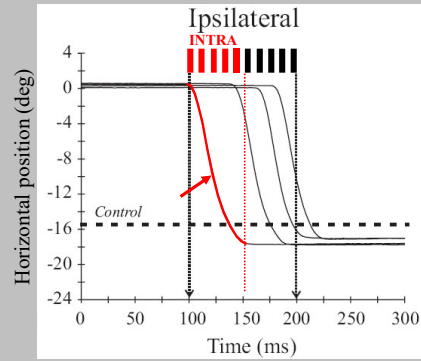
Inhibition of cFN

Right cFN (rebound saccades removed)



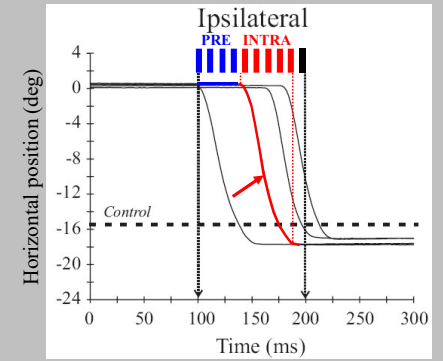
Time window of the perturbation

left caudal Fastigial Nucleus



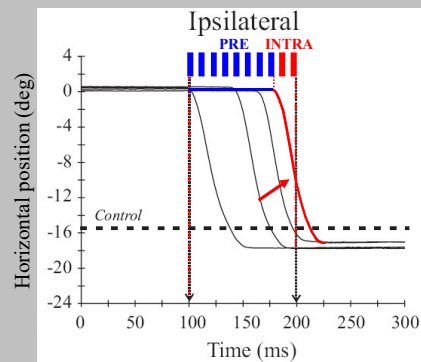
Time window of the perturbation

left caudal Fastigial Nucleus



Time window of the perturbation

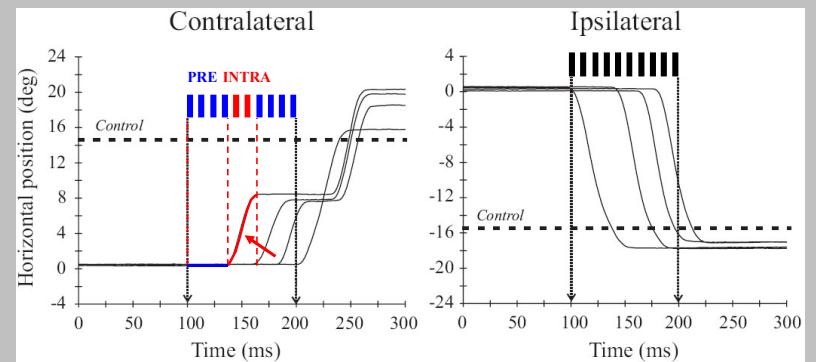
left caudal Fastigial Nucleus



Increasing the number of pre-saccadic pulses does not change the magnitude of hypermetria

Time window of the perturbation

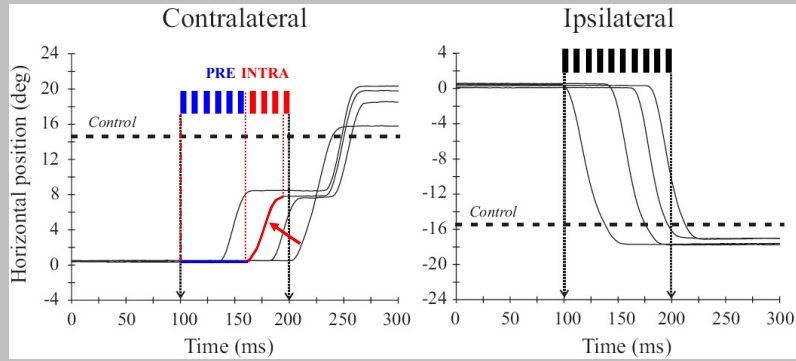
left caudal Fastigial Nucleus



Goffart & Quinet in preparation

Time window of the perturbation

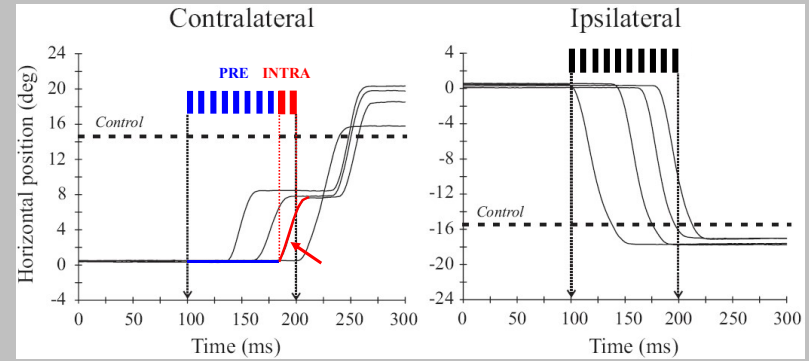
left caudal Fastigial Nucleus



Goffart & Quinet in preparation

Time window of the perturbation

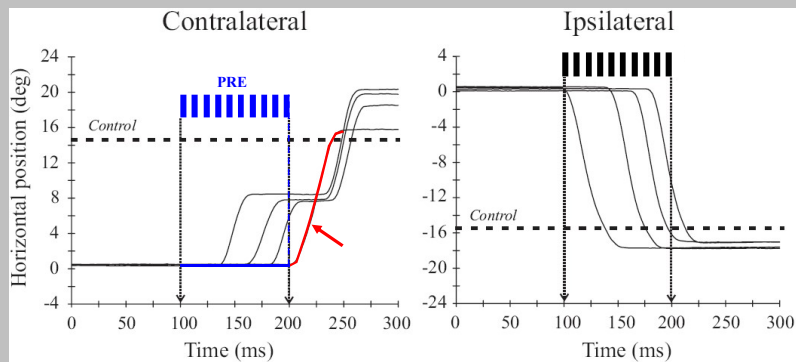
left caudal Fastigial Nucleus



Goffart & Quinet in preparation

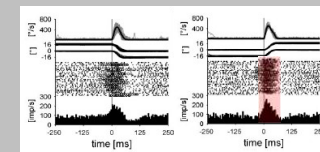
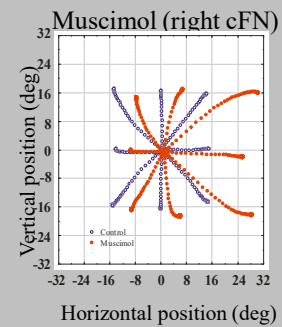
Time window of the perturbation

left caudal Fastigial Nucleus



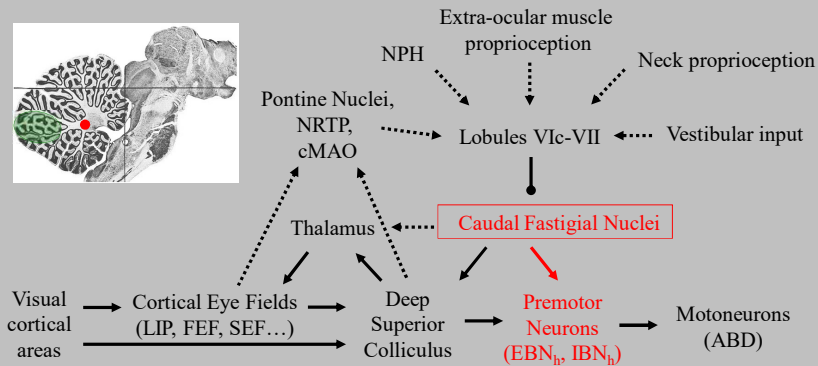
Goffart & Quinet in preparation

Horizontal dysmetria is due to the unilateral suppression of the saccade-related burst



modified from Kleine, Guan & Büttner JNP 2003

Fastigio-reticular projections and the cerebellar regulation of saccade amplitude

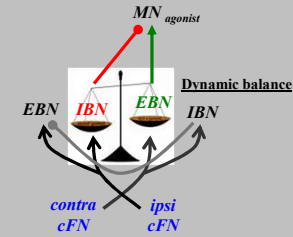


Bilateral hypothesis

J Neurophysiol 92: 3351-3367, 2004.
First published June 30, 2004; doi:10.1152/jn.01199.2003.

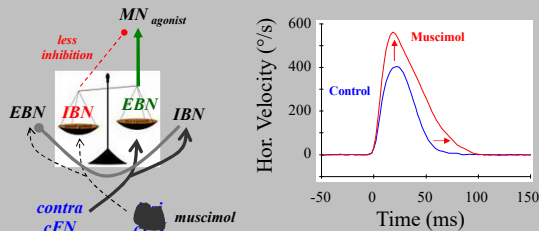
Goffart, Chen & Sparks, *JNP* 2004

For every saccade (horizontal, oblique or vertical), the left and right cFN regulate the balance of activity between excitatory input (EBNs) and inhibitory input (IBNs)



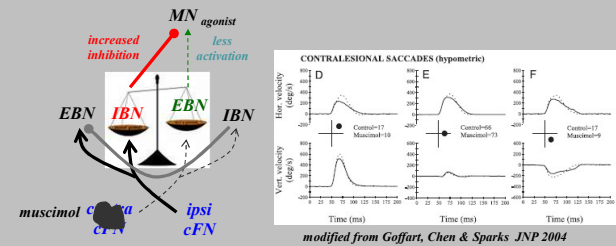
Bilateral hypothesis

Ipsilesional hypermetria

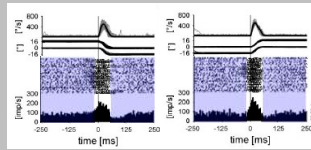


Bilateral hypothesis

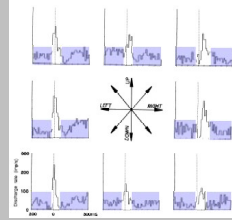
Contralateral hypometria



What about the sustained activity in cFN ?



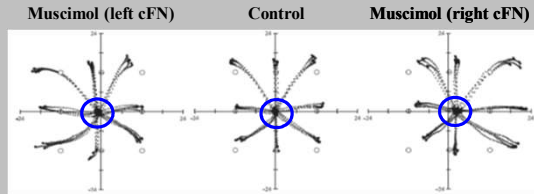
Kleine, Guan & Büttner JNP 2003



Ohtsuka & Noda JNP 1991

Ipsilesional fixation offset

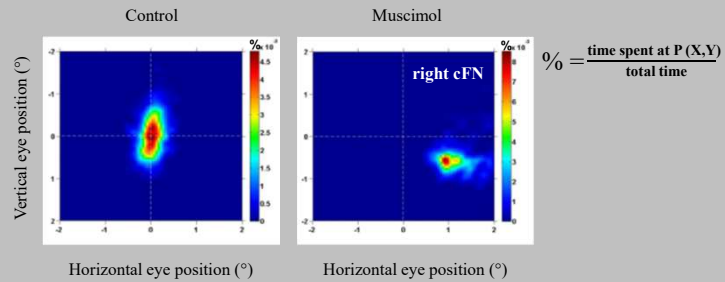
like in the head-unrestrained cat



Goffart, Chen & Sparks JNP 2004

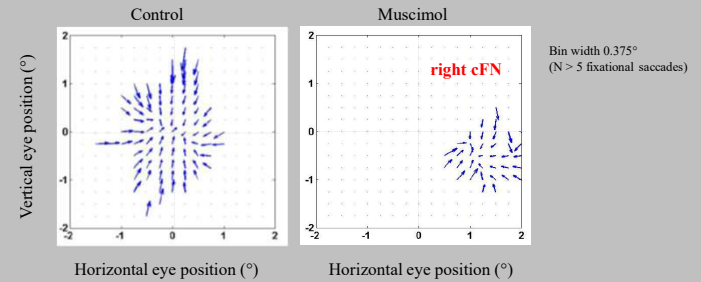
Fixation offset : ipsilesional shift in the scatter of eye position during fixation

Fixation offset



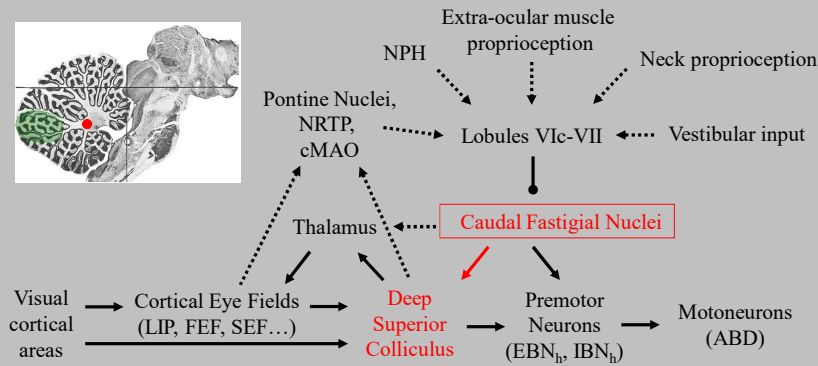
Monkey B

Direction of fixational saccades



Monkey B

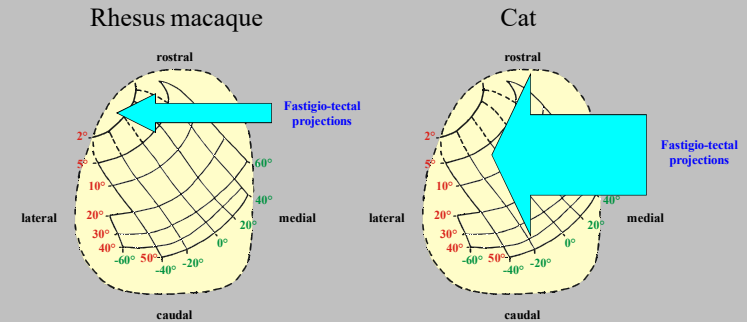
Fastigio-reticular projections and the cerebellar regulation of fixation



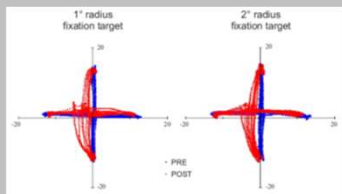
Behavioral and neuro-anatomical differences

In the monkey, a spatial deficit similar to that observed in the cat, is observed when one tests microsaccades generated when a visual target is being fixated.

This distinction could merely result from differences in the extent of fastigio-tectal projections.

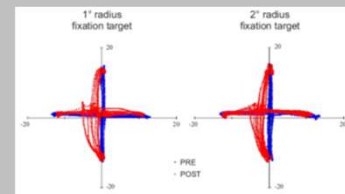


Experimental prediction : fixation offset after muscimol injection in the rostral SC

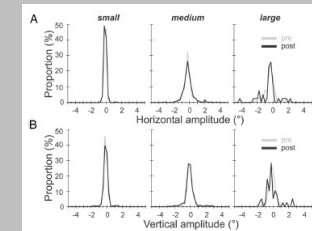


Ipsilesional fixation offset
Saccades to peripheral targets are accurate

Experimental prediction : fixation offset after muscimol injection in the rostral SC



Ipsilesional fixation offset
Saccades to peripheral targets are accurate

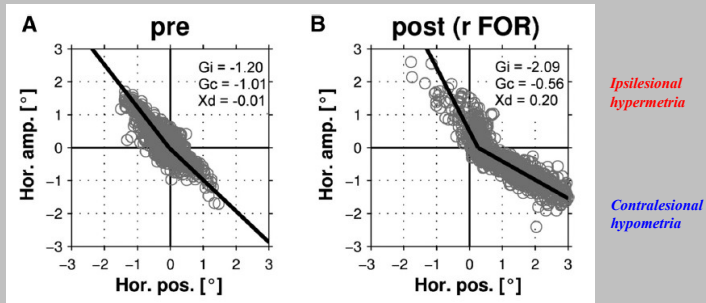


No asymmetry in the amplitude of fixational saccades

Goffart, Hafed & Krauzlis JN 2012

Amplitude of fixational saccades after muscimol injection in the caudal FN

Asymmetry (in contrast to muscimol in the SC)



Guerrasio, Quinet, Büttner & Goffart JNP 2010

Summary & conclusions

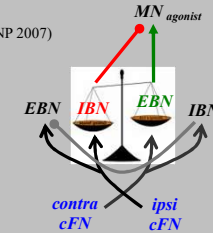
The medio-posterior cerebellum is involved, via the caudal fastigial nuclei, in mechanisms that ensure a spatial congruence between :

- the location of a visual target (foveal or peripheral, stationary or moving) and
- the impact of saccades toward this location (fixation or saccade).

The **bursts** emitted by saccade-related neurons in the two cFN regulate the **balance** between the excitatory and inhibitory input to the abducens motoneurons

→ this influence is visible in the **ipsipulsion** of eye saccades regardless of whether they are :

- ipsilateral, contralateral or vertical (Goffart et al. JNP 2004),
- fixational (Guerrasio et al. JNP 2010)
- generated during head-unrestrained gaze shifts (Quinet & Goffart JNP 2007)



Summary & conclusions

The medio-posterior cerebellum is involved, via the caudal fastigial nuclei, in mechanisms that ensure a spatial congruence between :

- the location of a visual target (foveal or peripheral, stationary or moving) and
- the impact of saccades toward this location (fixation or saccade).

The **bursts** emitted by saccade-related neurons in the two cFN regulate the **balance** between the excitatory and inhibitory input to the abducens motoneurons

→ this influence is visible in the **ipsipulsion** of eye saccades regardless of whether they are :

- ipsilateral, contralateral or vertical (Goffart et al. JNP 2004),
- fixational (Guerrasio et al. JNP 2010)
- generated during head-unrestrained gaze shifts (Quinet & Goffart JNP 2007)

The **sustained firing rate** emitted by the saccade-related neurons in the two cFN regulate the **balance** of activity between the left and right rostral SC

→ this influence is visible in the **offset** during fixation, regardless of whether it is made :

- with the head restrained (Goffart et al. JNP 2004; Guerrasio et al. JNP 2010)
- with the head unrestrained (Quinet & Goffart JNP 2005)

Summary & conclusions

The medio-posterior cerebellum is involved, via the caudal fastigial nuclei, in mechanisms that ensure a spatial congruence between :

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The **modulated firing rate** of smooth pursuit-related neurons in the two cFN also contribute to this SC **balance**

→ this influence is visible in the **offset** and **gain changes** during pursuit

- with the head restrained (Robinson et al. JNP 1997 ↔ Krauzlis et al. JNP 2000)

In the monkey, gaze dysmetria is due to dysmetric eye saccades

unlike in the head-unrestrained cat (dysmetric eye and head movements)

Quinet & Goffart JNP 2005

J Neurophysiol 93: 2343–2349, 2005.
First published November 24, 2004; doi:10.1152/jn.00705.2004.

Report

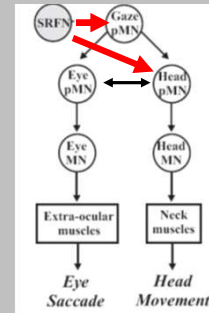
Saccade Dysmetria in Head-Unrestrained Gaze Shifts After Muscimol Inactivation of the Caudal Fastigial Nucleus in the Monkey

Quinet & Goffart JNP 2007

J Neurophysiol 98: 3269–3283, 2007.
First published October 10, 2007; doi:10.1152/jn.00741.2007.

Head-Unrestrained Gaze Shifts After Muscimol Injection in the Caudal Fastigial Nucleus of the Monkey

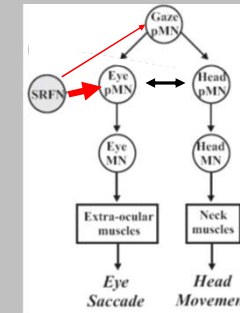
Cat



- Gaze dysmetria due to dysmetric **eye + head**
- Eye/head velocity **unchanged**
- Eye/head coupling **unchanged**

Goffart et al JNP 1998

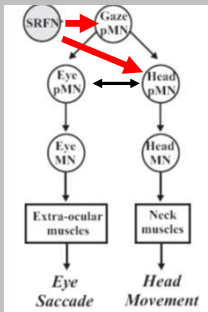
Primate



- Gaze dysmetria due to dysmetric **eye**
- Eye velocity **changed**, head velocity **unchanged**
- Eye/head coupling **changed**

Robinson et al. JCN 1994 (anatomy)
Quinet & Goffart JNP 2005, 2007 (inactivation & eye-head)
Quinet & Goffart JNP 2009 (microstimulation)
Fuchs et al JNP 2010 (unit recordings)

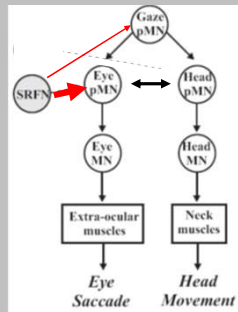
Cat



- Gaze dysmetria due to dysmetric **eye + head**
- Eye/head velocity **unchanged**
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Goffart et al JNP 1998

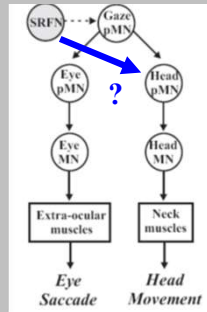
Primate



- Gaze dysmetria due to dysmetric **eye**
- Eye velocity **changed**, head velocity **unchanged**
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Robinson et al. JCN 1994 (anatomy)
Quinet & Goffart JNP 2005, 2007 (inactivation & eye-head)
Quinet & Goffart JNP 2009 (microstimulation)
Fuchs et al JNP 2010 (unit recordings)

Rodent, Amphibian



- Gaze dysmetria due to dysmetric **head** ?
- Head velocity **changed**, eye **unchanged** ?
- Eye/head coupling **changed** ?

Final conclusion

In the cat, the influence of the midline cerebellum concerns the generation of eye and head movements.

In the primate, it is restricted to the oculomotor system (system that transports the fovea).

More general hypothesis :

The medio-posterior cerebellum would compensate for intra- and inter-specific morphological variability - in the sensory organs used to detect events in the environment (afferents) and - in the motor plants (efferents) used to acquire them.

CONTROL OF SENSORY DATA ACQUISITION

James M. Bower

International Review of Neurobiology 41: 489-513, 1997

The preferred sensory system corresponds to the system associated with the largest neural mass.

Experiments in other vertebrate species (e.g., amphibian, rodent) will permit to verify the possibility of a deficit in orienting head movements.

Acknowledgments

Experiments in the caudal Fastigial Nucleus

Head-free cat

Denis Pélisson, PhD
Alain Guillaume, PhD

Head-restrained monkey

David L. Sparks, PhD Lorenzo Guerrasio, PhD
Longtang L. Chen, PhD Ulrich Büttner, MD PhD

Head-free monkey

Julie Quinet, PhD

Experiments in the deep Superior Colliculus

Ziad M. Hafed, PhD
Rich J. Krauzlis, PhD

