

UNDERSTANDING VESTIBULAR COMPENSATION after acute unilateral vestibular loss

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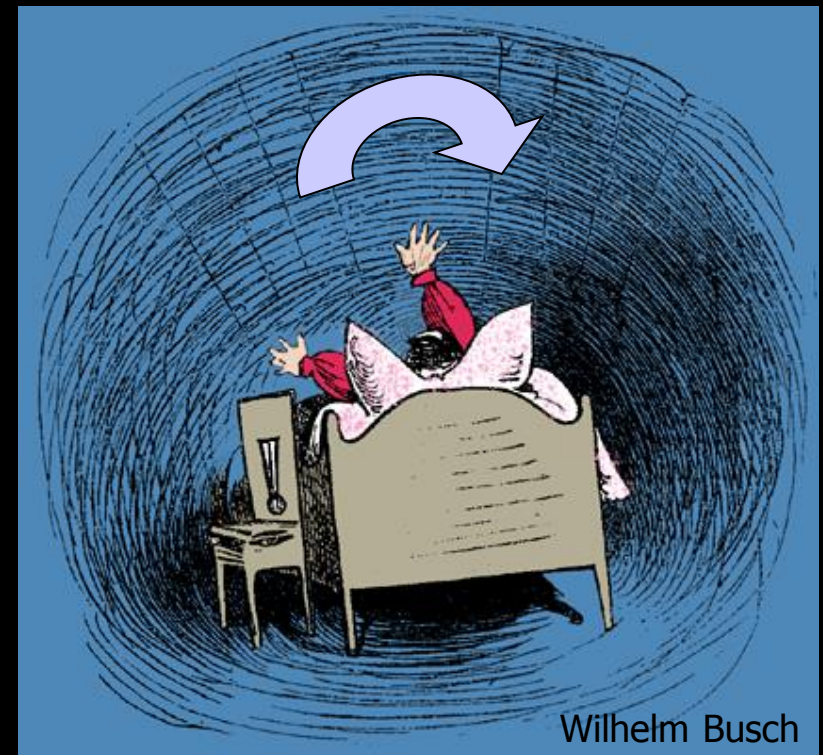
18th WORKSHOP on NEUROTOLOGY

*November 29th-30th
December 1st 2019*

KOLKATA
(India)

Key symptoms in patients with unilateral vestibular lesions

- Severe rotational vertigo
- Horizontal - rotatory SPN
- Blurred vision (oscillopsia)
- Falls towards the lesion side
- Nausea and vomiting



Wilhelm Busch

ACUTE STATIC DEFICITS

ACUTE DYNAMIC DEFICITS

Head/Body
Stationary

Head/Body
Movements

OCULOMOTOR
SYNDROME

PERCEPTIVE
SYNDROME

POSTURAL
SYNDROME

NYSTAGMUS
SKEW DEVIATION
OCULAR
CYCLOTORSION

VOR
ASYMMETRIES

VERTIGO
SUBJECTIVE VERTICAL

SPATIAL
DISORIENTATION

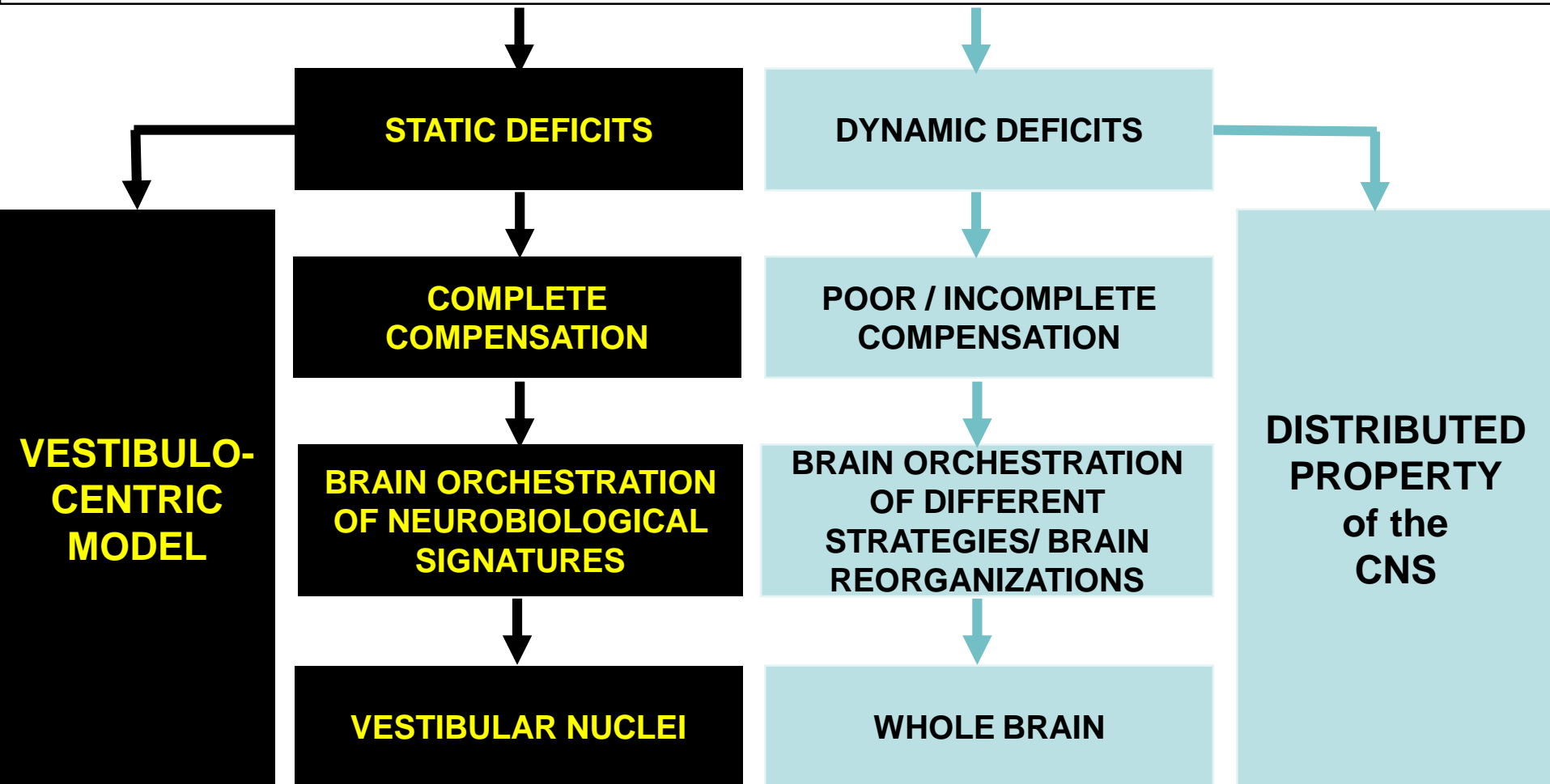
HEAD/BODY
TILT

LOSS of
HEAD
STABILIZATION

**VESTIBULAR COMPENSATION:
A MODEL OF NEURONAL PLASTICITY**

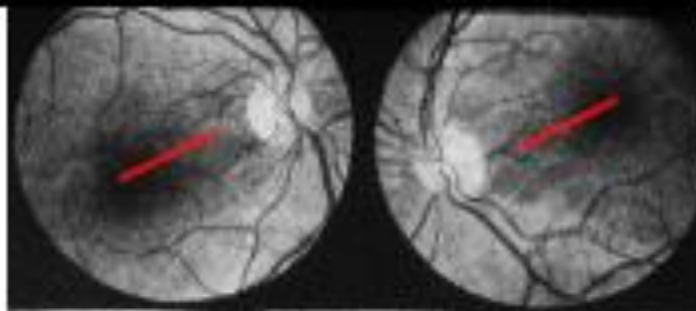
THE TWO MODELS OF VESTIBULAR FUNCTION RECOVERY

(Lacour, Current Med Res & Opinion, 2006; Lacour et al., Front Neurol, 2014)



COMPENSATION
of the
OCULAR AND
POSTURAL DEFICITS
(~3 months)
and of the
SUBJECTIVE VISUAL
VERTICAL
(~6 months-1 year)

Counterroll



Skew



Head Tilt



FULL RECOVERY OF THE STATIC VESTIBULAR FUNCTIONS

(Plastic events in the deafferented VN)

IEGs
NEUROTROPHINES
NEUROGENESIS

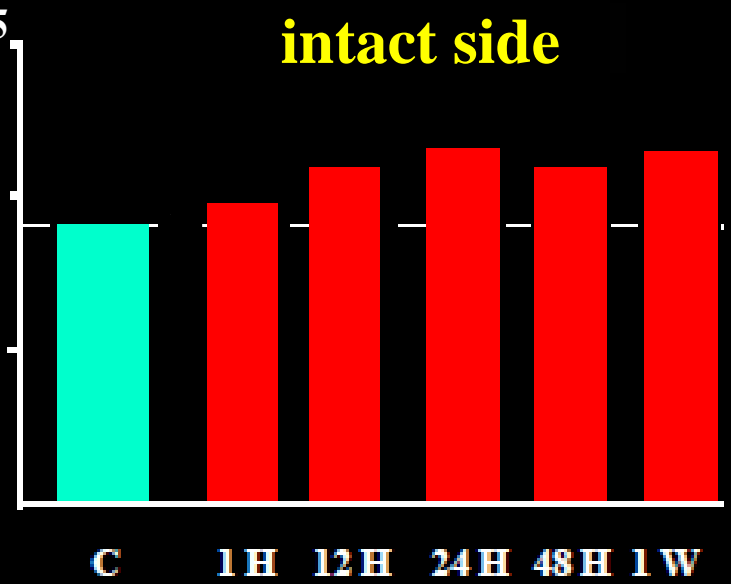
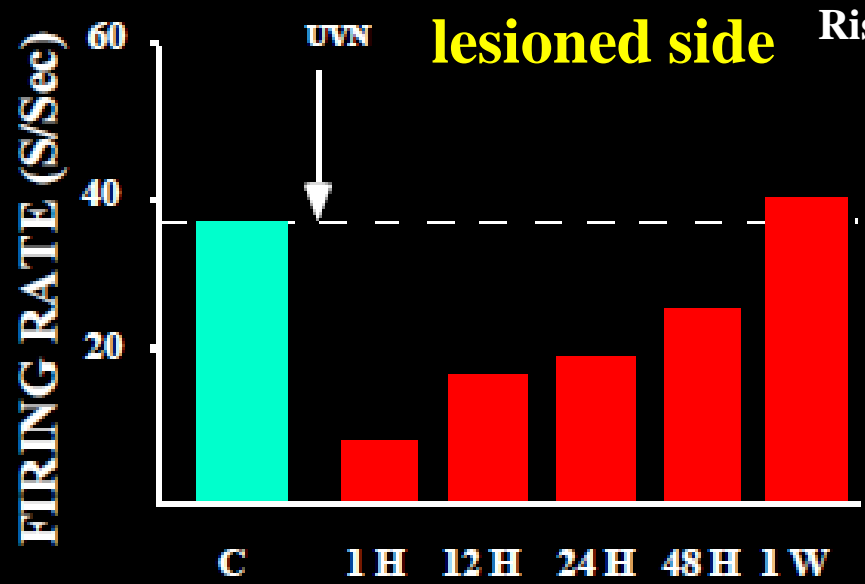
MODIFICATIONS OF THE MEMBRANE
PROPERTIES OF THE VN CELLS

REWEIGHTING OF
SENSORY INPUTS
(Vision, Proprioception)

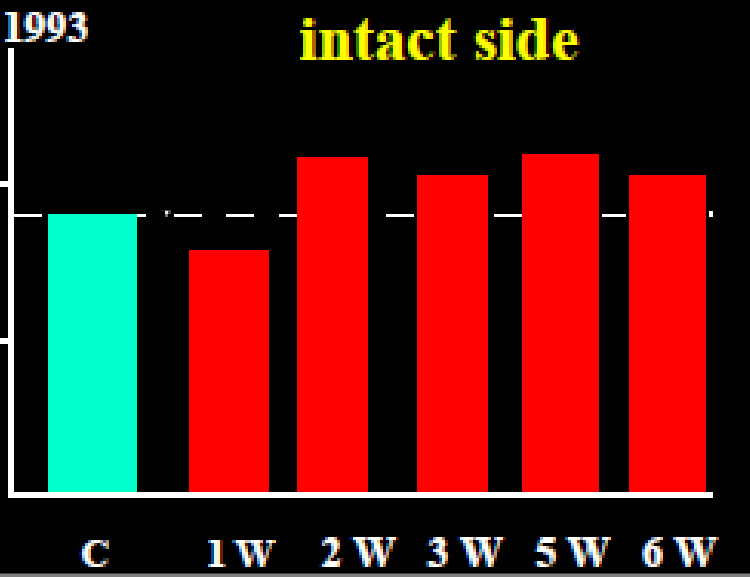
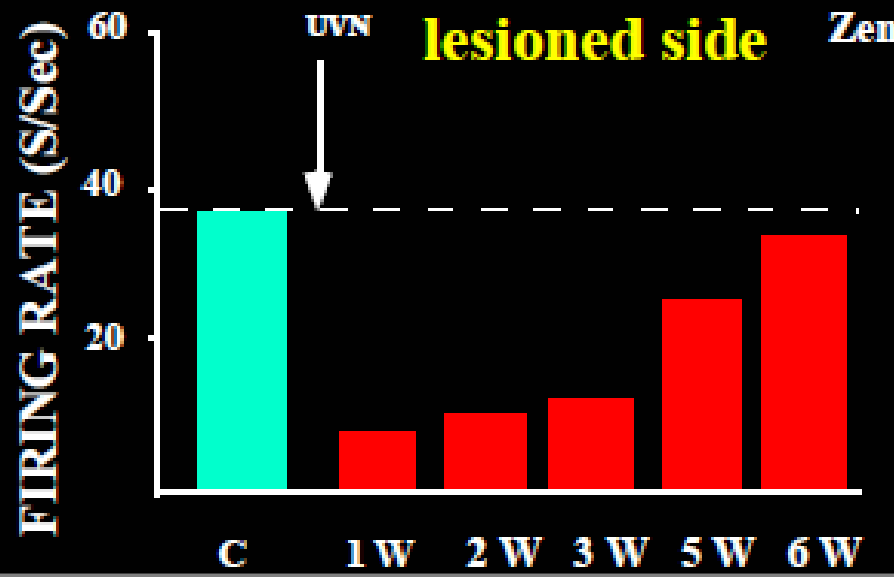
**RESTORATION OF NEURONAL
ACTIVITY ON THE LESION SIDE**
(Rebalance of the VN activity on both sides)

FULL COMPENSATION OF THE STATIC DEFICITS

REBALANCE OF THE VN ACTIVITY: A KEY PROCESS

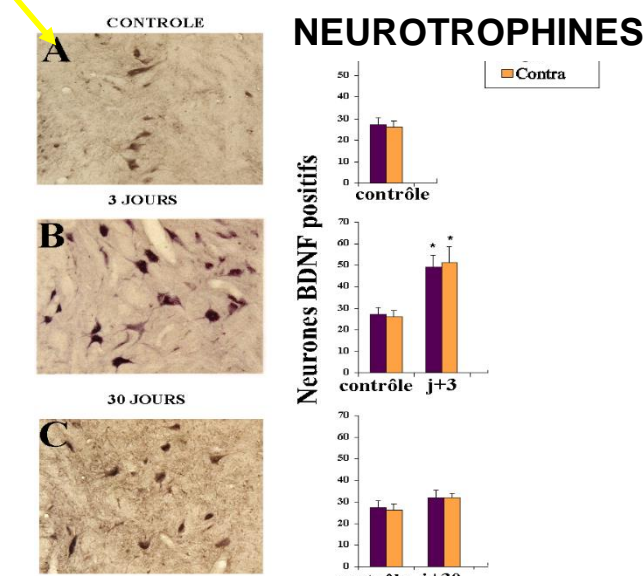
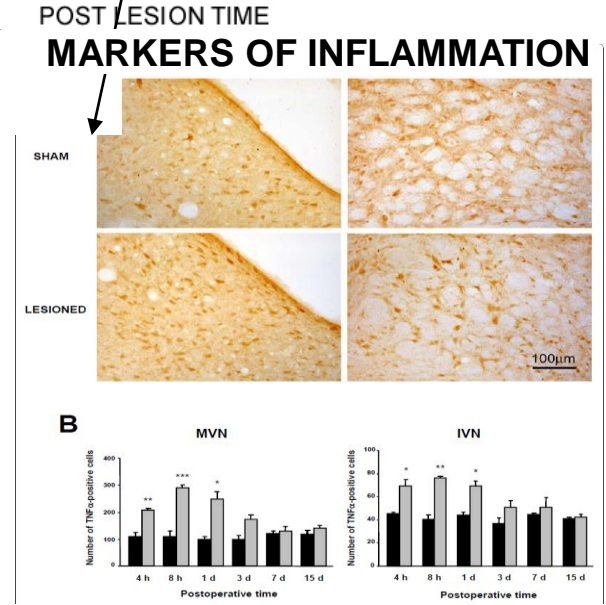
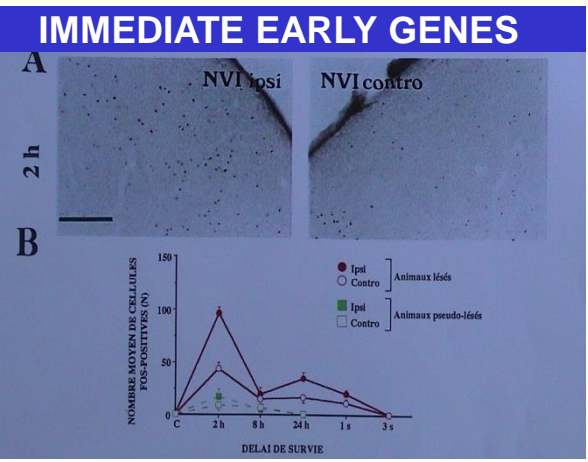
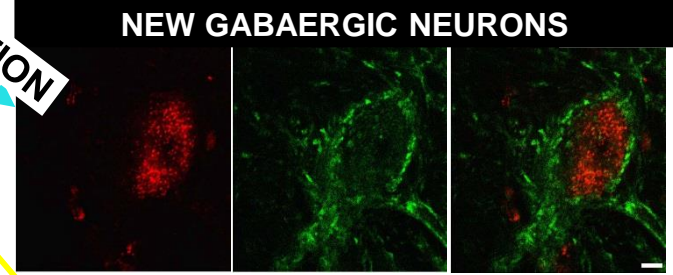
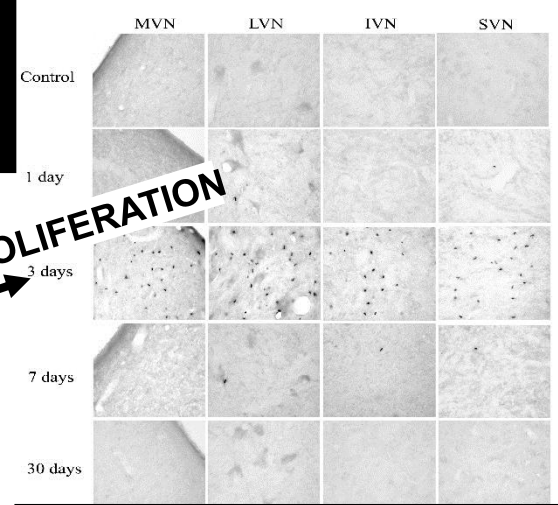
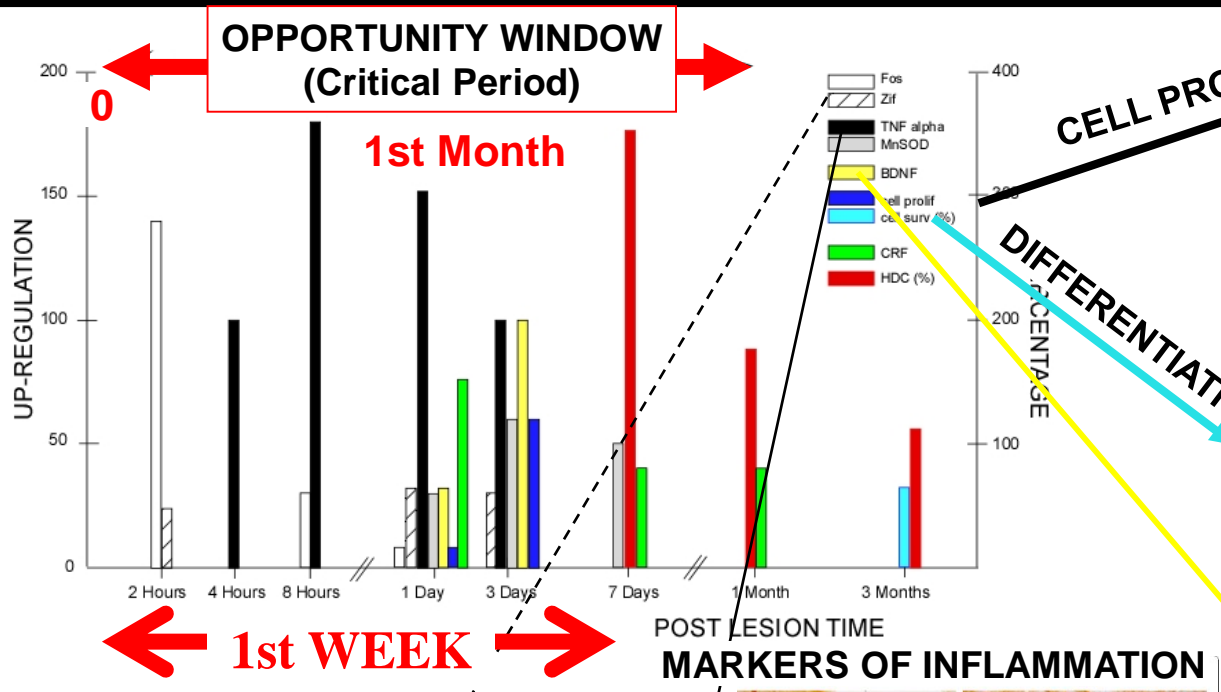


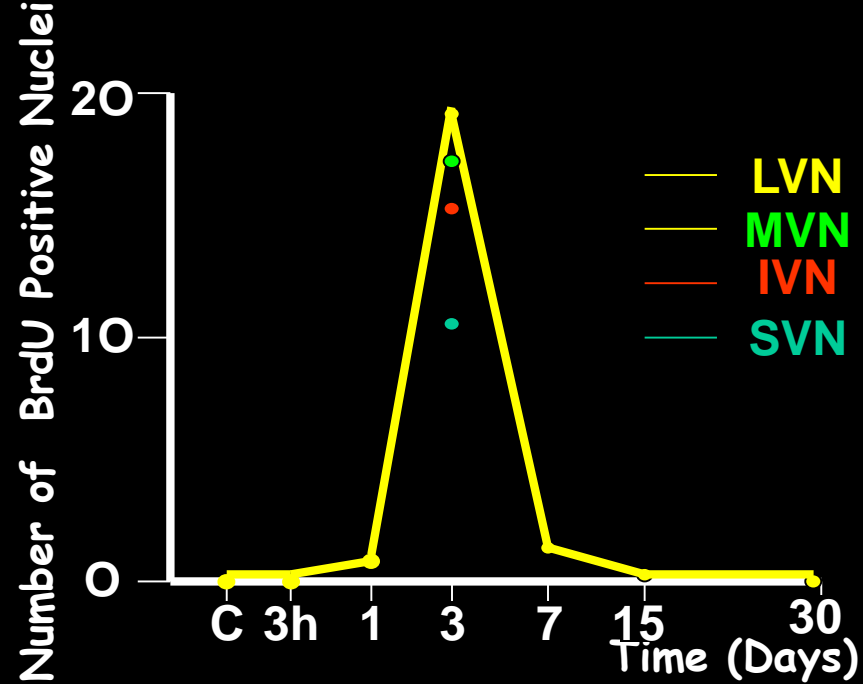
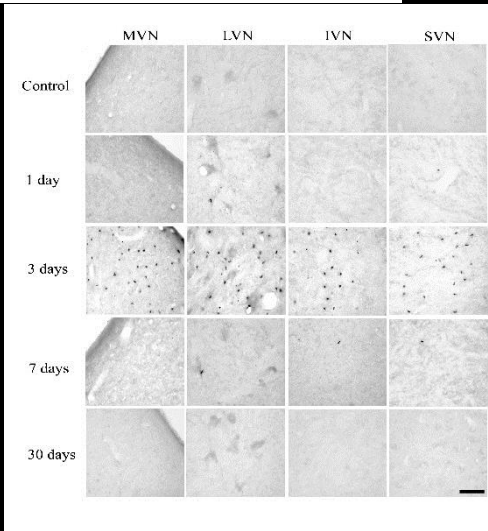
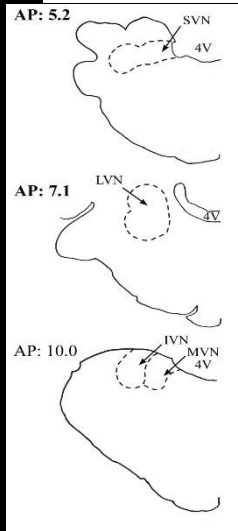
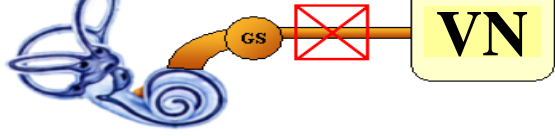
RODENT MODEL : 1 Week



CAT MODEL : 6 Weeks

RE-EXPRESSION OF DEVELOPMENTAL PLASTICITY MECHANISMS IN THE VN



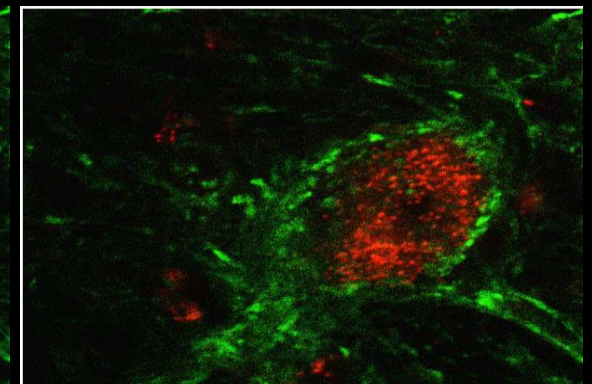
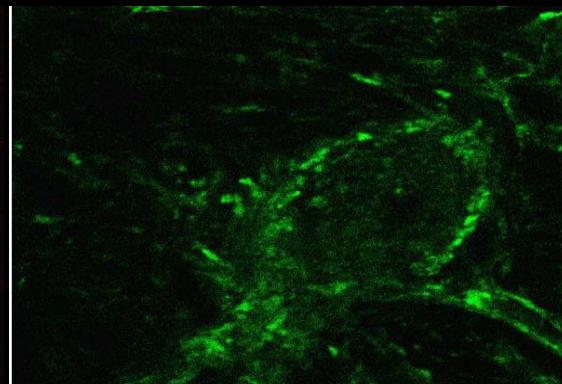
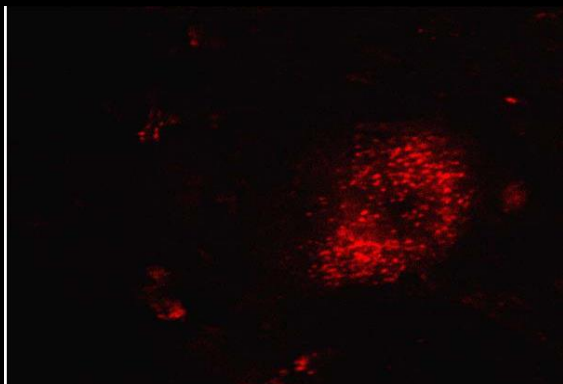


CELL PROLIFERATION IN THE VN (3 days)

BrdU

GAD 67

BrdU/GAD 67



CELL DIFFERENTIATION IN THE VN(1-2 months)

Tighilet, Brezun, Gustave Dit Duflo, Gaubert, Lacour (2007) Eur J Neurosci 25: 47-58

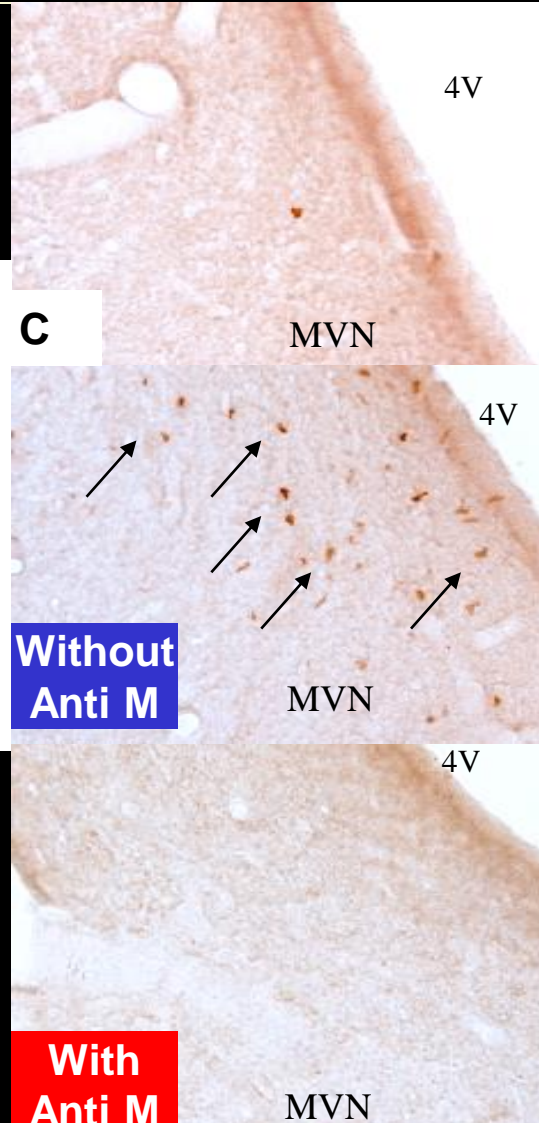
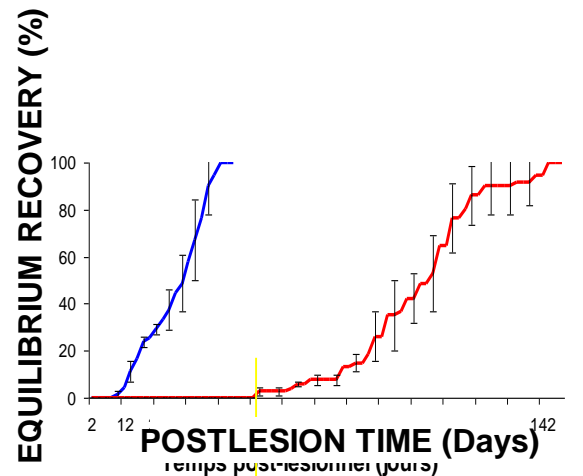
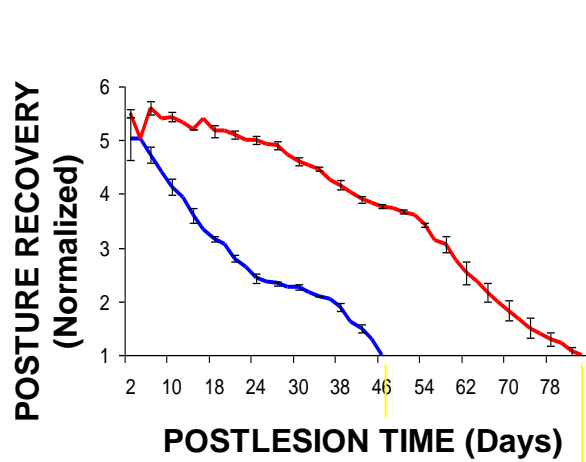
NEUROGENESE IN THE VN FACILITATES THE BEHAVIOURAL RECOVERY

VESTIBULAR LESION WITHOUT ANTIMITOTICS

VESTIBULAR LESION WITH ANTIMITOTICS

POSTURE

LOCOMOTION



6 WEEKS DELAY

14 WEEKS DELAY

RECOVERY TIME X 2

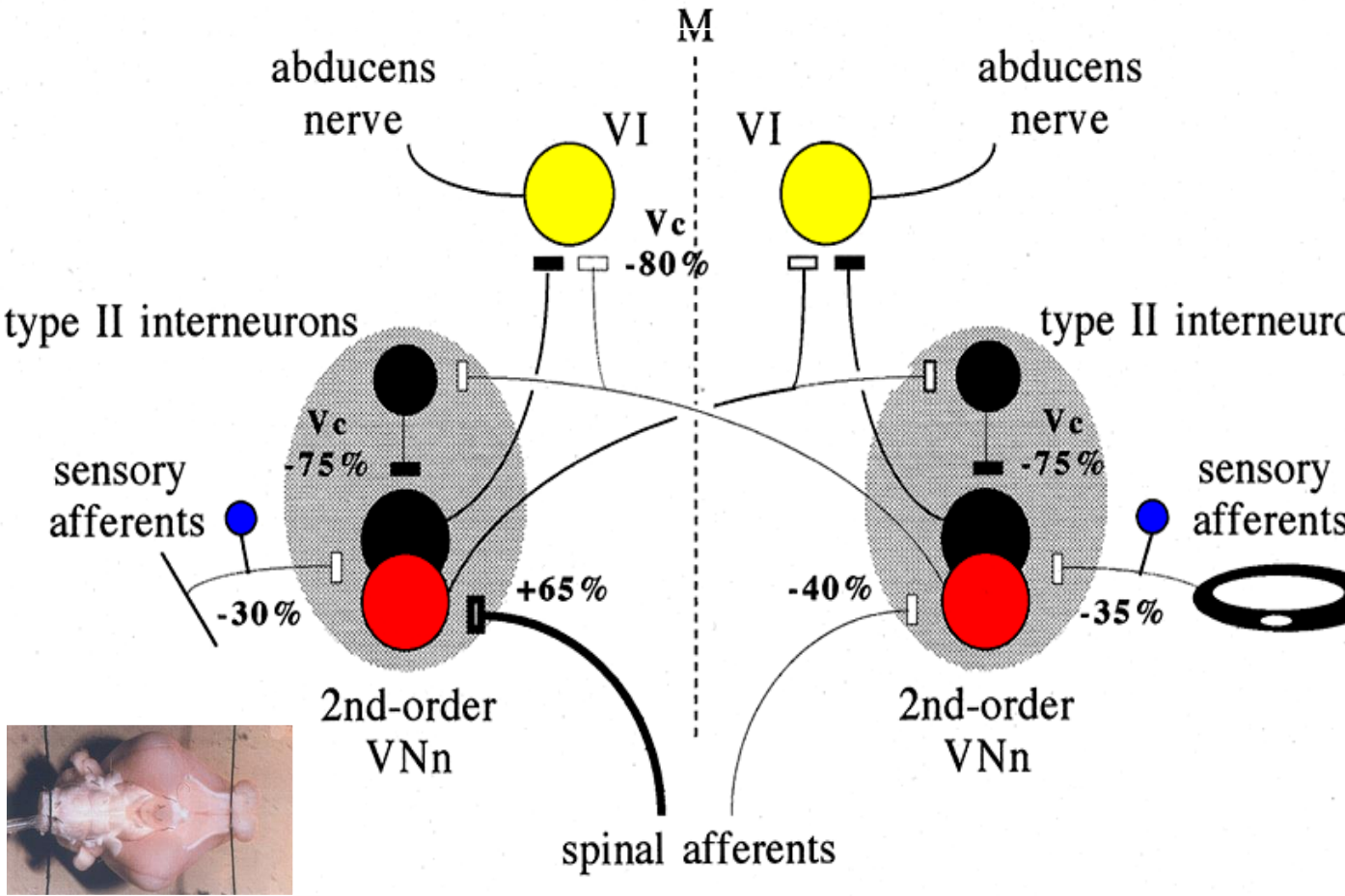
RECOVERY TIME X 3.5

With Anti M

MVN

MODIFICATIONS OF THE NEURONAL PROPERTIES OF THE VN CELLS

3 Days after unilateral vestibular lesion



LESIONED SIDE

INTACT SIDE

Lacour, Helmchen and Vidal, J Neurology (2016)

- Reduction of their sensitivity to inhibitory neurotransmitters (GABA) (decrease of the commissural inhibition)
- Increase of their intrinsic excitability
- Modulation of the neuronal activity on the lesion side by the contralateral side, which substitutes to the push/pull mechanism

POOR RECOVERY OF THE DYNAMIC VESTIBULAR FUNCTIONS

(Reorganization of the whole brain)

RETURN to the Initial Function

NEW OPERATIVE MODES
Distributed Property of the CNS

FUNCTIONAL RESTORATION

SENSORY SUBSTITUTION

BEHAVIOURAL SUBSTITUTION

**BRAIN REMODELINGS,
CHANGES IN BRAIN
FUNCTIONAL
CONNECTIVITY**

RETURN TO A GOOD QUALITY OF LIFE

RECOVERY OF THE DYNAMIC FUNCTIONS

1.

RESTORATION

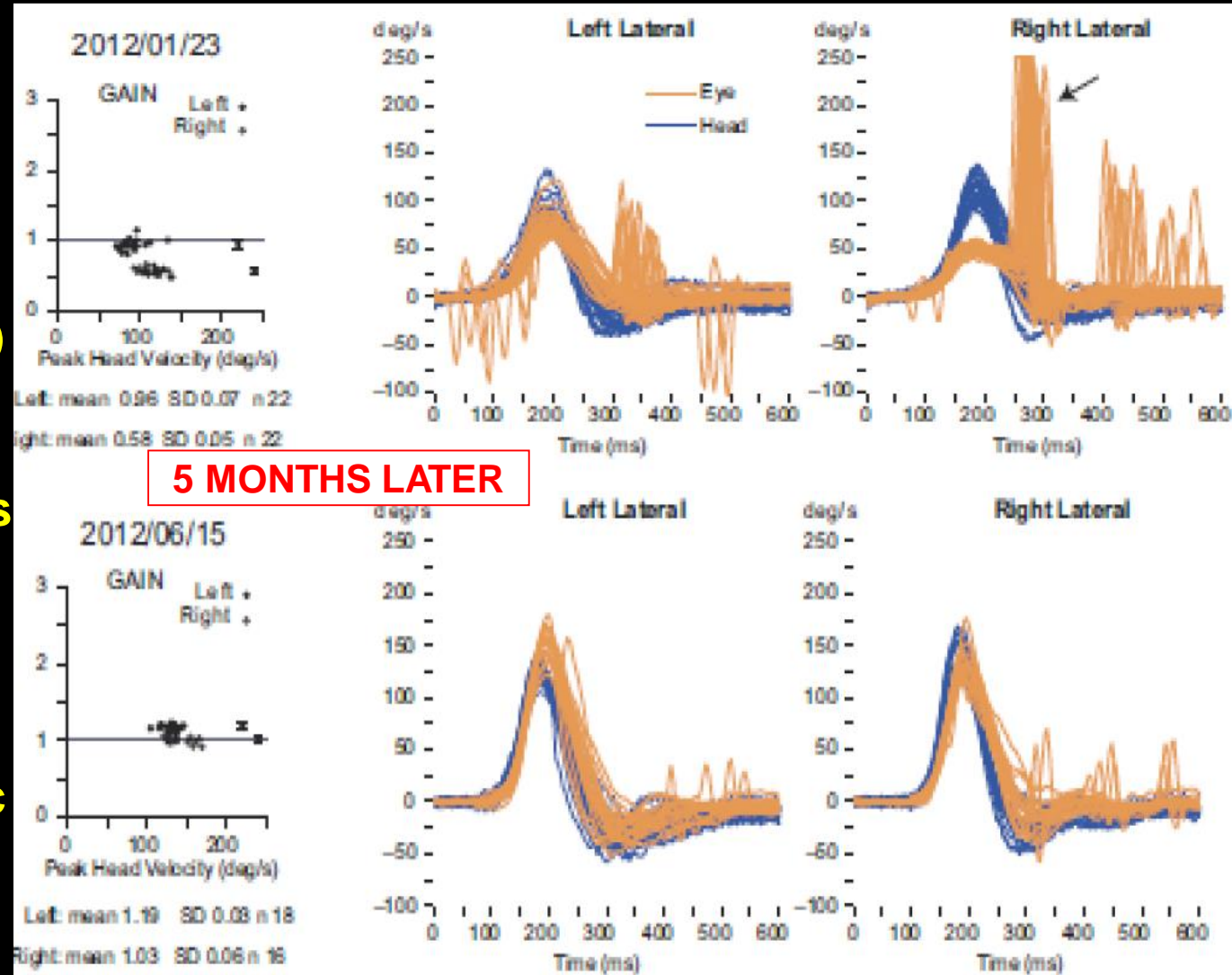
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graph TD; A[RESTORATION] --> B[RETURN TO THE SAME FUNCTION]
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**RETURN TO THE
SAME FUNCTION**

RECOVERY OF THE VOR (Patient with a right vestibular neuritis)

HYPOTHESIS

1. Repair of vestibular terminal afferents (periphery)
2. Reoccupation of vacant synaptic sites by sprouting of remaining vestibular afferents (in the VN)
3. Increased synaptic weight of intact vestibular afferent fibres (in the VN)



COMPENSATION OF THE DYNAMIC DEFICITS

2.

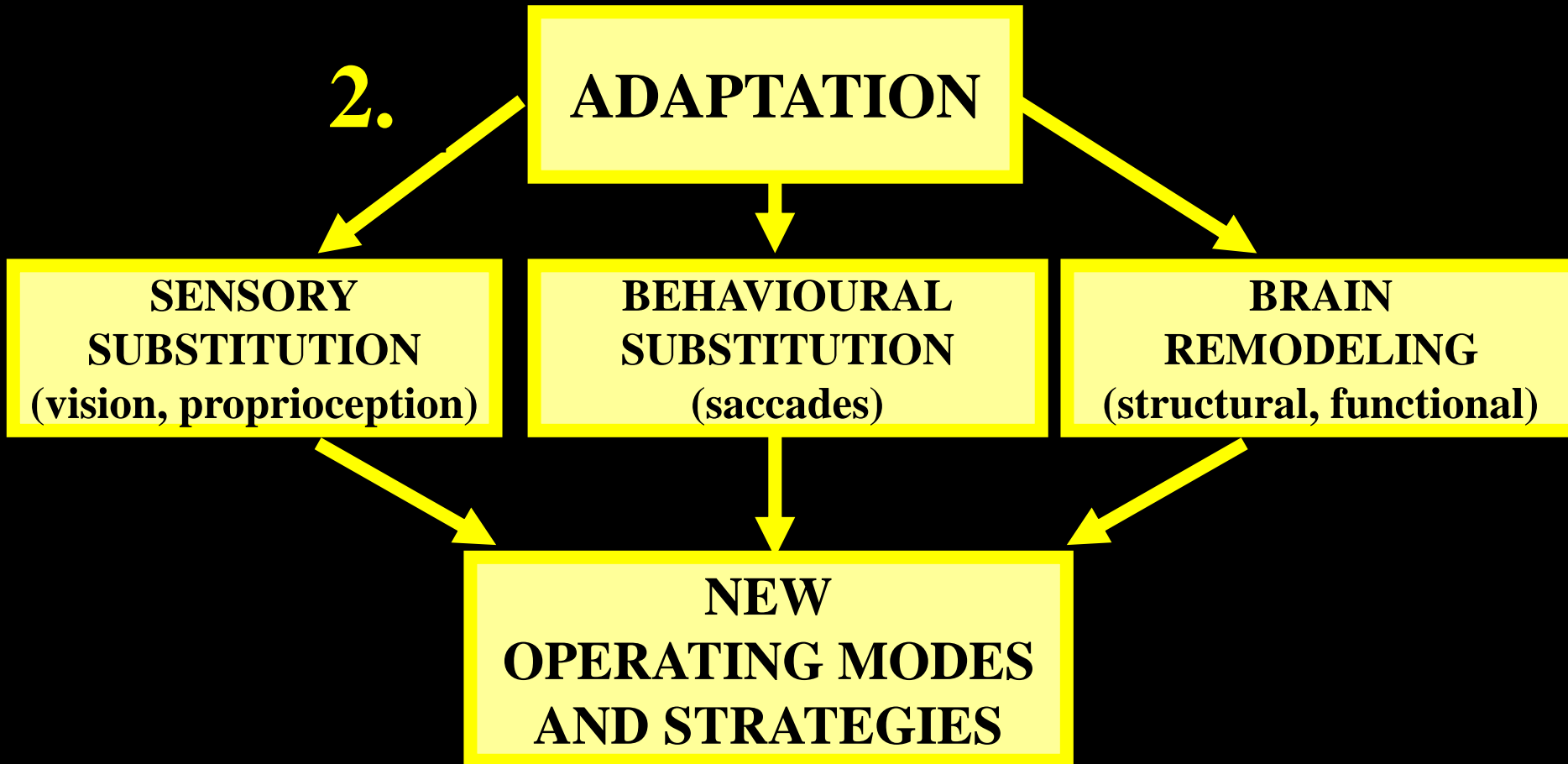
ADAPTATION

**SENSORY
SUBSTITUTION**
(vision, proprioception)

**BEHAVIOURAL
SUBSTITUTION**
(saccades)

**BRAIN
REMODELING**
(structural, functional)

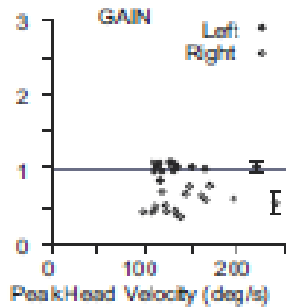
**NEW
OPERATING MODES
AND STRATEGIES**



THE SACCADIC SUBSTITUTION: a behavioural adaptation (Patient with a right vestibular neuritis)

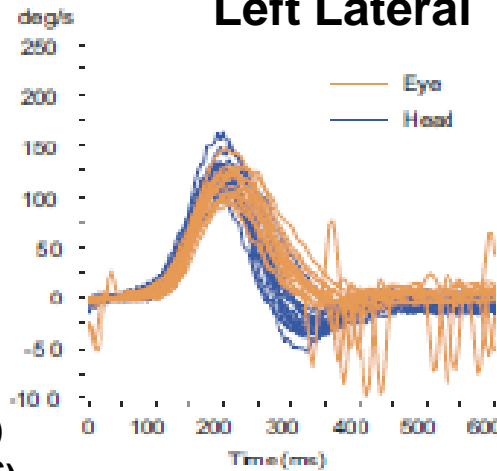
ACUTE STAGE

10/06/2011

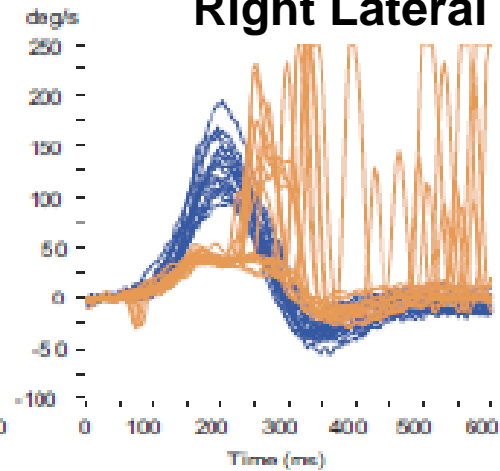


Left: 1.03 ± 0.07 (n=16)
 Right: 0.56 ± 0.13 (n=16)

Left Lateral

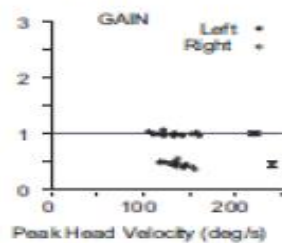


Right Lateral



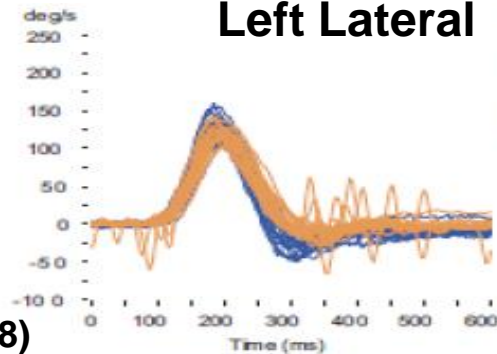
COMPENSATED
 STAGE
 (11 months later)

08/05/2012

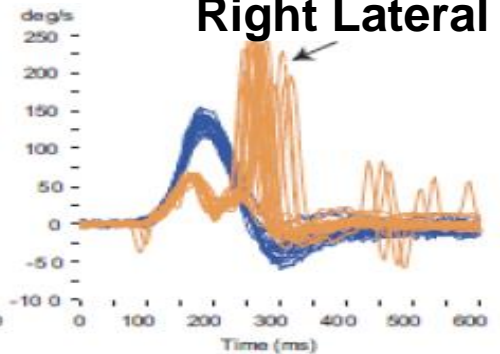


Left: mean 1.01 ± 0.03 (n=18)
 Right: 0.46 ± 0.05 (n=19)

Left Lateral



Right Lateral



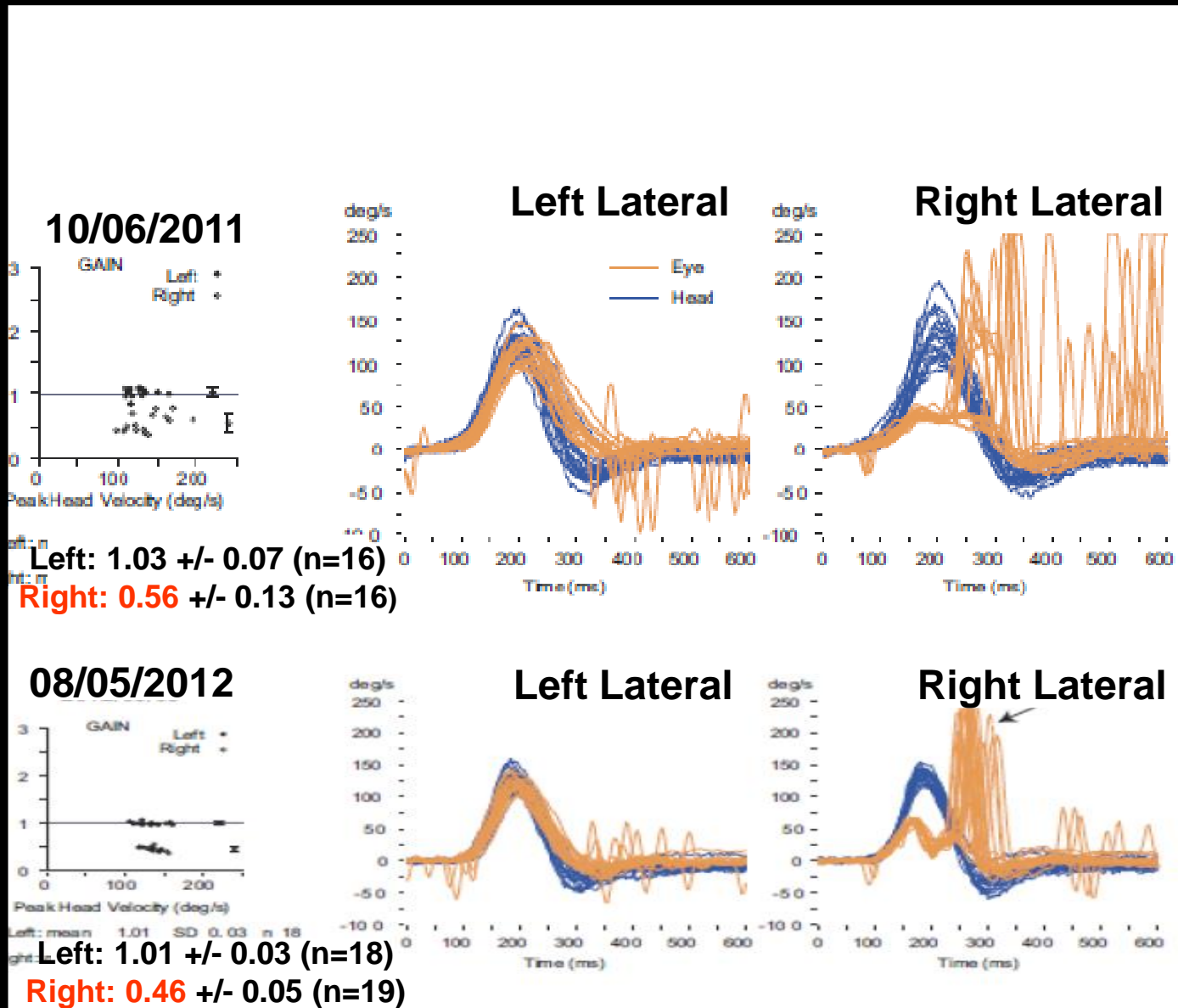
THE SACCADIC SUBSTITUTION: a behavioural adaptation (Patient with a right vestibular neuritis)

HYPOTHESES

1. Pre-programmation of an ocular saccade in the direction of the missing slow phase of the VOR (covert saccade)

2. Suppression of vision during the saccade (decrease of retinal slip and of its perception)

3. Proprioception ?
Cerebellum ?
Efference copy ?
Retinal slip



BRAIN REMODELING AFTER A VESTIBULAR LOSS

INCREASE OF WHITE MATTER:

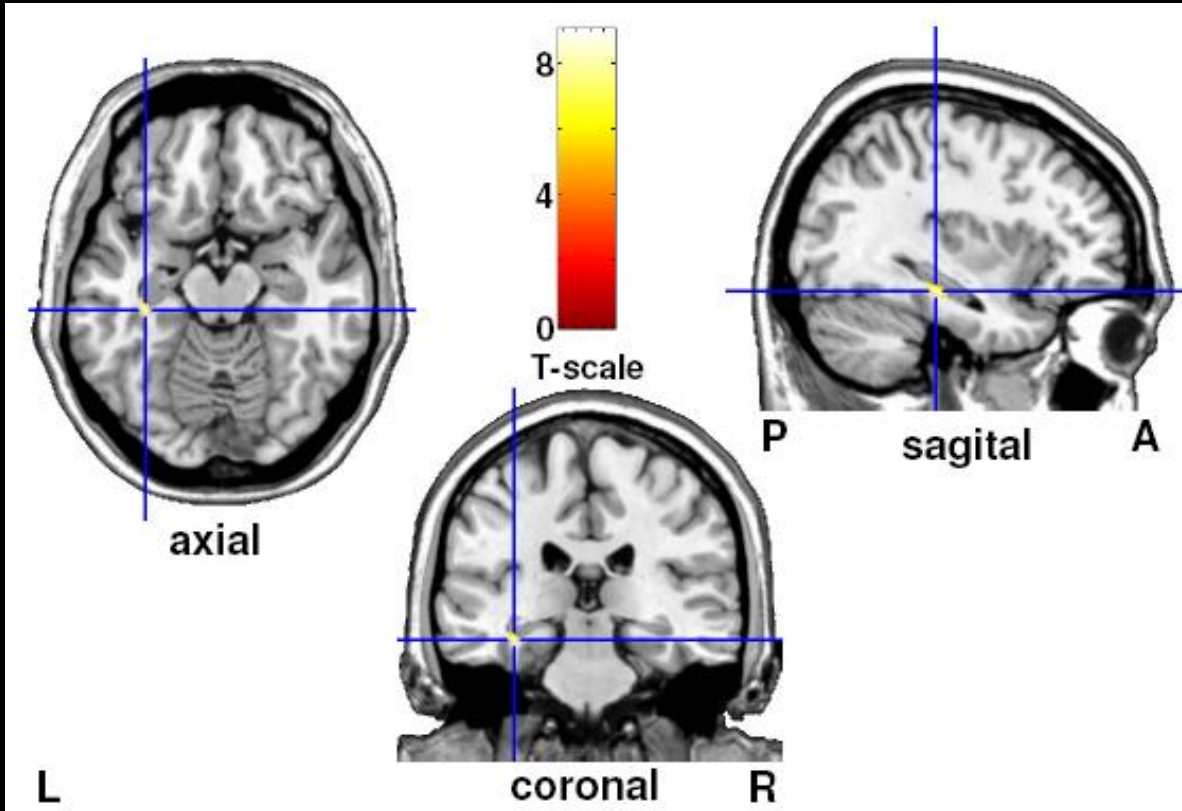
- In the commissural system
(modulation of the VN activity on the lesion side by the intact side)
- in the somatosensory system
(Gracilis Nucleus, relay of the somatosensory inputs)
- in the areas MT/V5
(role in the perception of visual motion)

Indicating that these pathways are reinforced during the central compensation process

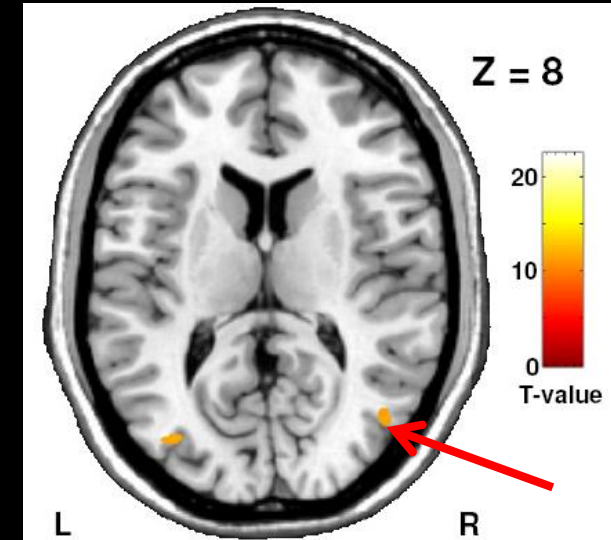
Central Compensation after Vestibular Neuritis or acoustic neurinoma surgery

increased activity in visual/somatosensory areas

(zu Eulenburg et al., Ann Neurol 2010)



(Helmchen et al., JNNP, 2010)



Residual paresis of SCC
> 2 y. after VN:

**→ bilateral increase
in visual areas
(MT / V5)**

Relative atrophy: - left posterior hippocamp
- right superior temporal gyrus

Stronger hippocamp atrophy in Bilateral Loss (17%)

(Brandt et al., Brain, 2005)

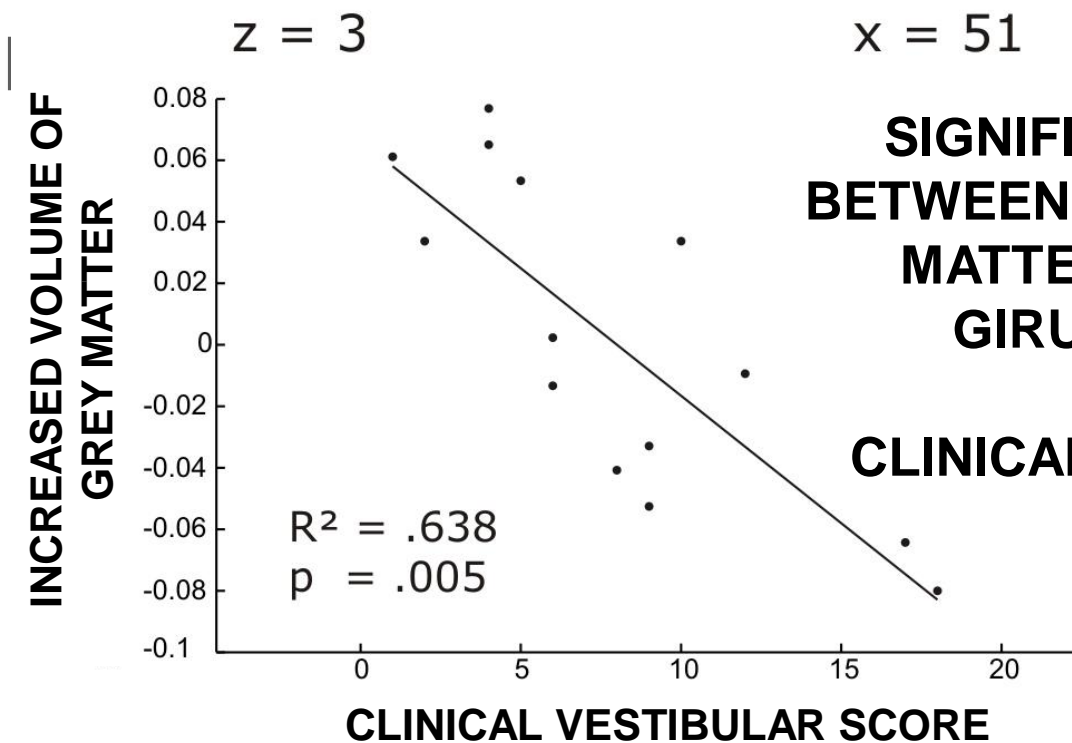
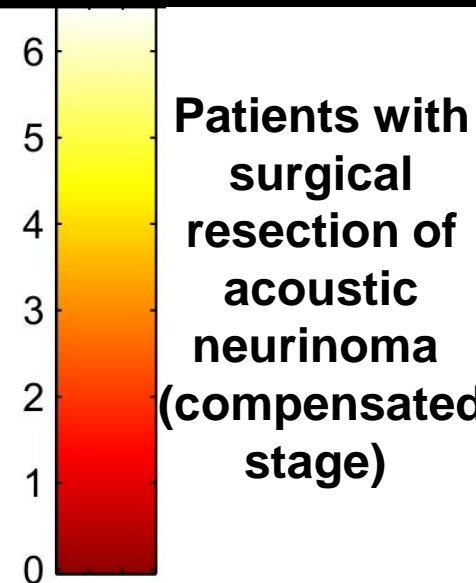
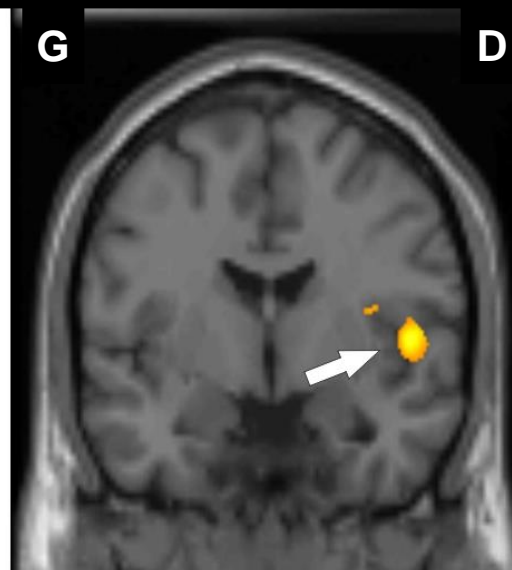
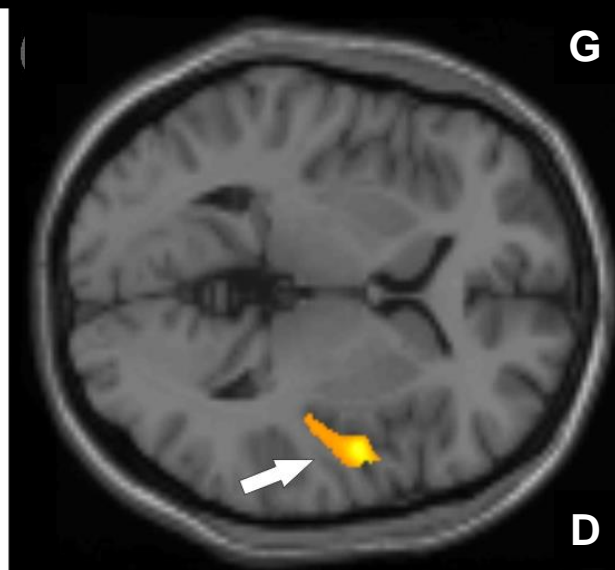
BRAIN REMODELING AFTER A VESTIBULAR LOSS

INCREASE OF GREY MATTER:

- in the superior temporal gyrus
- in the posterior insula

Indicating that new functional connections have been formed in these multisensorial cortical areas in which the vestibular afferences project (synaptogene)

STRUCTURAL BRAIN CHANGES AND BEHAVIOURAL CORRELATES



SIGNIFICANT CORRELATION BETWEEN THE VOLUME OF GREY MATTER (POST TEMPORAL GIRUS / POST INSULA) AND THE CLINICAL VESTIBULAR SCORE

DON'T FORGET:

IN ADDITION TO THE POSTURAL/OCULAR MOTOR DEFICITS, UVL PATIENTS SHOW ALSO...

- . Difficulty to focus attention, decrease of the capability to concentrate**

(Yardley et al., 1998; Gurvich et al., 2013 for review)

- . Difficulty during dual-tasking**

(Yardley et al., 2001)

- . Loss of short-term memory (antibiotic ototoxicity)**

(Risey and Briner: 1990; Yardley et al., 2002; Redfern et al., 2004)

- . Impaired spatial memory**

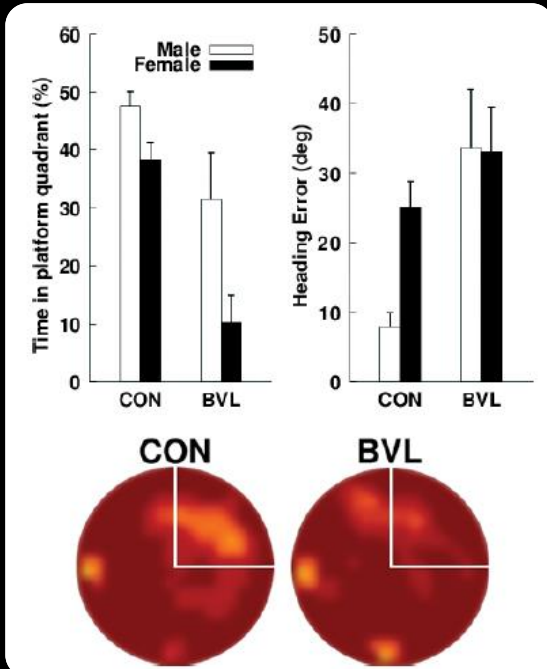
(Brandt et al., 2005; Hübner et al., 2007; zu Eulenburg et al., 2010)

- . Deficits in motor imagery, mental rotation (VPPB, Neuritis)**

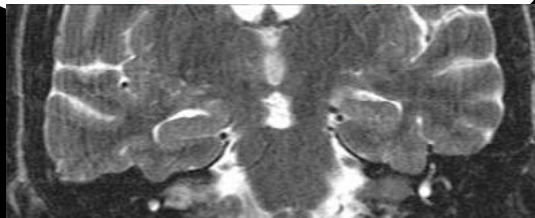
(Péruch et al., 2011; Candidi et al., 2013)

ALTERATION OF THE VISUO-SPATIAL FUNCTION

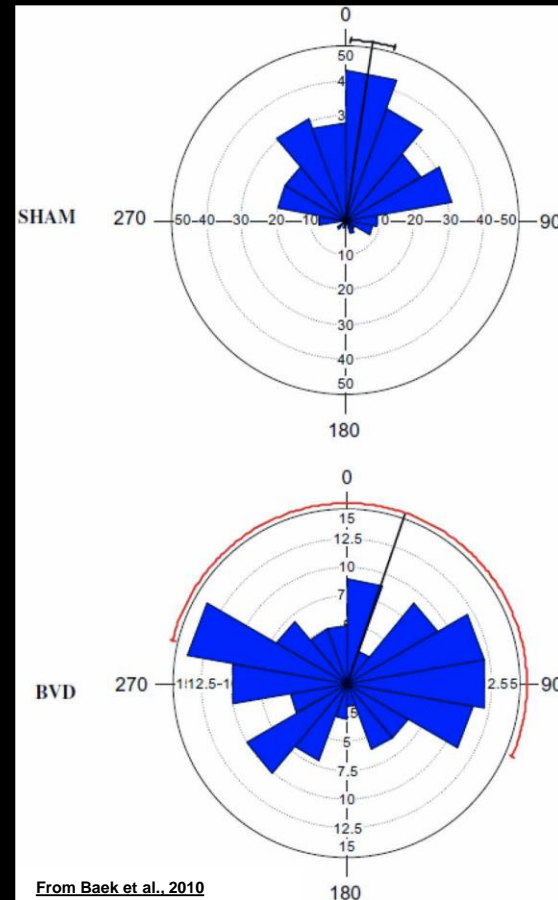
→ SPATIAL MEMORY



The
Virtual
Morris
Water
Maze
Test
(patient)



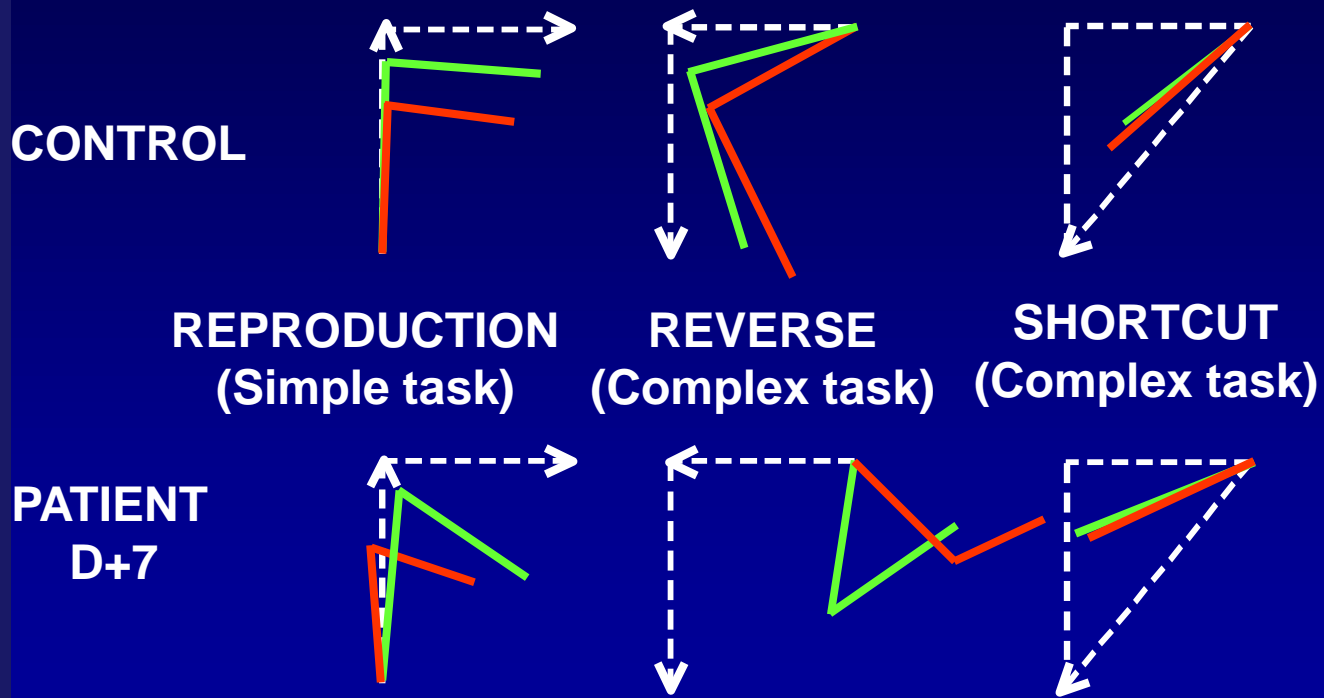
Brandt et al. (2005) *Brain*



The
Morris
Water
Maze
Test
(rat)

From Baek et al., 2010

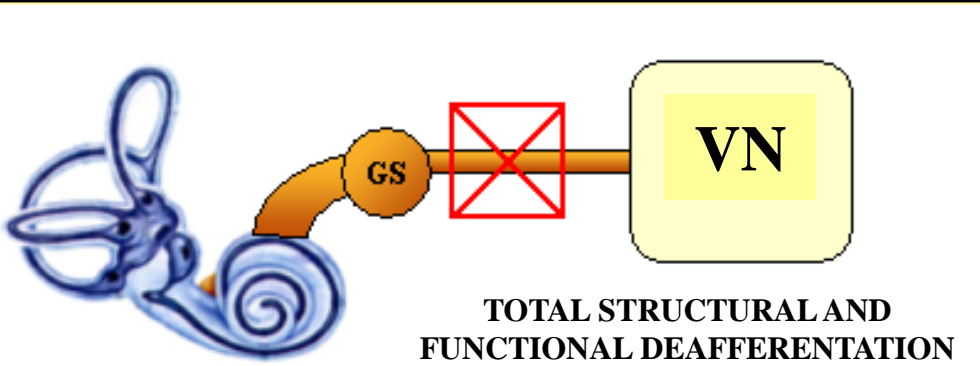
— VIRTUAL NAVIGATION (mental representation or path imaging)
— NAVIGATION IN DARKNESS



Peruch, Borel, Lacour, Cognitive Brain Research 2005

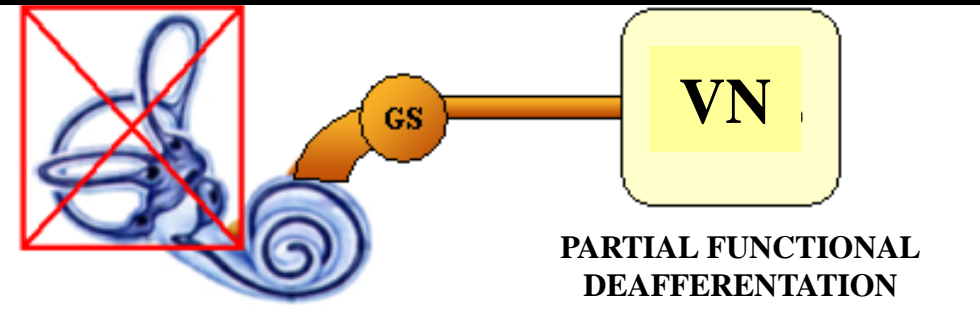
UNILATERAL
VESTIBULAR
LOSS
PATIENTS

THE RECOVERY MECHANISMS AND THE RECOVERY TIME COURSE DEPEND ON THE NATURE OF THE VESTIBULAR DEAFFERENTATION



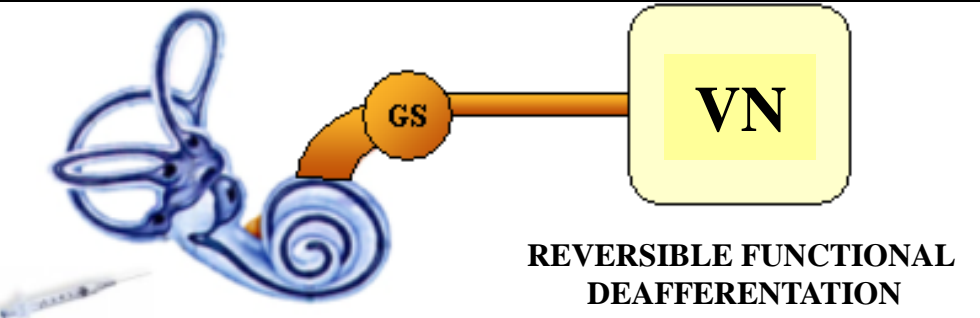
UNILATERAL VESTIBULAR NEURECTOMY (UVN)

Sudden Loss of Vestibular Function
(vestibular neuritis, 8th nerve surgery)



UNILATERAL LABYRINTHECTOMY (UL)

Gradual Loss of Vestibular Function
(aging, ototoxic drugs, head trauma)



TETRODOTOXINE BLOCKADE (TTX)

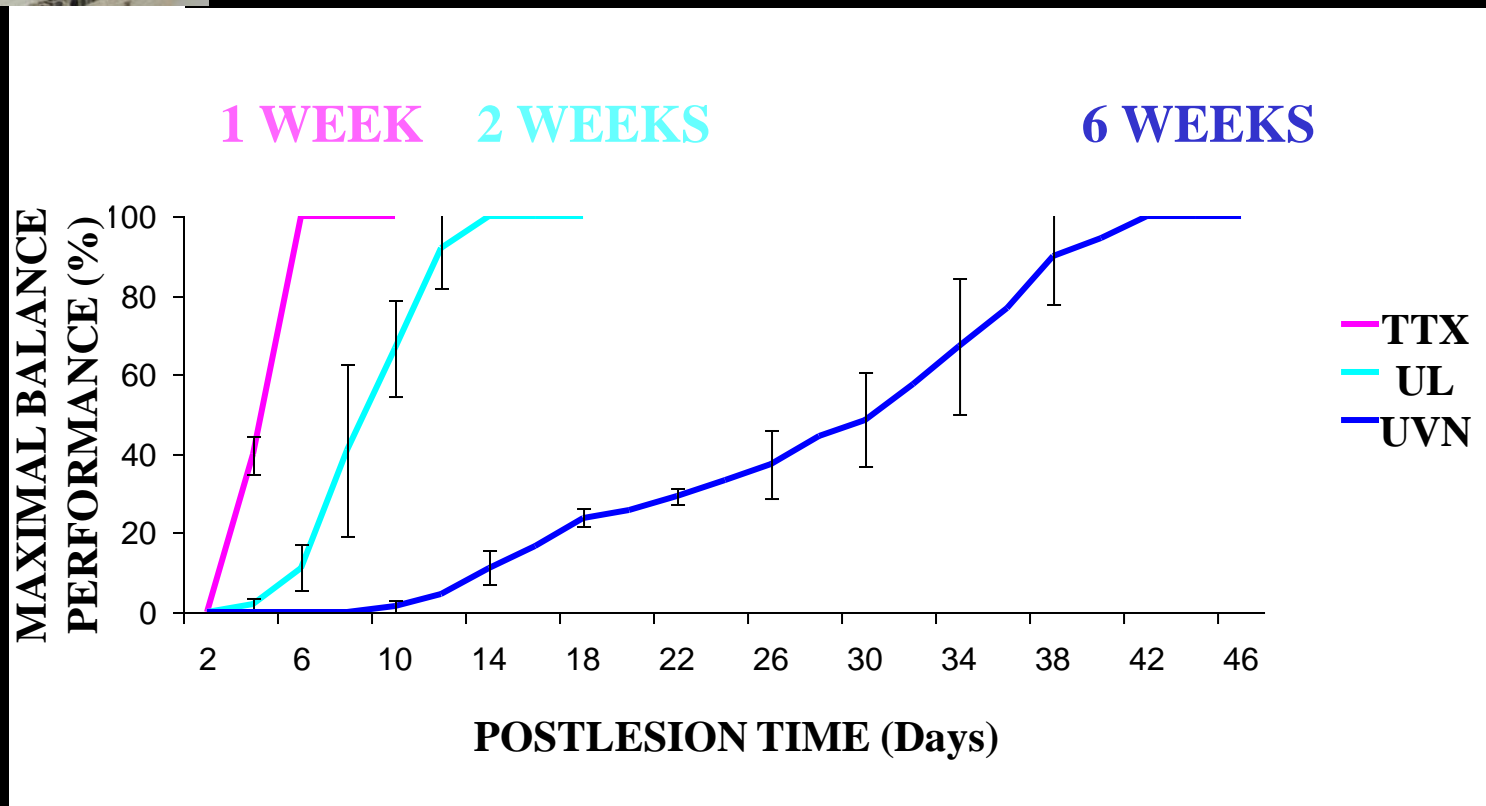
Reversible Loss of Vestibular Function
(BPPV ? Menière's disease ?)

VESTIBULAR COMPENSATION DEPENDS ON THE TYPE OF VESTIBULAR DEAFFERENTATION



Dutheil S, Brezun JM, Léonard J, Tighilet B, Lacour M (2009) *Neurosci* 164: 1444-1456

Recovery of the equilibrium function



Functional recovery is faster after TTX and UL deafferentation
compared to UVN



**I THANK YOU
FOR
YOUR ATTENTION**