# fMRI AND CNS DAMAGE

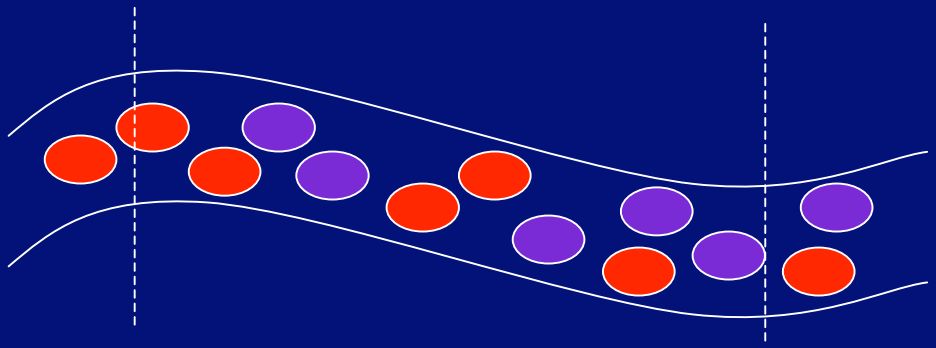
## Outline of the presentation

- What is measured by fMRI?
- Does fMRI disclose “sensible” changes?
- Are those changes correlated with structural damage?
- Which is the role of fMRI changes?
- Are fMRI changes sensitive to disease evolution?
- Can fMRI be a tool to monitor treatment?

# fMRI AND CNS DAMAGE

## What is measured by fMRI?

Basal state

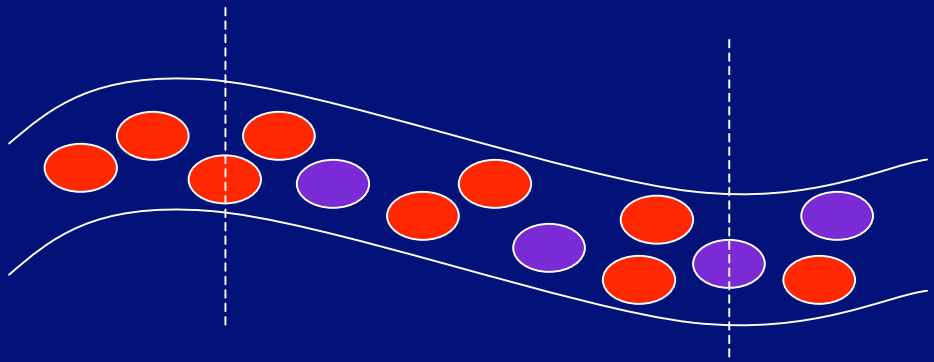


- normal flow
- basal level [Hbr]
- basal CBV
- normal MRI signal

HbO2

Hbr

Activated state



- increased flow
- decreased [Hbr]
- increased CBV
- increased MRI signal

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# fMRI AND CNS DAMAGE

## "Sensible changes"? Lessons learned from stroke

Enlarged activation of the SMC of the damaged hemisphere (contralateral to movement).

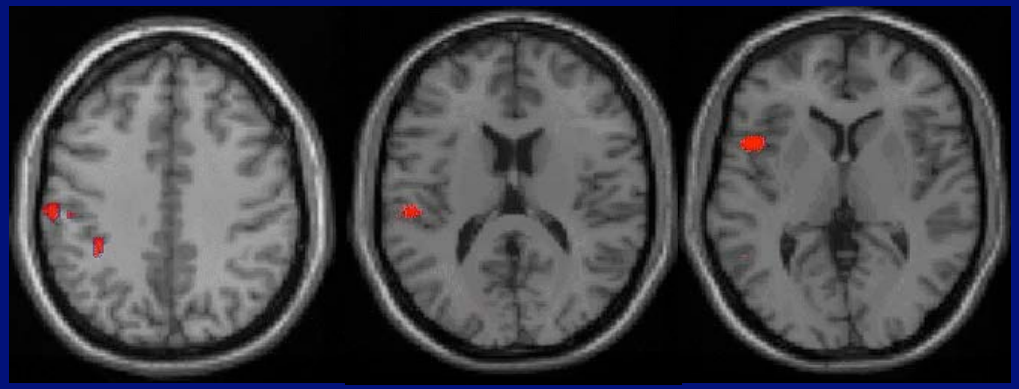
Recruitment of the primary SMC in the undamaged hemisphere (ipsilateral to the movement), with a shift of the center of activation.

Recruitment of secondary motor cortices (SMA, premotor cortex, cingulate areas) and somatosensory cortex in the lesioned hemisphere.

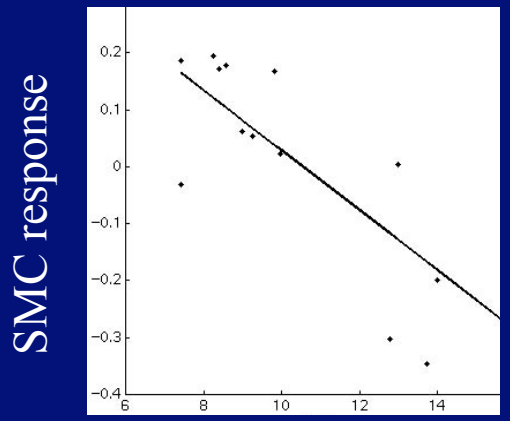
Chollet et al. 1992, Weiller et al. 1992, 1993, Cramer et al. 1997, Cao et al. 1998, Rossini et al. 1998, Pineiro et al. 2001

# fMRI AND CNS DAMAGE

## "Sensible changes"/CIS

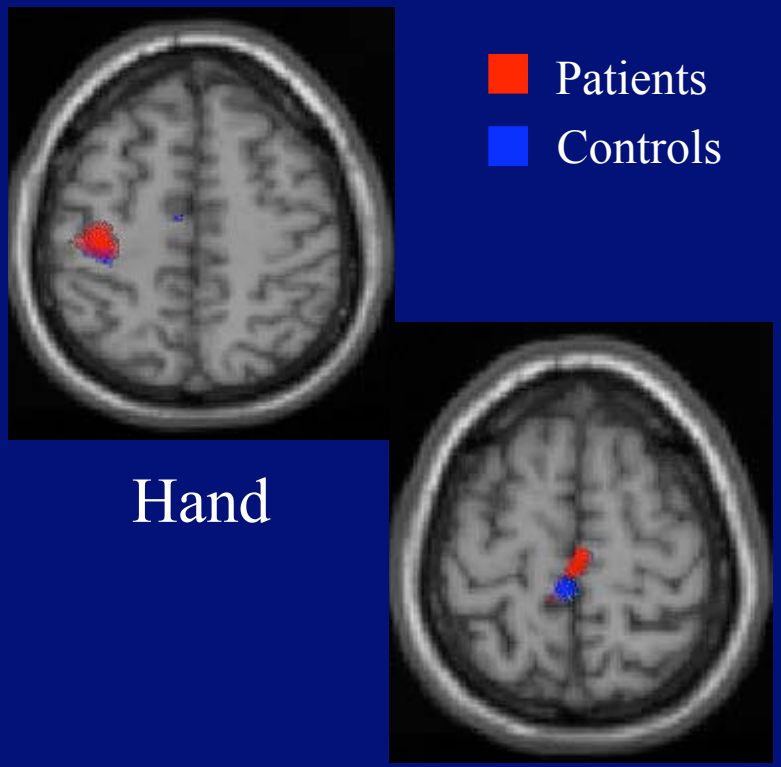


SMC SII IFG




Whole brain NAA [mMol]

Rocca et al., NeuroImage 2003




Hand

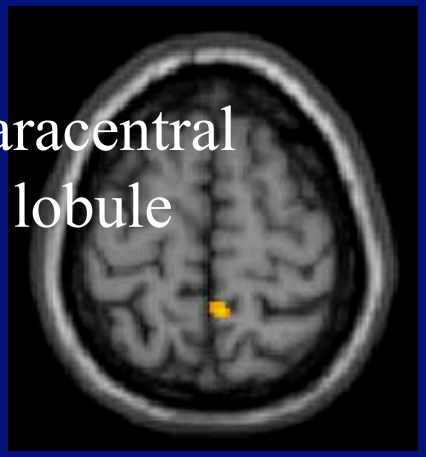
Foot

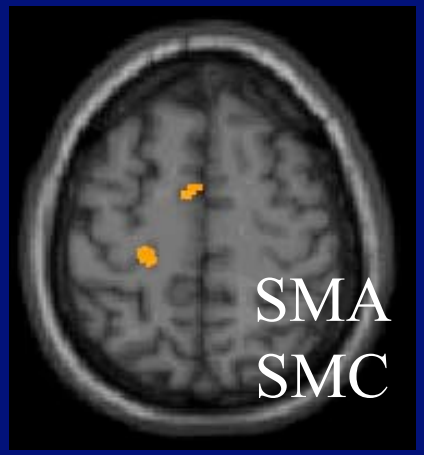
Filippi et al., Hum Brain Mapp 2004

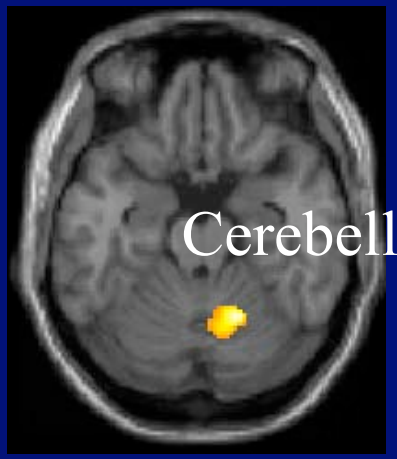
# fMRI AND CNS DAMAGE

## "Sensible changes"/CIS

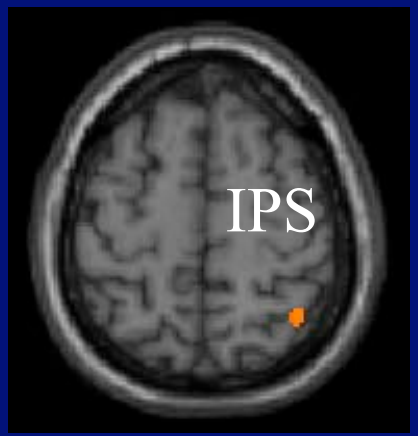
Without disease evolution

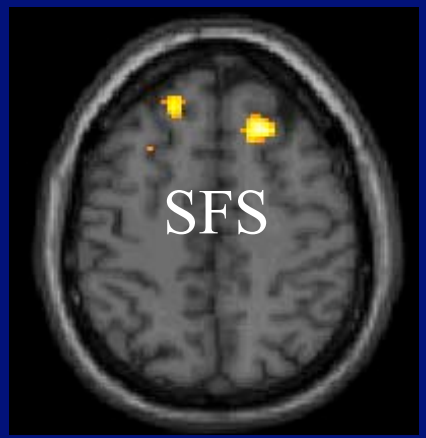


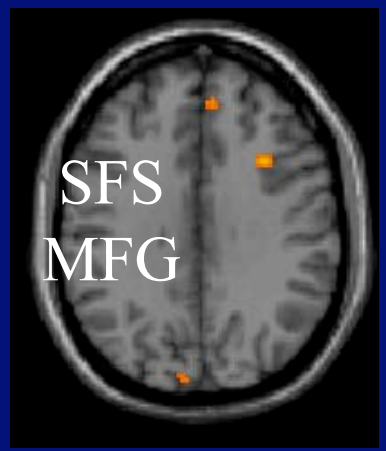



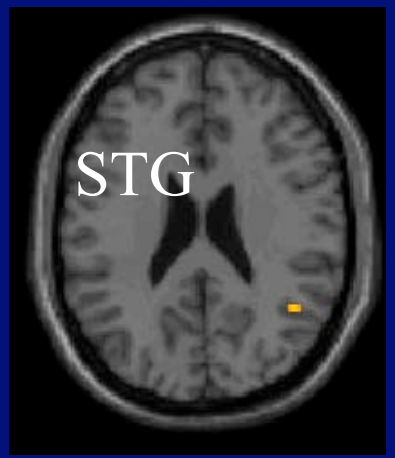




With disease evolution




Rocca et al., AJNR 2005

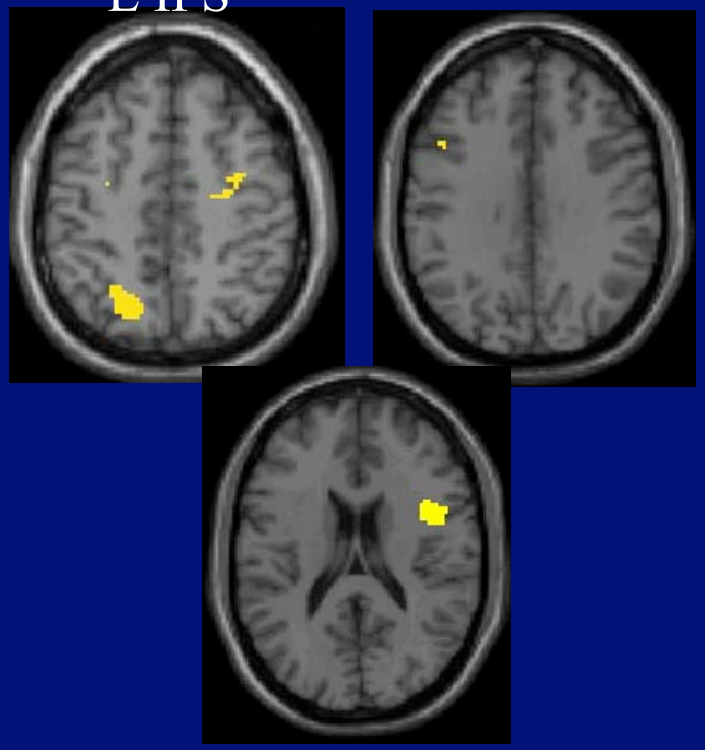
# fMRI AND CNS DAMAGE

## "Sensible changes"/ Inefficiency of recovery mechanisms

### SPMS

Bilateral MFG
L IPS

L MFG

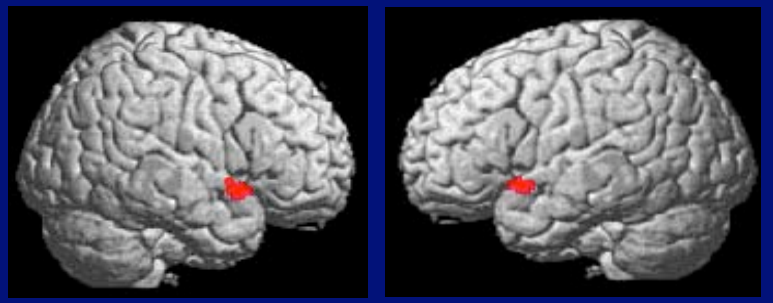


R IFG

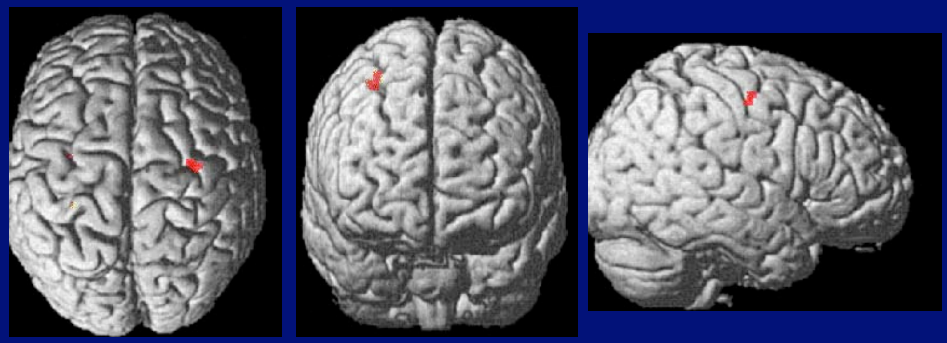
Rocca et al., NeuroImage 2003

### PPMS

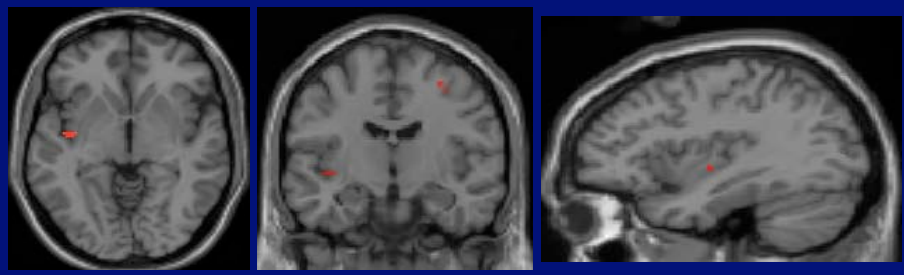
STG



MFG



Insula/claustrum

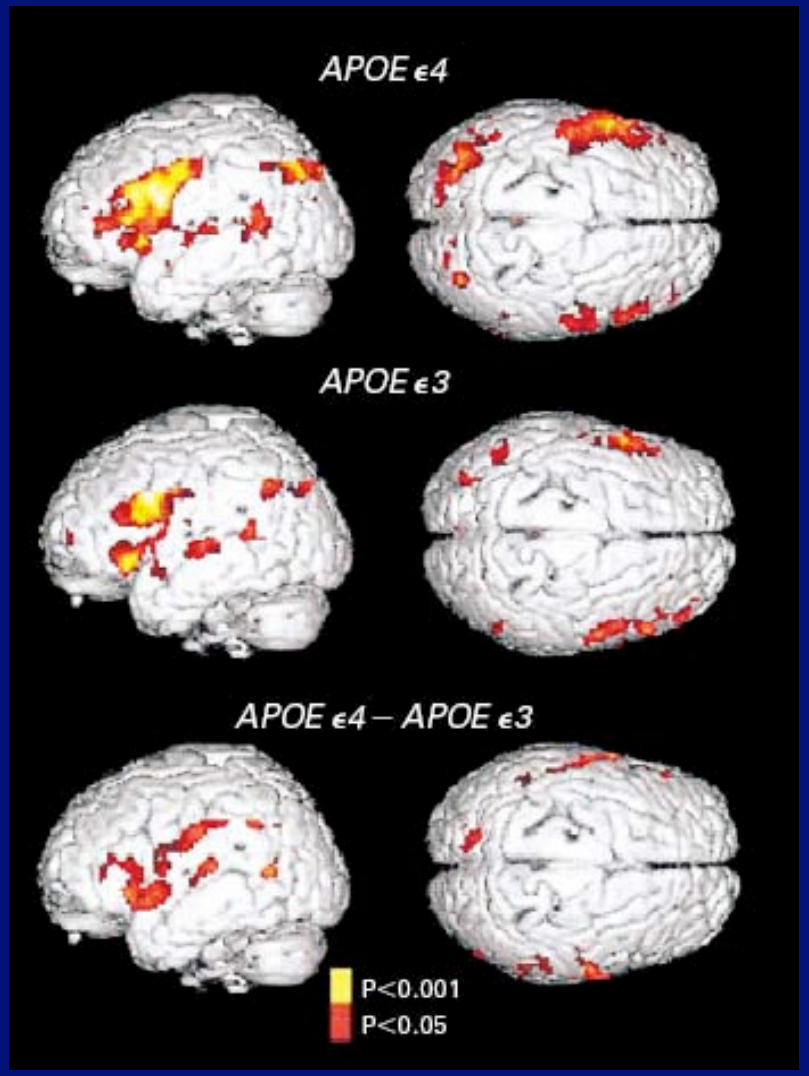


Filippi et al., NeuroImage 2002;
Rocca et al., Neurology 2002

# fMRI AND CNS DAMAGE

## "Sensible changes"/ Normals and AD

30 cognitively normal subjects (16 Apoε4 allele, 14 Apoε3 allele) Word memory task



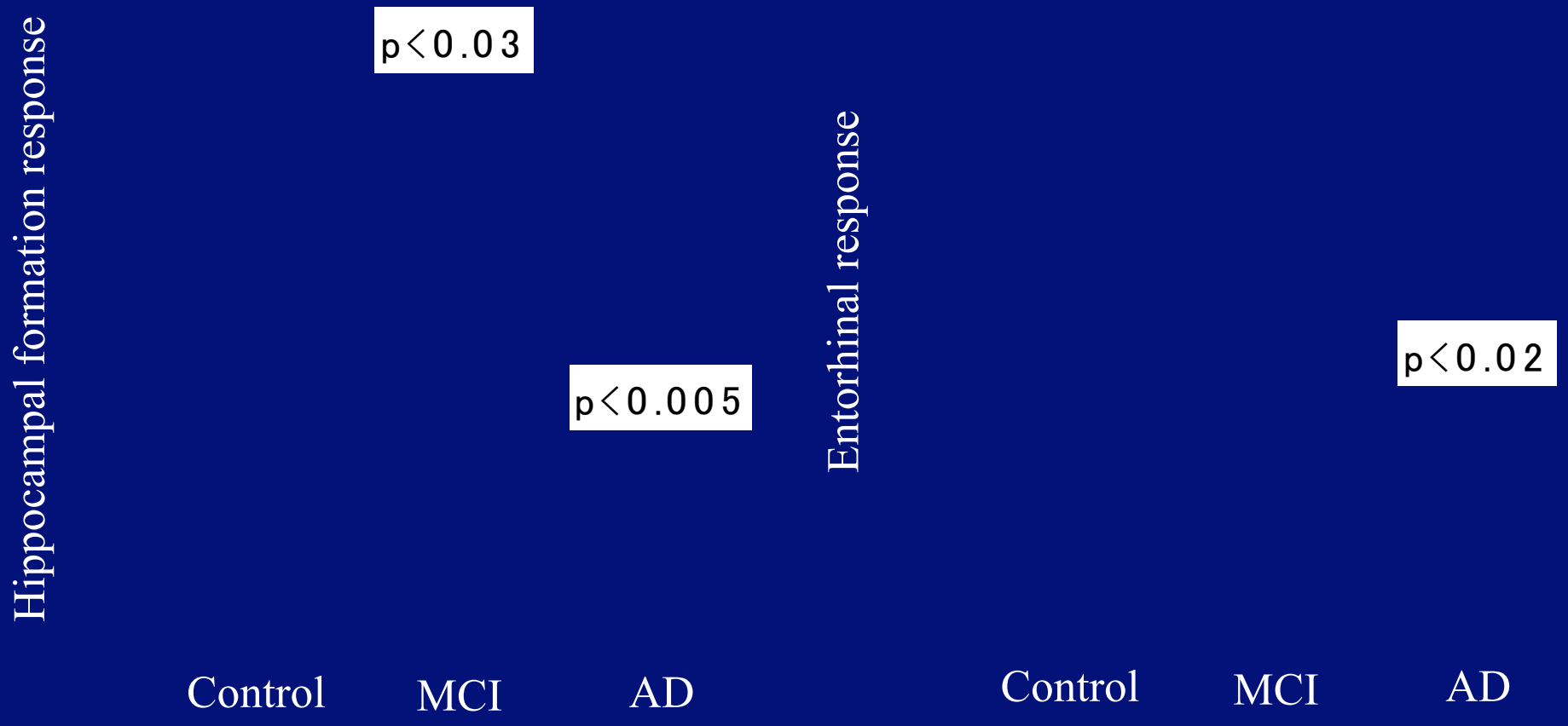

Hippocampal gyrus, dorsal prefrontal cortex, parietal lobe, temporal lobe, anterior cingulate gyrus

Bookheimer et al., New Engl J Med 2000

# fMRI AND CNS DAMAGE

## "Sensible changes"/ MCI and AD

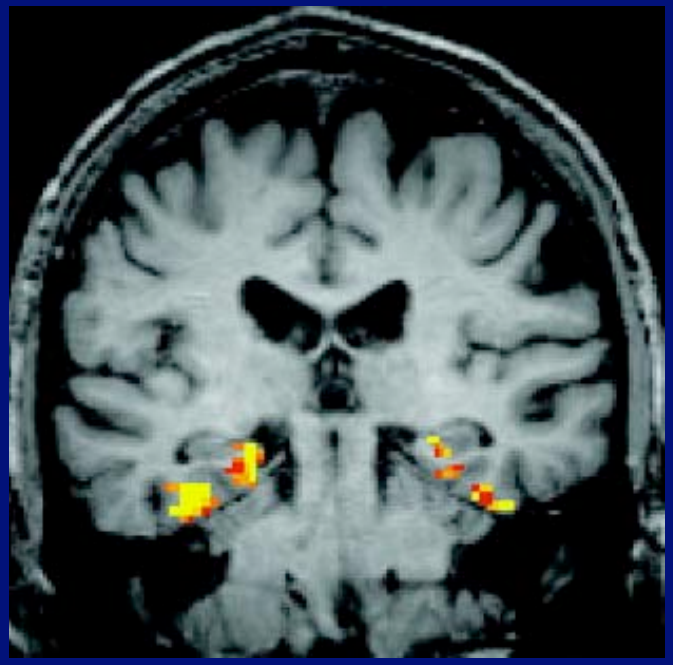
Face-name associative encoding task



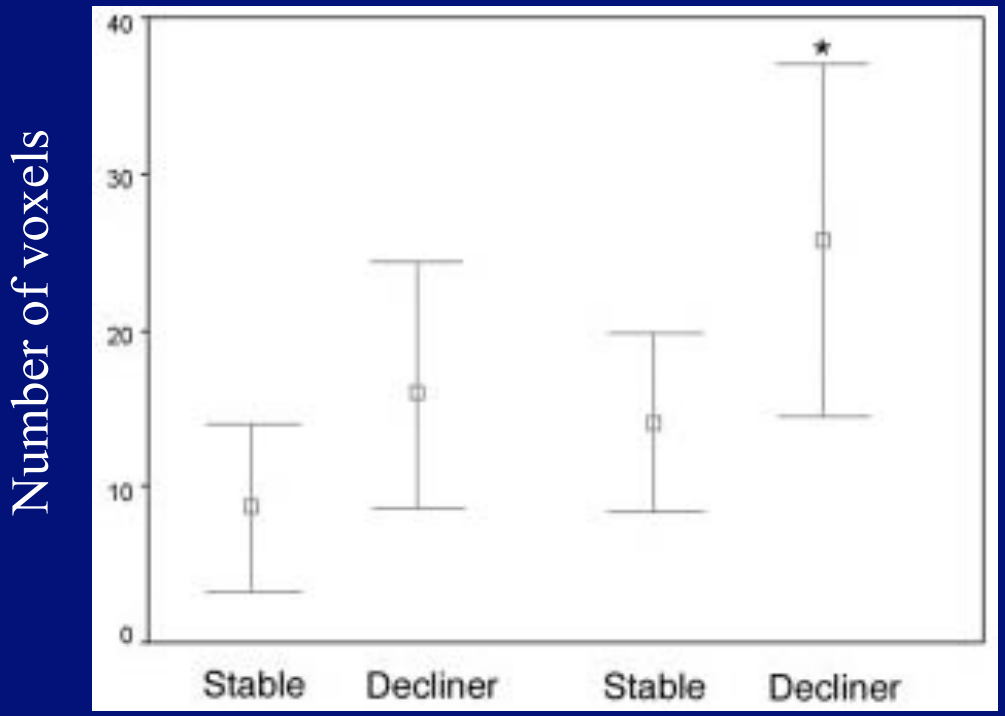

Dickerson et al., Neurology 2005

# fMRI AND CNS DAMAGE

## "Sensible changes"/ MCI



Visual encoding task
MTL activation




R Hippocampal Formation

R Prehippocampal gyrus

Dickerson et al., Ann Neuol 2004

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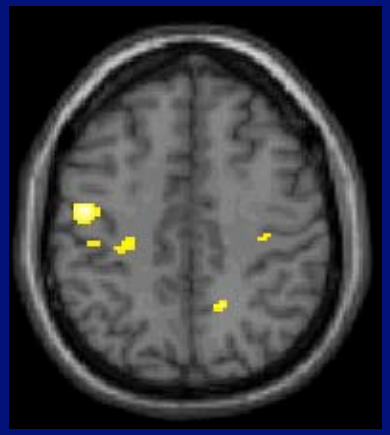
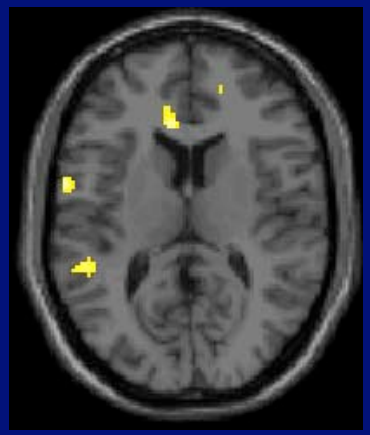
# fMRI AND CNS DAMAGE

## MS / Cortico-spinal tract lesions

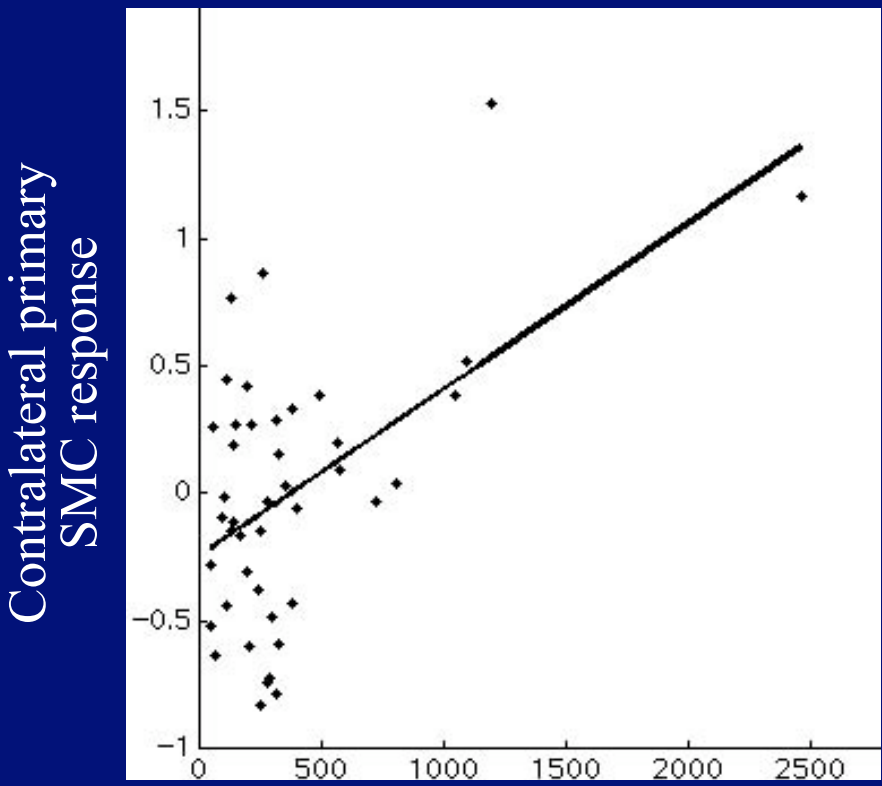
Right SMC



Bilateral SMC, right precuneus



Bilateral CMA, left SII and inferior central sulcus

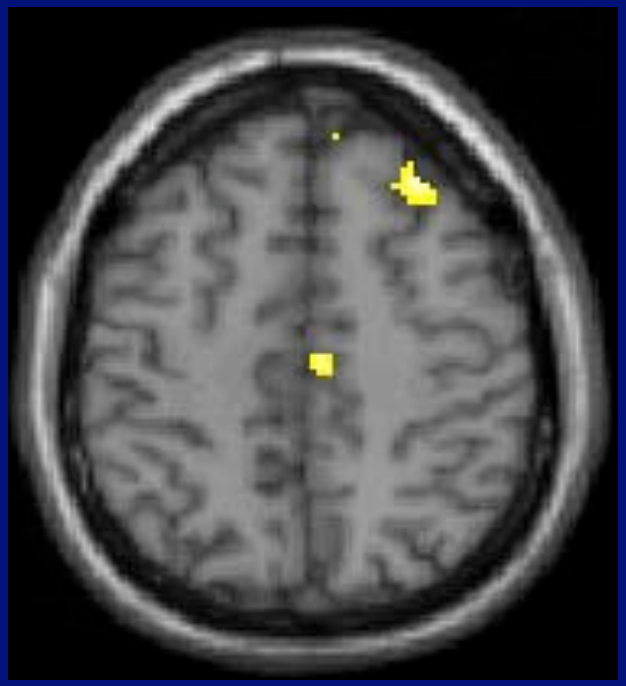



Left cortico-spinal tract T2 lesion load (ml)

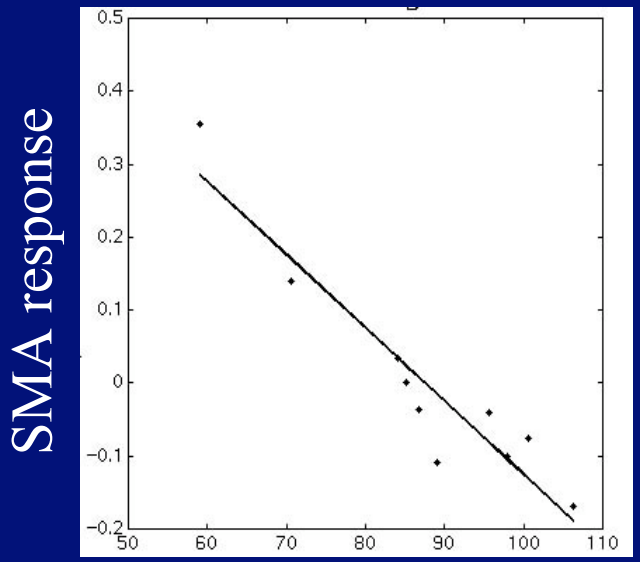
Rocca et al., NeuroImage 2004

# fMRI AND CNS DAMAGE

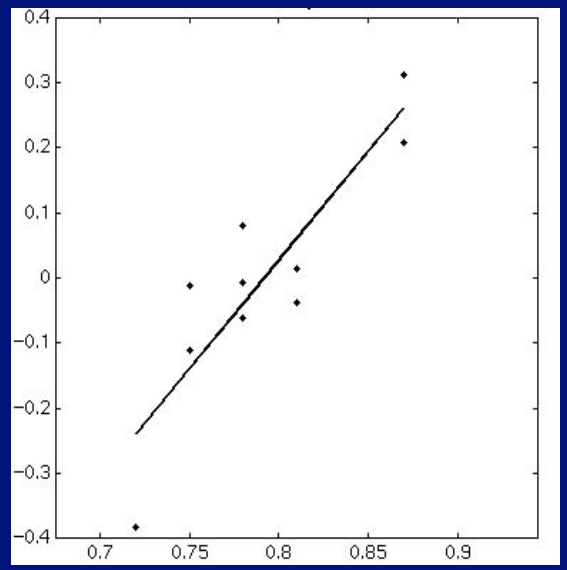
## CDMS and no T2 lesions/Amount of brain damage



**SMA**
**Superior frontal sulcus**




NAGM $\overline{D}$ histogram
peak height [‰]

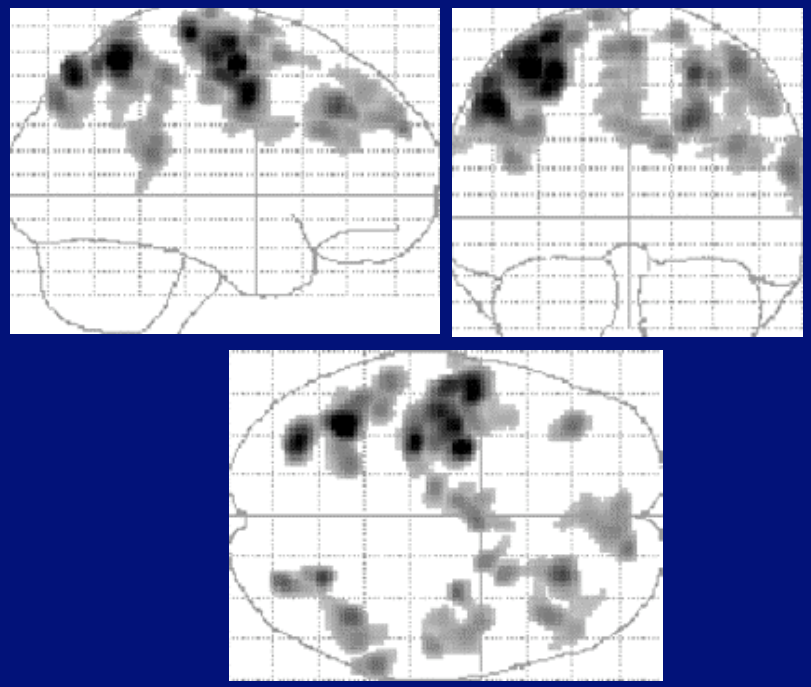



NAGM $\overline{D}$ histogram
peak location [$mm^2/s$]

Rocca et al., NeuroImage 2003

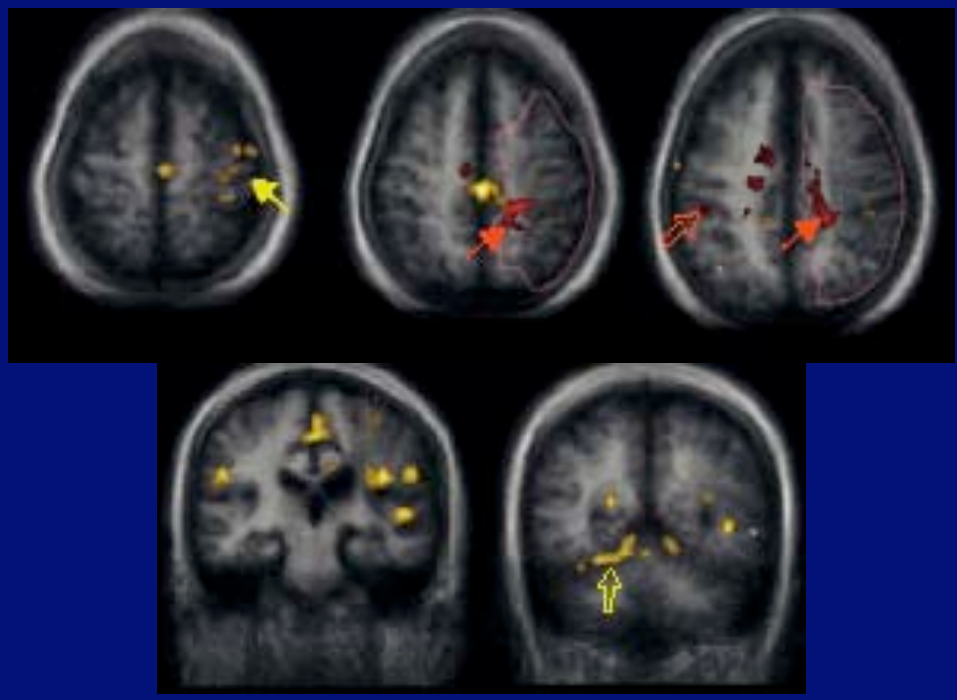
# fMRI AND CNS DAMAGE

## Stroke / Site of lesion



Significant correlations between CST functional integrity and motor-task related brain activations

Ward et al., Brain 2006



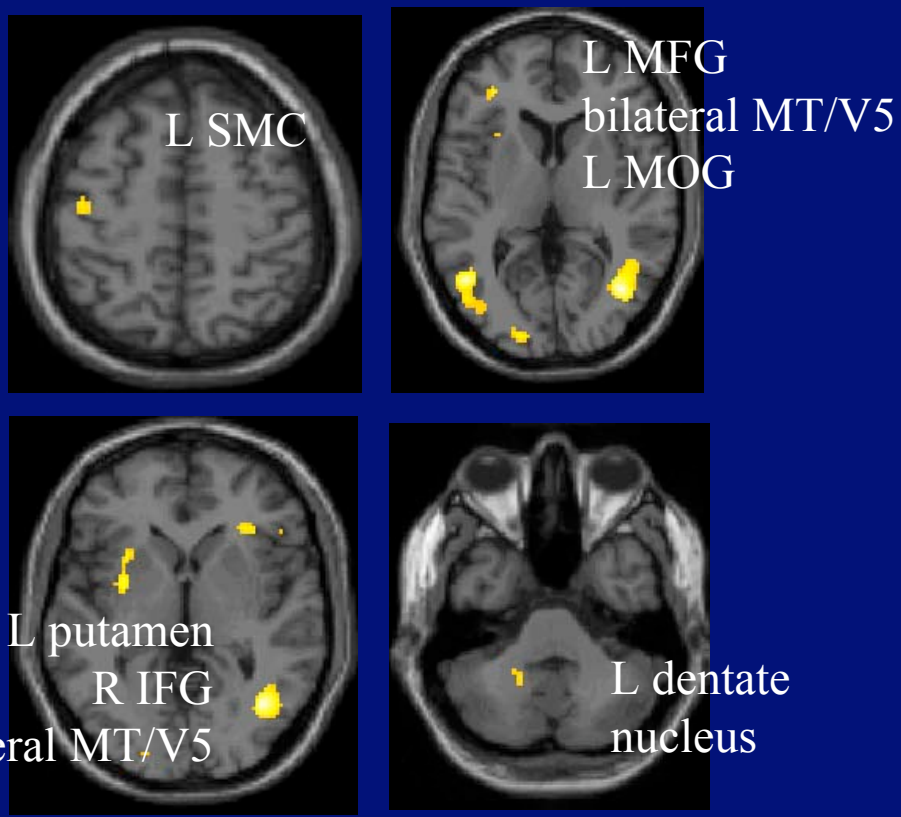
- Cortical strokes
- Subcortical strokes

Luft et al., NeuroImage 2004

# fMRI AND CNS DAMAGE

## NPSLE and CADASIL / Amount of brain damage

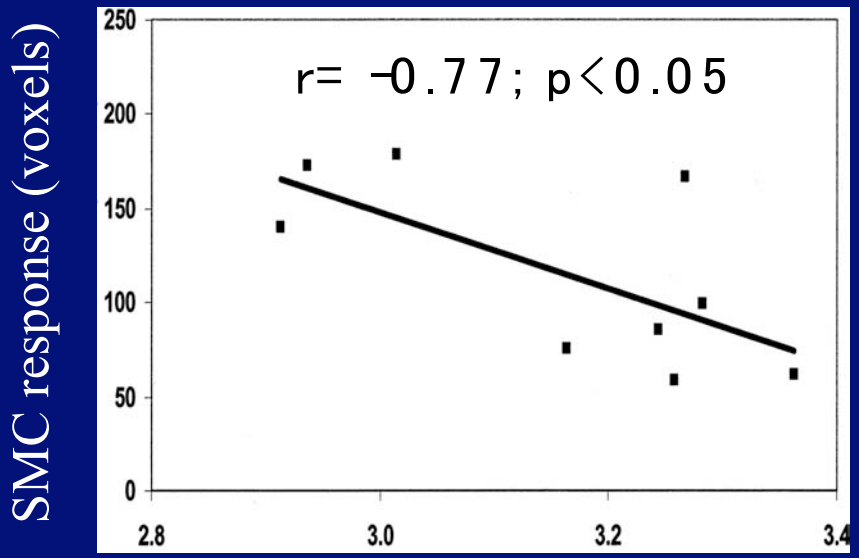
NPSLE patients *vs.* healthy volunteers




fMRI *vs.* structural MRI: r (0.79- 0.87), p <0.001

Rocca et al., NeuroImage 2005

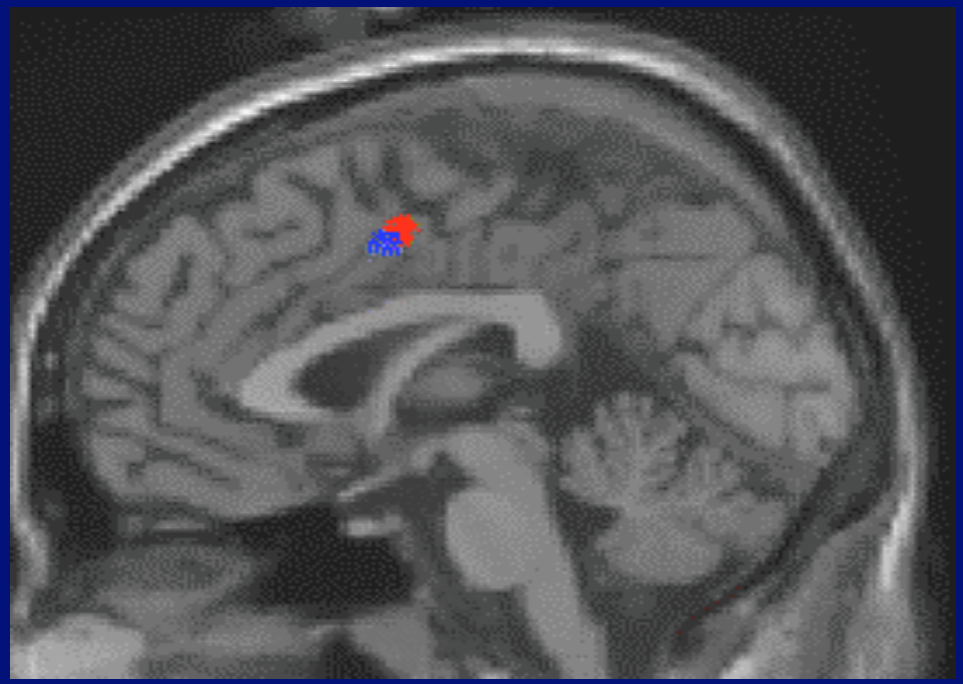
Patients with CADASIL




Reddy et al., Stroke 2001

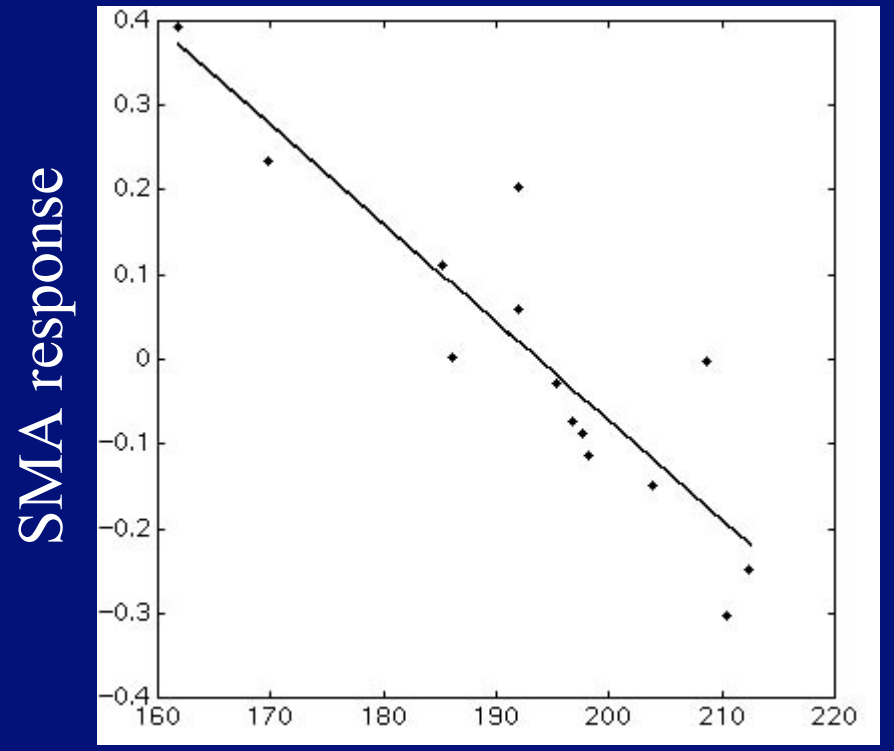
# fMRI AND CNS DAMAGE

## Migraine / Amount of brain damage



Patients with migraine

Controls

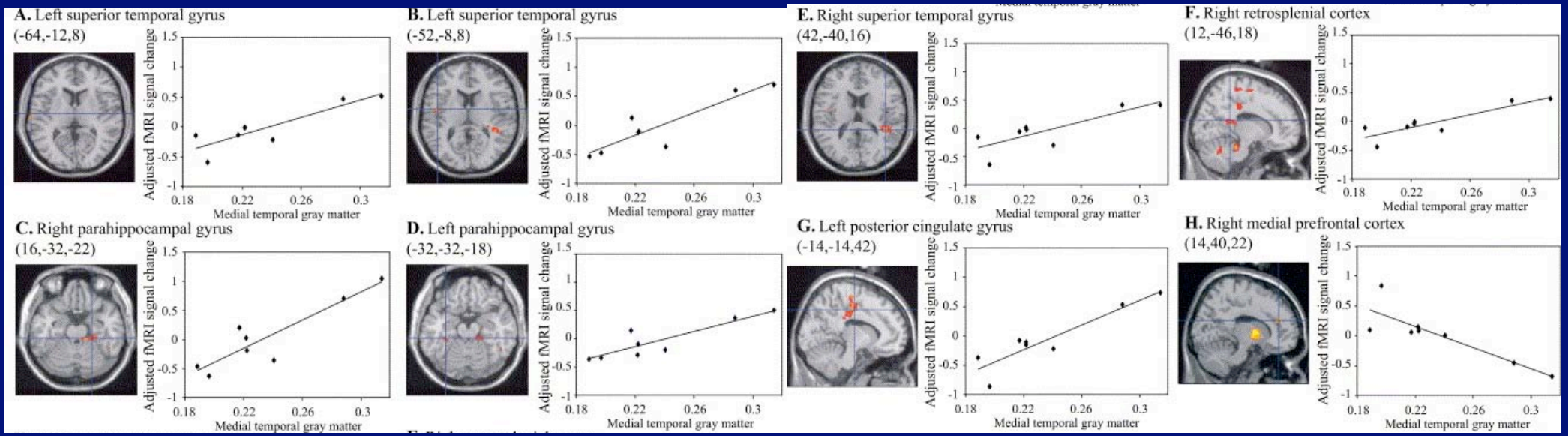



NAWM $\bar{D}$ histogram peak height [‰]

Rocca et al., Stroke 2003

# fMRI AND CNS DAMAGE

## AD / Amount of GM loss



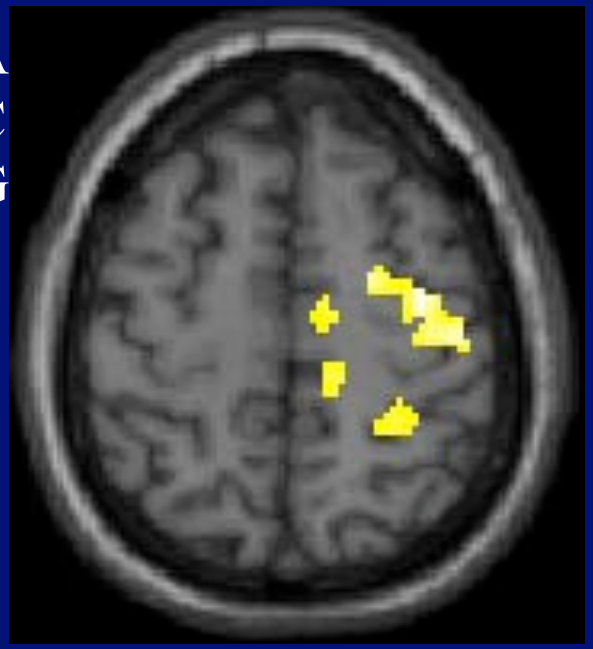

Remy et al., NeuroImage 2005

# fMRI AND CNS DAMAGE

## Isolated cord myelitis / Amount of cord damage

### Cervical cord myelitis

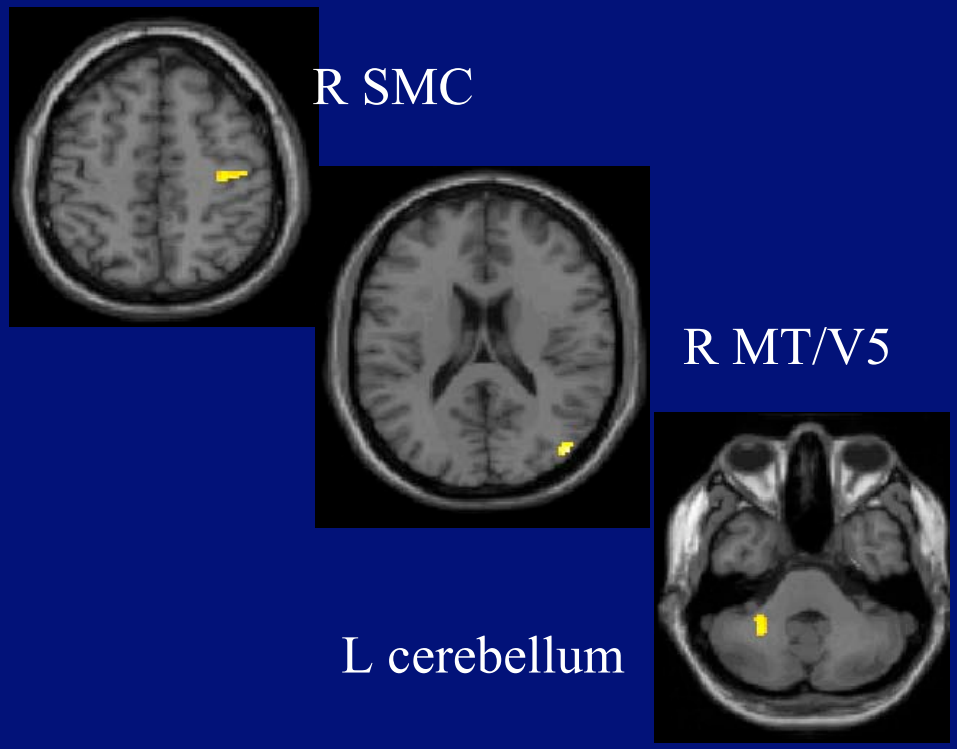
SMA
SMC
MFG



fMRI activations *vs*. structural cord damage:
r = -0.87 to -0.91; p<0.001

Rocca et al., Neurology 2003

### Dorsal cord myelitis

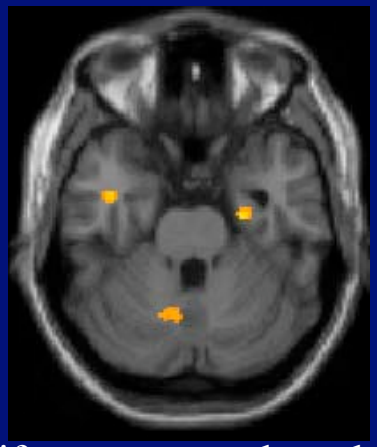



fMRI activations *vs*. structural cord damage:
r = -0.72 to -0.88; p<0.001

Rocca et al., NeuroImage 2005

# fMRI AND CNS DAMAGE

## NMO / Amount of cord damage

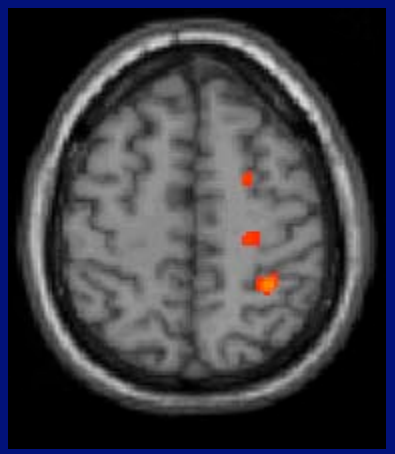


L fusiform gyrus and cerebellum
R parahippocampal gyrus

R temporal lobe

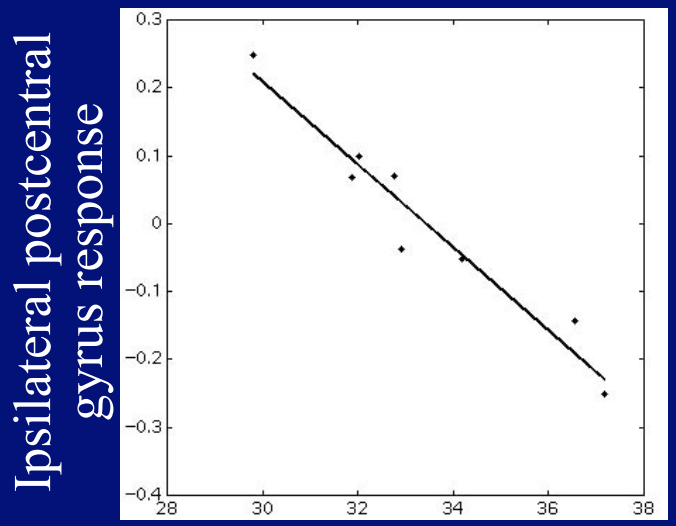
R rolandic operculum,
SII, MT/V5

R precuneus



R MFG, SMC

Bilateral SMC




Rocca et al., NeuroImage 2004

# fMRI AND CNS DAMAGE

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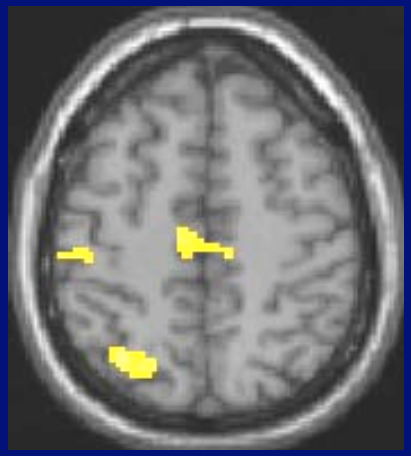
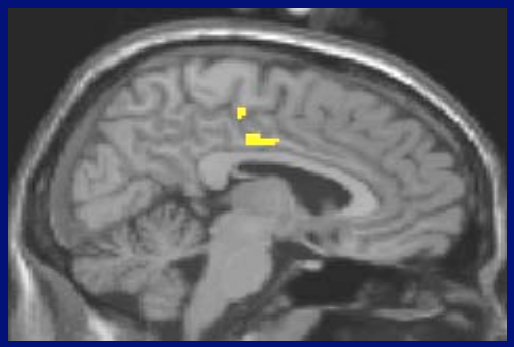
# fMRI AND CNS DAMAGE

## Adaptive role? / RRMS and no clinical disability

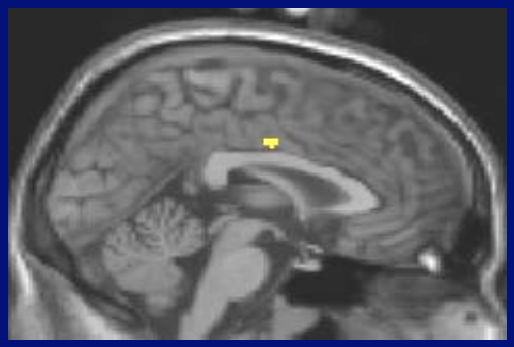


SMC, SMA, IPS

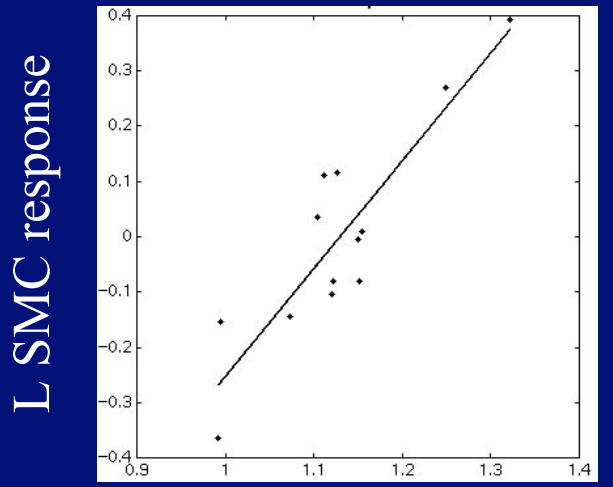
SII



SMA, CMA

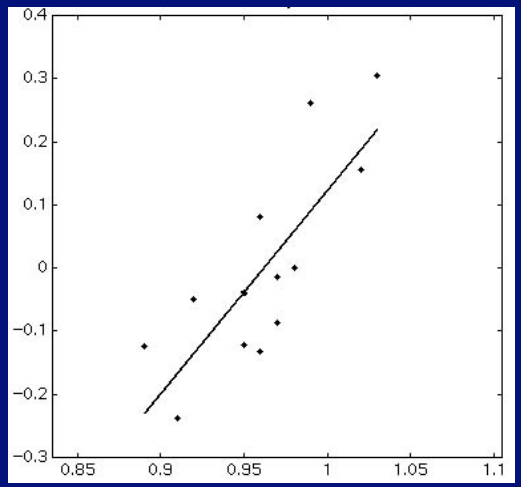


CMA




r = 0.88

p < 0.001




r = 0.81

p < 0.005

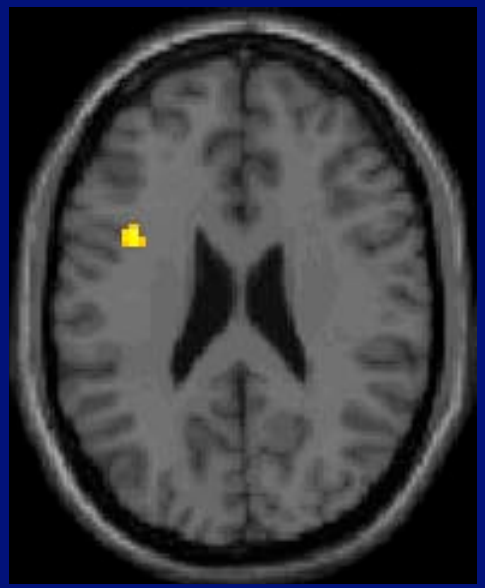
Rocca et al., Ann Neurol 2002

# fMRI AND CNS DAMAGE

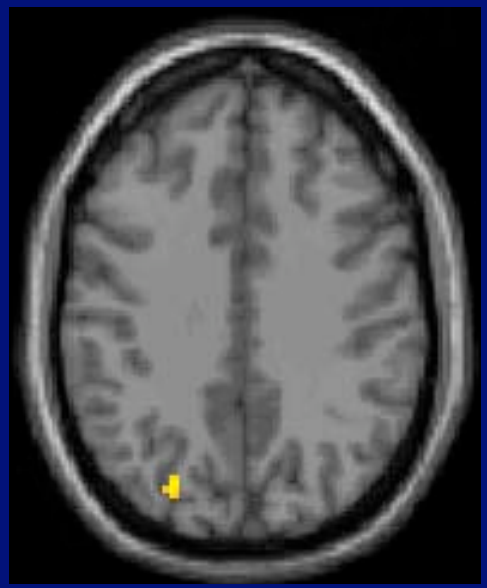
## Adaptive role? / RRMS

Healthy subjects: object manipulation

MS patients: simple motor task

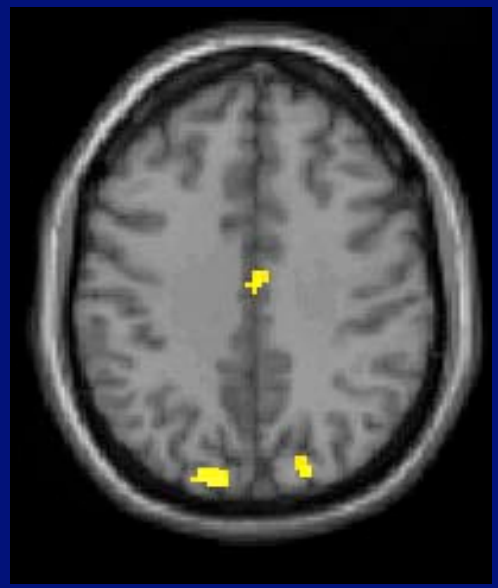


IFG



IPS

IFG
SII



IPS
SMA

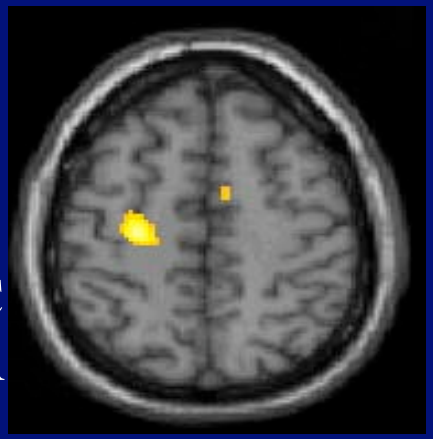
Filippi et al., NeuroImage 2004

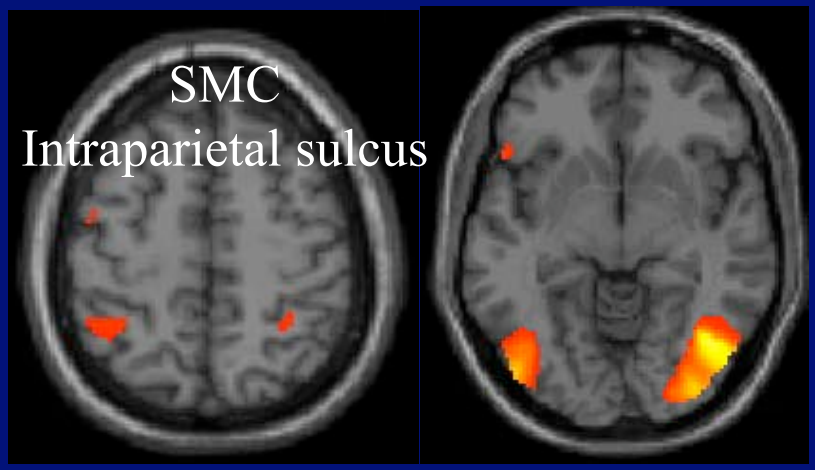
# fMRI AND CNS DAMAGE

## Adaptive role? / RRMS – Mirror system

**Simple task**
Patients
*vs.* controls

SMC
SMA



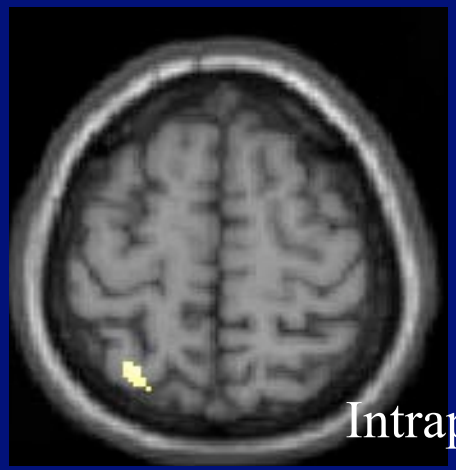



**Mirror task**
Patients and
controls

IFG
MT/V5 complex

**Mirror task**
Patients
*vs.* controls

IFG

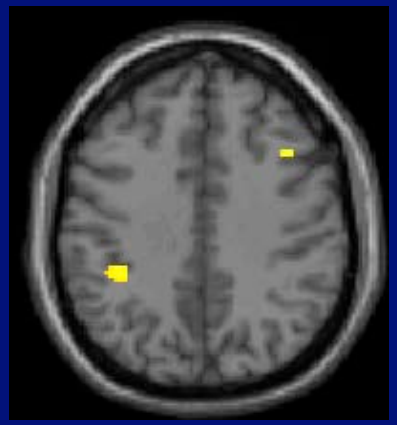


**Simple and mirror tasks interaction**
Patients *vs.* controls

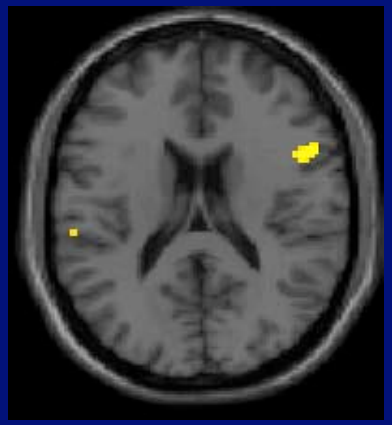
Intraparietal sulcus

# fMRI AND CNS DAMAGE

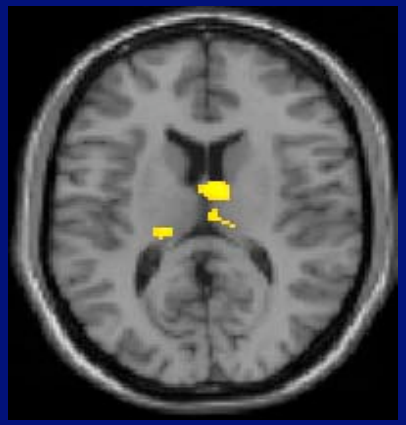
## Adaptive role? / CIS patients – Complex motor task



MFG
Postcentral gyrus

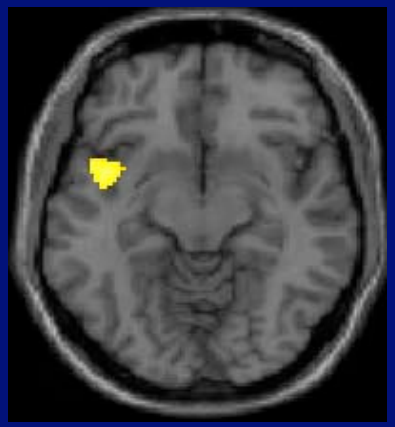


SII, IFG



Thalami

IFG

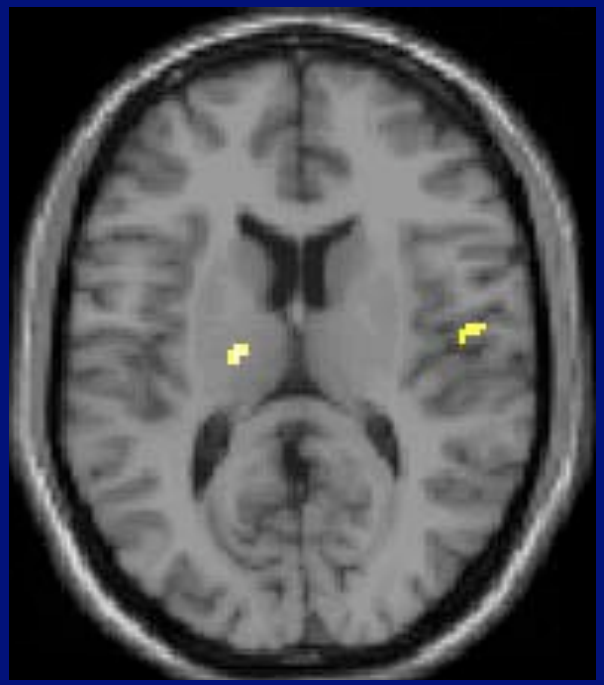


Insula

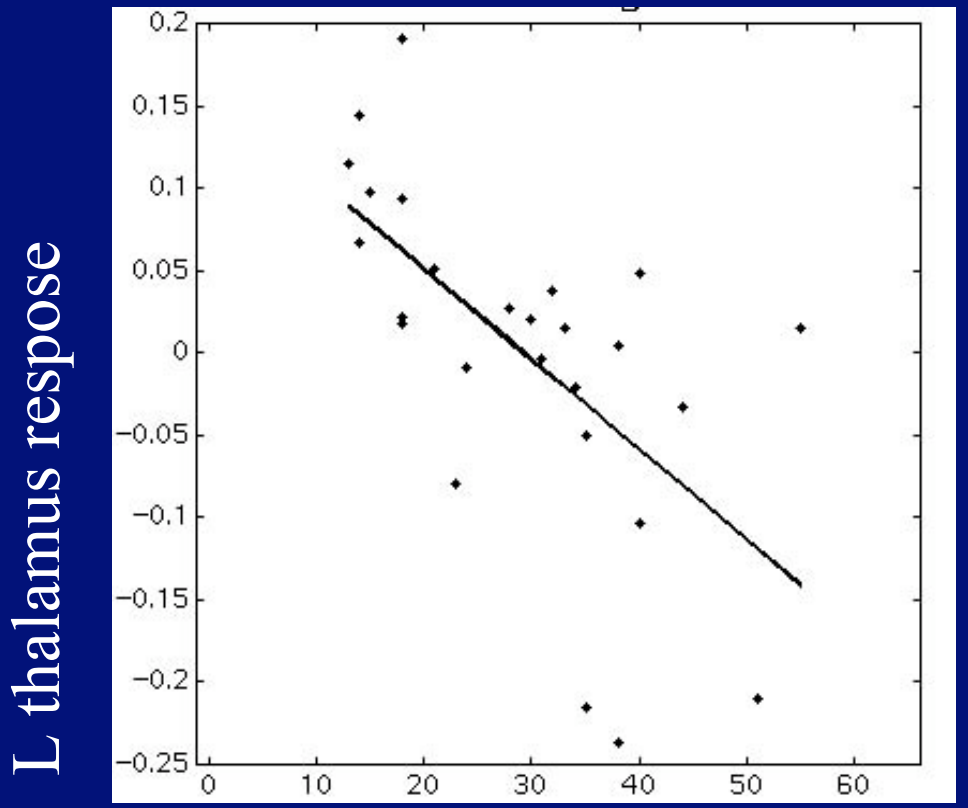
Filippi et al., Hum Brain Mapp 2004

# fMRI AND CNS DAMAGE

## Adaptive role? / NF *vs.* F MS patients



Thalamus
Rolandic operculum




**FSS score**
r = -0.62; p<0.001

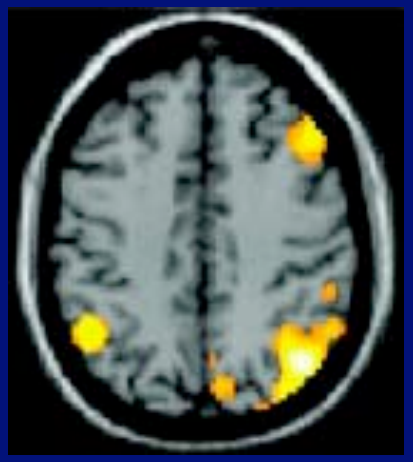
Filippi et al., NeuroImage 2002

# fMRI AND CNS DAMAGE

## Adaptive role / AD

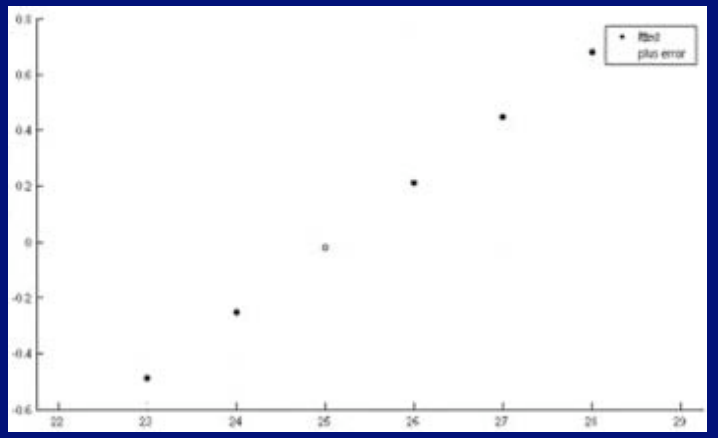
**Memory task AD *vs.* controls**

Hypoactivation of the right hippocampus



Hyperactivation of frontal and parietal regions

**Inferior parietal response *vs.* MMSE**




Pariente et al., Ann Neurol 2005

# fMRI AND CNS DAMAGE

## Outline of the presentation

- What is measured by fMRI?
- Does fMRI disclose “sensible” changes?
- Are those changes correlated with structural damage?
- Which is the role of fMRI changes?
- Are fMRI changes sensitive to disease evolution?
- Can fMRI be a tool to monitor treatment?

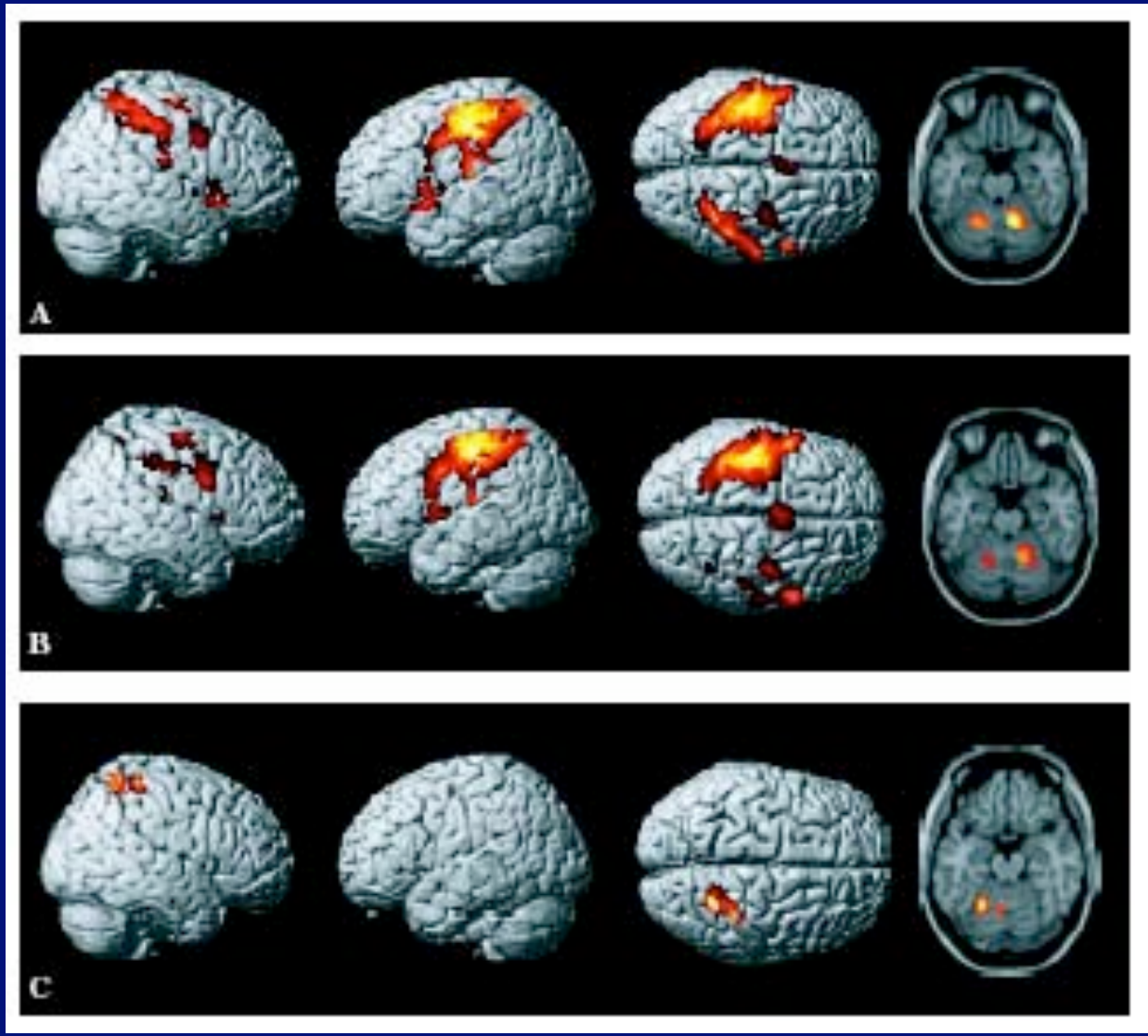
# fMRI AND CNS DAMAGE

## Sensitivity to changes / RRMS

Baseline

15-26 months

Baseline *vs*. follow-up



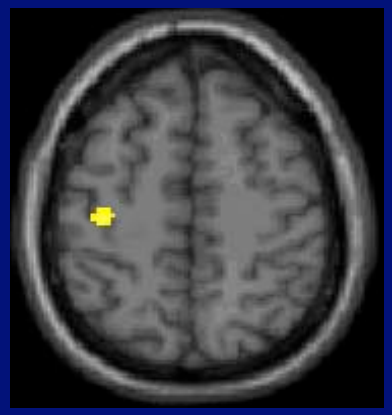

Pantano et al., Brain 2005

# fMRI AND CNS DAMAGE

## Sensitivity to changes / MS evolution

**CIS *vs.* non-disabled RRMS**

SMC

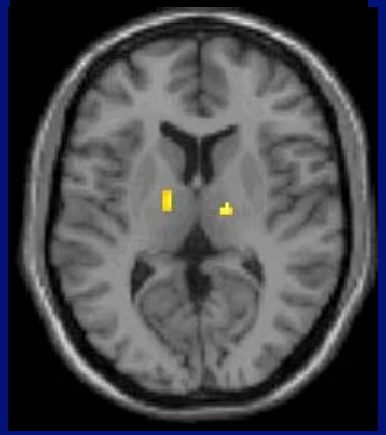


**Non-disabled *vs.* mildly disabled RRMS**

SMC, SMA

**Mildly disabled RRMS *vs.* SPMS**

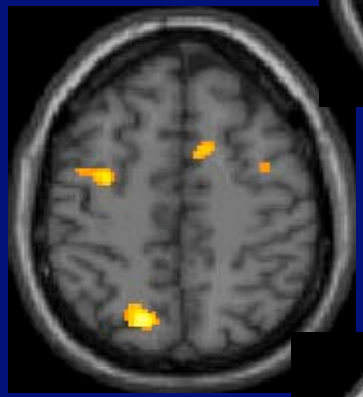
SII



Thalamus

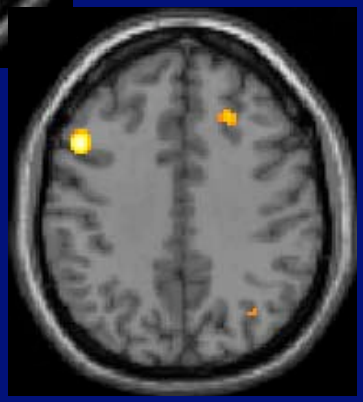
**SPMS *vs.* mildly disabled RRMS**

Precuneus, IPL, MFG



Precuneus, CMA, MFG

MFG, IPL



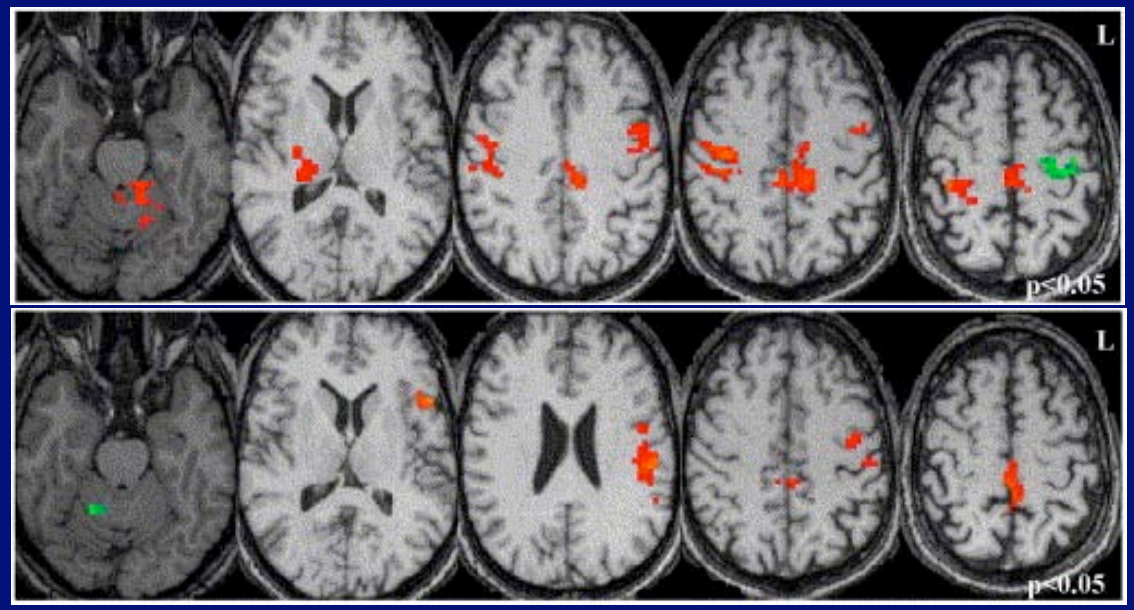
Rocca et al., Lancet Neurol 2005

# fMRI AND CNS DAMAGE

## Sensitivity to changes / Stroke and motor recovery

Early and transient compensatory network

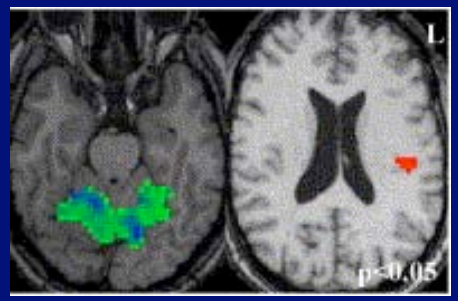
20 days post-stroke




4 months post-stroke

Late compensatory network

1 year post-stroke




Tombari et al., NeuroImage 2004

# fMRI AND CNS DAMAGE

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# fMRI AND CNS DAMAGE

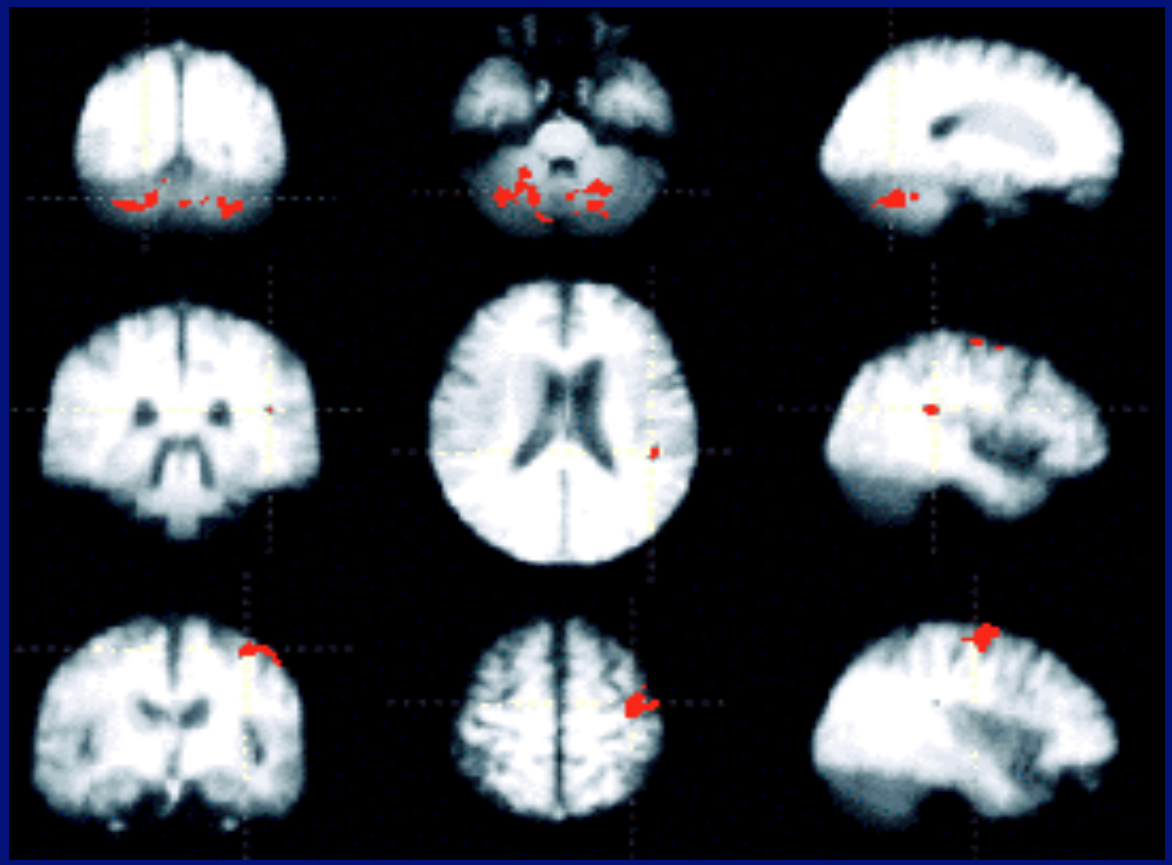
## Monitoring treatment / Rehabilitation in stroke

**Correlation map between therapy-related improvements and fMRI activity**

**Cerebellum**

**SII**

**SMC**

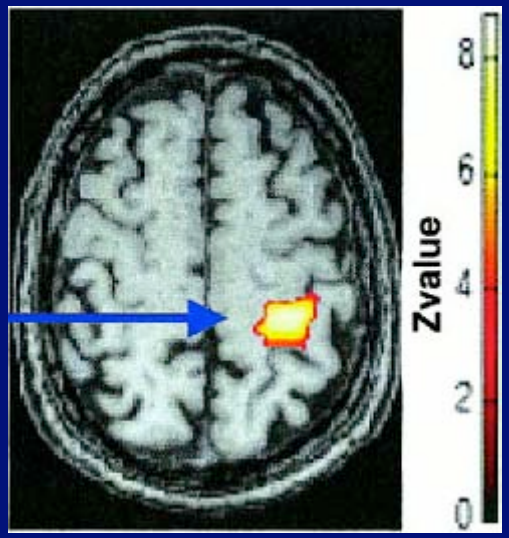


Johansen-Berg et al., Brain 2002

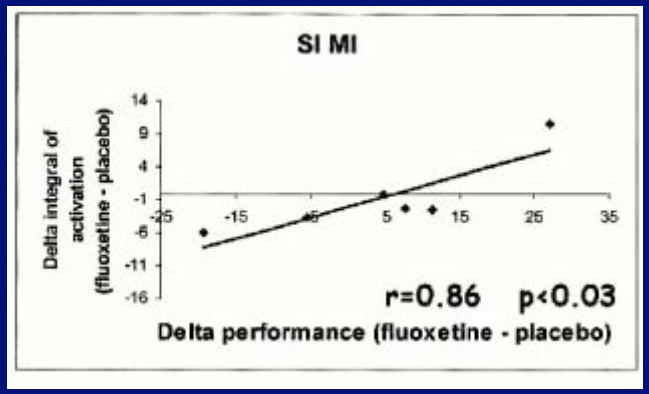
# fMRI AND CNS DAMAGE

## Monitoring treatment / Stroke and fluoxetine

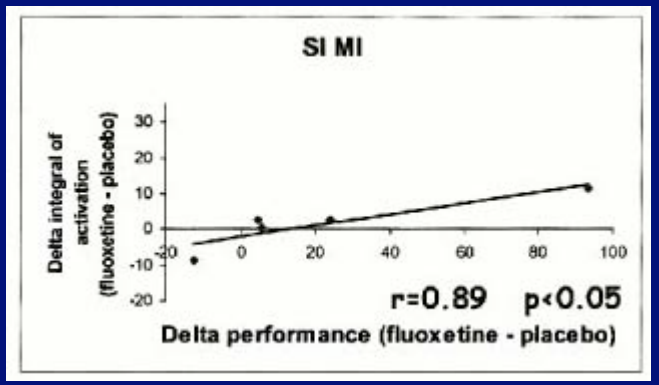
**Contralateral SMC**




**Finger tapping**



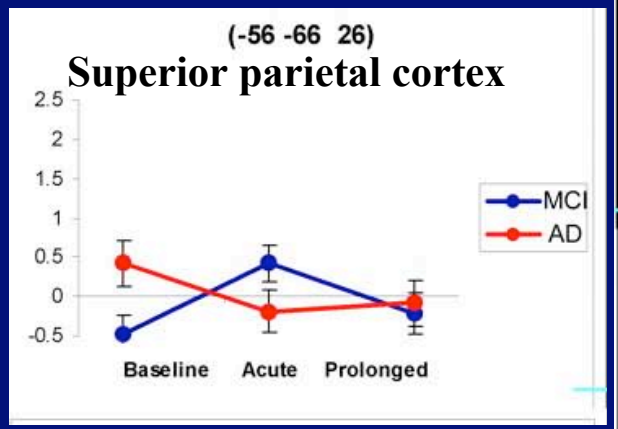

**Dynamometer**

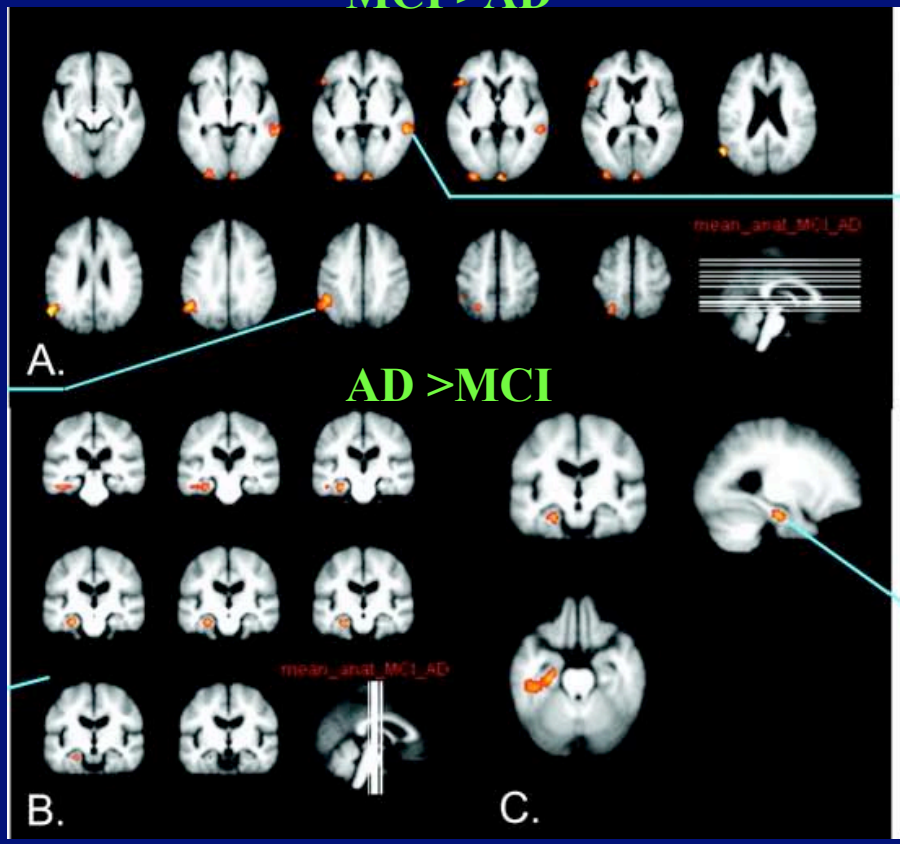


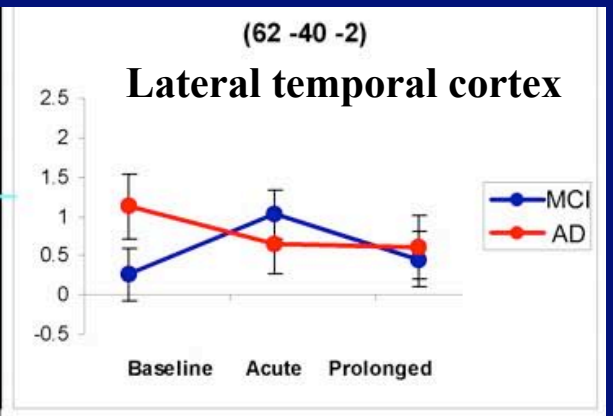

Pariente et al., Ann Neurol 2001

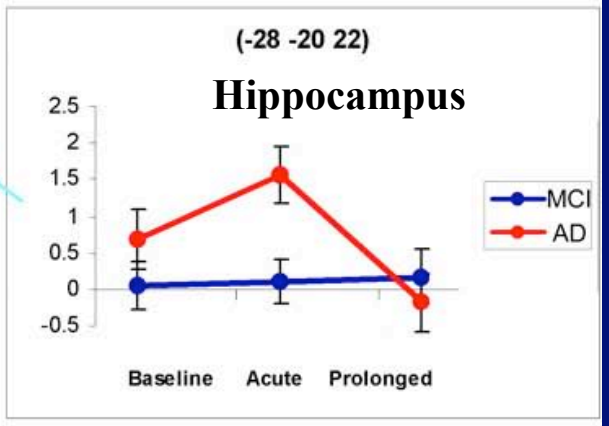
# fMRI AND CNS DAMAGE

## Monitoring treatment / AD and galantamine



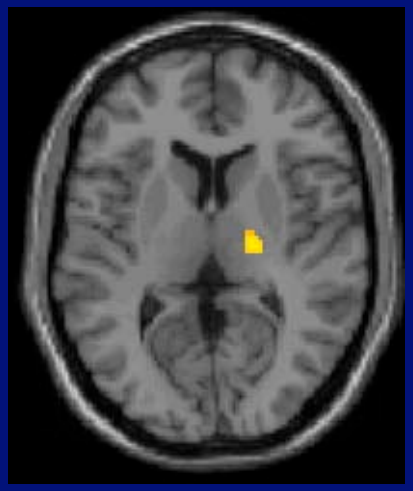




Goekoop et al., Brain 2006

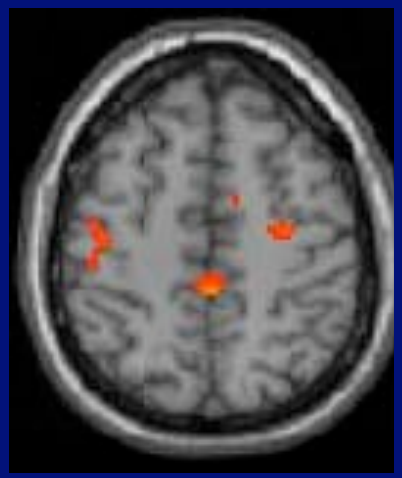
# fMRI AND CNS DAMAGE

## Monitoring treatment / MS fatigue and IFN beta 1a

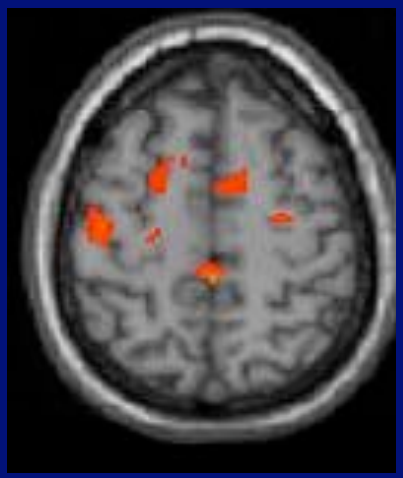
F MS day 1 *vs*. baseline + day 4



R thalamus



L SMC, R MFG,
SMA, CMA



L SMC, MFG,
SMA, CMA

Rocca et al., Hum Brain Mapp 2006

# fMRI AND CNS DAMAGE

## Conclusions

- Common phenomenon in patients with CNS damage
- Likely to limit the clinical consequences of irreversible tissue injury
- Progressive failure of these mechanisms due to accumulating tissue damage may contribute to accumulation of disability
- Dynamic phenomenon over the course of the disease
- Elicited by macroscopic lesions as well as by the presence of ‘occult’ damage (brain + cord)
- Possible role in future trials