Neuroplasticity: functional MRI techniques

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fMRI & MS

Outline of the presentation

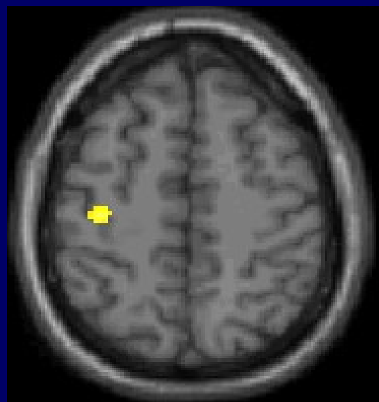
- Does fMRI disclose “sensible” changes in MS phenotypes?
- Which is the role of fMRI changes?
- Are those changes correlated with structural damage?
- Investigating the resting brain: a valuable approach?
- Function of the spinal cord GM?
- Can fMRI have a prognostic role?
- Can fMRI be useful to monitor treatment effects?

fMRI & MS

MS phenotypes

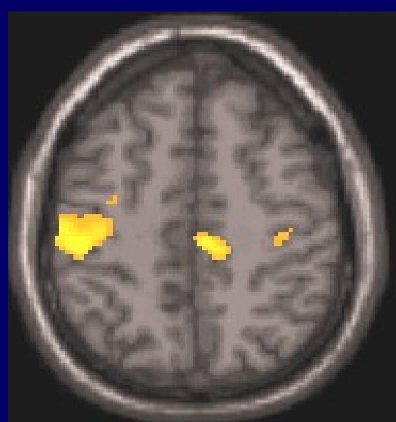
CIS *vs* non-disabled RRMS

SMC

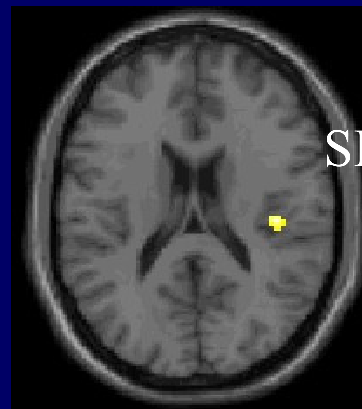


Non-disabled *vs* mildly disabled RRMS

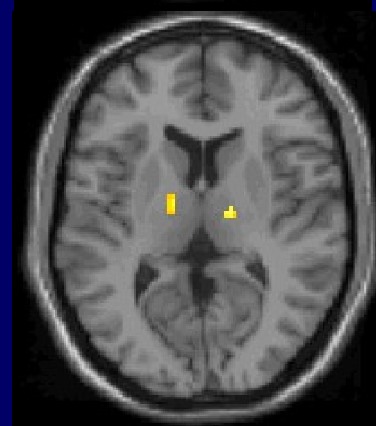
SMC, SMA



Mildly disabled RRMS *vs* SPMS



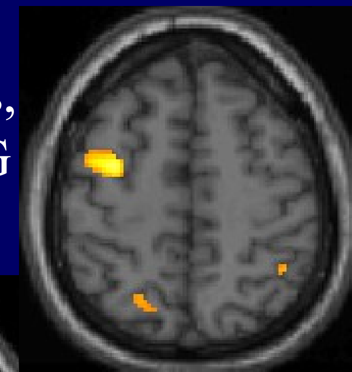
SII

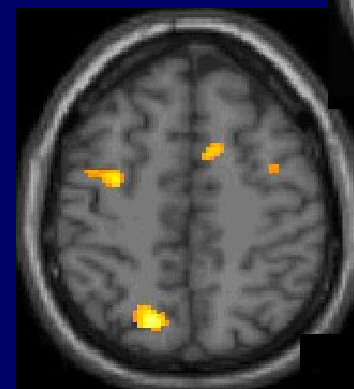


Thalamus

SPMS *vs* mildly disabled RRMS

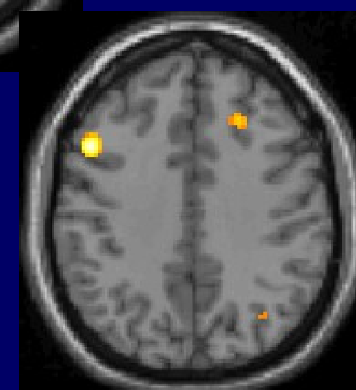
Precuneus, IPL, MFG





Precuneus, CMA, MFG

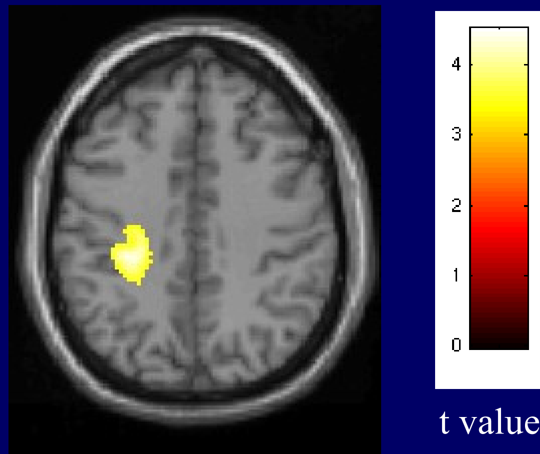
MFG, IPL



Rocca et al., Lancet Neurol 2005

fMRI & MS
Adaptive role

BMS

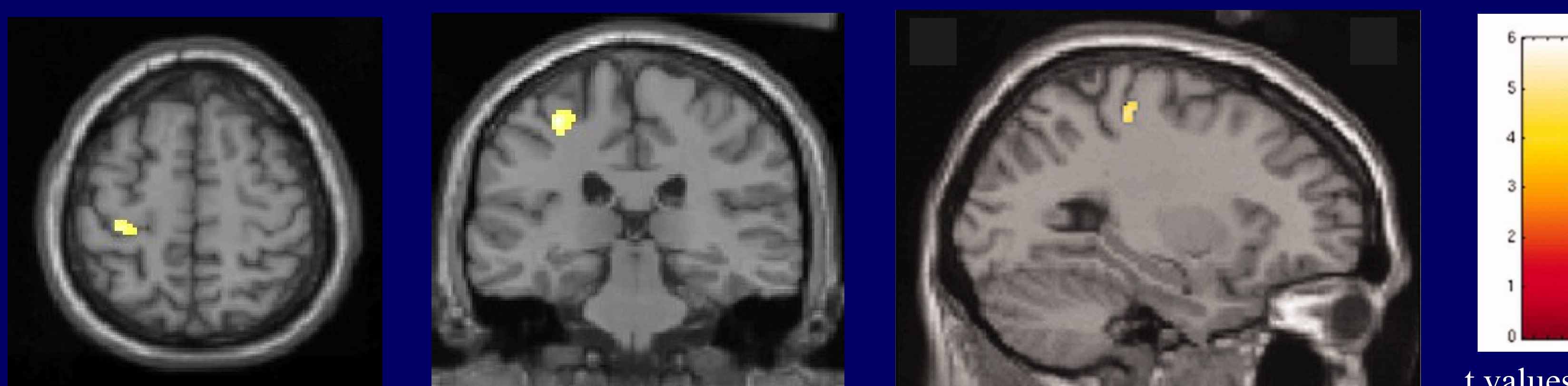


t values

L SMC *vs* T2 lesion volume:
$r = 0.78$, $p < 0.001$

Rocca et al., Neurology 2010

Pediatric MS



t values

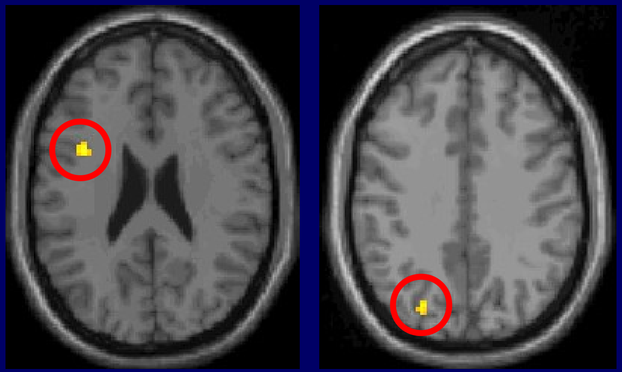
L SMC *vs* T2 lesion volume: $r = 0.78$, $p < 0.001$

Rocca et al., Hum Brain Mapp 2009

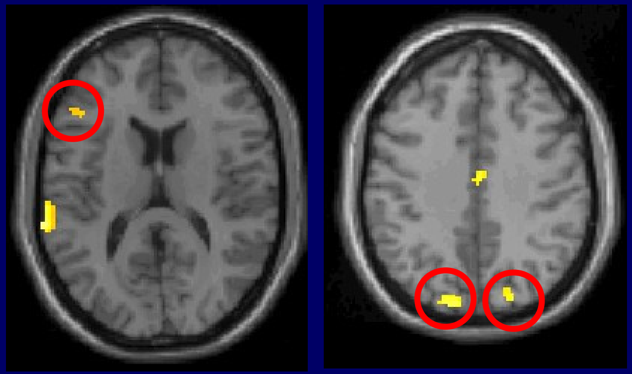
fMRI & MS
Adaptive role

Object manipulation

Healthy subjects: object manipulation



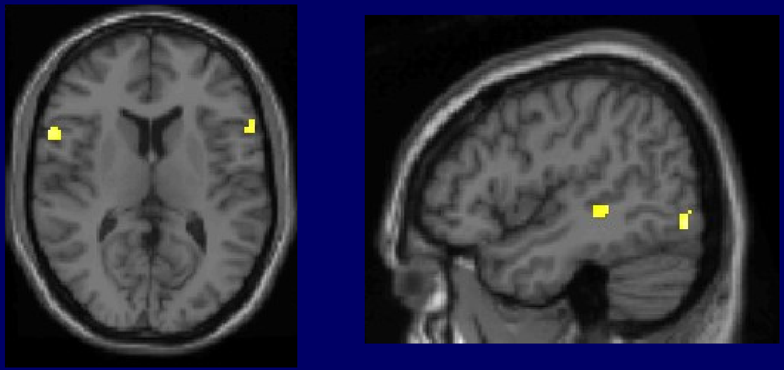
MS patients: simple motor task



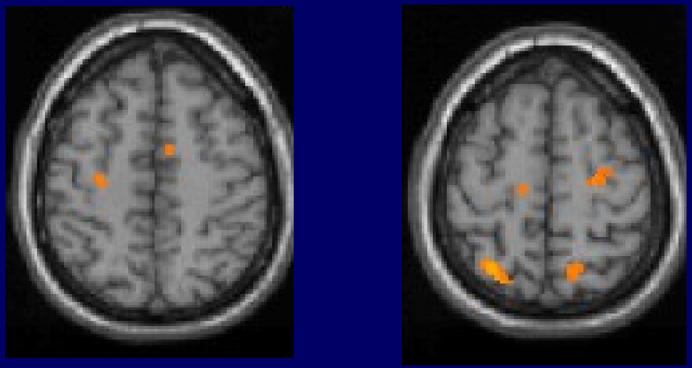
Filippi et al., NeuroImage 2004

MNS task

MNS task: patients *vs* controls



Simple and MNS tasks interaction: patients *vs* controls

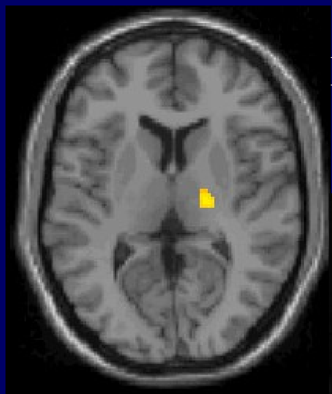


Rocca et al., Neurology 2008

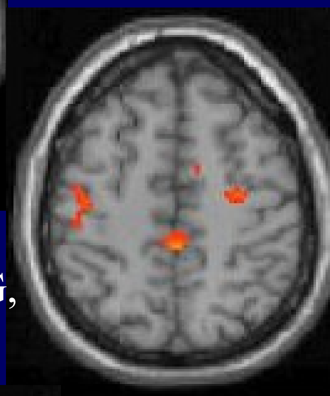
fMRI & MS

Maladaptive role

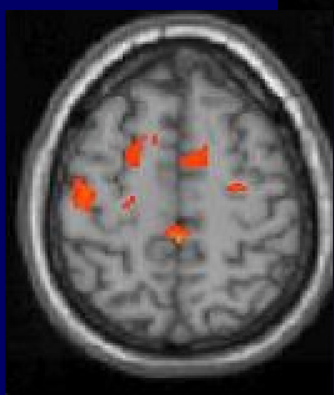
F MS day 1 *vs* baseline + day 4



R thalamus



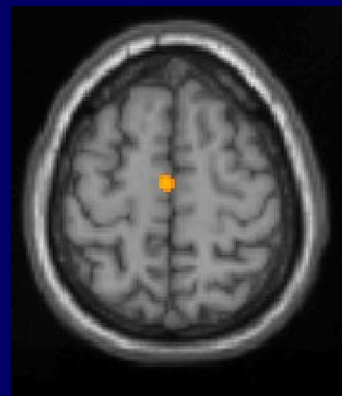
L SMC, R MFG, SMA, CMA



L SMC, MFG, SMA, CMA

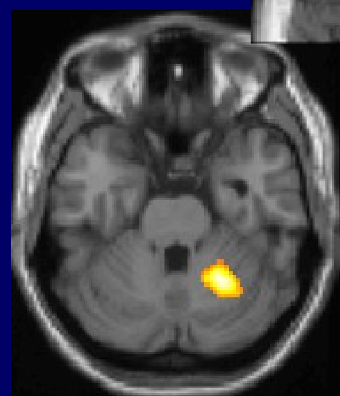
Rocca et al., Hum Brain Mapp 2007

SPMS (reduced activations)



L SMA

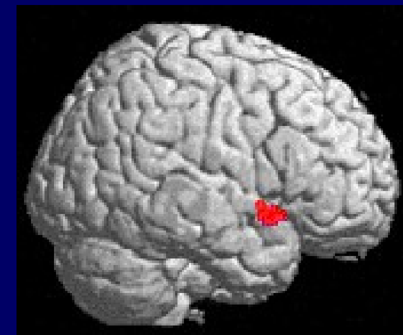
L putamen



R cerebellum

Rocca et al., Neurology 2010

PPMS



STG

MFG

Insula

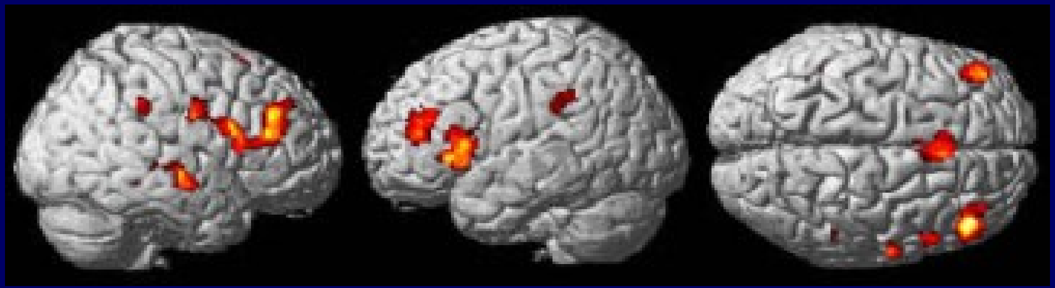
Filippi et al., NeuroImage 2002

fMRI & MS

Adaptive-Maladaptive role

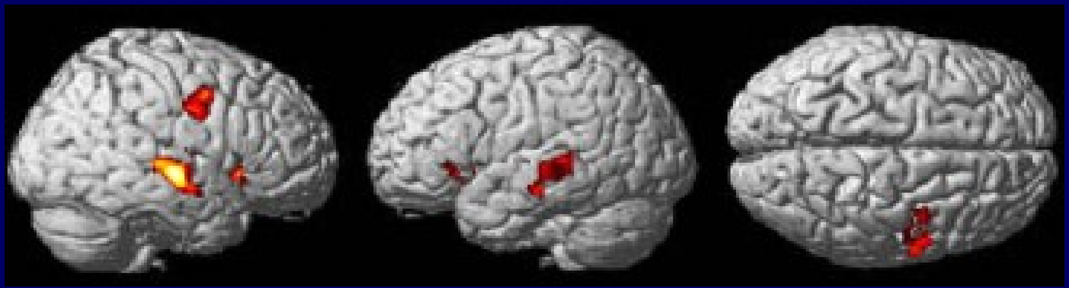
MS patients *vs* controls

PASAT



IFG, MFG, IP cortex, STG, MTG, bilaterally; SMA; R anterior cingulate

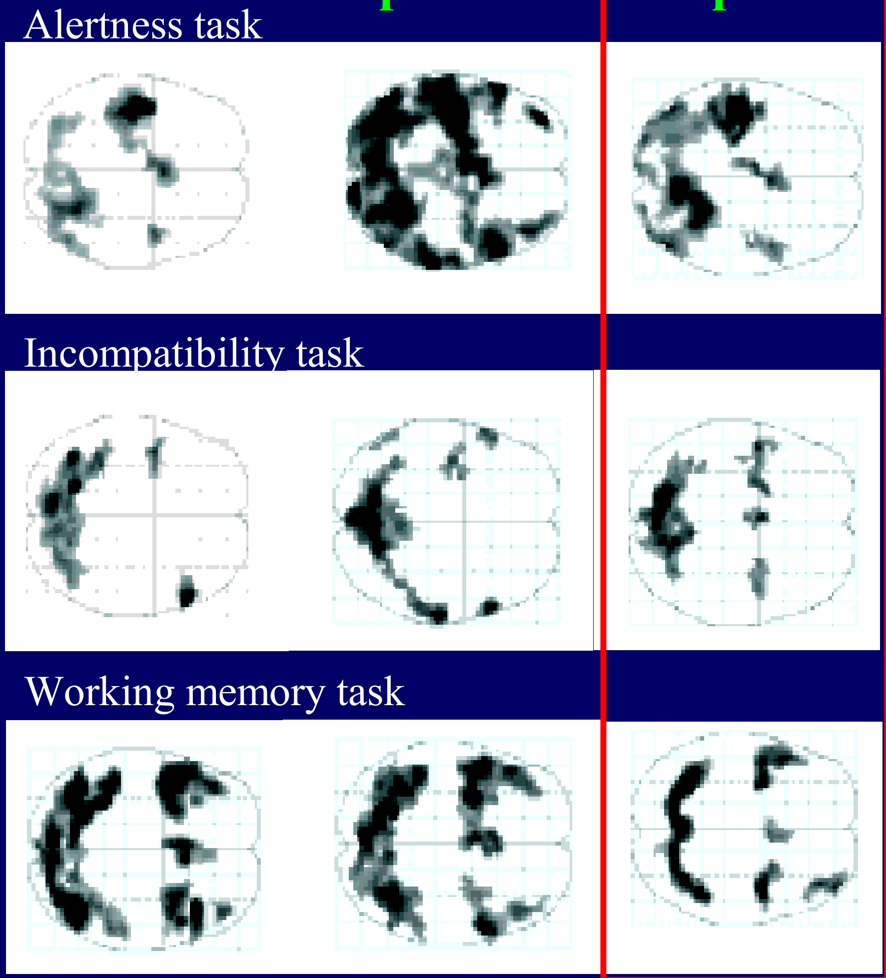
Recall Task



IFG, MFG, STG, MTG, transverse TG, BG, bilaterally; R lateral premotor area; L thalamus

Mainero et al., NeuroImage 2004

Controls | **Mildly impaired** | **Severely impaired**

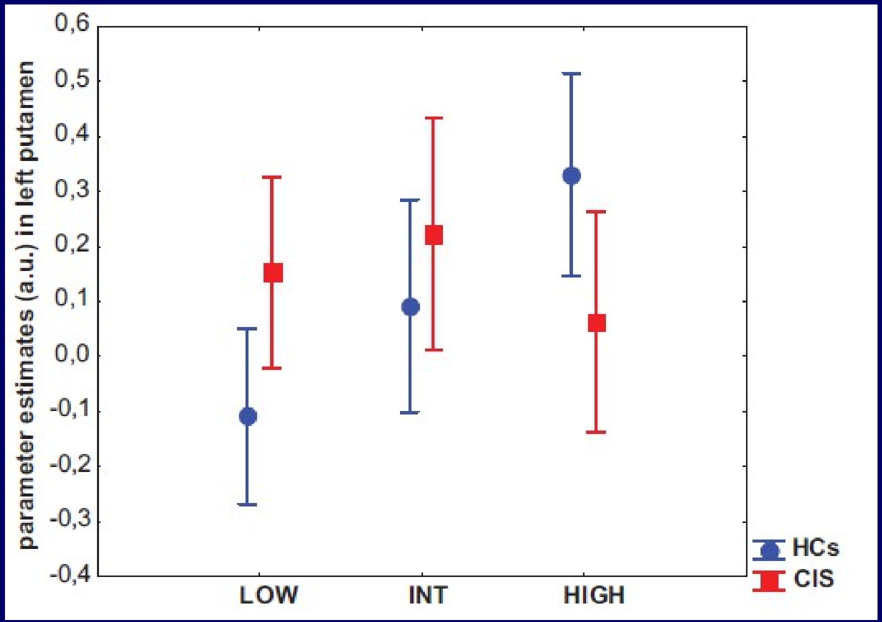


Penner et al., J Neurol 2003

fMRI & MS

Impaired functional reserve

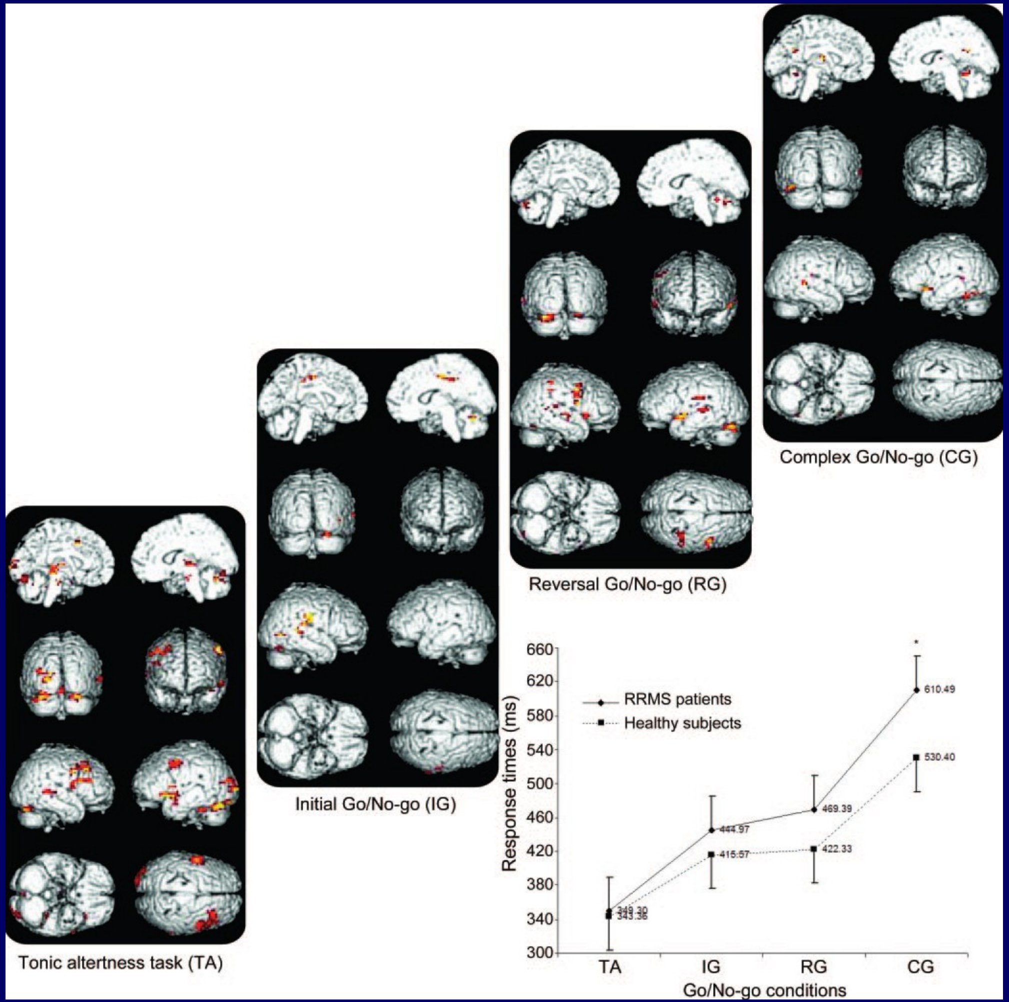
Controls *vs* CIS
(Variable attentional control task)



Load-related abnormalities in the recruitment of putamen in CIS patients

Tortorella et al., MSJ 2013

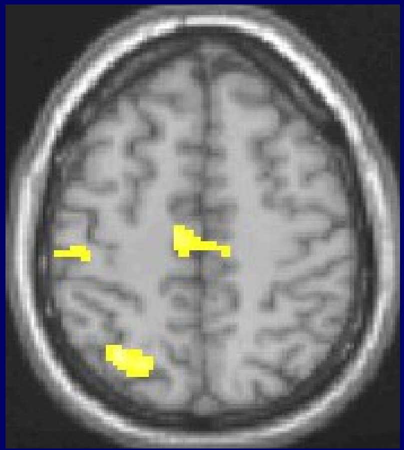
RRMS patients (Go-NoGo task)



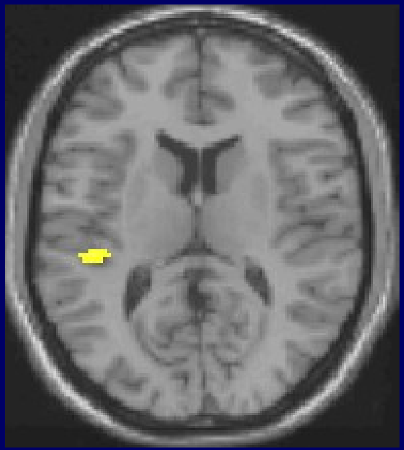
Bonnet et al., Neurology 2010

fMRI & MS

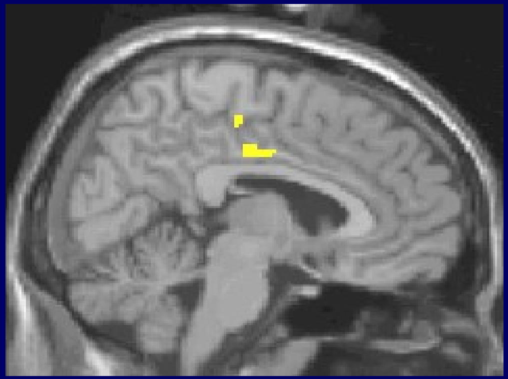
fMRI *vs* structural damage



SMC, SMA, IPS

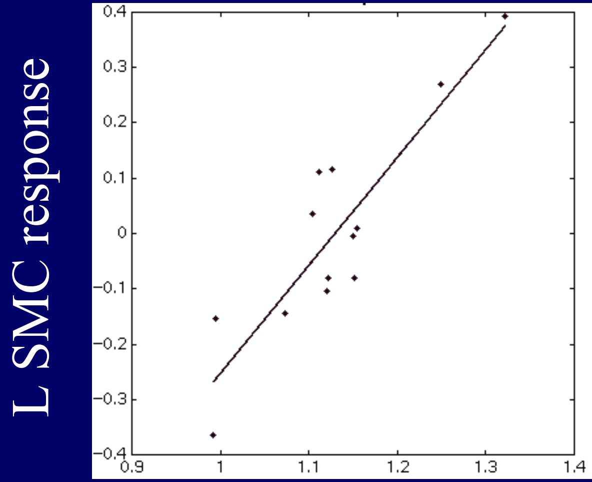


SII



SMA, CMA

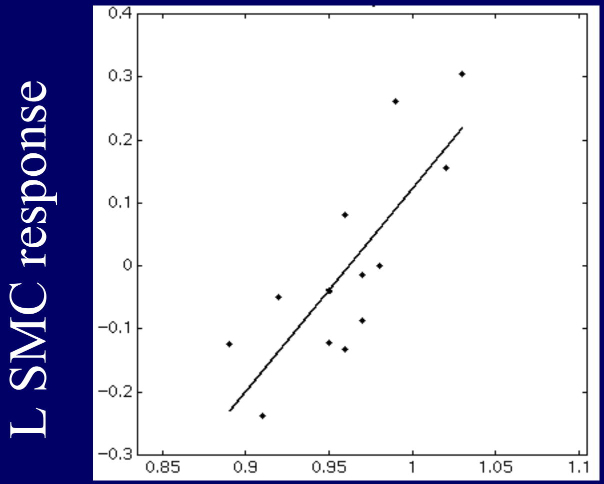
CMA



$r = 0.88$

$p < 0.001$

Average lesion MD [mm^2s^{-1}]



$r = 0.81$

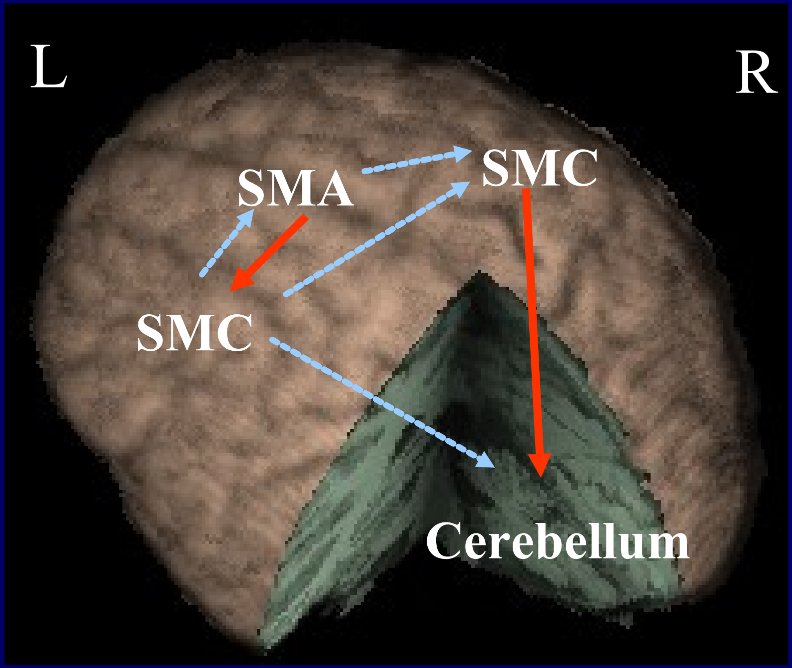
$p < 0.005$

MD of the NABT [mm^2s^{-1}]

Rocca et al., Ann Neurol 2002

fMRI & MS

fMRI *vs* structural damage



Increased connectivity in patients

Similar connectivity in patients and controls

SMA to L primary SMC:

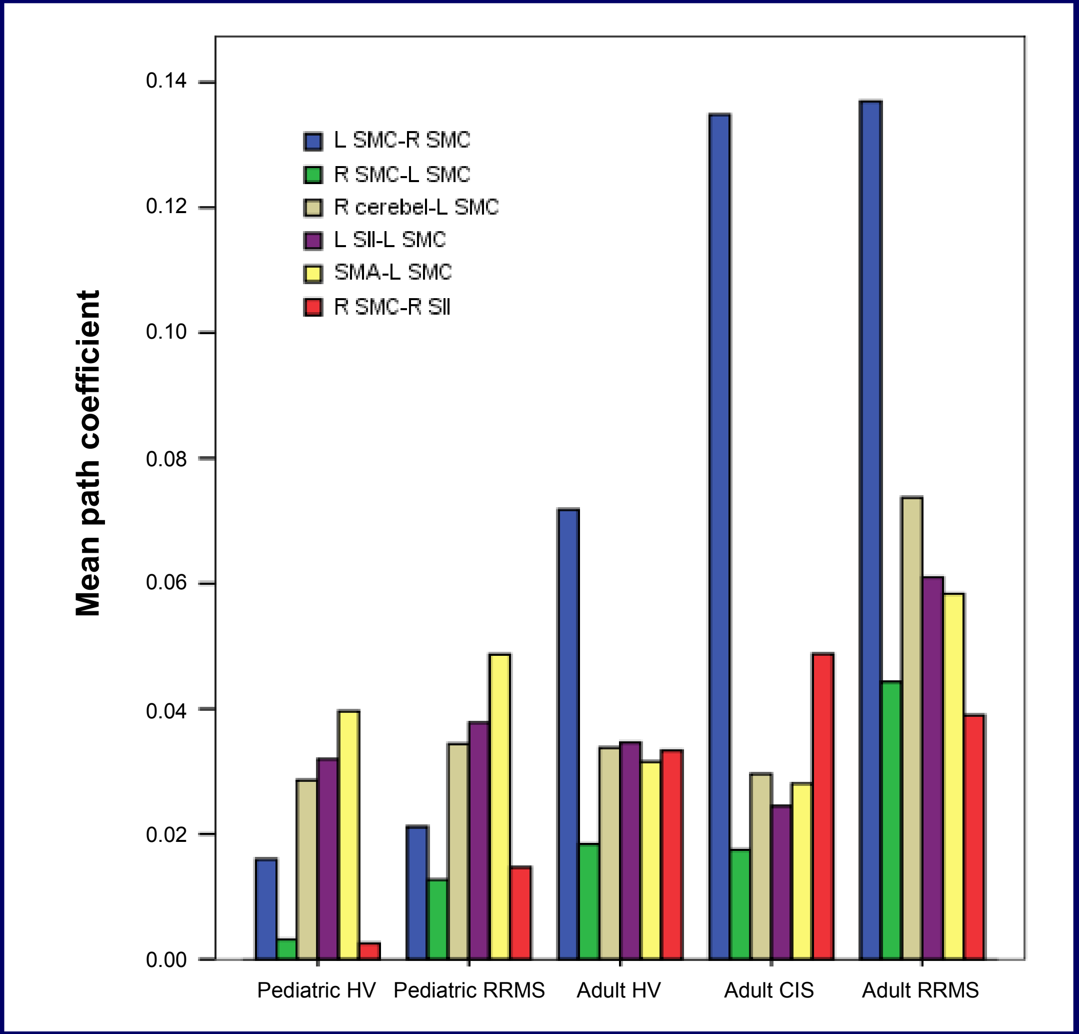
CST LL ($r = 0.64$, $p = 0.04$)

R SMC to cerebellum:

DRT-FA ($r = -0.73$, $p = 0.02$)

DRT-MD ($r = 0.85$, $p = 0.004$)

Rocca et al., Neurology 2007



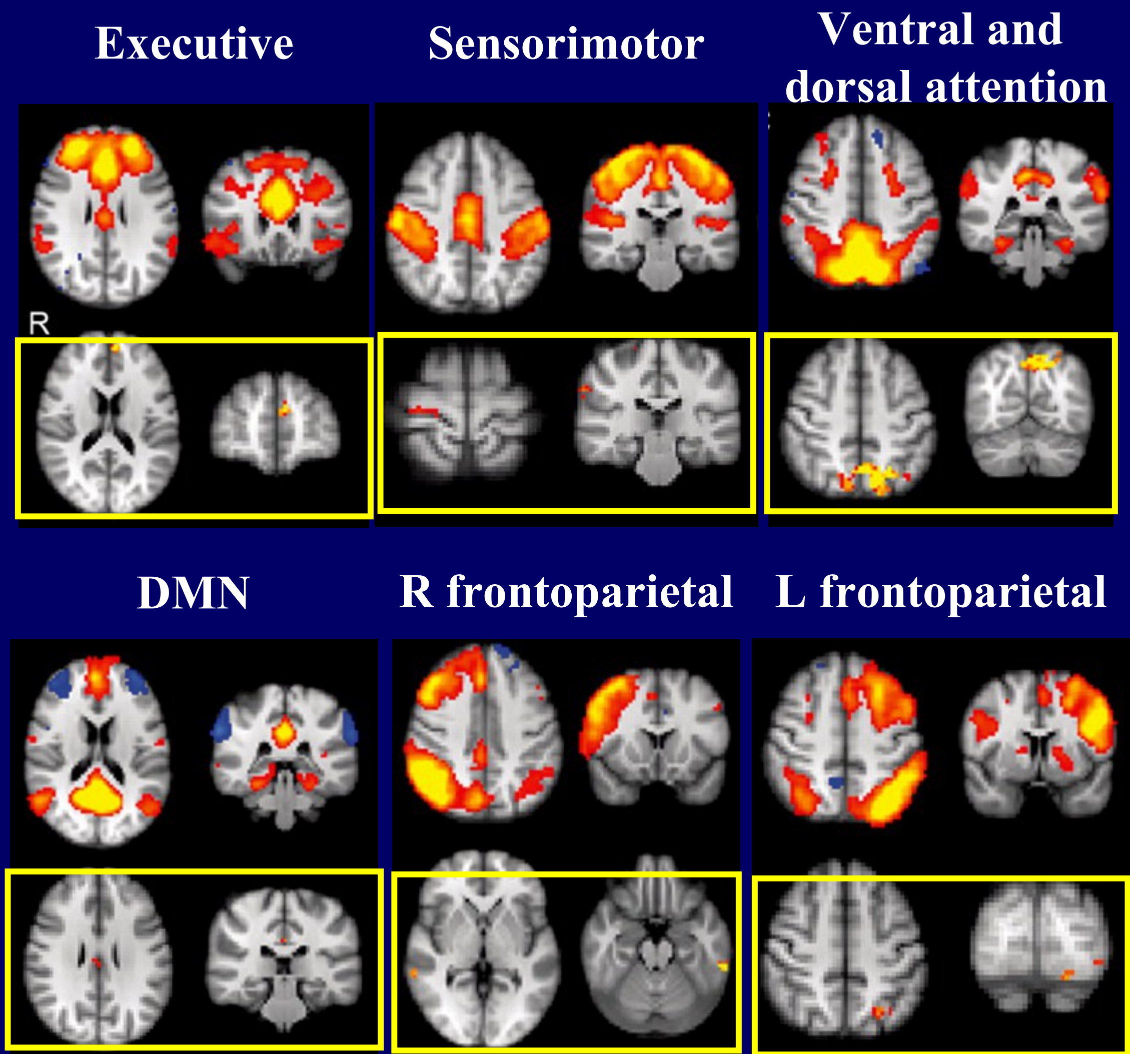
Connectivity coefficients *vs* CC and CST damage ($r = -0.34$ to 0.40)

Rocca et al., Radiology 2010

fMRI & MS

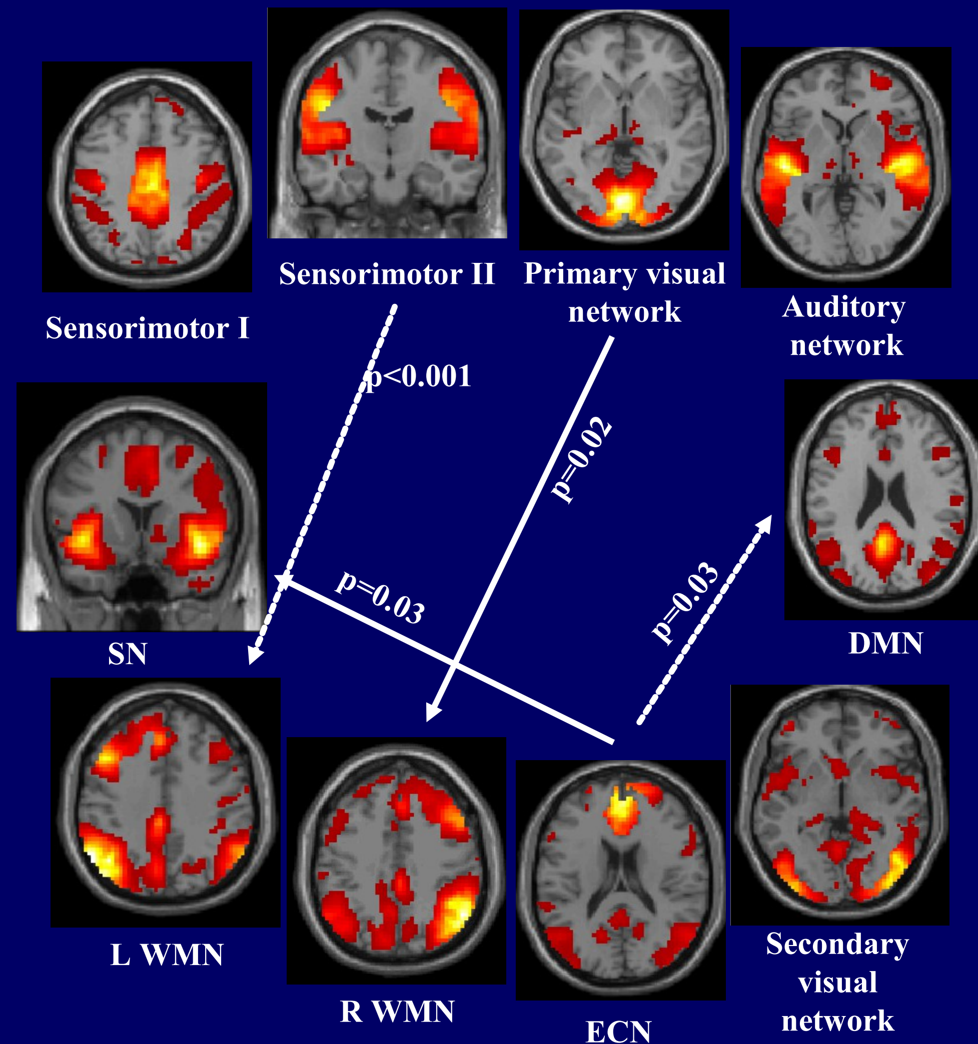
From regions to networks

Within-network abnormalities



Roosendaal et al., Brain 2010

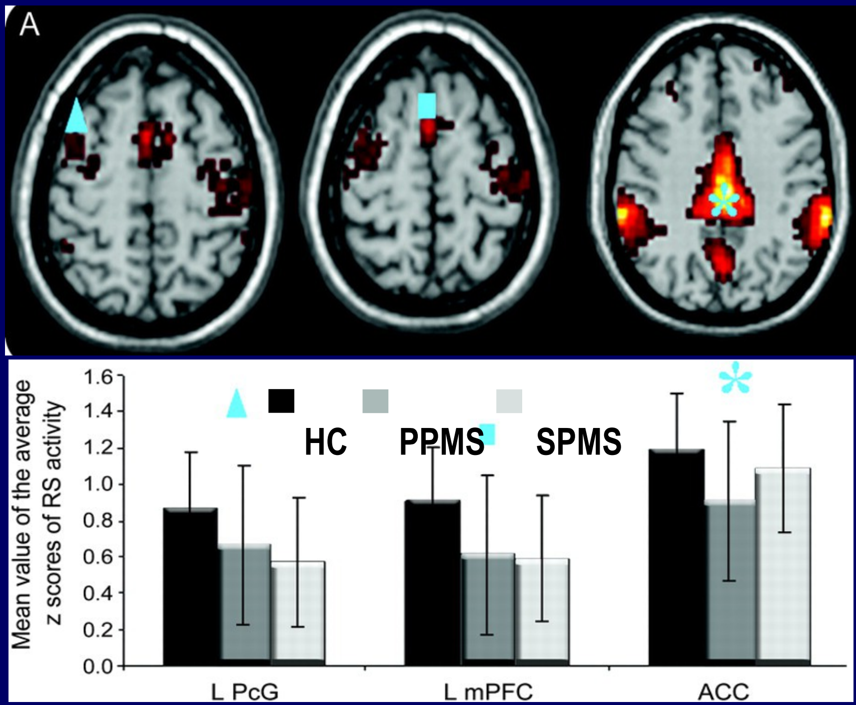
Inter-network abnormalities



Rocca et al., Neurology 2012

fMRI & MS
From regions to networks

↓ DMN RS FC in progressive MS

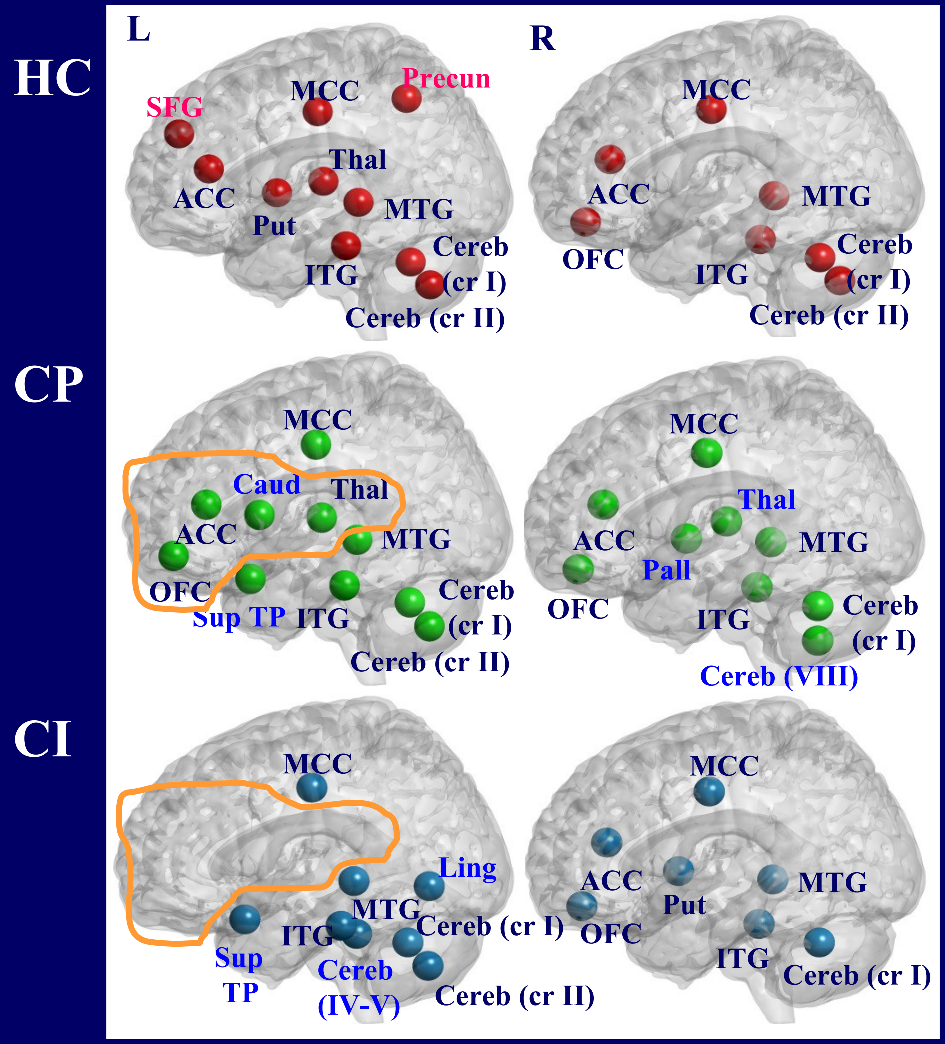


Correlations between ↓ DMN RS FC and:

PASAT (r=0.42, p<0.001)
CC FA and JD (r from 0.54 to 0.87, p<0.001)
Cingulum FA (r=0.83, p<0.001)

Rocca et al., Neurology 2010

MS connectome



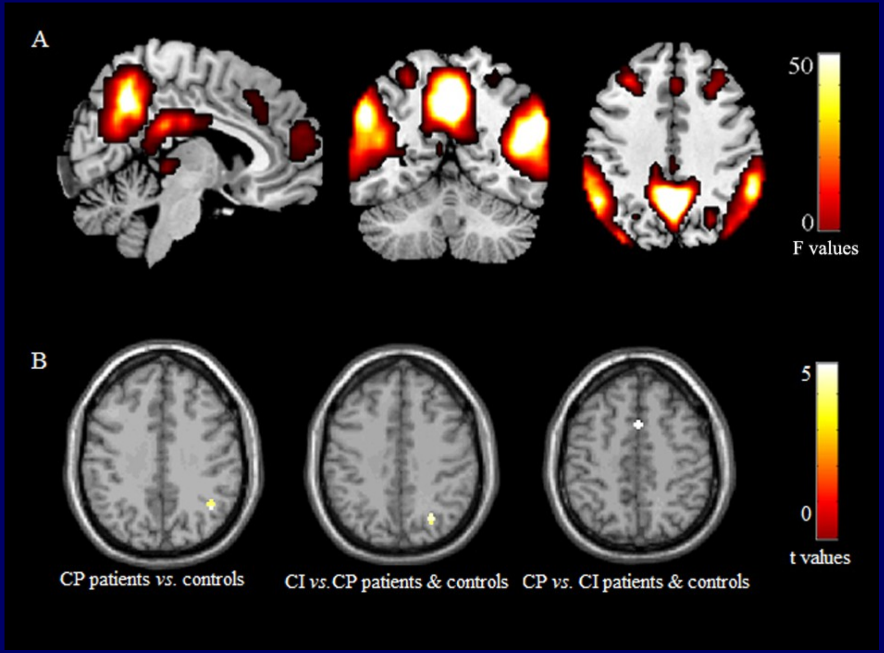
Rocca et al., Brain Struct & Funct 2014

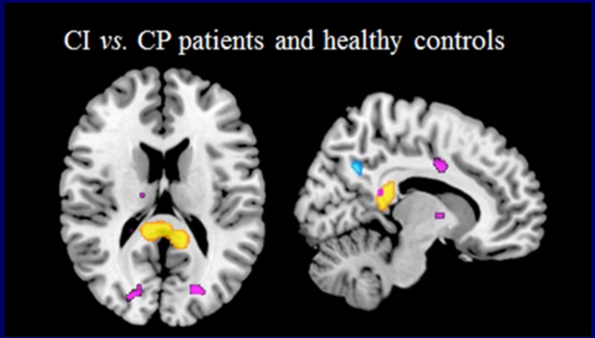
fMRI & MS

From regions to networks

Intra/Inter-network abnormalities in pediatric MS

Intra-network abnormalities



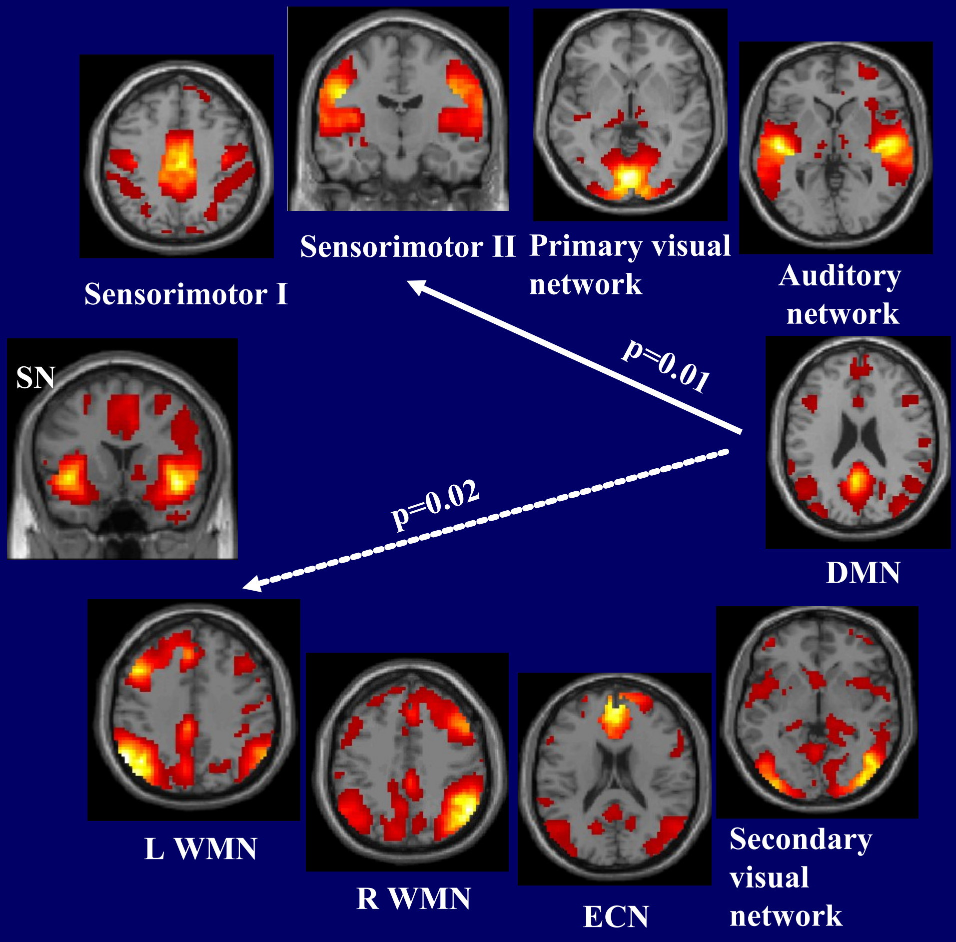


CI explained by:
- **cingulum FA**
- **CC MD**
- **R precuneus RS FC**

C-index=0.99

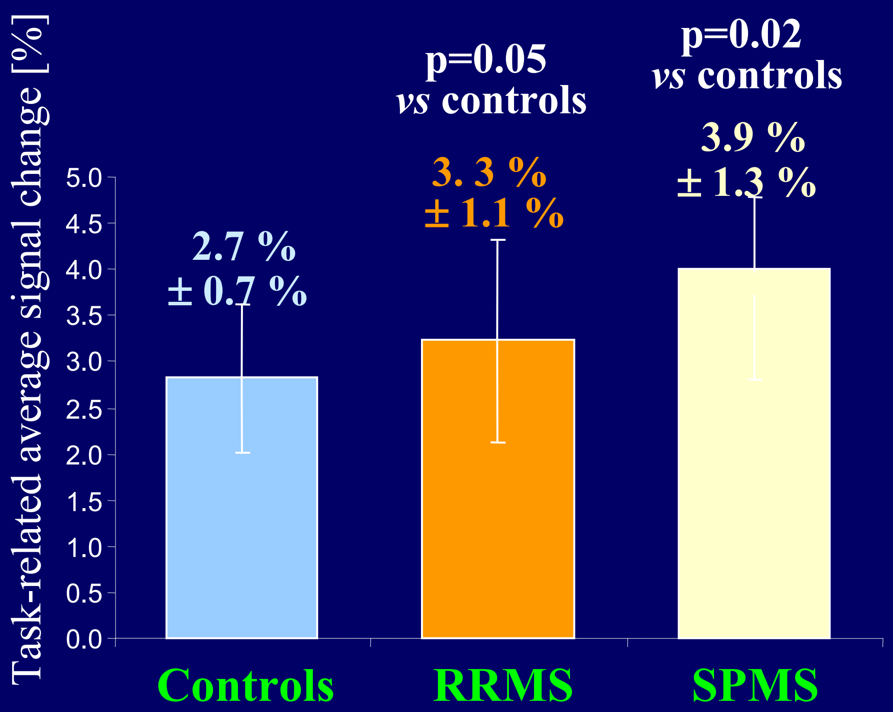
Rocca et al., Neurology 2014

Inter-network abnormalities



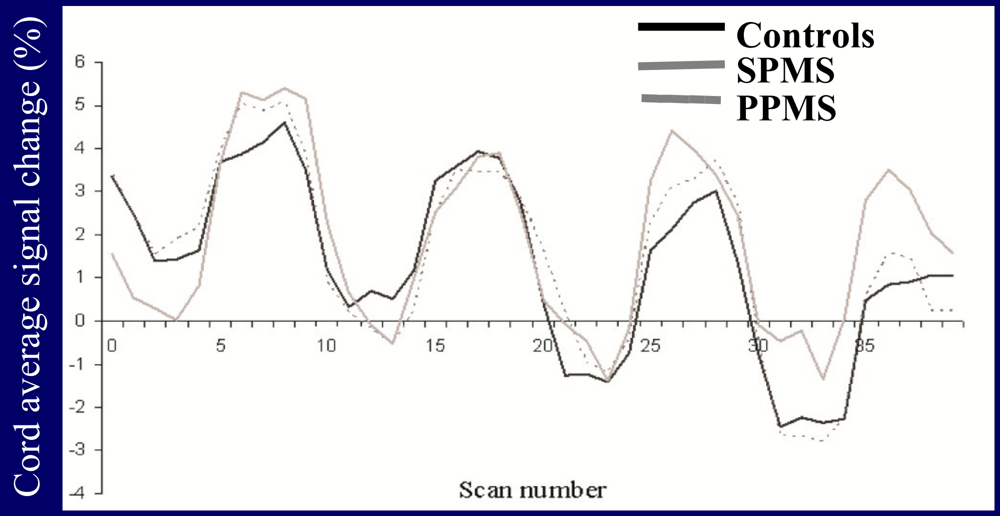
Rocca et al., Human Brain Mapp 2014

fMRI & MS
Cervical cord



Valsasina et al., JNNP 2010

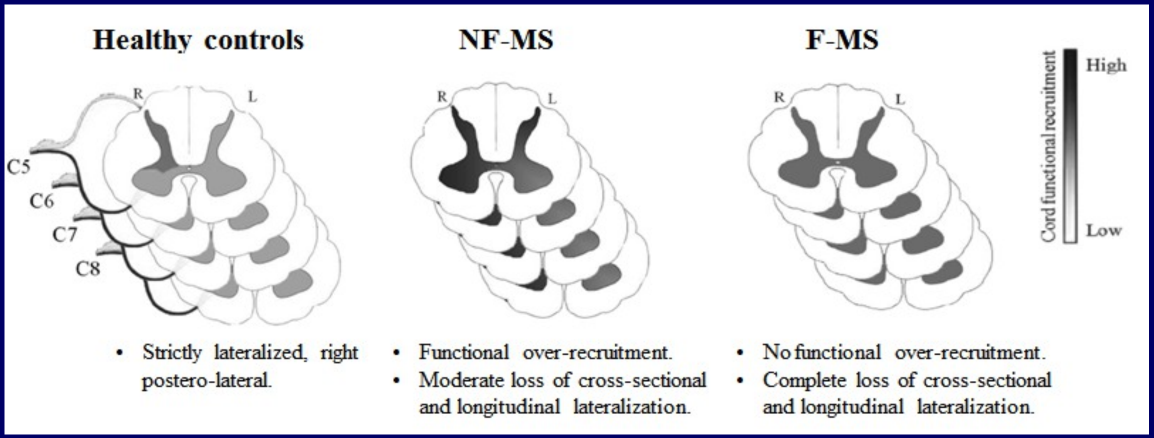
Cord fMRI in progressive MS



Valsasina et al., Hum Brain Mapp 2011

Progressive MS *vs* controls: p=0.003
SPMS *vs* PPMS: p=0.05

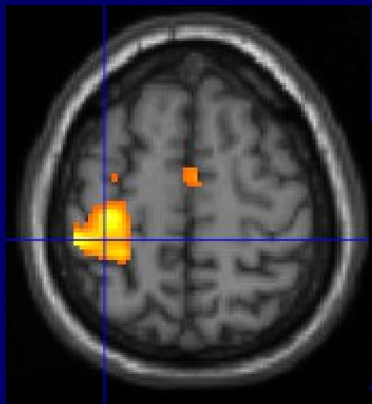
Cord fMRI *vs* fatigue



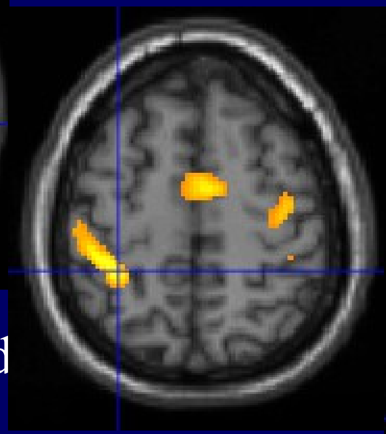
Rocca et al., Mult Scler 2012

fMRI & MS

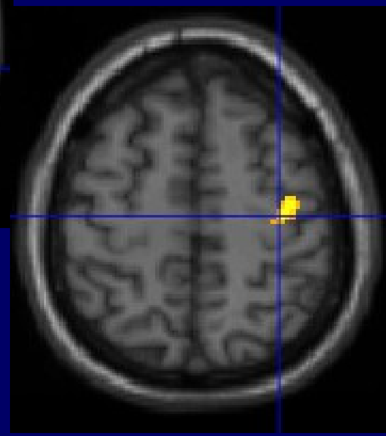
Prognosis



Unimpaired hand



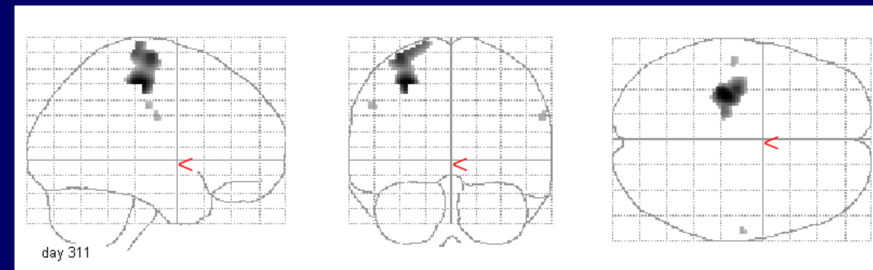
Impaired hand



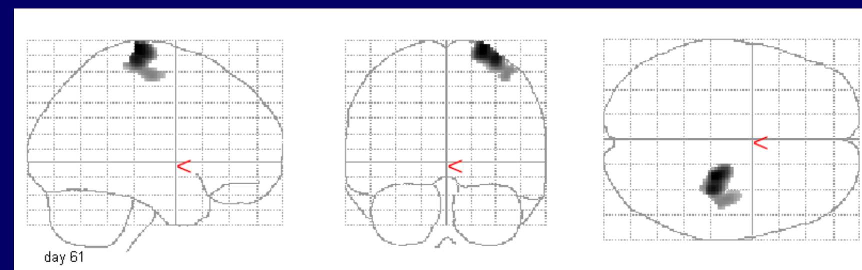
Impaired *vs.* unimpaired hand

One-year follow up

Good clinical recovery



Poor clinical recovery



Mezzapesa et al., Hum Brain Mapp 2007

fMRI & MS

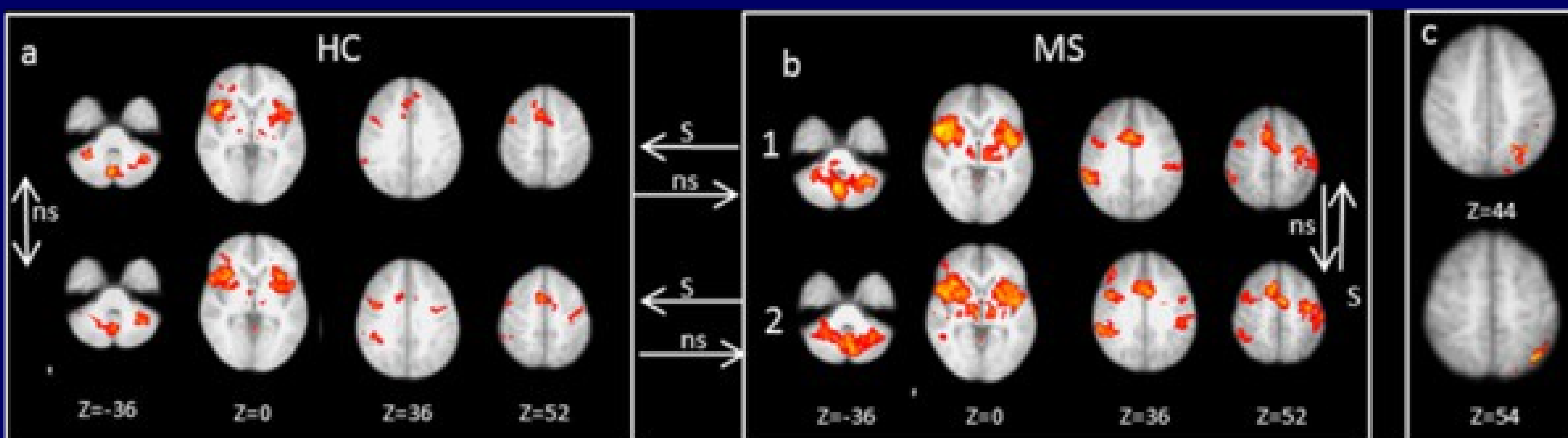
Longitudinal changes

CIS/R DLPFC 1 year activation change

Cognitively improved
vs stable patients

Audoin et al., Mult Scler 2008

Early RRMS /L IPL 1 year activation change



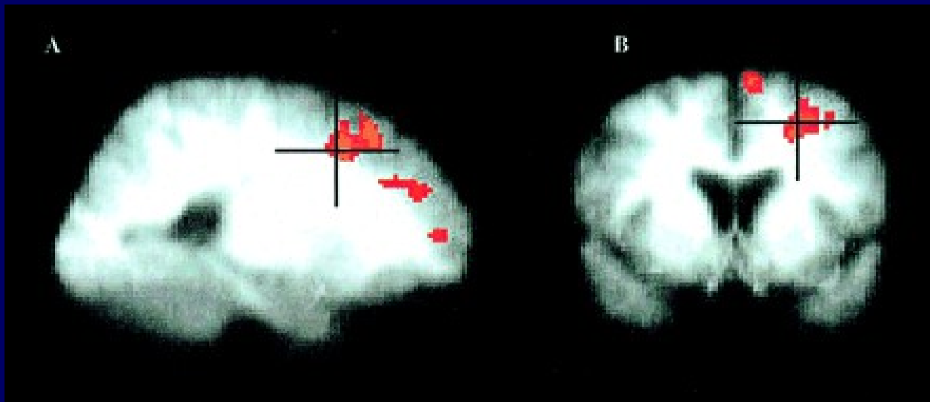
L IPL *vs*
worse
SDMT
performance

Loitfelder et al., PlosOne 2014

fMRI & MS

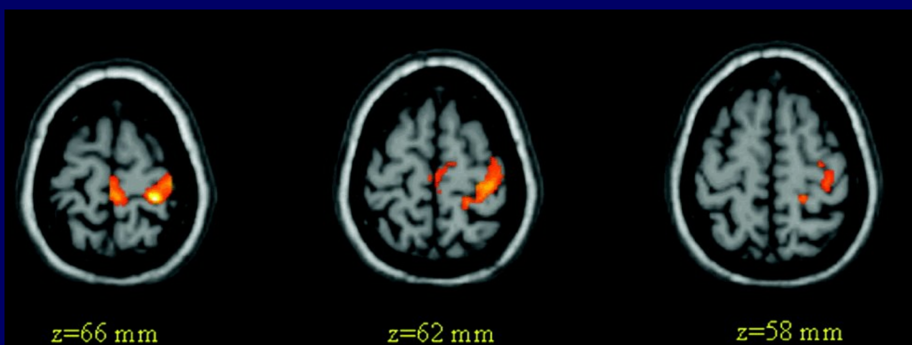
Monitoring treatment

Stroop task and rivastigmine



Parry et al., Brain 2003

3, 4-diaminopyridine *vs* placebo

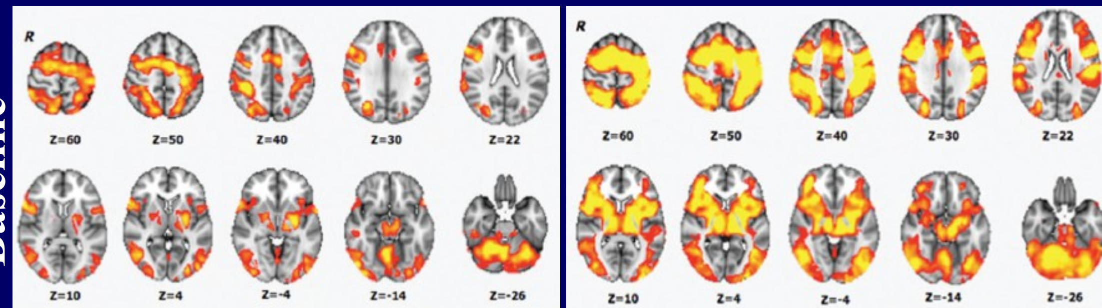


Mainero et al., Neurology 2004

Controls

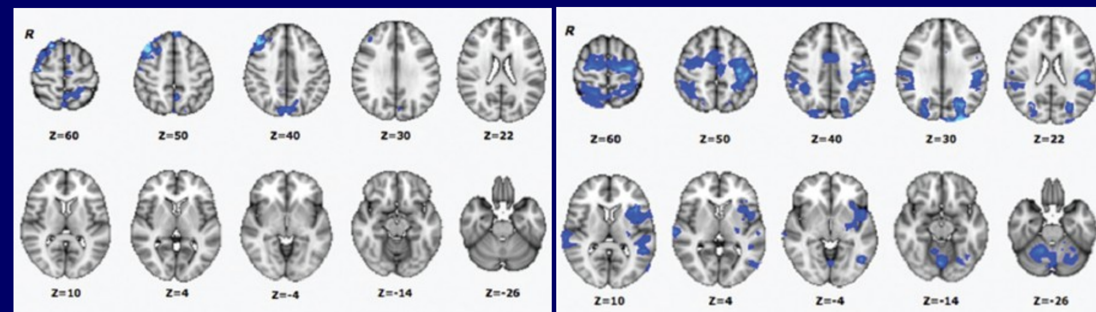
MS patients

Baseline

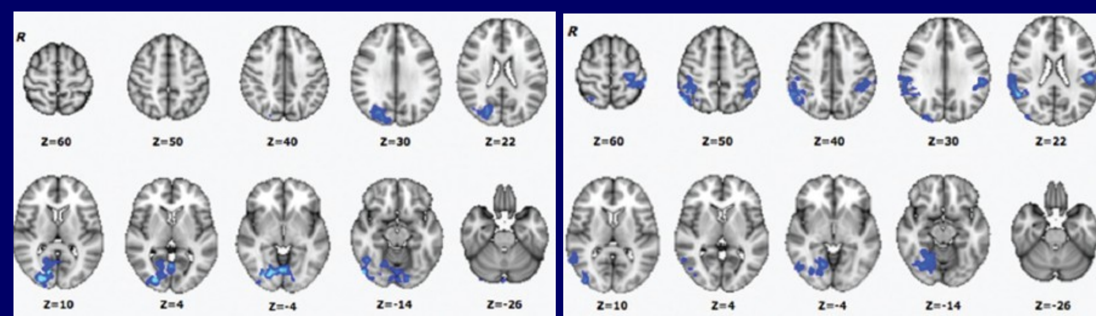


Performance improvement *vs* fMRI activity

1 session



2 weeks



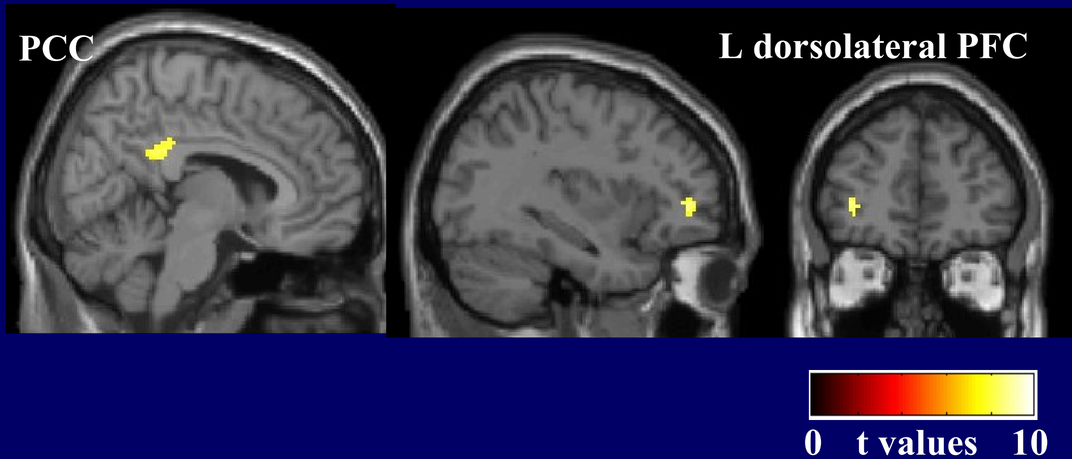
Tomassini et al., Neurorehabil Neural Repair 2012

fMRI & MS

Monitoring treatment

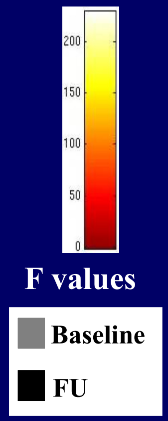
Stroop task *vs* cognitive rehabilitation

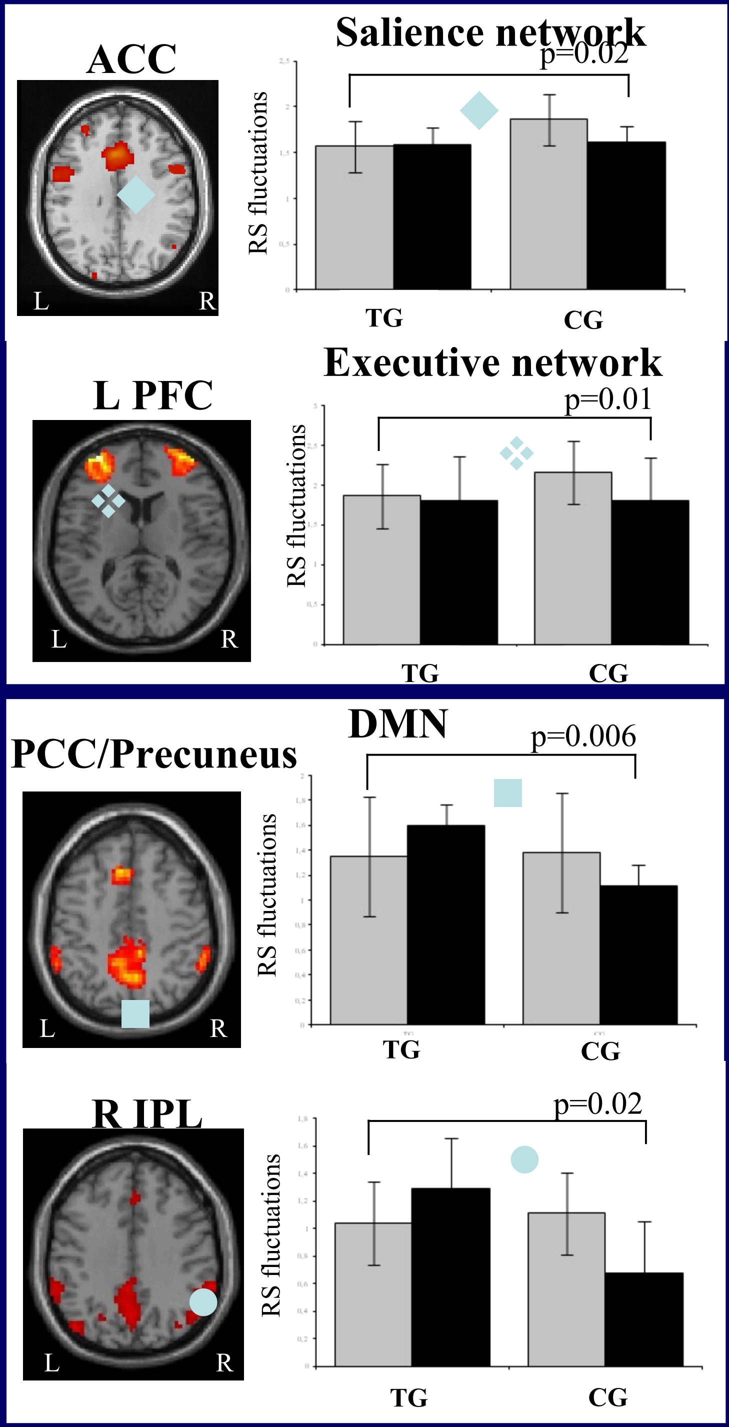
Stroop facilitation condition: TG *vs* CG



Stroop interference condition: TG *vs* CG

RSN

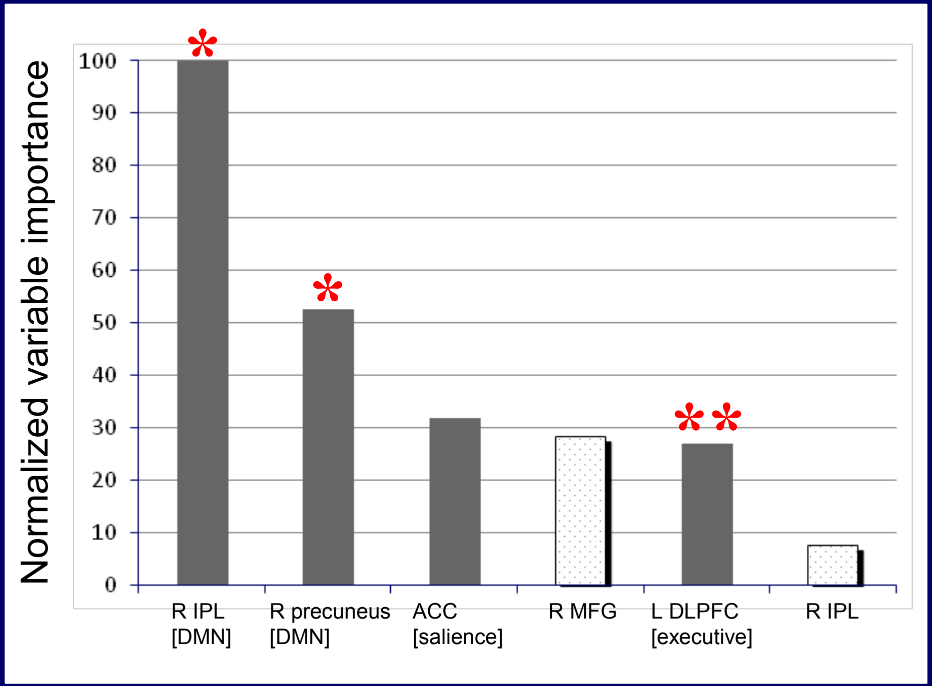




Filippi et al., Radiology 2011

fMRI & MS
Monitoring treatment

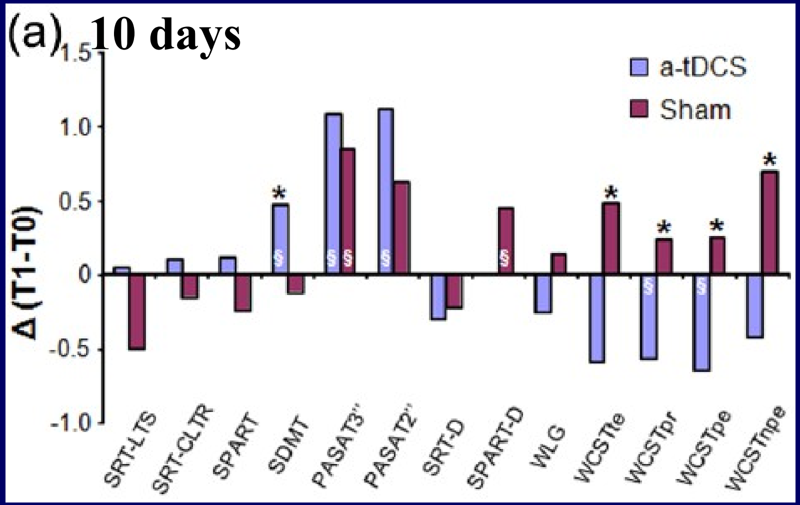
6 month follow up

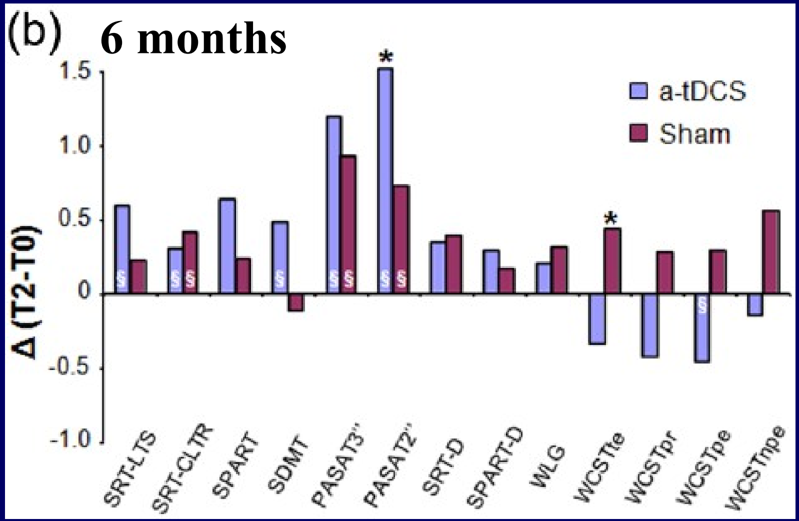


*Depression **QoL

Parisi et al., MSJ 2014

L DLPFC anodal tDCS stimulation

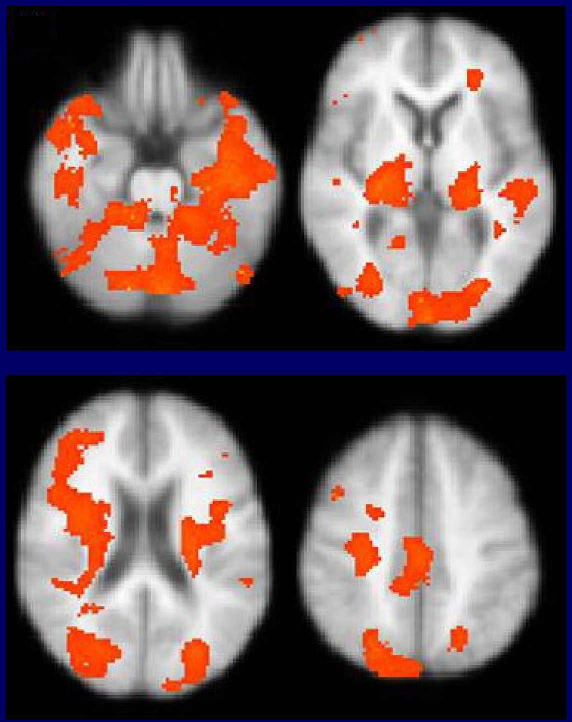




Mattioli et al., MSJ 2015

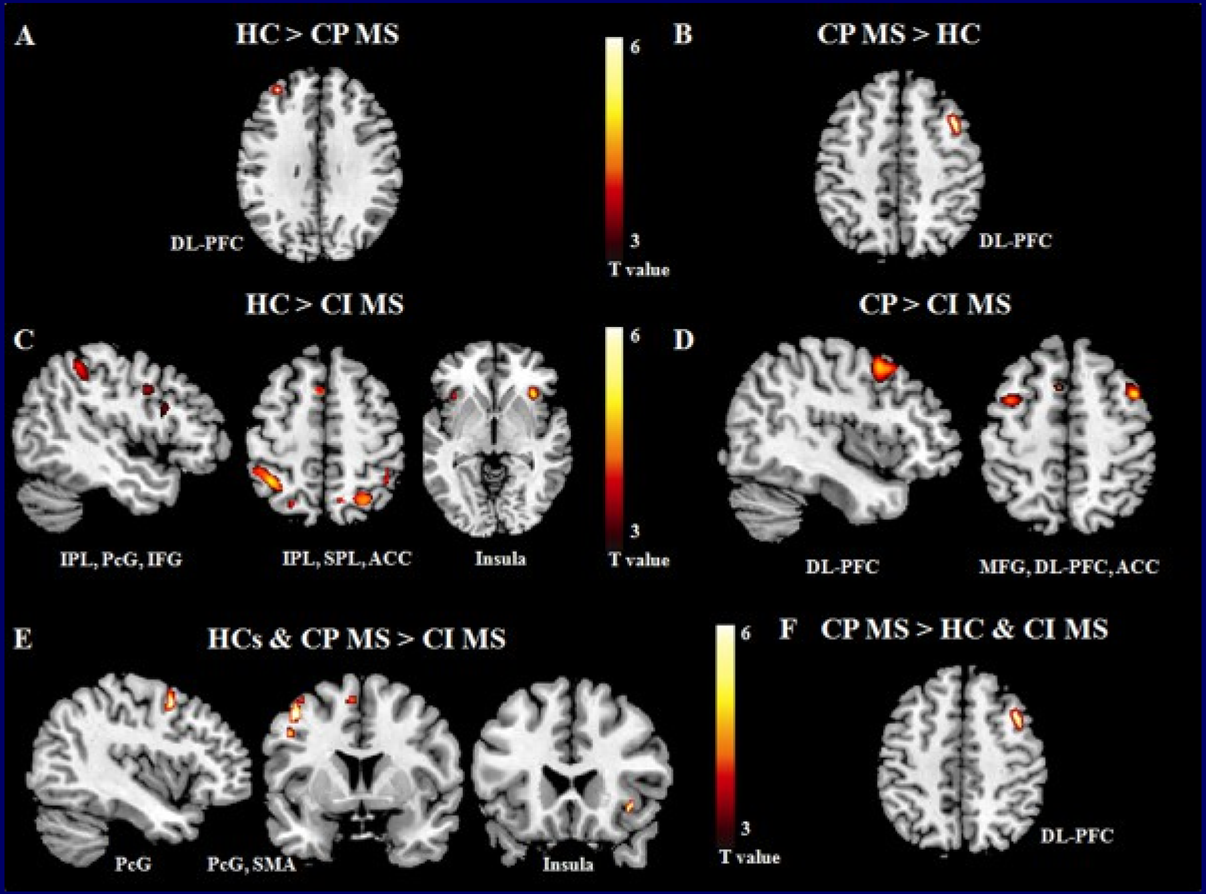
fMRI & MS
Multi-centre studies

Motor task



Wegener et al., Eur J Neur 2007
Rocca et al., Hum Brain Mapp 2009

Cognitive task



Rocca et al., Hum Brain Mapp 2014

fMRI & MS

Conclusions

- Brain functional reorganization is a common phenomenon in MS patients independent of disease duration and clinical phenotype.
- Variable patterns of cortical rewiring with the potential to limit the functional consequences of tissue damage occur in MS patients, suggesting that their disability is likely to result from the balance between structural damage and brain reorganization, rather then being a mere reflection of tissue disruption.
- Together with adaptive plasticity, maladaptive plasticity can occur in brain systems, which contributes to accumulation of disability and cognitive impairment.
- Improved understanding of recovery mechanisms may guide the development of new recovery-oriented strategies in MS.