Universitätsklinikum Hamburg-Eppendorf

RIMS 2012
Rehabilitation in Multiple Sclerosis -
17th Annual Conference
31.May.-02. June 2012

Major topic 2:"Towards evidence-based motor system regeneration"

Fundamentals in neurosciences & implications for rehabilitation

What can we learn from system neurosciences (fMRI, TMS)?

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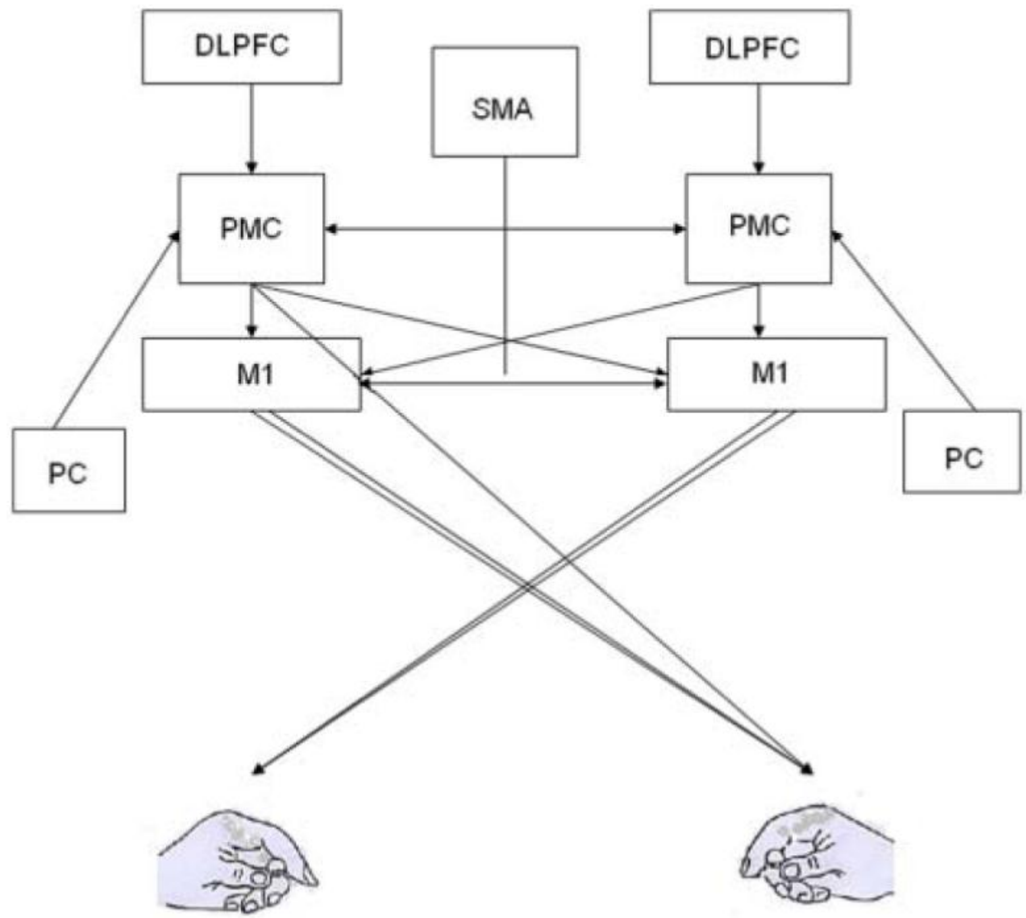
- The control and execution of motor behavior (e.g., reach, grasp etc.) is represented by a cortical network of primary and secondary motor areas

- This network has the potential to reorganize after focal lesions or structural changes

- How can systems neuroscience help to understand reorganization, functional relevance, prediction of recovery or select therapeutic interventions



Kantak et al. 2012

- Representation of unimanual movements in healthy subjects and in patients
- What is the functional meaning of activation patterns in healthy subjects and in patients
- Can we potentially predict recovery patterns and processes
- Can systems neuroscience provide a basis for patient-individualized treatments?

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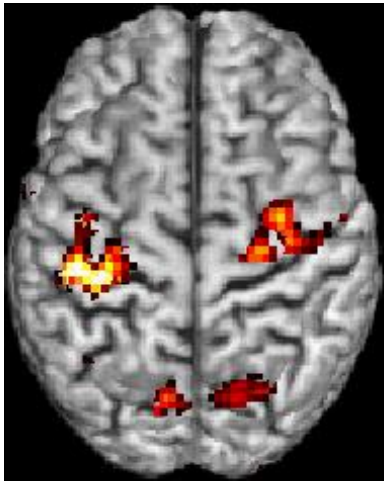
Representation of unimanual movements in healthy subjects and in patients

Healthy subjects

fMRI activation in young and old healthy subjects during a right-hand, motor task (Mattay et al. 2002, Ward et al. 2006, Sailer et al. 2000)

Stroke



fMRI activation in chronic stroke patients during a right-hand, motor task (Lotze et al. 2006, Ward et al. 2003, Grefkes et al. 2008)

MS

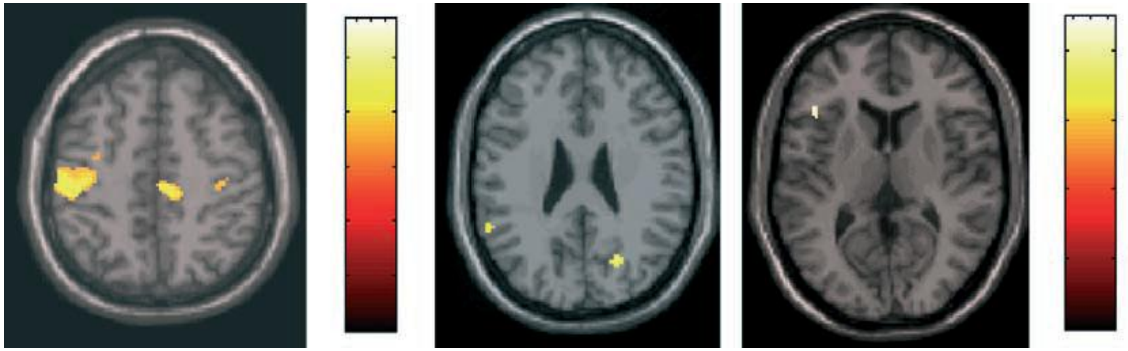
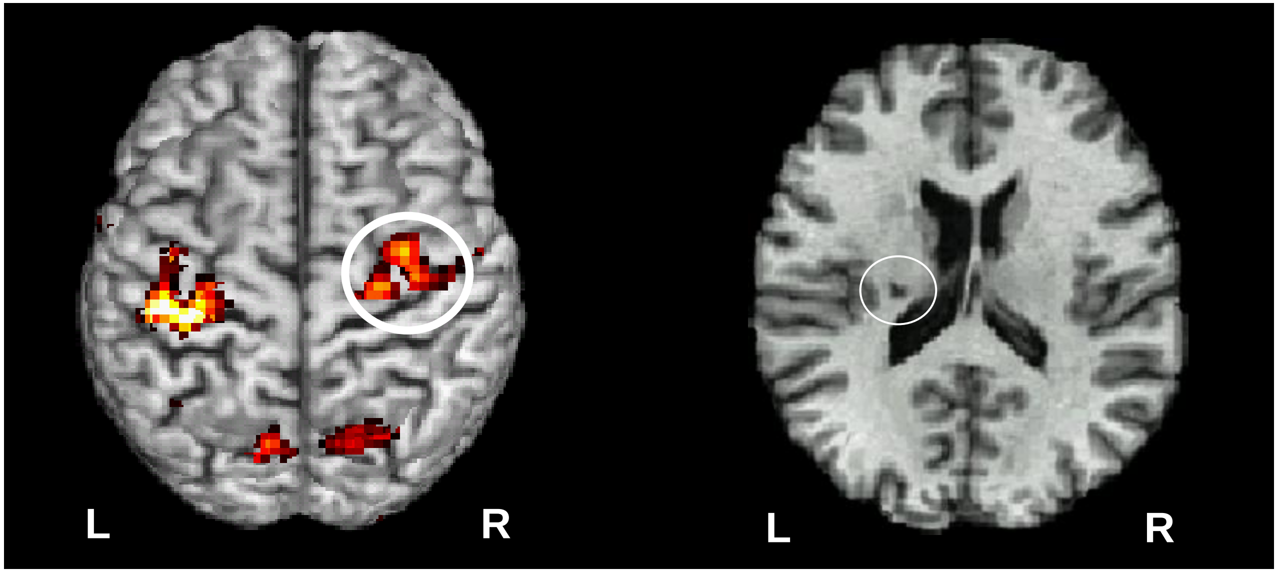


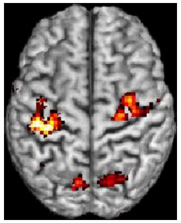
Figure 3: Comparisons of patients with RRMS without disability and patients with RRMS with mild disability during a simple, right-hand, motor task (Rocca et al. 2005, Pantano et al. 2002)

Virtual Lesion: Is there a causal link?

- Have cortical areas that are active during functional neuroimaging a causal link to a certain function?



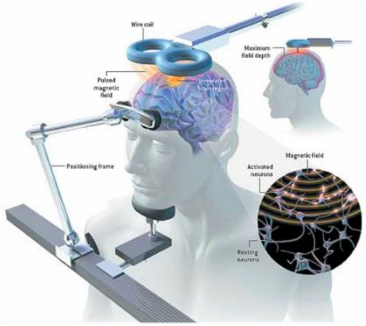
Ipsilateral motor cortex in MS patients; Is there a causal link?



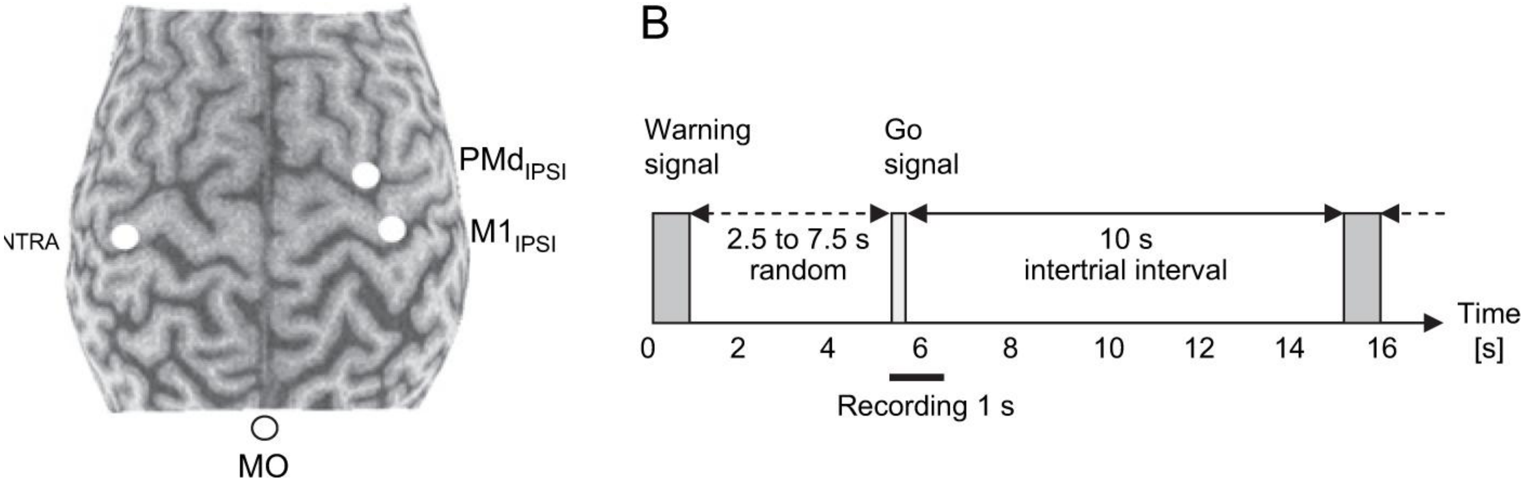
Functional role of ipsilateral motor areas in multiple sclerosis

Daniel Zeller,[1] Su-Yin Dang,[1] Katja Stefan,[1] Armin Biller,[3,4] Andreas Bartsch,[3,4] Dorothee Saur,[2] Martin Bendszus,[3,4] Peter Rieckmann,[1,5] Klaus V Toyka,[1] Joseph Classen[1,2]

JNNP 2011



- n=26 MS, 26 controls
- Virtual lesion TMS approach
- neuronavigated



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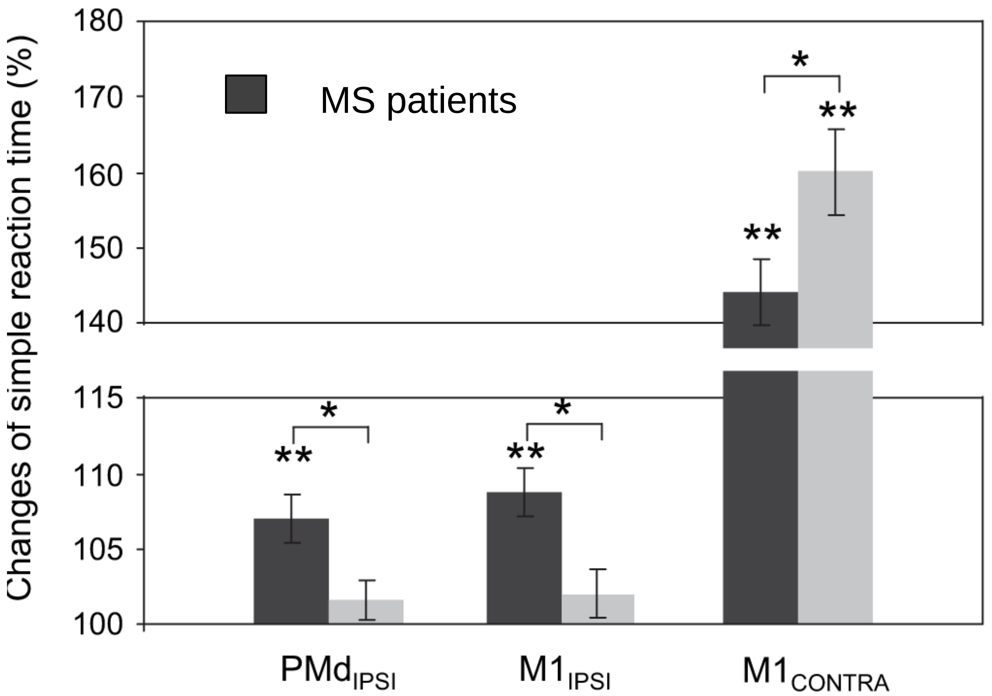
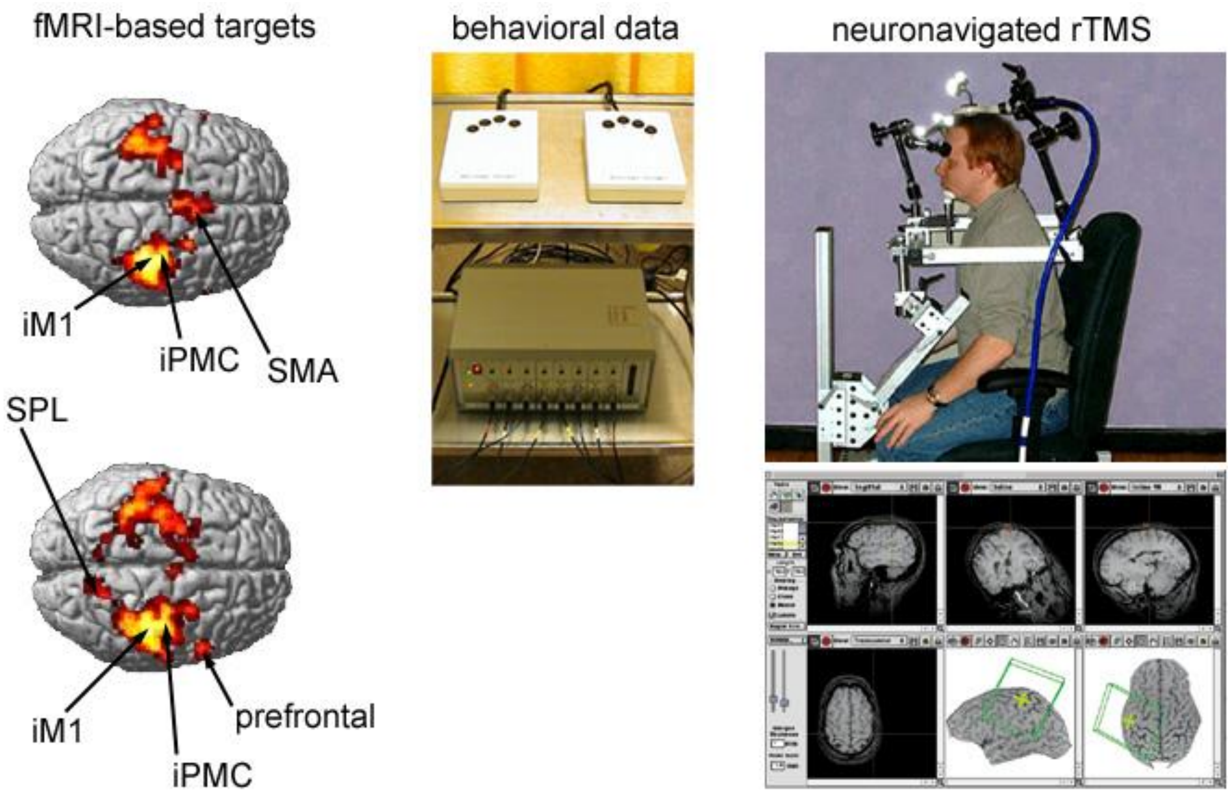
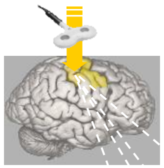
JNNP 2011



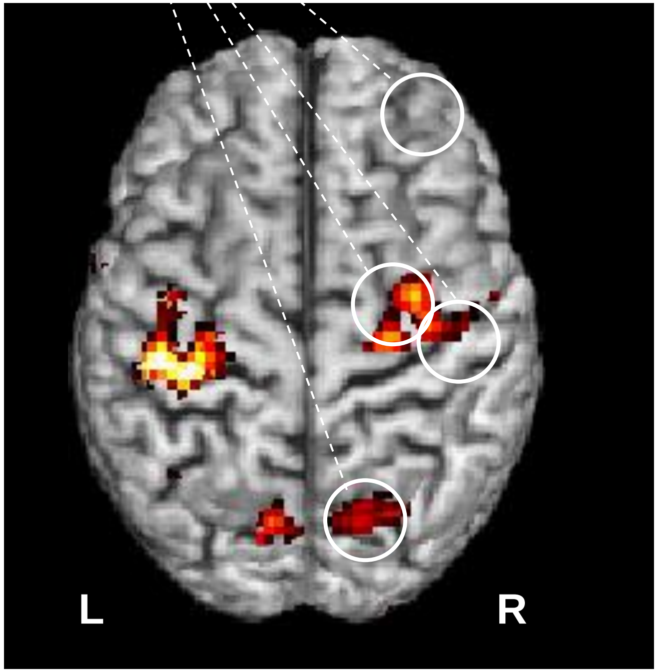
Disturbance of the ipislateral M1, PMd led to impaired reaction times

- preparation and execution of complex movement sequences?

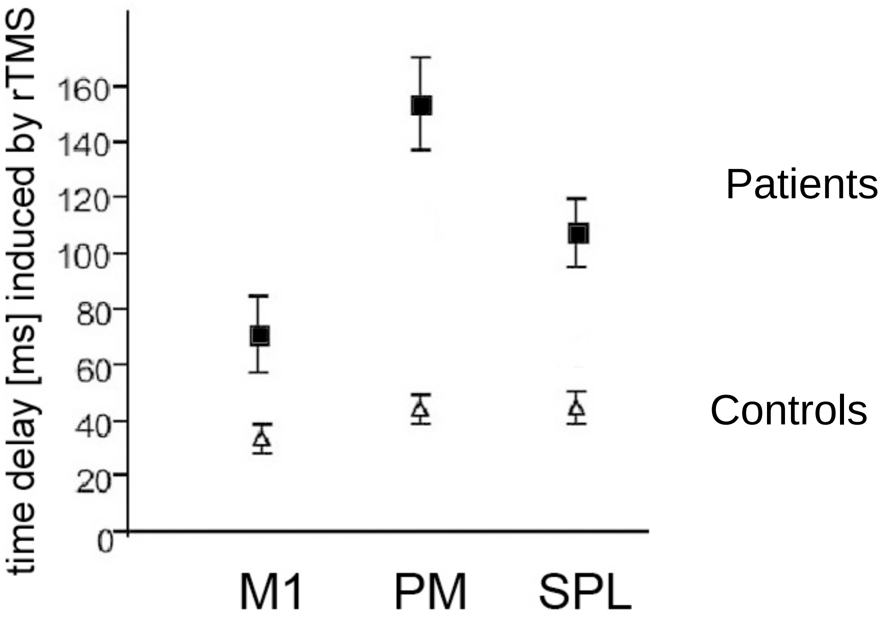




Virtual Lesion Approach



Individual Patient-Data
(fMRI during a motor fingersequence)



Functional relevance of secondary motor areas

Lotze et al J Neurosci 2006

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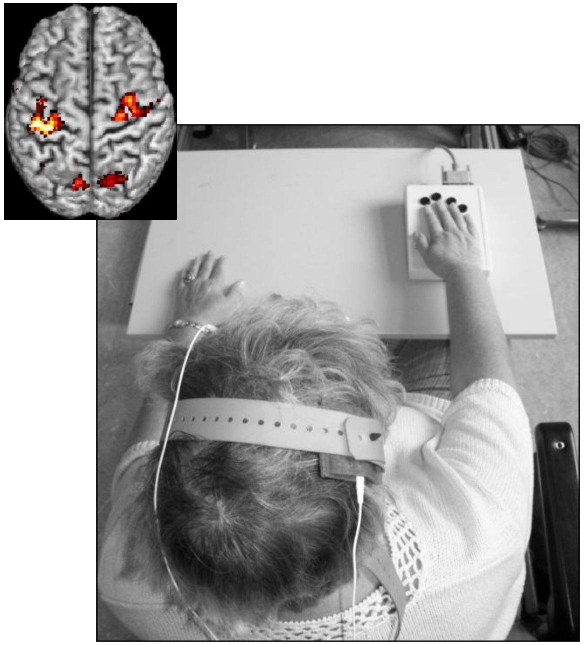
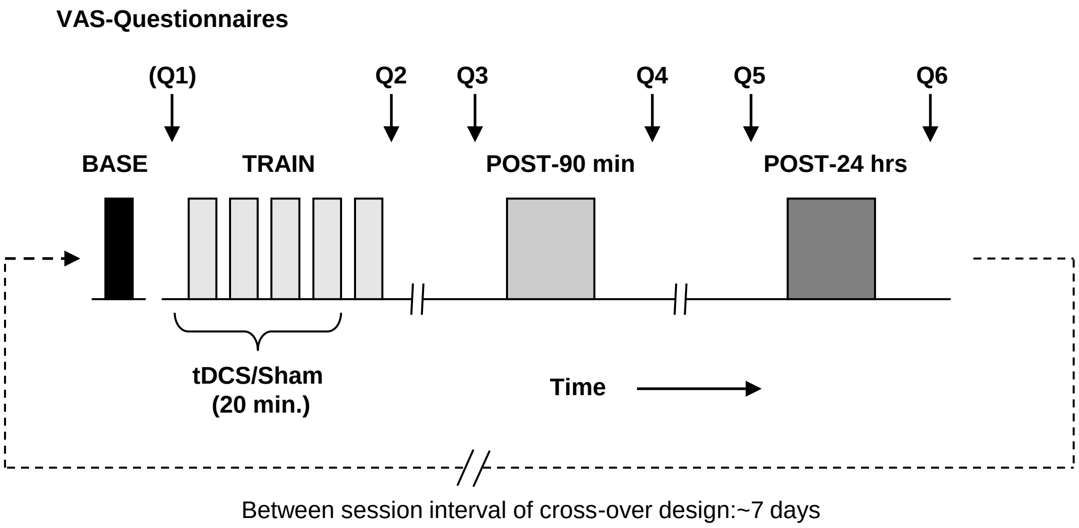
Ipsilateral motor cortex and motor learning in aged subjects





Zimerman et al., (submitted)

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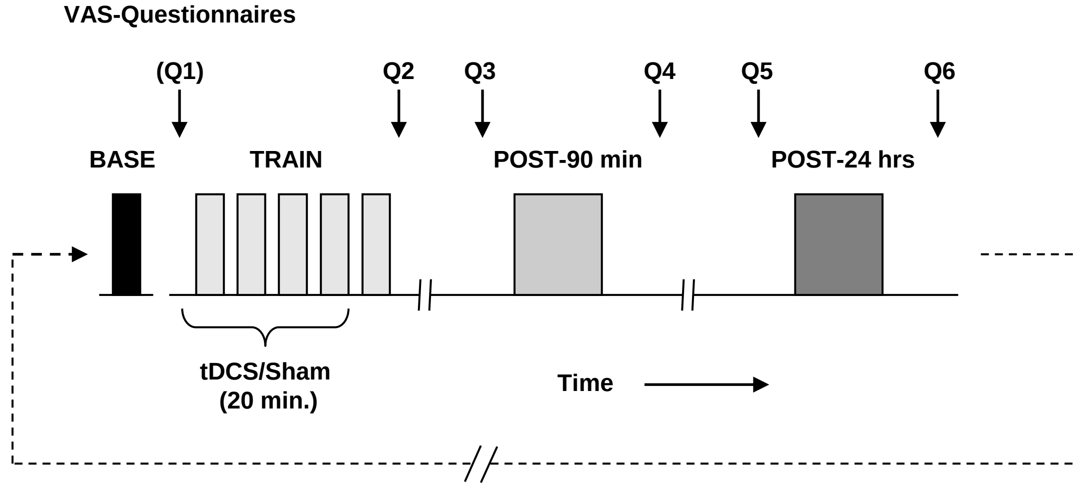
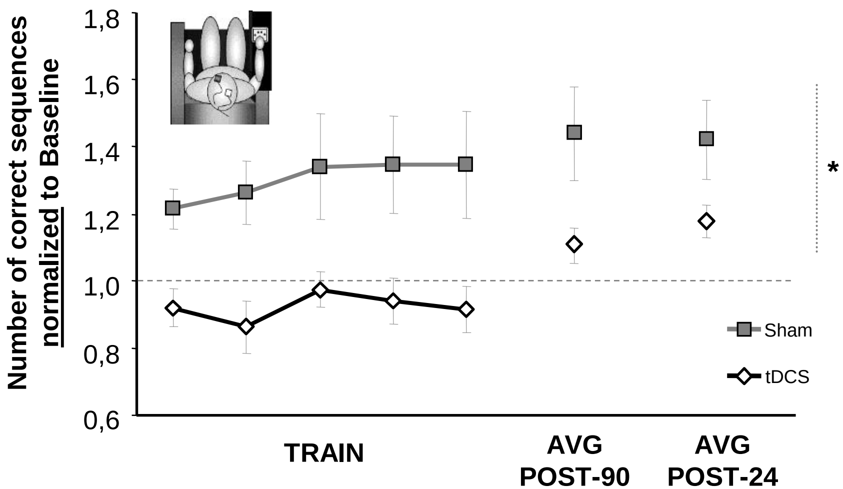
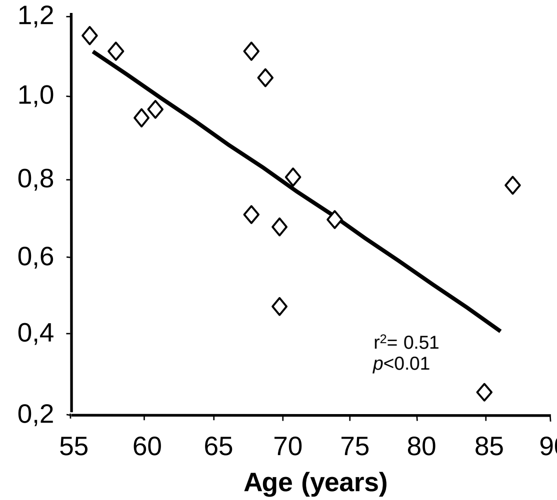
Ipsilateral motor cortex and motor learning in aged subjects



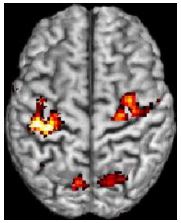
Between session interval of cross-over design:~7 days

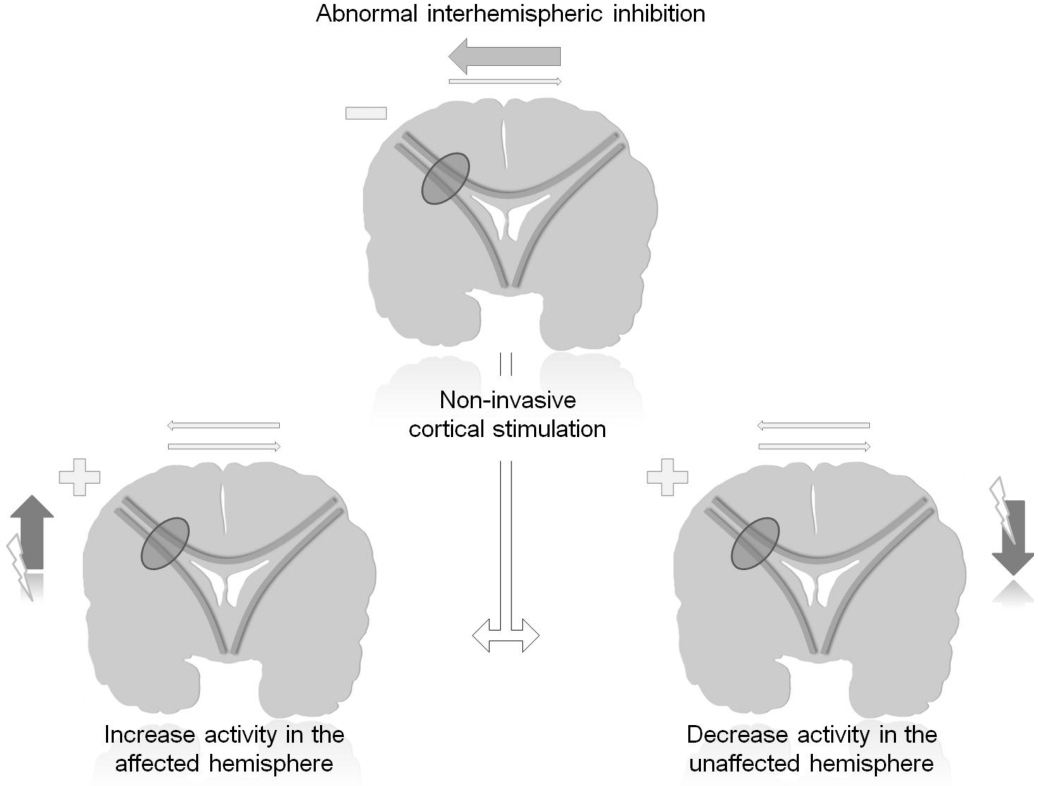


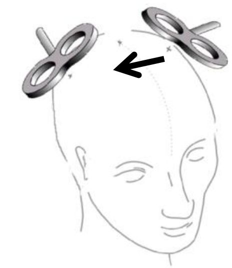


Zimerman et al., (submitted)

Ipsilateral motor cortex and motor learning in stroke patients



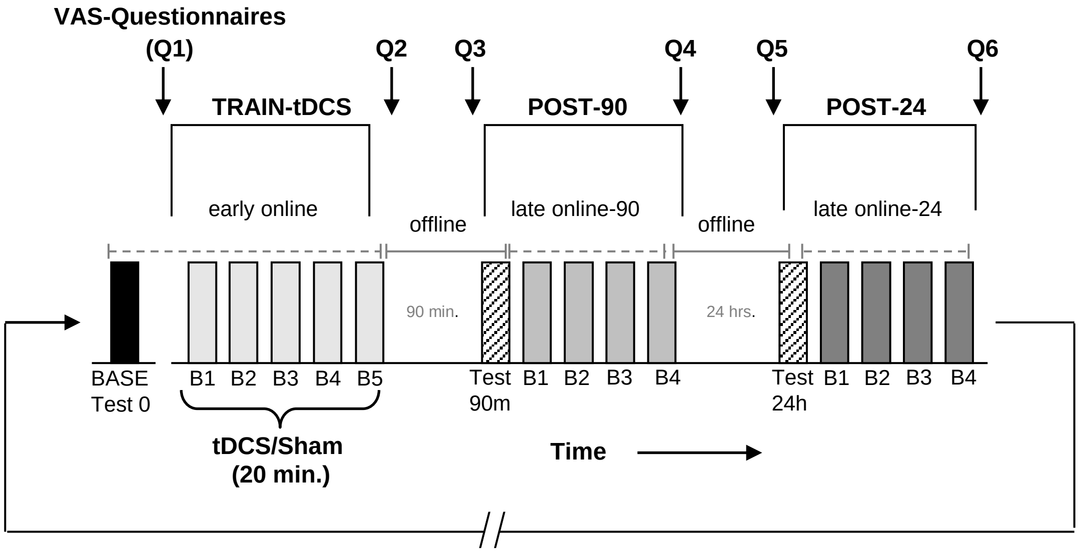




Murase *et al.* Ann Neurol 2004, Duque *et al.* NIMG 2005, Hummel & Cohen Lancet Neurol 2006, Grefkes *et al*. Ann Neurol 2008

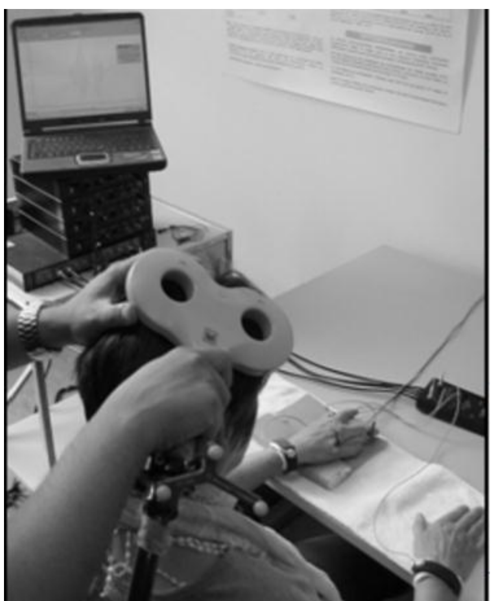
Ipsilateral motor cortex and motor learning in stroke patients

A. Behavioural experiment – Motor skill acquisition

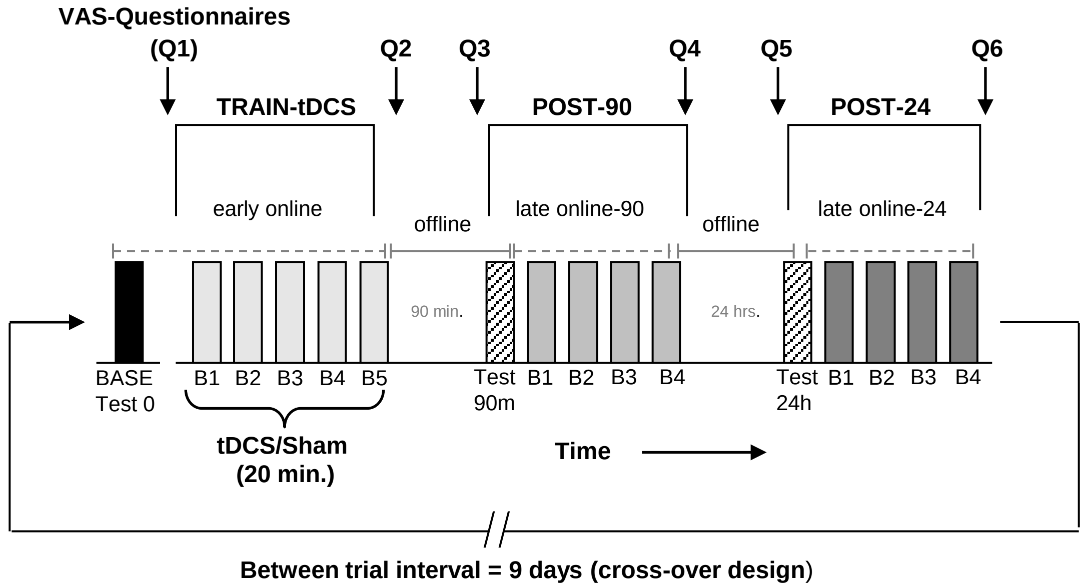


Between trial interval = 9 days (cross-over design)

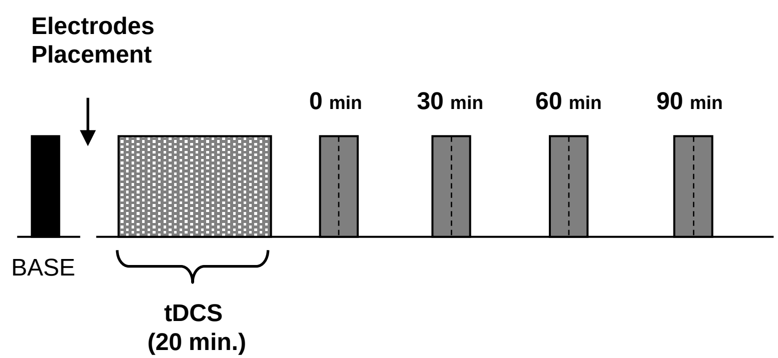
Ipsilateral motor cortex and motor learning in stroke patients



A. Behavioural experiment – Motor skill acquisition

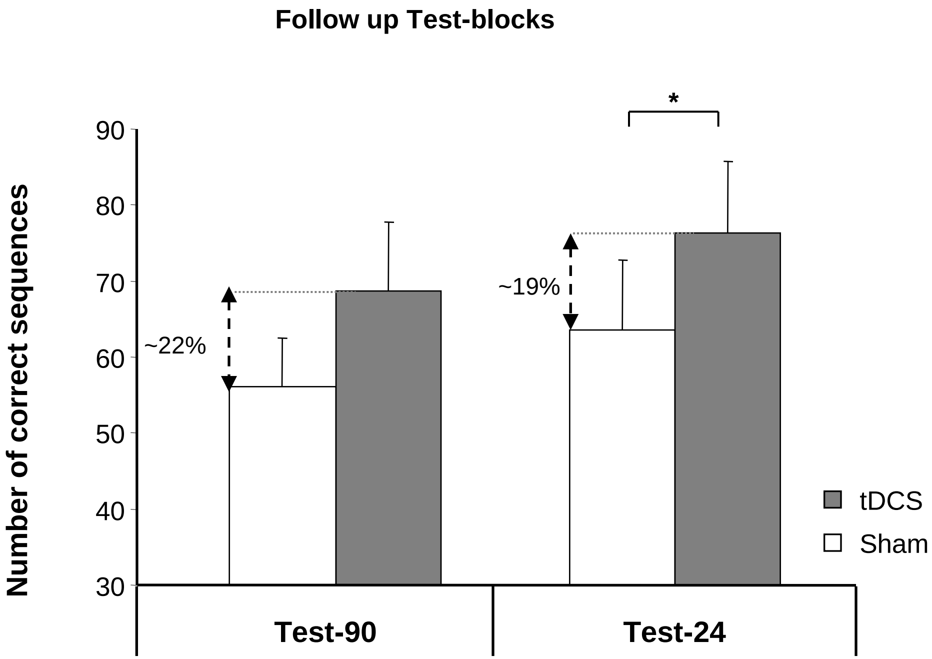


B. Neurophysiological measurements– Motor cortex excitability changes at rest



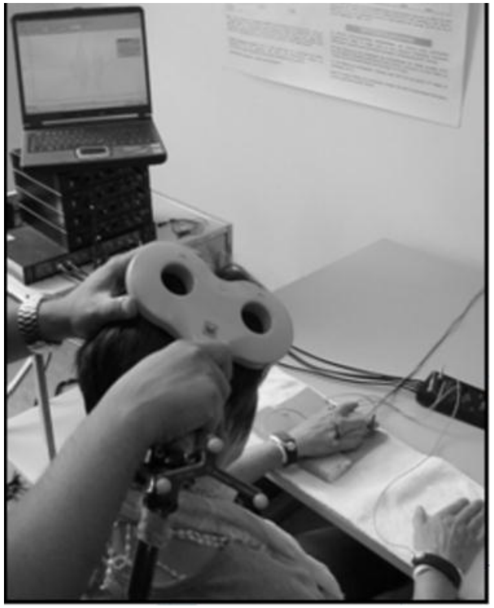
Zimerman et al., *Stroke* (2012)

Ipsilateral motor cortex and motor learning in stroke patients

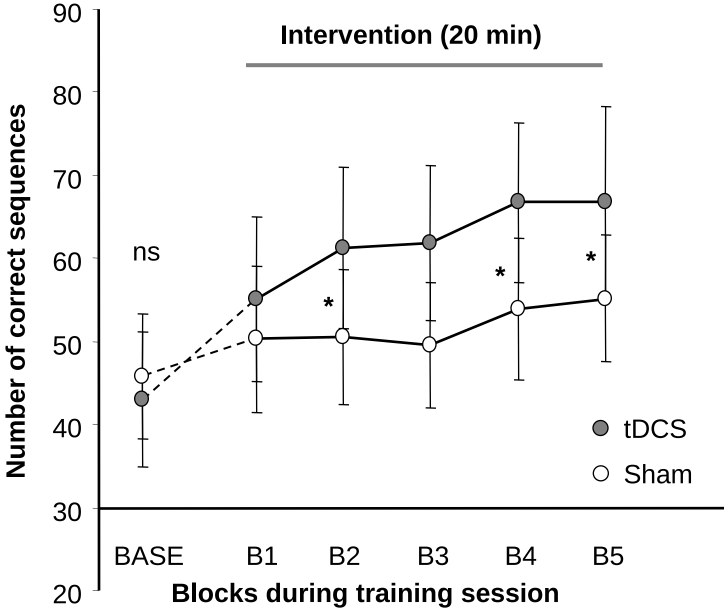


Zimerman et al., *Stroke* (2012)

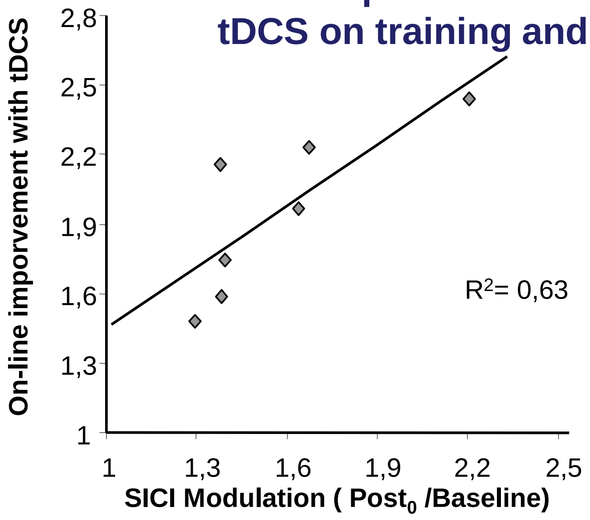
Ipsilateral motor cortex and motor learning in stroke patients



Training Session (tDCS vs. Sham)

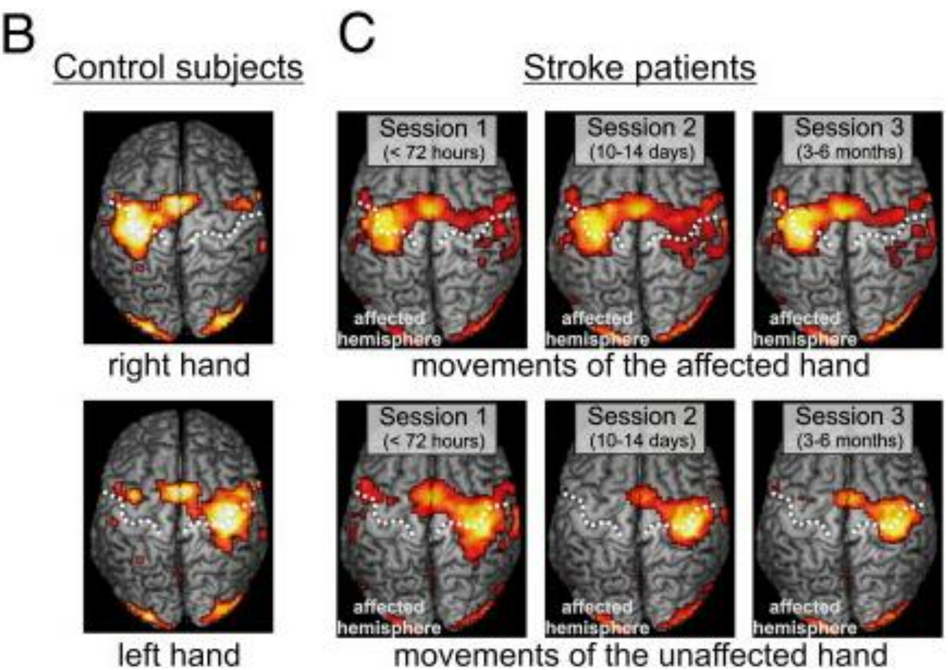


Relationship between the effects of tDCS on training and on SICI

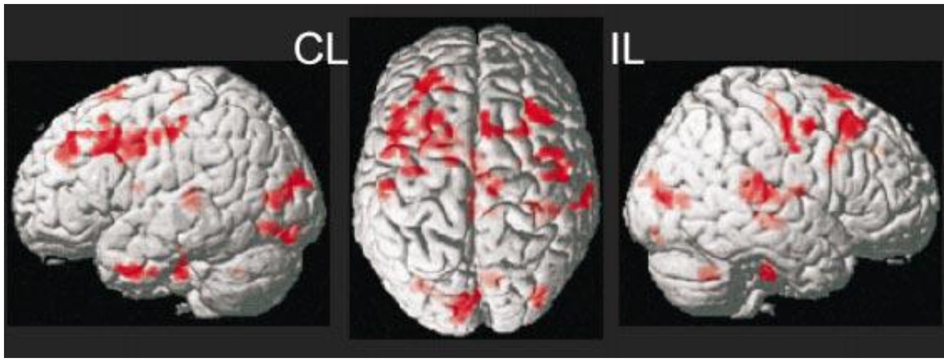


motor areas and functional recovery: functional brain imaging- longitudinal

- Activation patterns change over the time of functional regeneration (Ward et al. 2004, Grefkes et al. 2008, Calautti et al. 2005)
  - Patterns (e.g. ipsilateral to the paretic hand) differ depending on patients characteristics (Ward et al. 2004, Grefkes et al. 2008, Calautti et al. 2005)



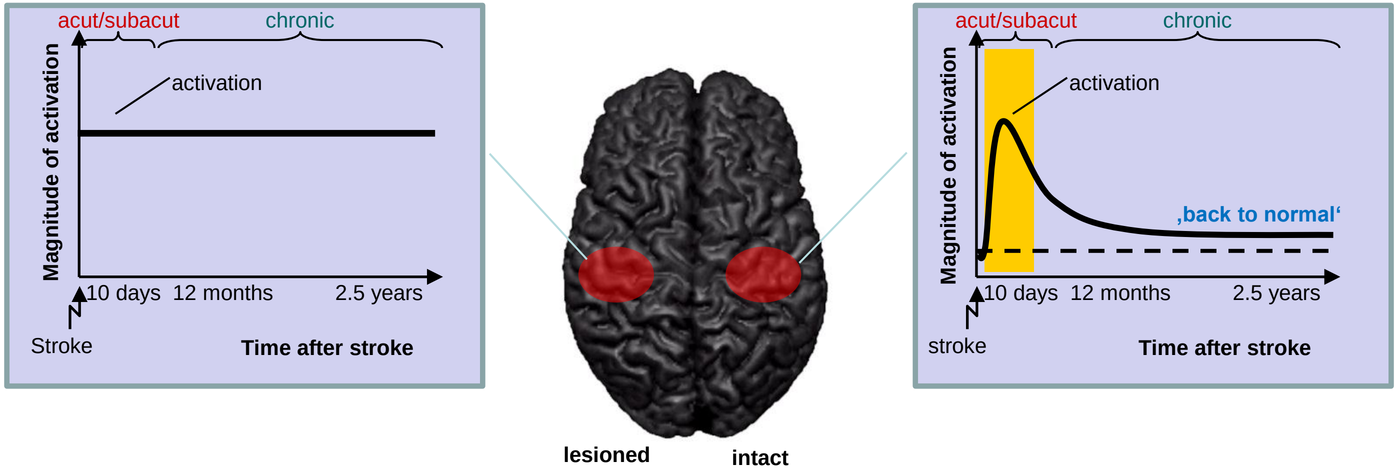
Rehme et al. 2011



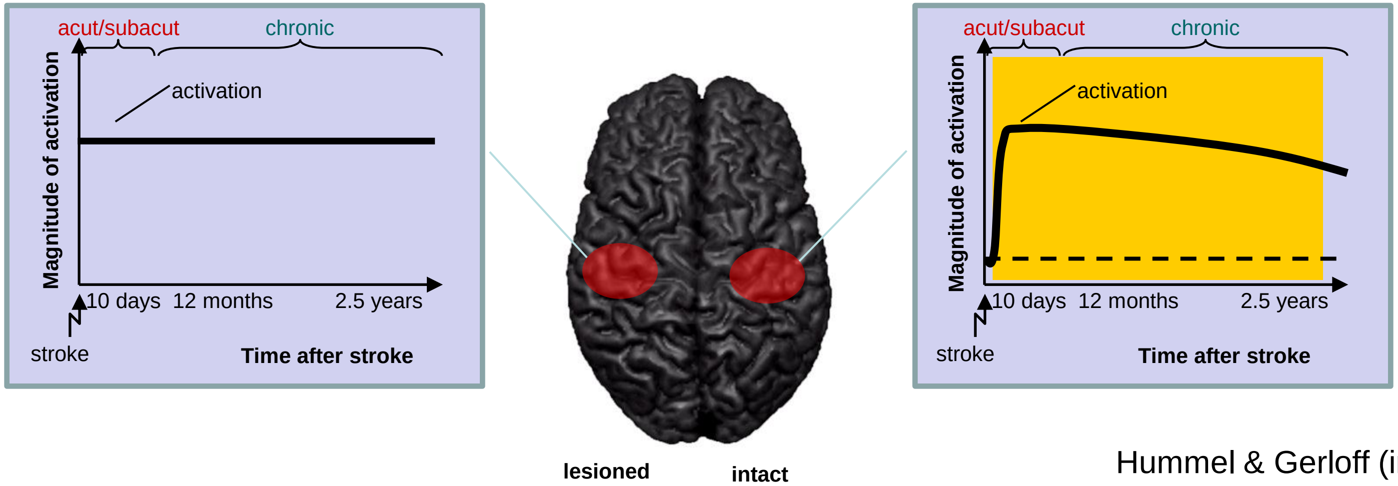
Ward et al. 2003

motor areas and functional recovery: functional brain imaging- longitudinal

Subcortical Stroke, good recovery

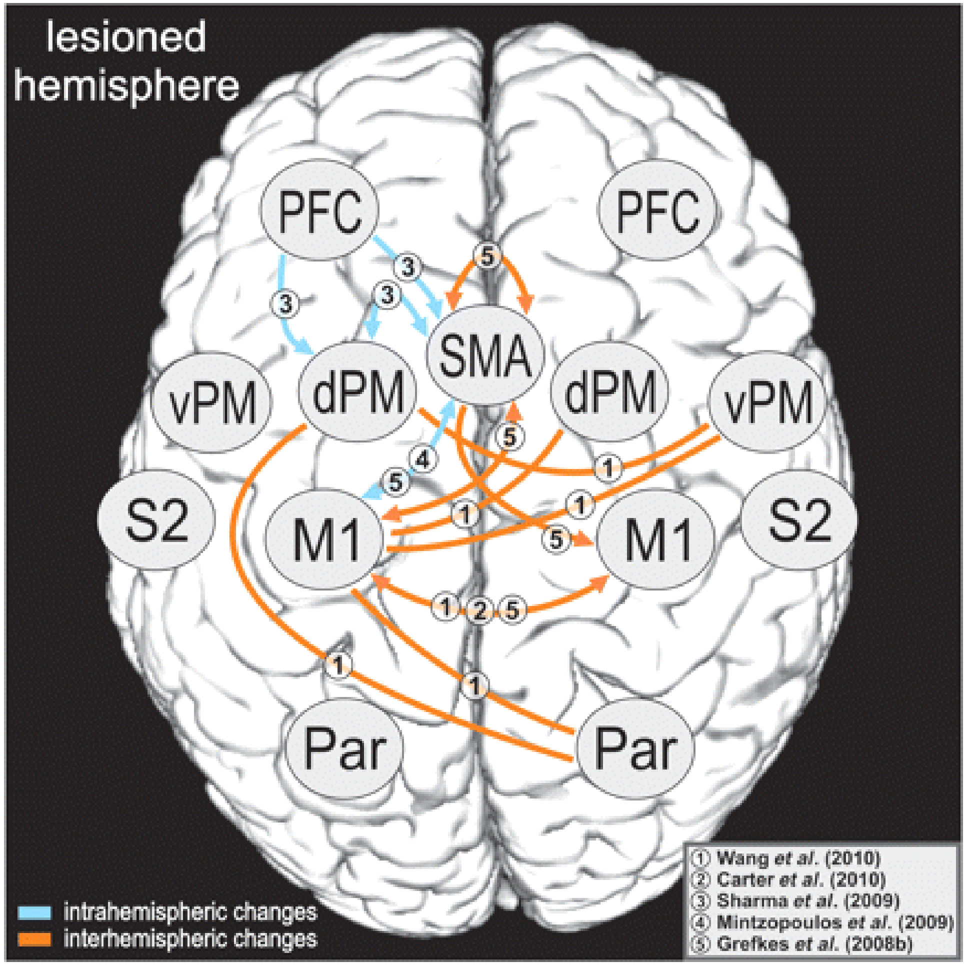


Cortical Stroke, limited recovery



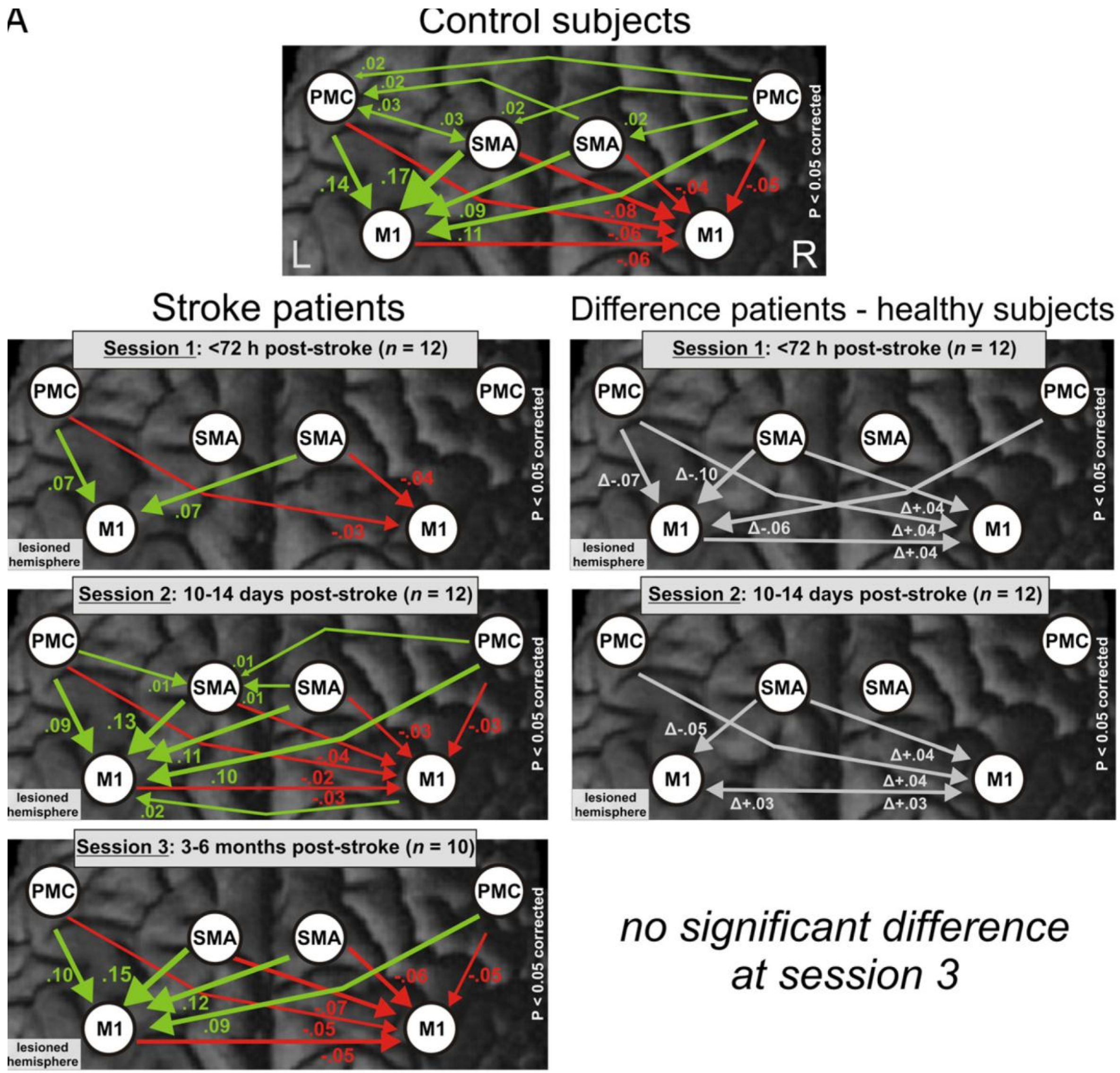
Hummel & Gerloff (in press)

motor areas and functional recovery: functional brain imaging - connectivity



Grefkes & Fink Brain 2011

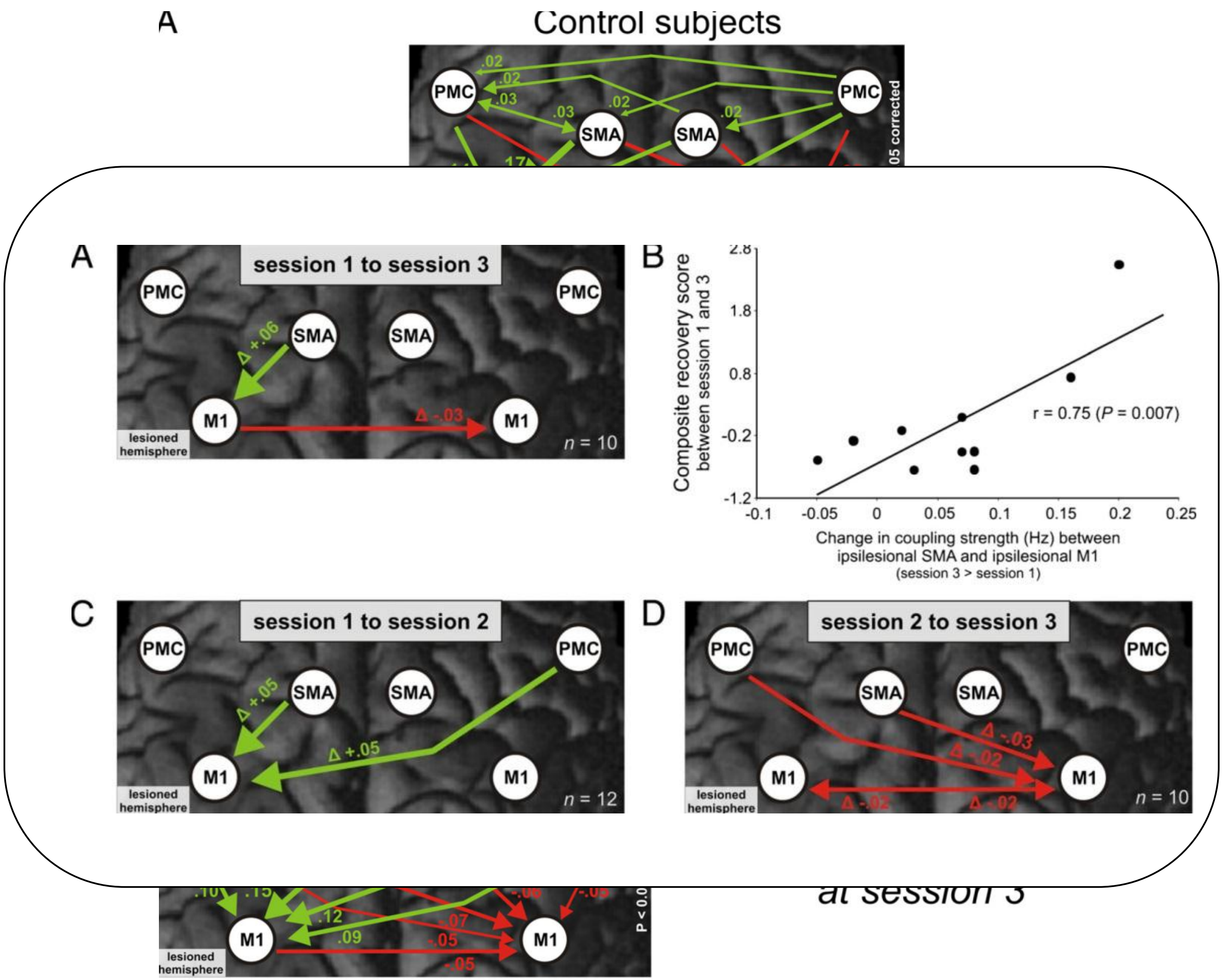
motor areas and functional recovery: functional brain imaging - connectivity



no significant difference at session 3

Rehme et al. NIMG 2011

motor areas and functional recovery: functional brain imaging - connectivity



Rehme et al. NIMG 2011

EJN fens EUROPEAN JOURNAL OF NEUROSCIENCE

European Journal of Neuroscience, Vol. 33, pp. 1256–1263, 2011 doi:10.1111/j.1460-9568.2011.07623.x

NEUROSYSTEMS

A multicentre study of motor functional connectivity changes in patients with multiple sclerosis

Paola Valsasina,[1] Maria A. Rocca,[1] Martina Absinta,[1] Maria Pia Sormani,[2] Laura Mancini,[3] Nicola De Stefano,[4] Alex Rovira,[5] Achim Gass,[6] Christian Enzinger,[7] Frederik Barkhof,[8] Christiane Wegner,[9] Paul M. Matthews[9,10] and Massimo Filippi[1]

Secondary motor areas and functional recovery: functional brain imaging - connectivity

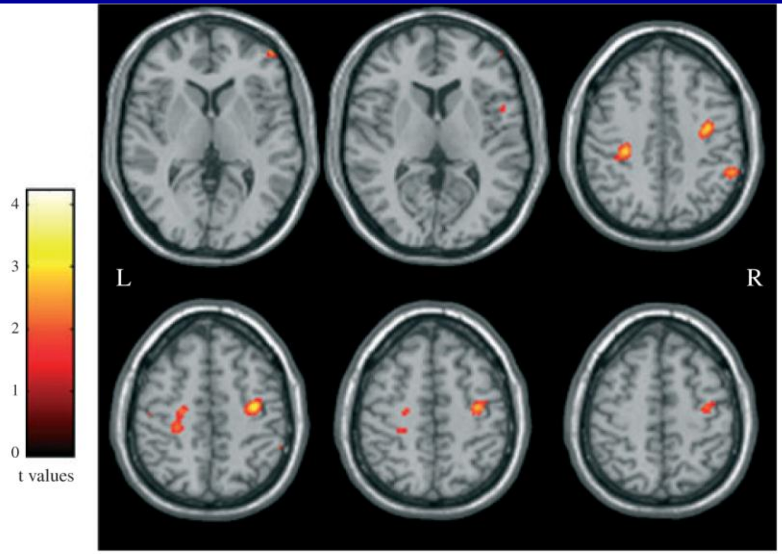


FIG. 2. Statistical parametric maps (ANOVA model, $P < 0.05$, SVC for multiple comparisons) showing brain regions with significantly increased FC with the left primary SMC in MS patients as compared with controls. Images are presented according to neurological convention L, left; R, right.

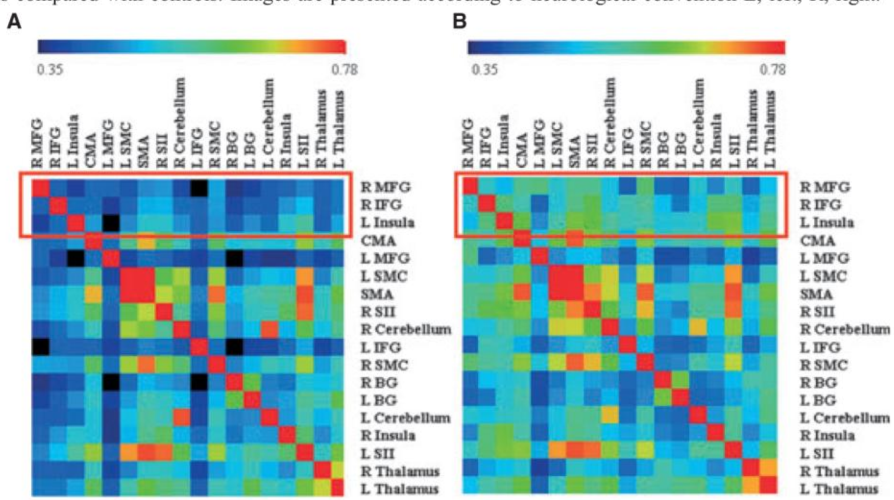
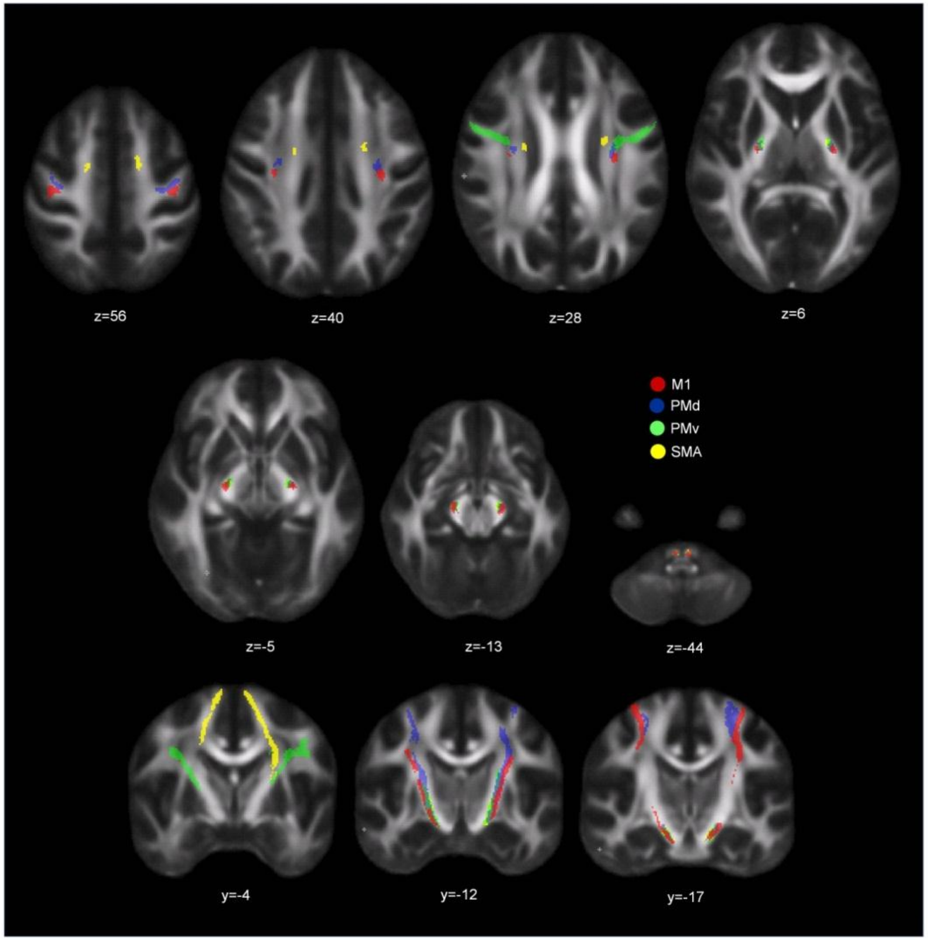


FIG. 3. Colour-coded connectivity matrices representing the degree of correlation between pairs of brain regions in control subjects (A) and MS patients (B). Note that these matrices are symmetrical, because Pearson correlation coefficients between pairs of regions are symmetrical. The brain regions shown include: left (L) and right (R) MFG; left and right IFG; left and right insula; CMA; left and right primary SMC; SMA; left and right SII; left and right cerebellum (dentate nucleus); left and right basal ganglia (BG) (putamen); and left and right thalamus. These regions have been ordered according to the number of connections that are significantly different between controls and MS patients (that is, the first region in the matrix is the one with the greatest number of increased connections in MS patients as compared with controls). Most of the connections involving the right MFG, the right IFG and the left insula show an overall increase in MS patients as compared with controls, as highlighted from the black boxes surrounding the first three lines of the left (A) and the right (B) connectivity matrices. See text for further details.

Secondary motor areas and functional recovery: structural analyses

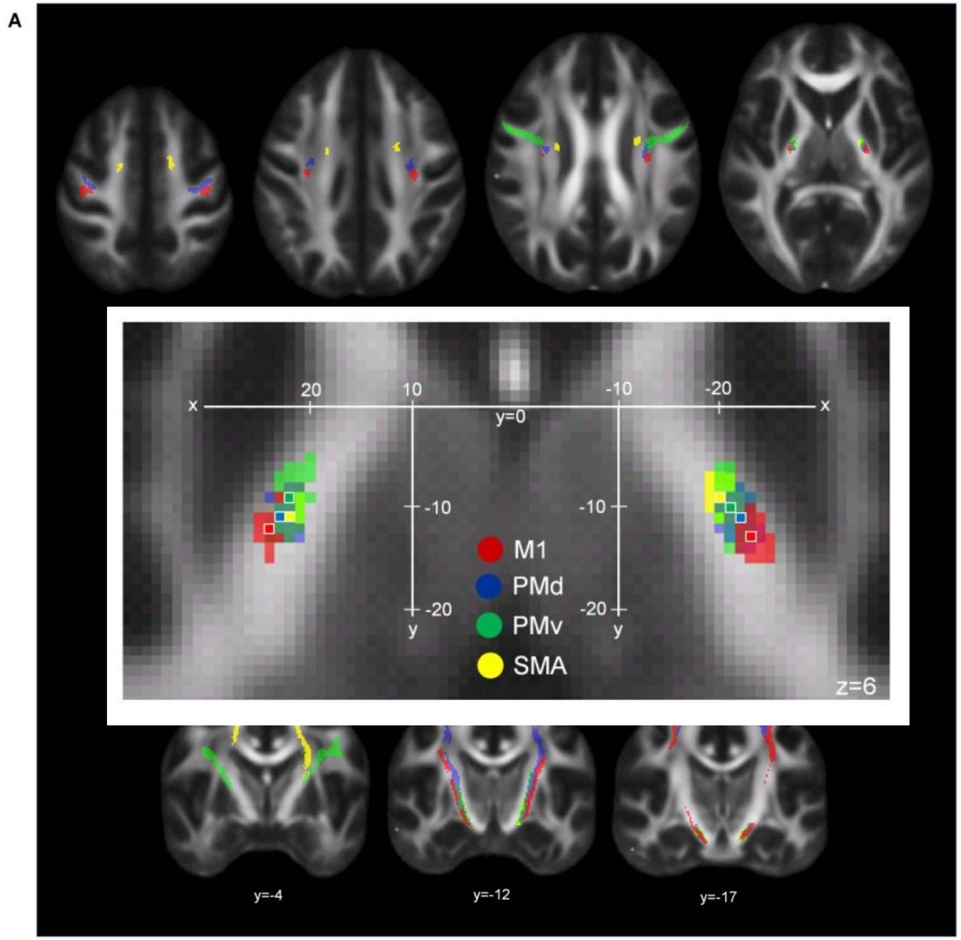
A



- Probabalistic tractography
- Cortical seeds based on fMRI
- Chronic stroke

Schulz *et al.* Stroke (in press)

Secondary motor areas and functional recovery: structural analyses



- Probabalistic tractography
- Cortical seeds based on fMRI
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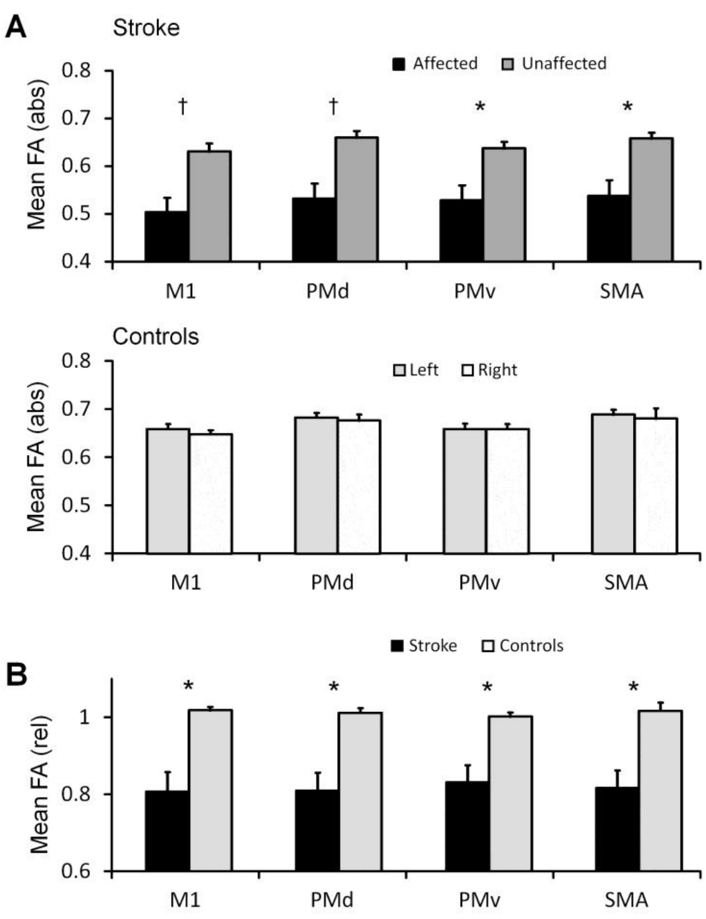
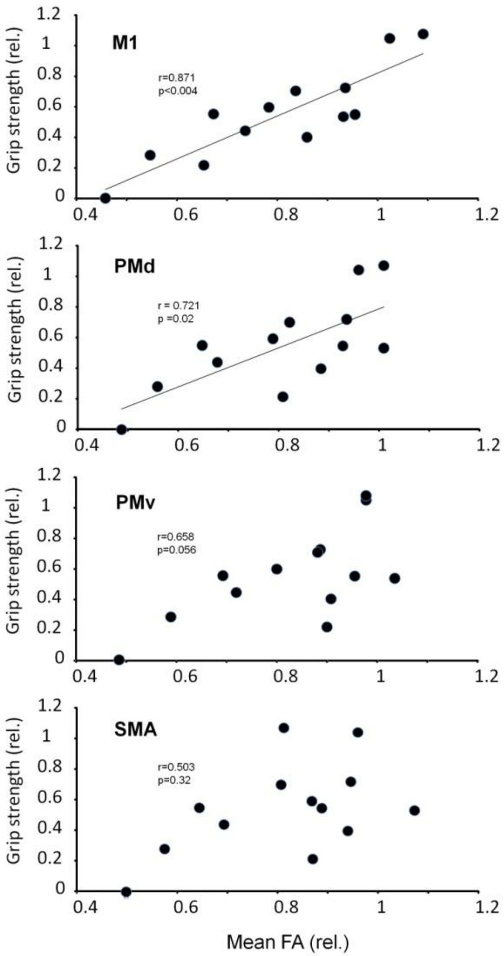
Schulz *et al*. Stroke (in press)

Motor cortex and premotor cortex tract specific FA associated with function (Riley et al. 2011, Lindenberger et al. 2010)





Schulz et al Stroke (in press)

Lancet Neurol 2010; 9: 1228–32

Published Online October 28, 2010 DOI:10.1016/S1474-4422(10)70247-7

See In Context page 1153

Prediction of recovery of motor function after stroke

Cathy Stinear

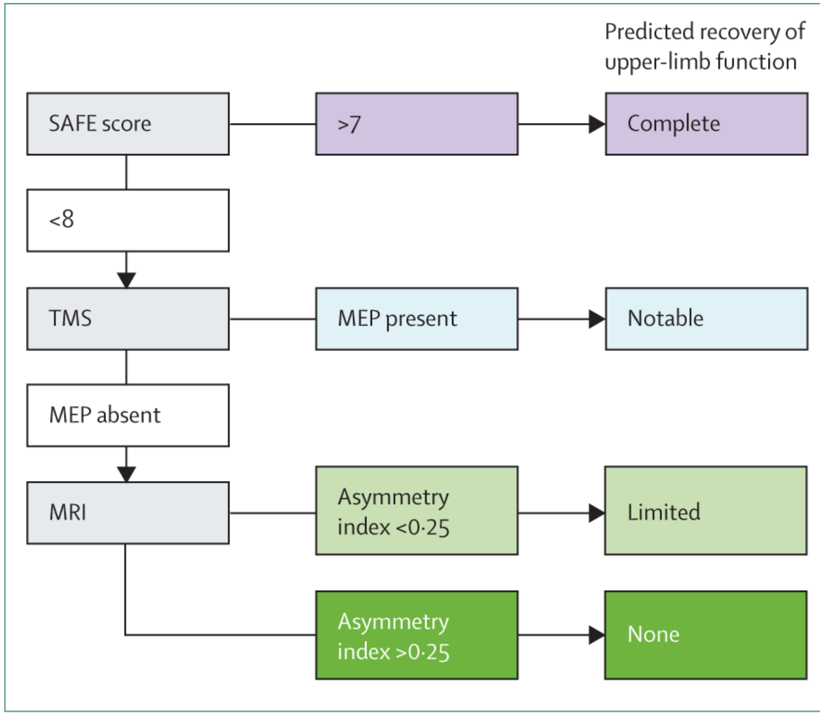


***Figure* 2: Suggested sequence of tests to predict recovery of motor function in patients with subacute stroke**

Predicted recovery of upper-limb function refers to recovery in the weeks after stroke. Although this particular algorithm requires validation, it illustrates a potentially efficient progression from simple to more complex predictive measures, which might be a useful direction for future research. SAFE=sum of the shoulder abduction and finger extension Medical Research Council muscle grades 72 h after stroke. TMS=transcranial magnetic stimulation. MEP=motor evoked potentials in affected upper limb. Asymmetry index=asymmetry index of fractional anisotropy in the posterior limbs of the internal capsules measured with diffusion-weighted MRI.[15]

Summary

- Factors like *lesion location*, *size*, *structural background and integrity*, *time* after ictal event and others influence the course of impairment and functional regeneration
- Approaches of systems neuroscience provide the option to evaluate adaptive, maladaptive plastic changes after brain lesions
- Approaches of systems neuroscience might provide the option to predict functional reorganization, outcome and direct an individual patient-targeted therapy.
- Approaches of systems neuroscience might provide a platform to evaluate innovative novel treatment strategies (pharmacological, brain stimulation etc,)

Vielen Dank für ihre Aufmerksamkeit!

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Max Wessel
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Pablo Celnik

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Ralf Veit
Andrea Caria
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