Non-invasive transcranial brain stimulation (NTBS) in Cognitive Neuroscience: A "connectivity" account

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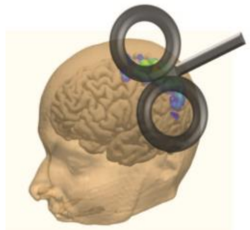
Introduction

Non-invasive transcranial brain stimulation ⇔ Brain Connectivity

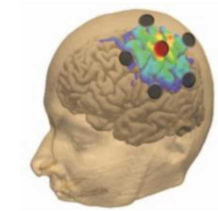
Non-invasive transcranial brain stimulation (NTBS)

Transcranial magnetic stimulation



- Single-pulse, burst, rTMS
- High-intensity TMS
- Inductive electrical stimulation
  Electrical=>Magnetic=>Electrical
- Tissue conductivity:
  Skull is no problem, brain tissue and CSF are a problem.
- Suprathreshold intensity
  (action potential=>synaptic)

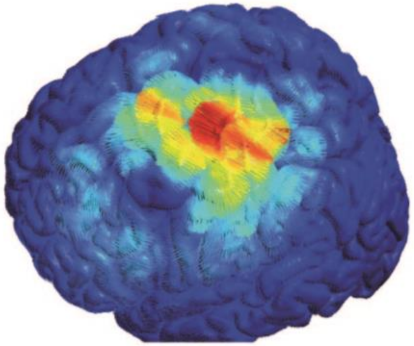
Transcranial electrical stimulation



- Constant (DC), Alternating (AC)
- Low-intensity TES
- Electrical stimulation all the way to (and through) the brain !
- Tissue conductivity:
  Skull is THE problem, brain tissue and CSF are a problem.
- Subthreshold intensity
  (membrane potential=>synaptic)

Which spots are we stimulating ?

Figure-8 TMS and monopolar TES are reasonably focal.



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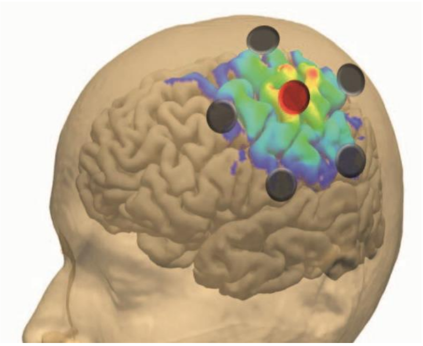

TMS with round or cap coil is non-focal but superficial.

Bipolar TES is non-focal and NOT suited for anatomical localization (Distortions by holes in the skull, skull thickness, both sites are stimulated, current orientation in tissue: tangential vs vertical).

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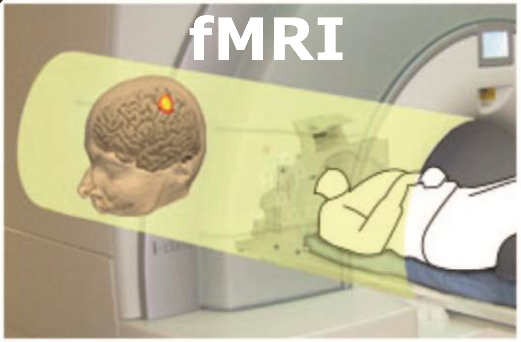
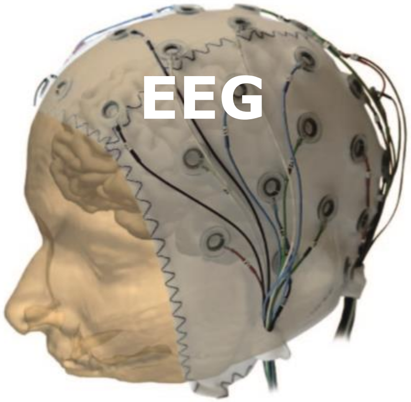
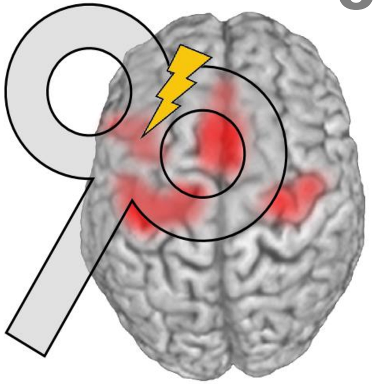
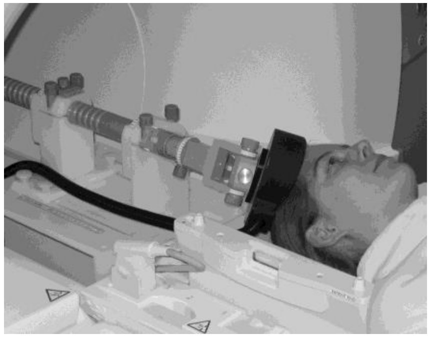
Mapping the neural netwerk effects of NTBS:
Online versus offline approaches



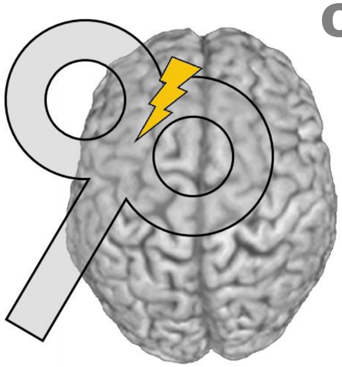


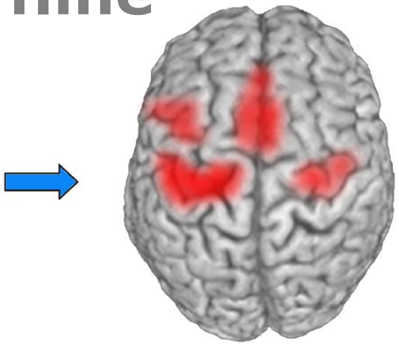
online



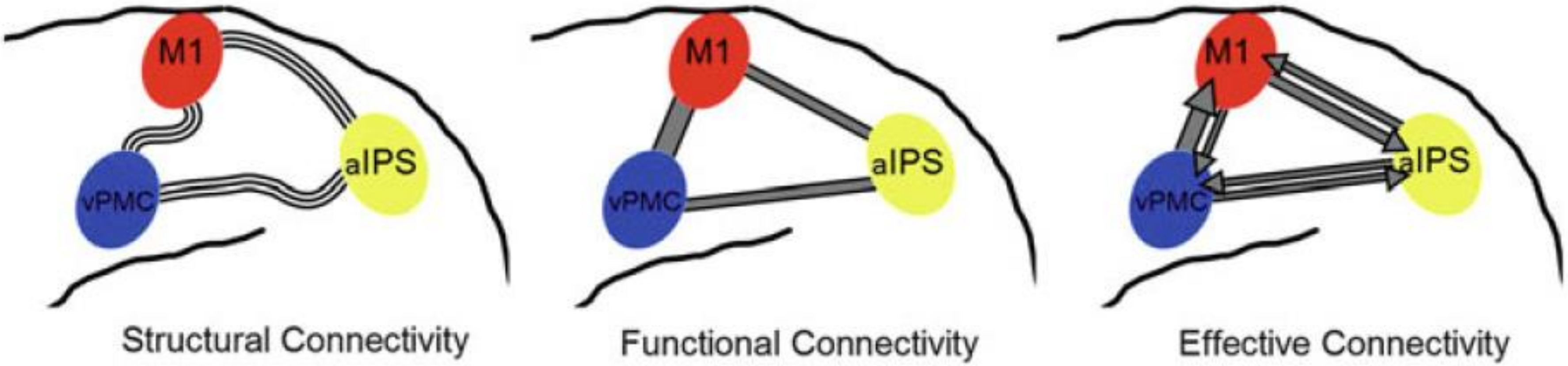


offline





Effective connectivity describes the influence of one brain area over another area



Structural Connectivity	Functional Connectivity	Effective Connectivity
Anatomical connections between brain areas forming a network.	Temporo-spatial covariance between brain areas forming a network.	The influence that brain areas exert over another in a given network.
Setting the frame for functional interactions.	No claims regarding directionality (undirected edges).	Claiming directionality, causality, and the flow of information.

A simple grasping network: vPMC = ventral premotor cortex
M1 = primary motor hand area, aIPS = anterior intraparietal sulcus

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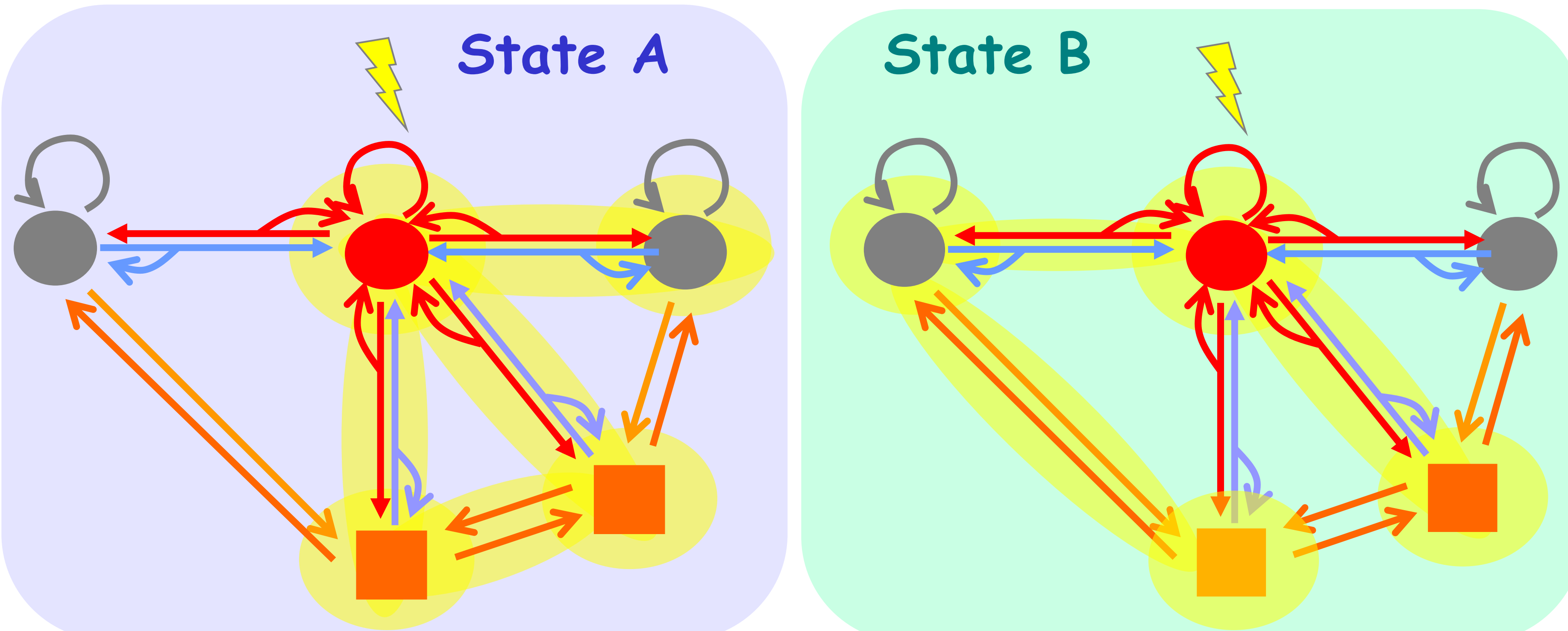
TMS induces state-dependent network effects

x "state" = "shape"

- Stimulated cortex
- Connected cortical area
- Connected subcortical area

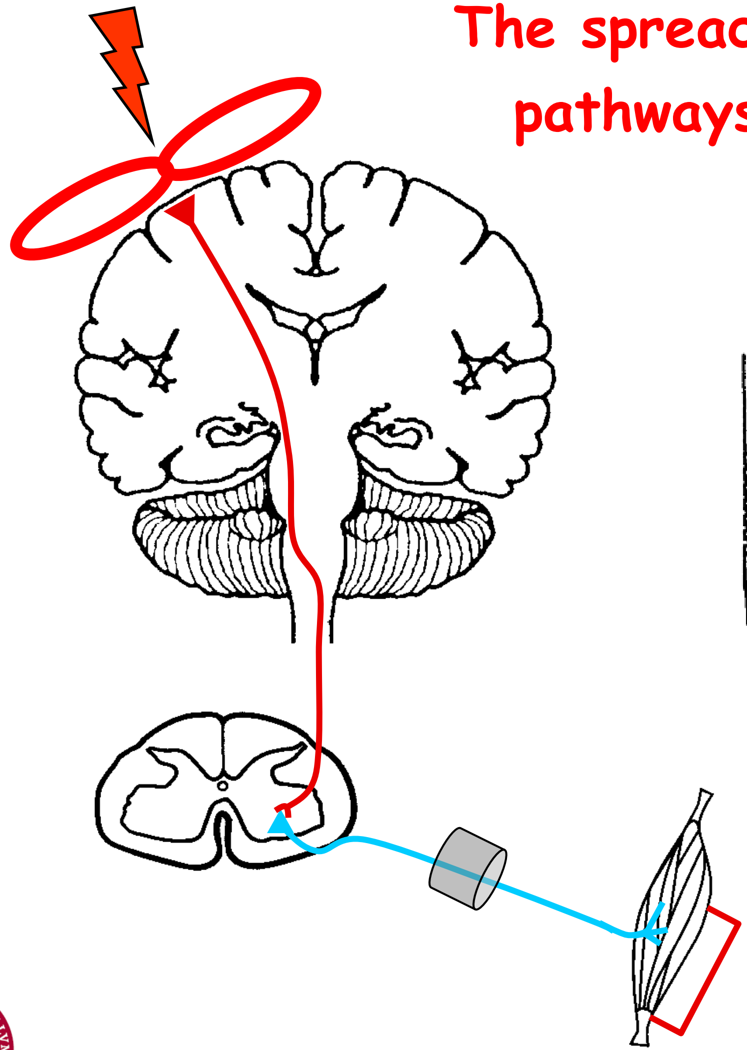


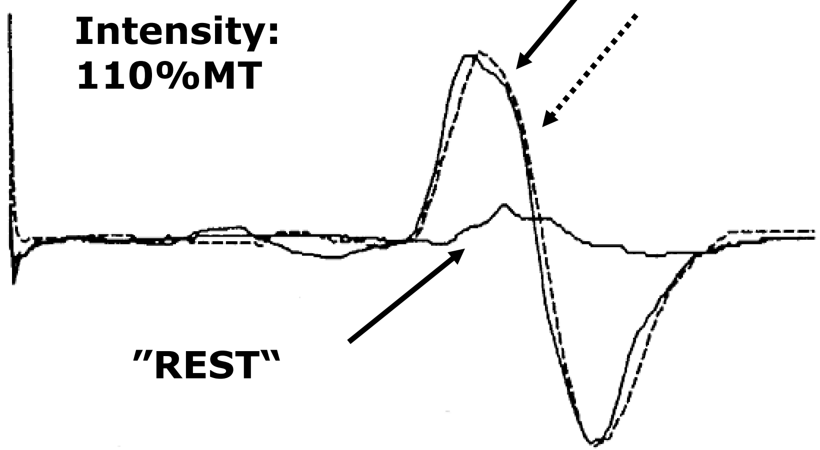
Spread of excitation to connected sites in the brain:

Orthodromic and antidromic excitation

TMS can be used to trace effective cortico-to-motor connectivity

The spread of action potentials along neural pathways depends on the "neural state"





Neural context
"State dependency"

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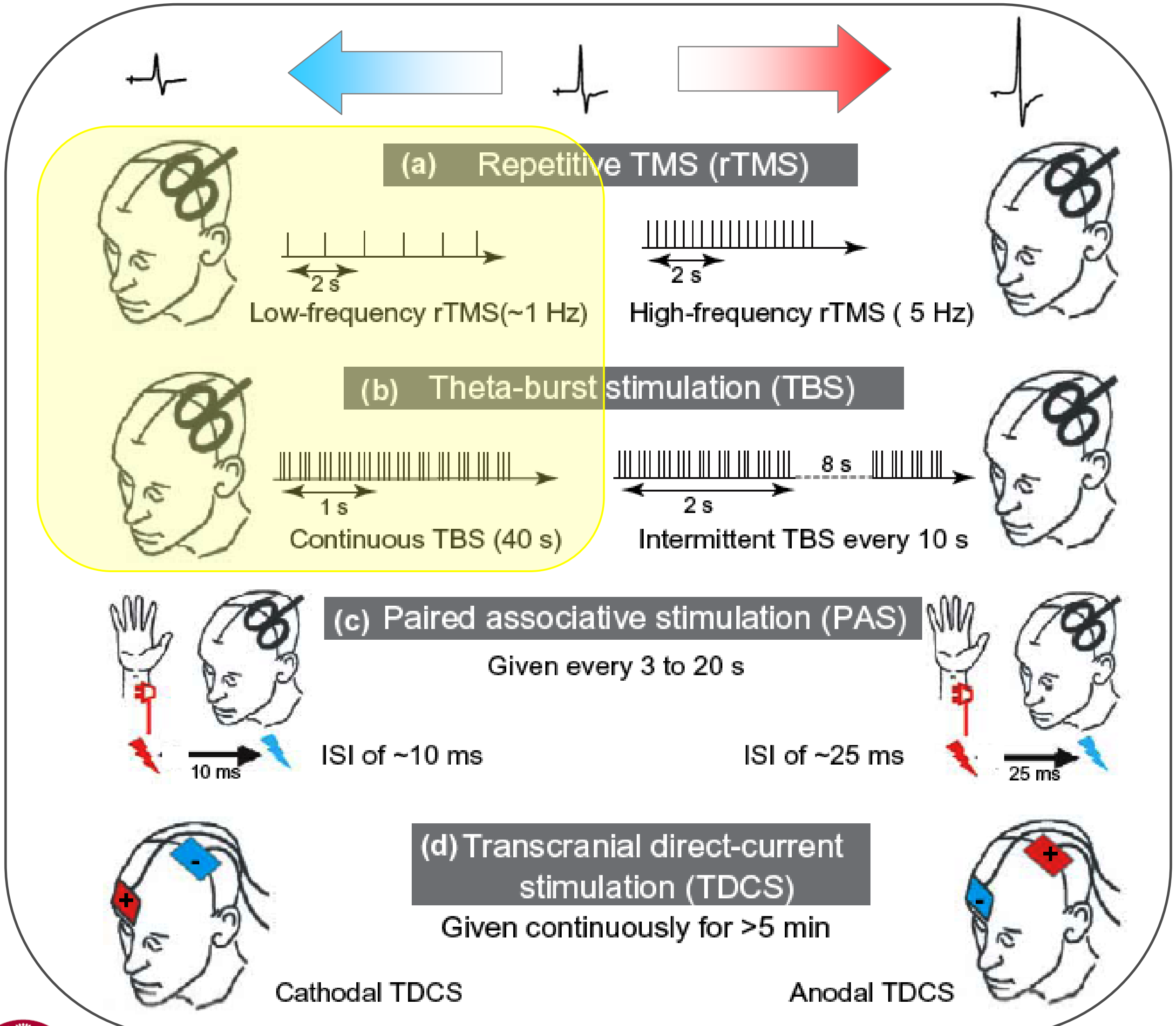
Inducing lasting bidirectional changes in corticospinal excitability with rTMS



Quartarone, Siebner, Rothwell Trends Neurosci 2006

More recent protocols:

- Quadripulse TMS
- High-frequency PAS
- Cortico-cortical PAS
- Sinusoidal TDCS
- TACS
- Random noise stimulation

Ziemann et al. Brain Stimulation 2008

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Repeated-measure within-subject design including a real and sham rTMS session

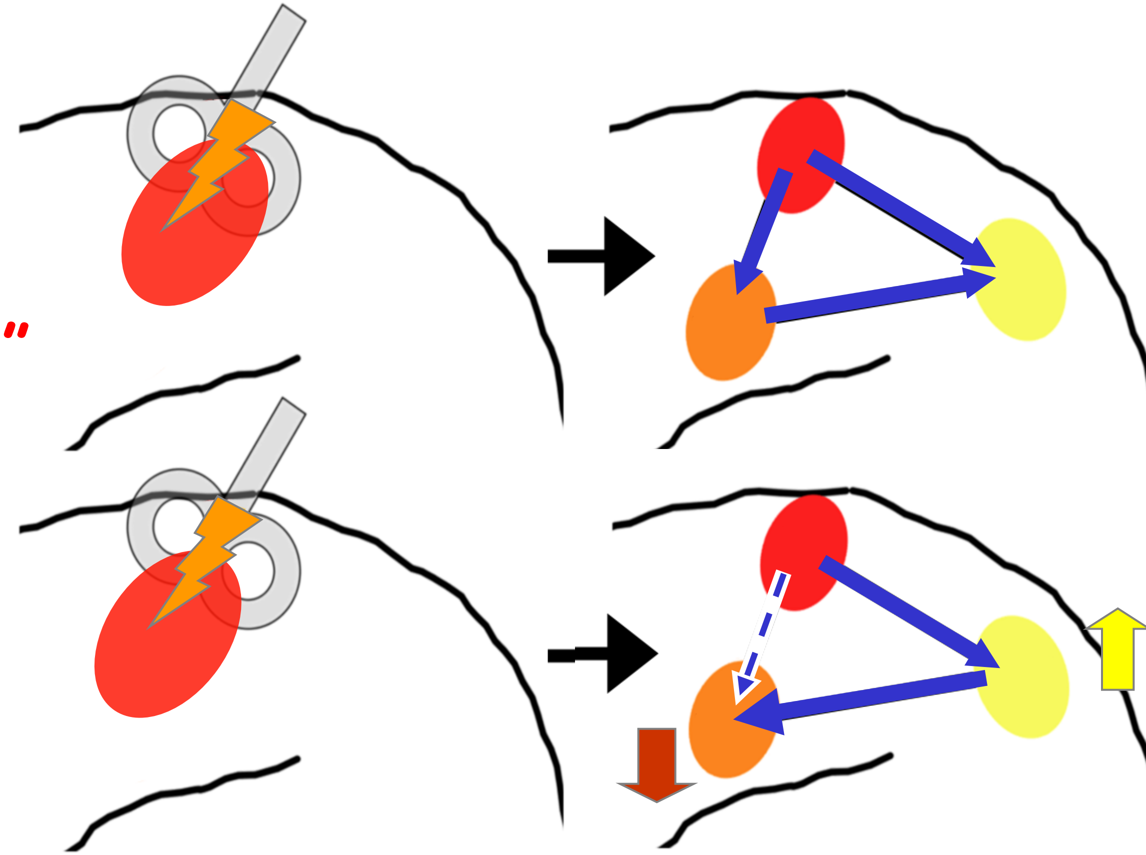
Offline TMS - fMRI: condition and map approach

TMS protocol 1

"control protocol"

TMS protocol 2

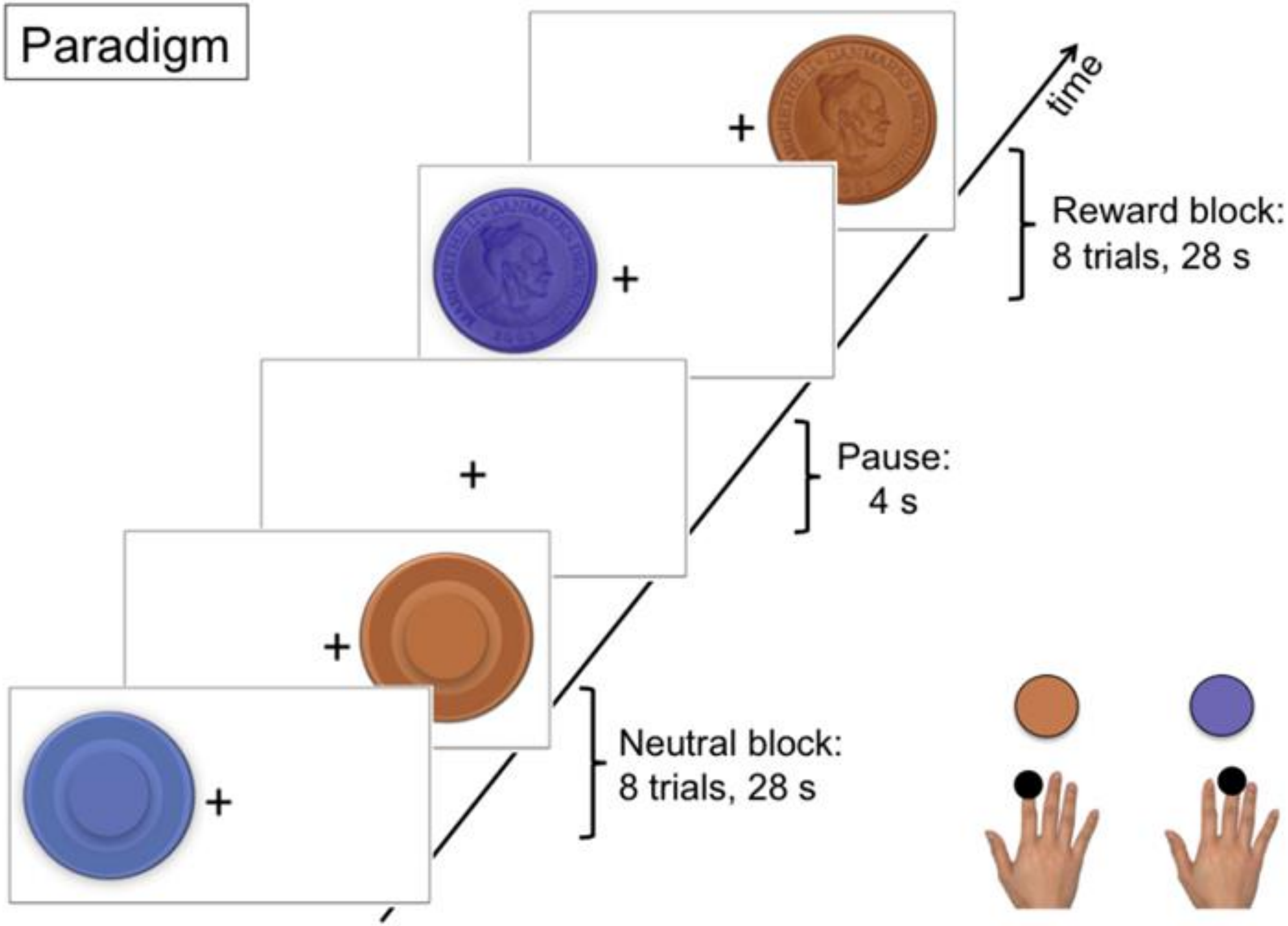
"real protocol"



Study 1: Offline TMS of pre-SMA
Improving control over impulsive response tendencies

Collaboration: K. Richard Ridderinkhof
Cognitive Science Center Amsterdam, The Netherlands

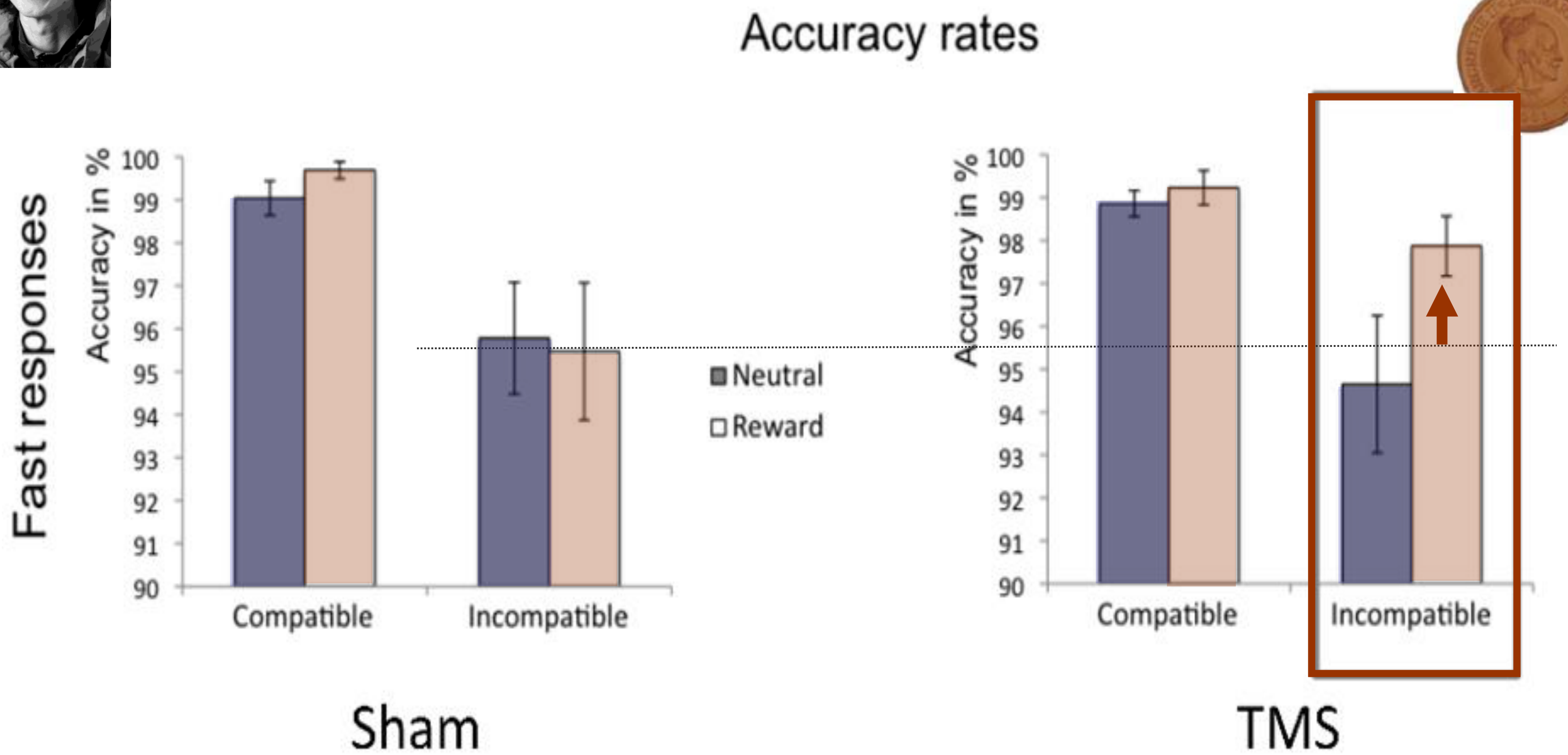
Dealing with response interferences in a context of high motivation (potential reward)



Herz et at. J Neurosci 2014

Solving a response conflict: Context-dependent effect of 1Hz rTMS over pre-SMA on accuracy

Impairing pre-SMA function by noninvasive brain stimulation improved control over impulsive response tendencies



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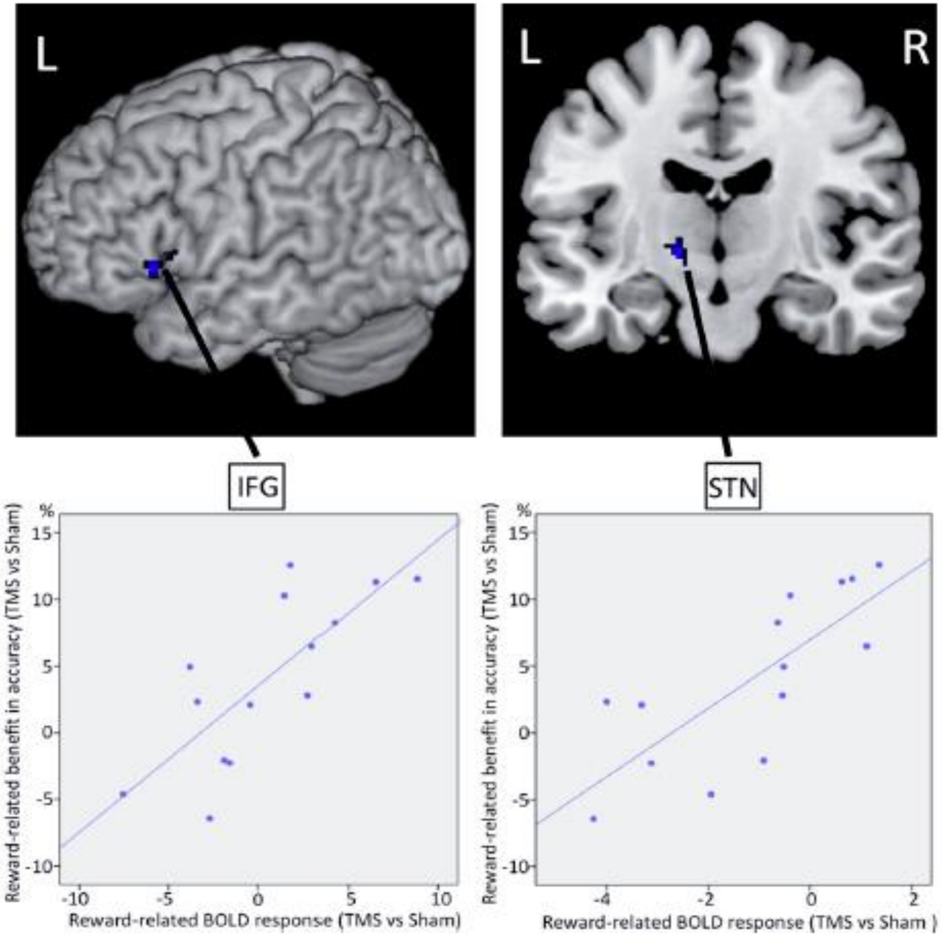
Change in accuracy ⇔ Change in activity

Activity in left IFG & left STN was predicted by individual differences in the rTMS-dependent reward related benefit in accuracy.

The higher the benefit in motor control, the stronger both areas were activated.

=> DCM analysis of effective connectivity



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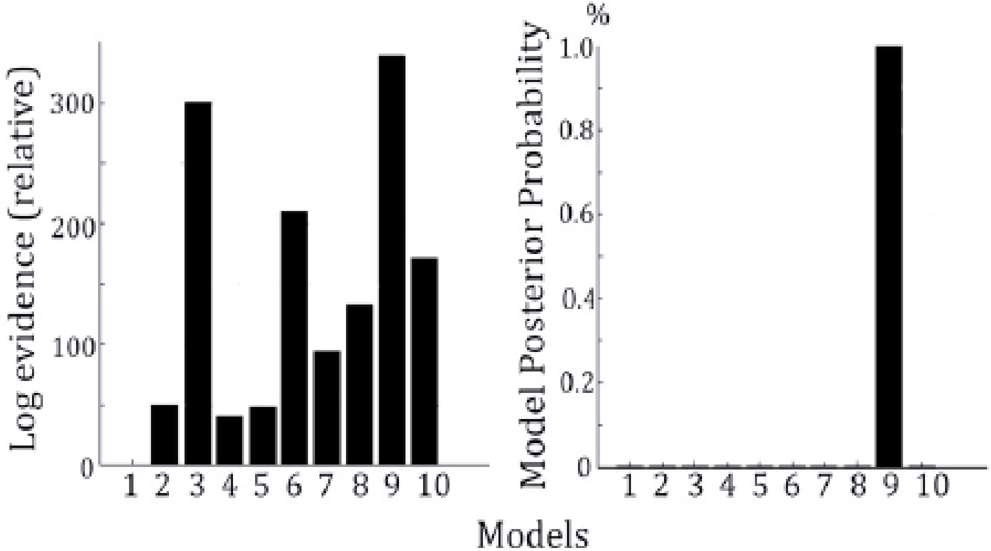
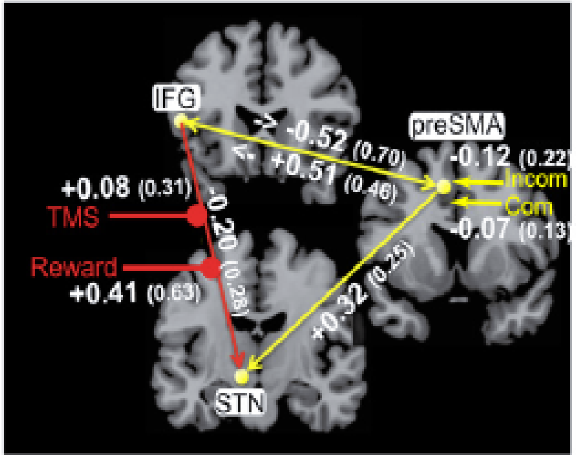
Bayesian model selection (BMS) focusing on a left-hemispheric per-SMA, IFG and STN network

BMS yielded strong evidence for the model postulating that both Prospect-of-reward and TMS modulated the connection from IFG to STN (model 9).





The models differed with regards to the modulated connection (pre-SMA-STN, IFG—STN, or both) and the experimental modulator (Prospect-of-reward, TMS, or both).
We also created a null model (M-1) with no connections being modulated.

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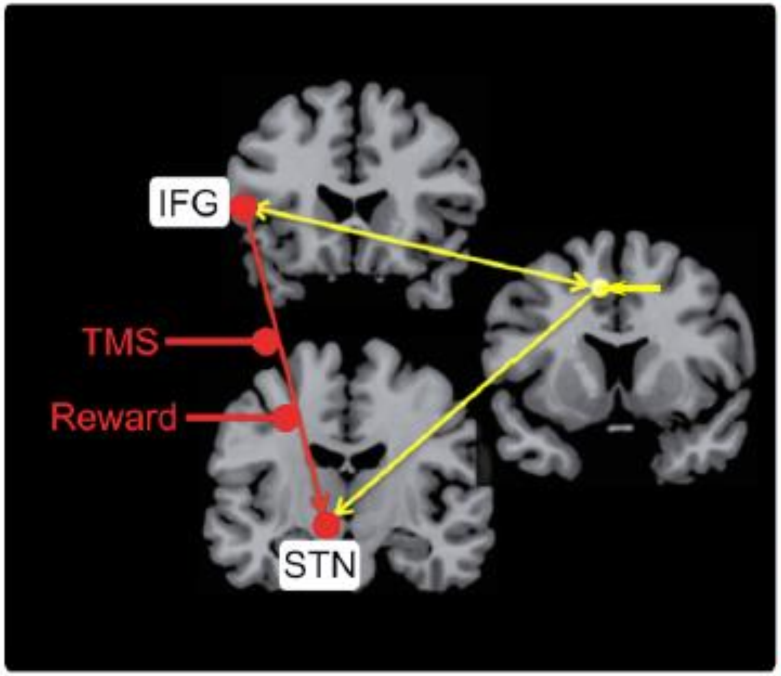
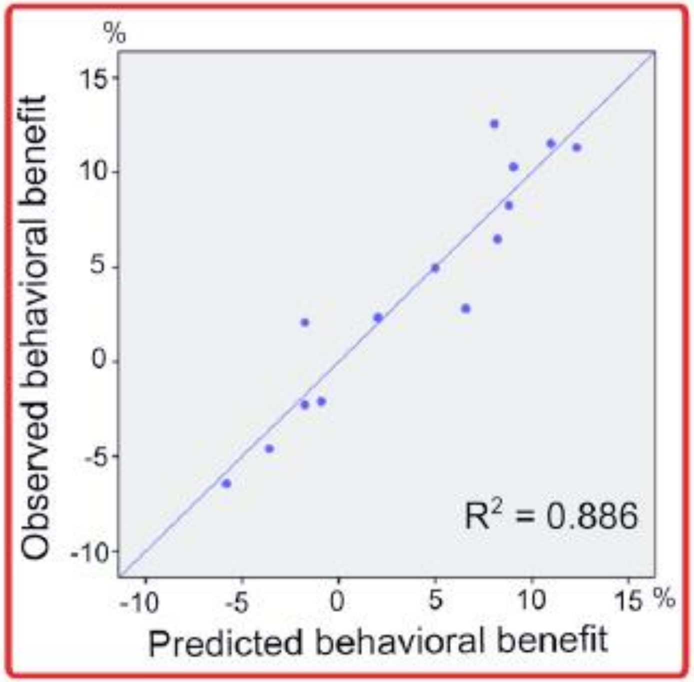
Hierarchical multiple linear regression analysis:

Change in accuracy ⇔ Change in activity & connectivity

The regression model comprising modulation of activity and connectivity of the IFG-STN pathway predicted88% variance of the behavioral benefit (p=0.001).





Entering connectivity values from the DCM analysis reflecting modulation of coupling by Prospect-of-reward and TMS (B-matrix) significantly improved model predictions of the behavioral benefit (reward-related benefit in accuracy after rTMS) with an R 2-change of 0.124 (p = 0.036).
The independent variables (predictors) of the regression model are marked in red.

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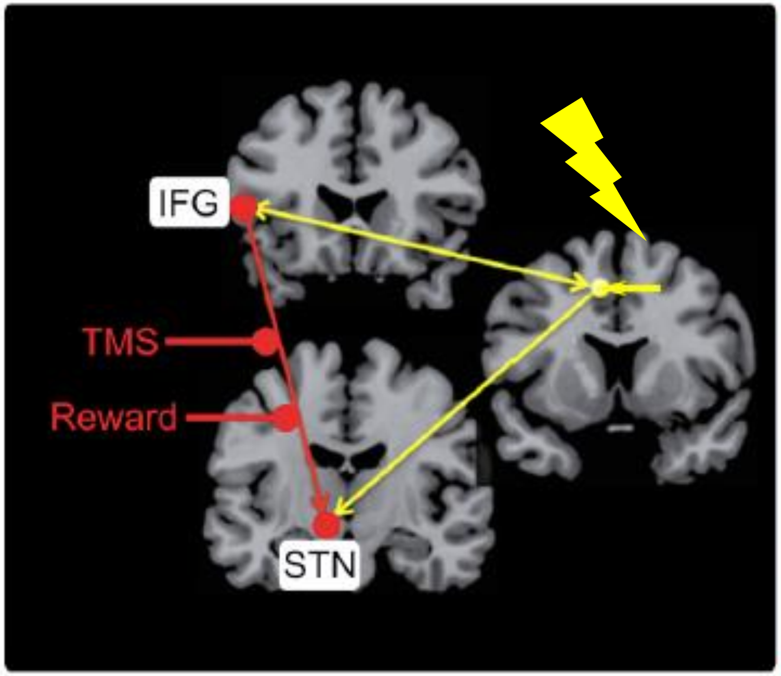
Summary slide - Study I

Parallel vs hierarchical model of the pre-SMA - IFG - STN pathway



The results of the current study provide causal evidence for parallel organization of the pre-SMA–STN and IFG–STN pathways,since improved control over impulsive responses was linked to an enhancedIFG–STN connectivity after pre-SMA had been disrupted.

Herz et at. J Neurosci 2014

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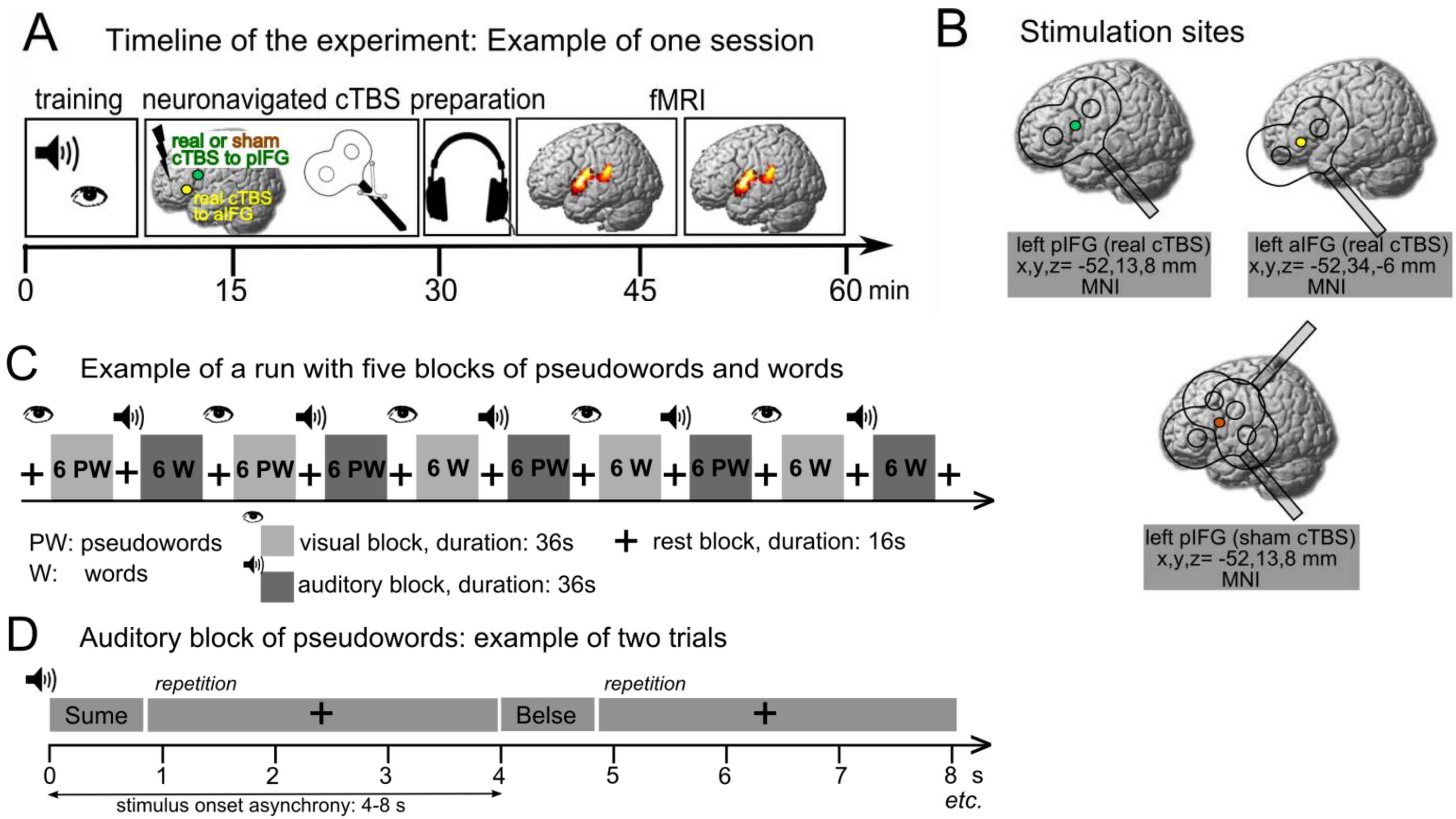
Study 2: Offline TMS of left IFG
Effects on pseudo-word repetition
Inter-hemispheric compensation

Collaborators: Dorothee Saur, Department of Neurology, University of Leipzig, Germany
Cathy J. Price, Wellcome Trust Centre for Neuroimaging, University College London, UK
Annette Baumgaertner, Hochschule Fresenius Hamburg, Germany

Inter-hemsipheric adaptive plasticity between right-left IFG

Short-term reorganization related to pseudoword repetition



Hartwigsen et al., *Proc Natl Acad Sci USA* 2013

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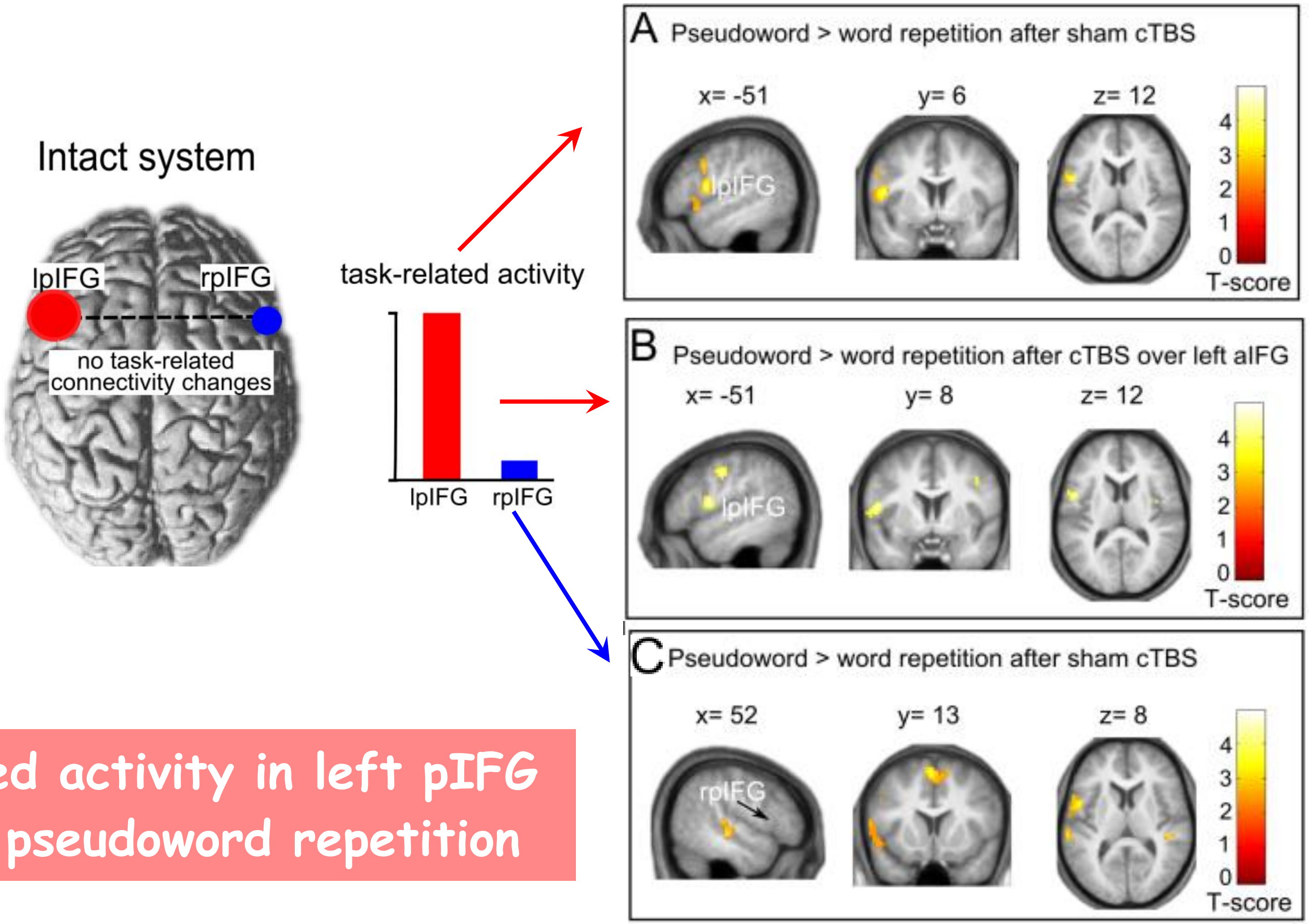
Adaptive plasticity in the language system

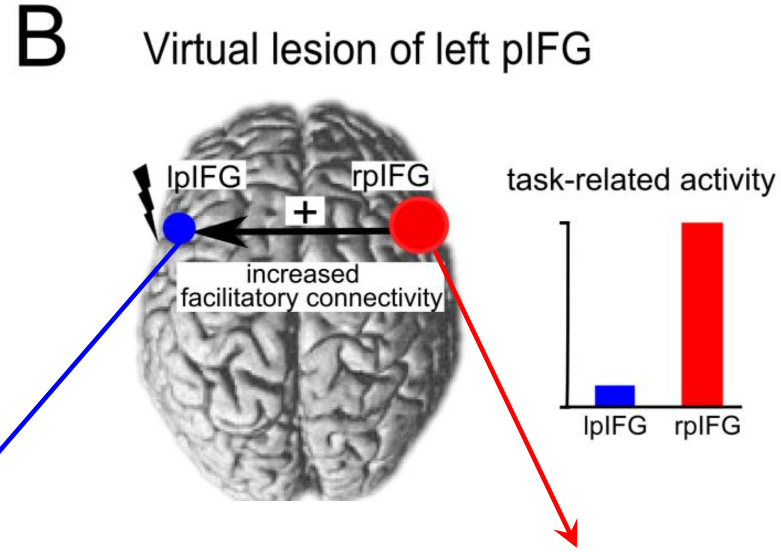


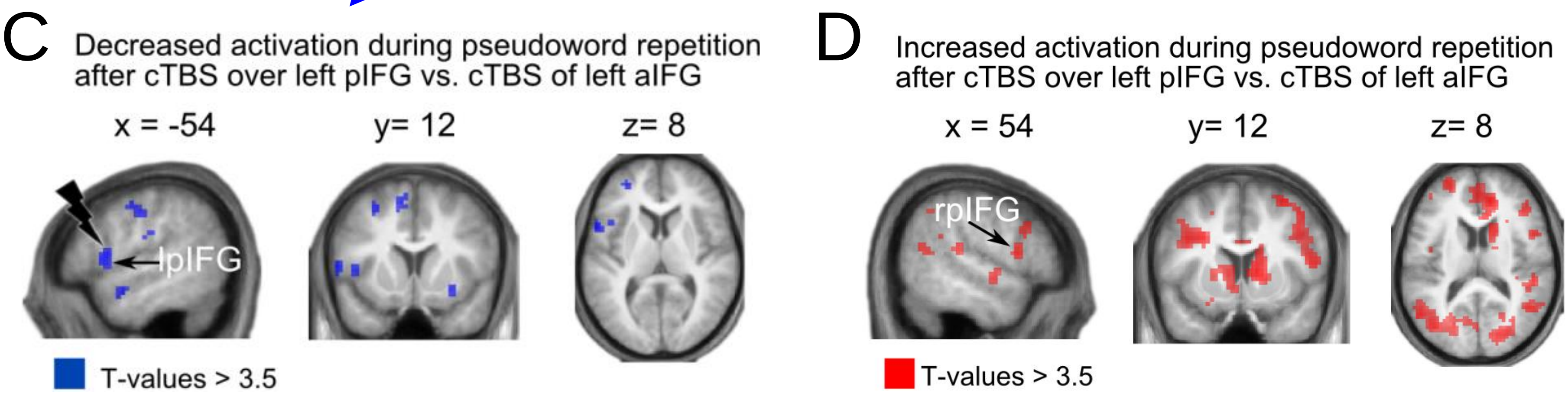
Increased activity in left pIFG during pseudoword repetition

Hartwigsen et al., *Proc Natl Acad Sci USA* 2013

Adaptive plasticity in the language system

Adaptive upregulation of the right pIFG to maintain task function





Hartwigsen et al., *Proc Natl Acad Sci USA* 2013

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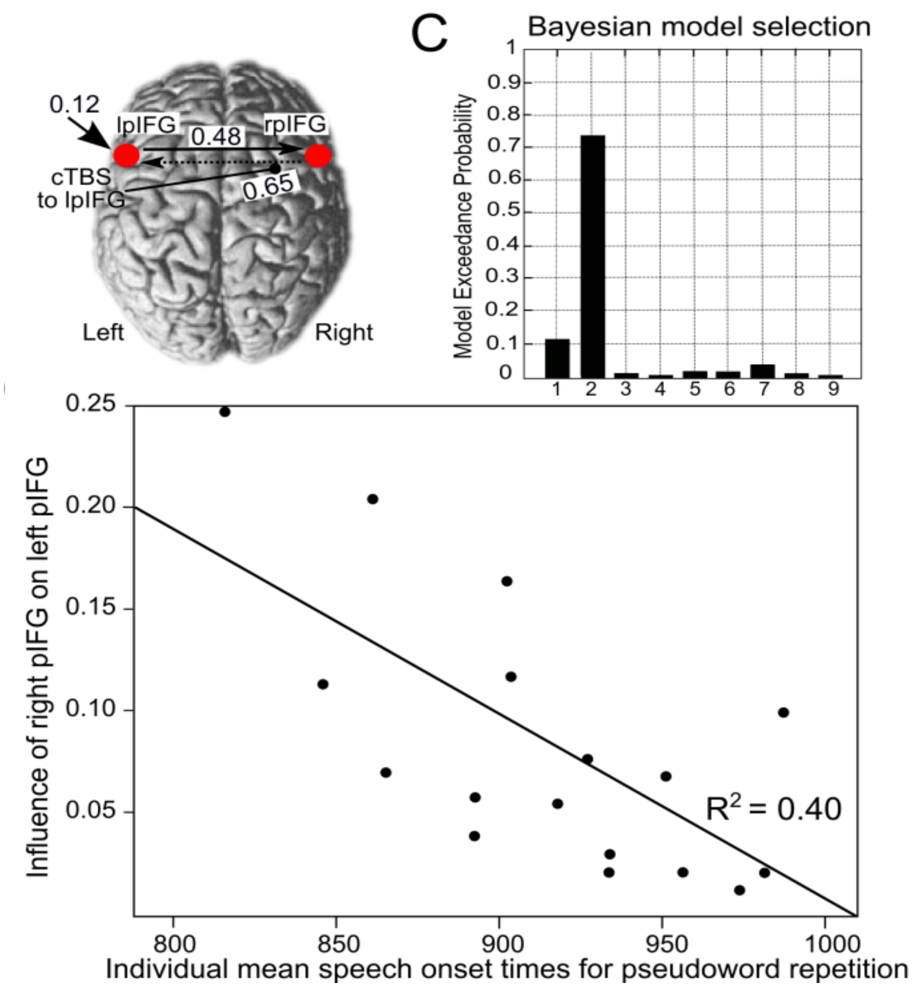
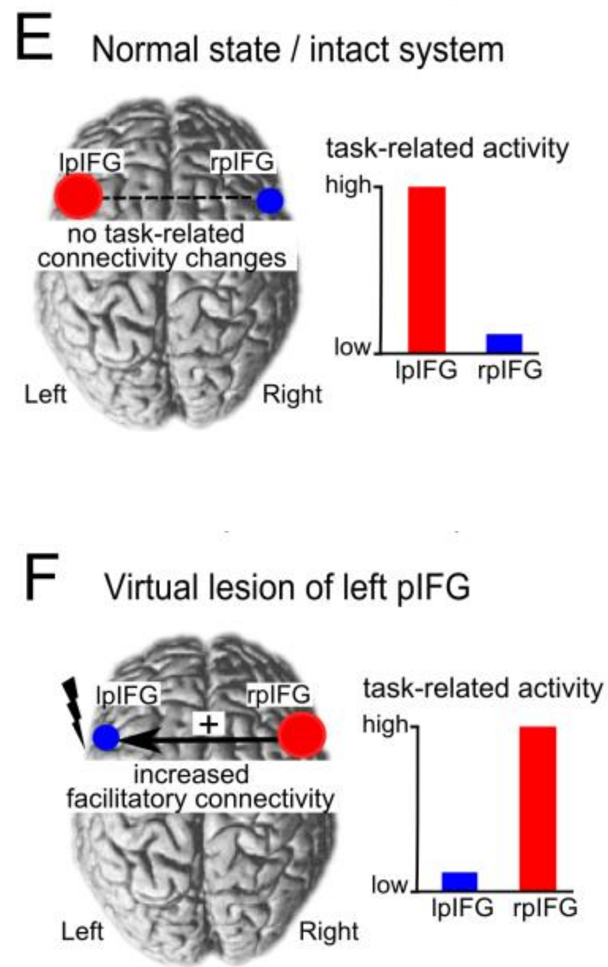
Adaptive plasticity in the language system

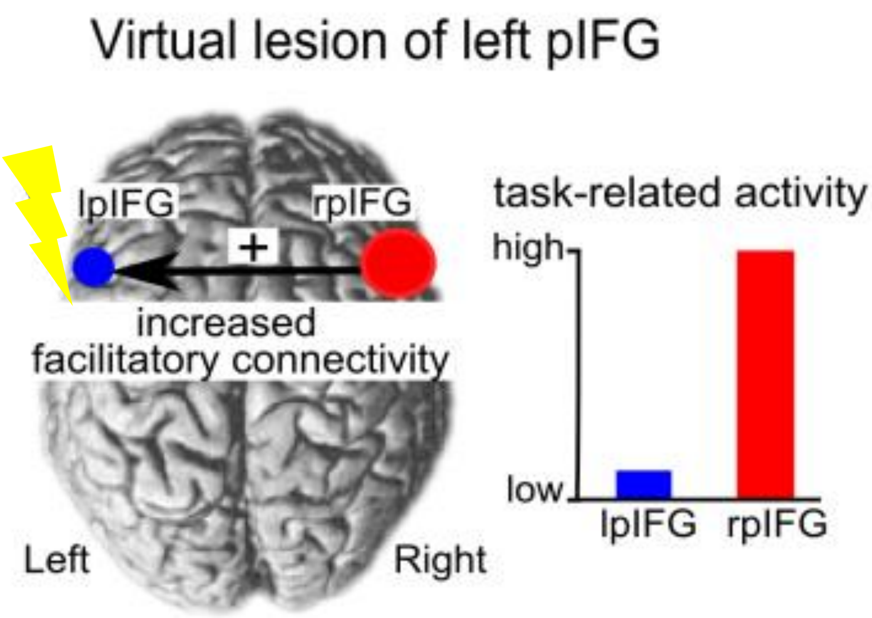




Increased connectivity from right to left pIFG after virtual lesion of left pIFG

Hartwigsen et al., *Proc Natl Acad Sci USA* 2013

Adaptive tuning of inter-hemispheric interaction between left and right pIFG



The results of the current study provide causal evidence for acute re-weighting of task related activity and effective connectivity between left and right pIFG.

Hartwigsen et al., *Proc Natl Acad Sci USA* 2013

TMS is a valuable tool to shape effective connectivity of cogitive brain networks and relate these effects to behavior:

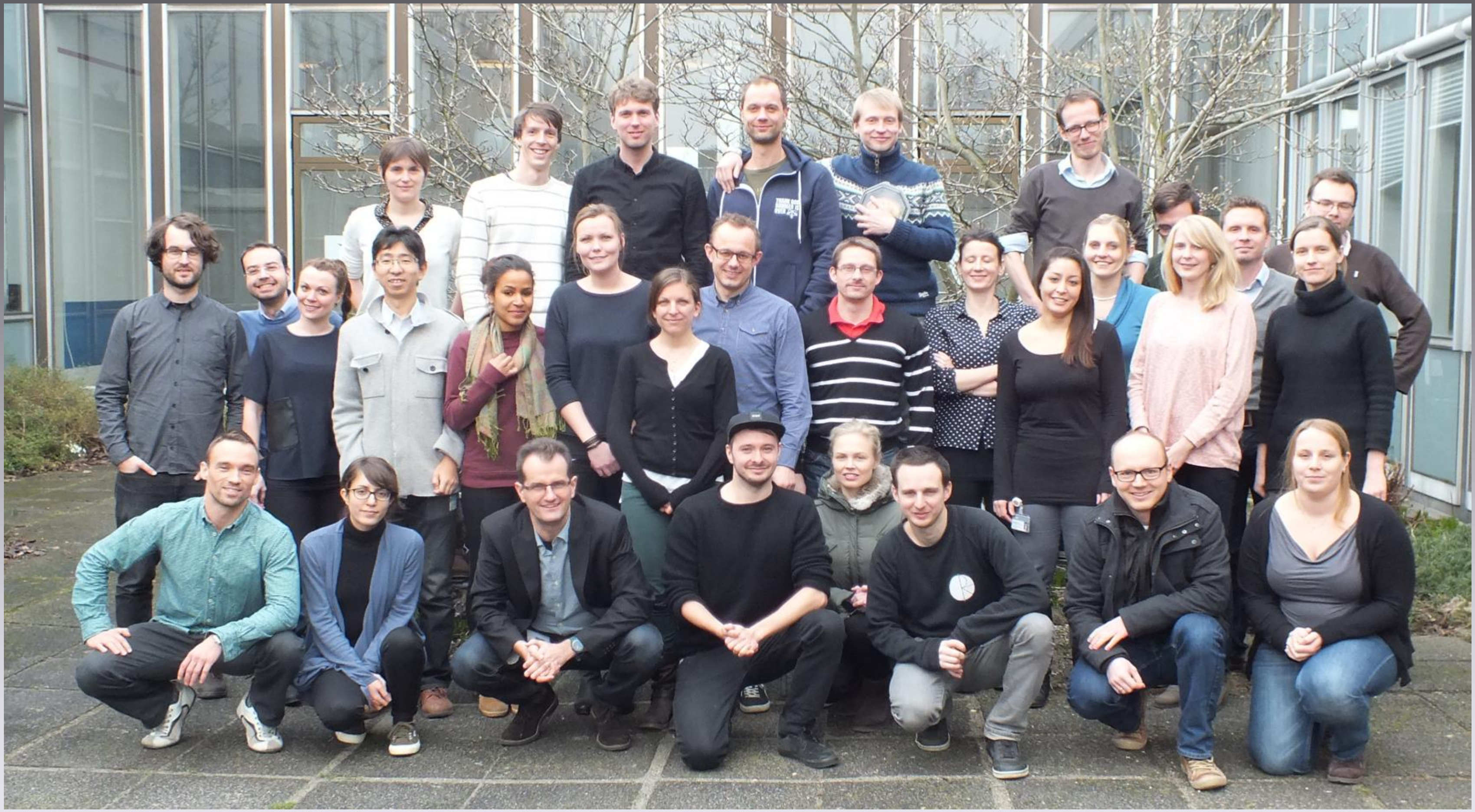
Study I: 1Hz rTMS to pre-SMA

Modulation of intrahemispherical cortico-subcortical connectivity between IFG-STN

=> Better control over impulsive response tendencies

Study II: cTBS to left pIFG

Inter-hemispheric cortico-cortical connectivity between right & left pIFG during pseudo-word repetition => Compensation



*The **contact** group February 2014*