



Central European Institute of Technology
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Multimodal approach - combination of NTBS and imaging

L'ubomíra Anderková,

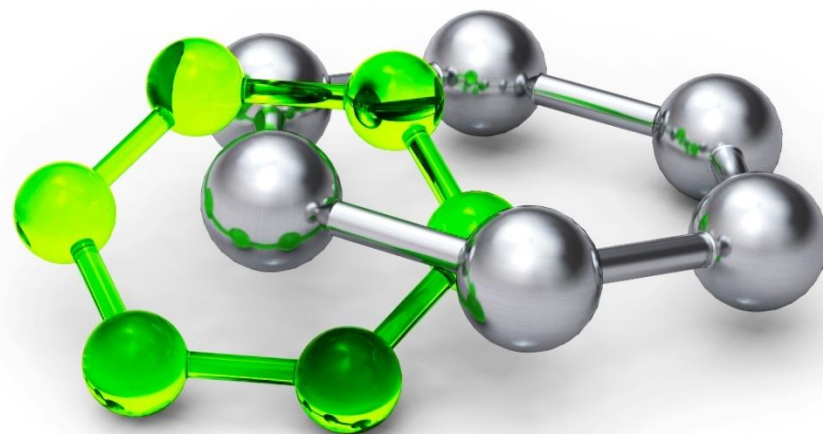
CEITEC MU, Masaryk University, CZ



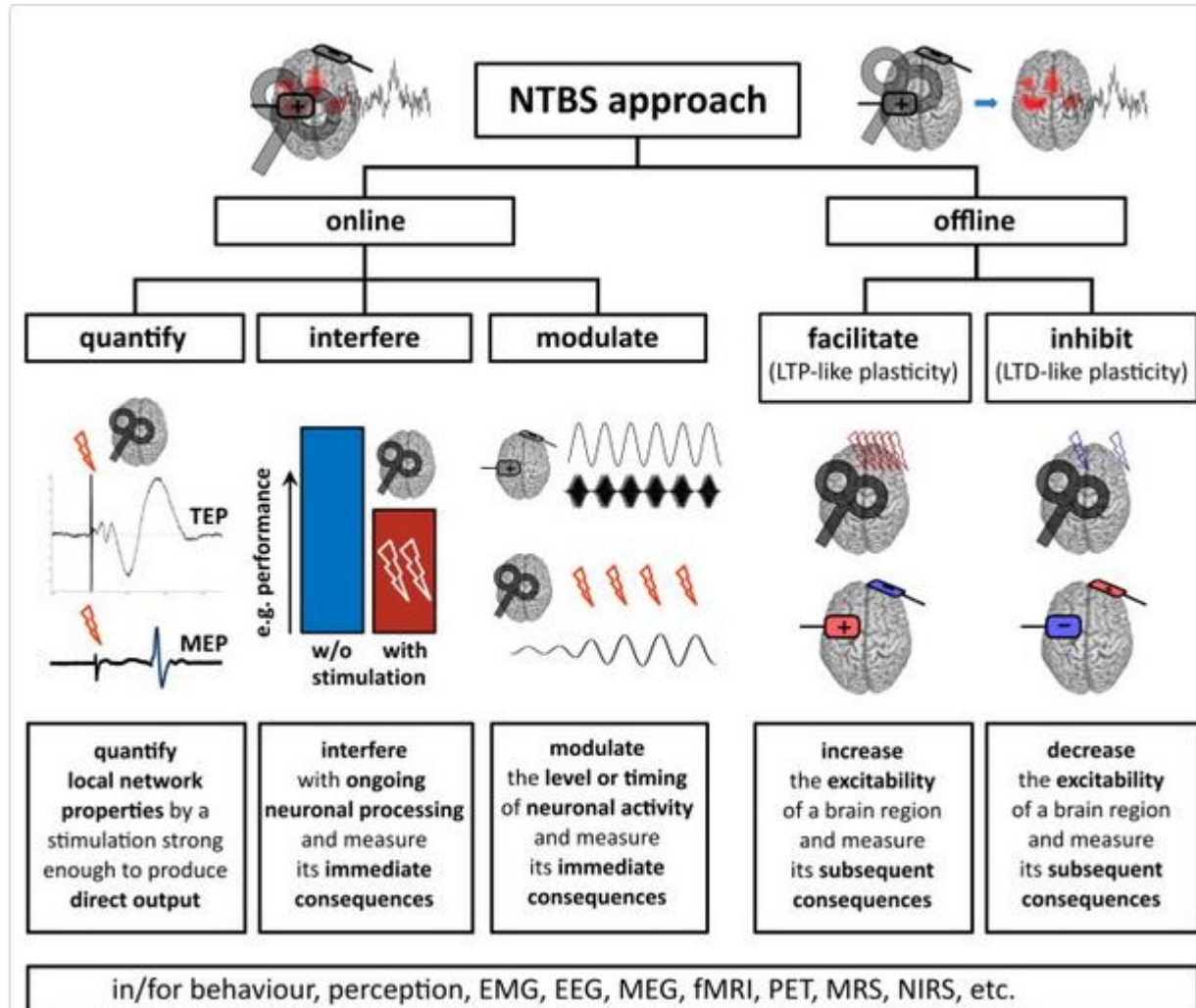
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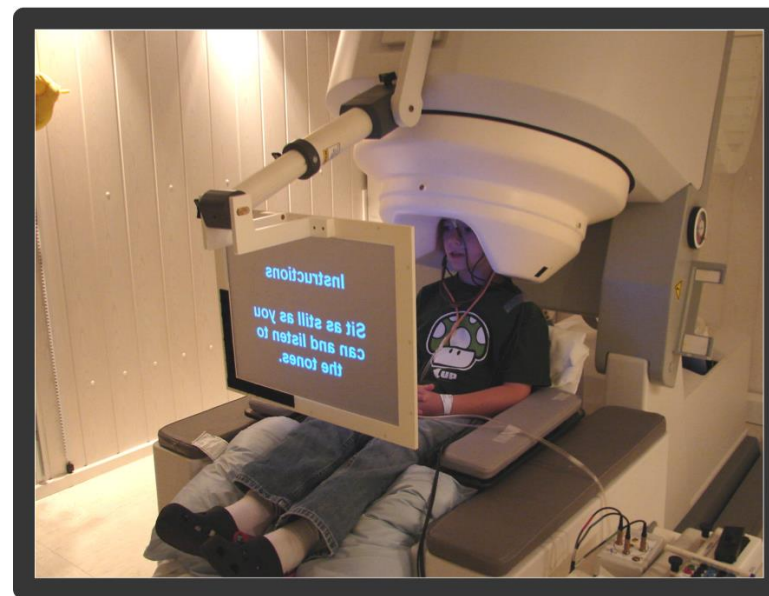
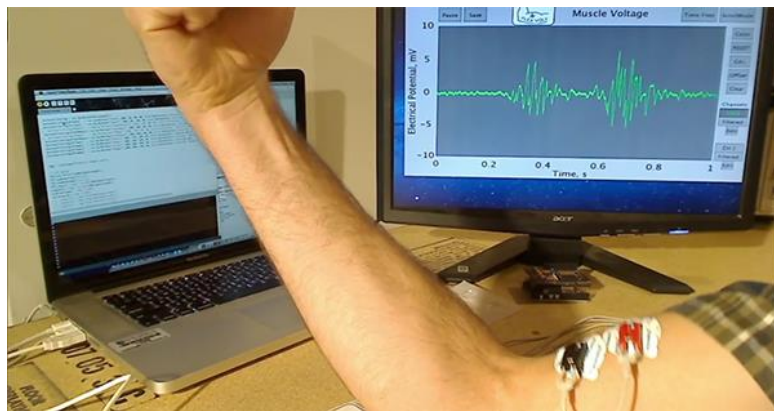
OP Research and
Development for Innovation



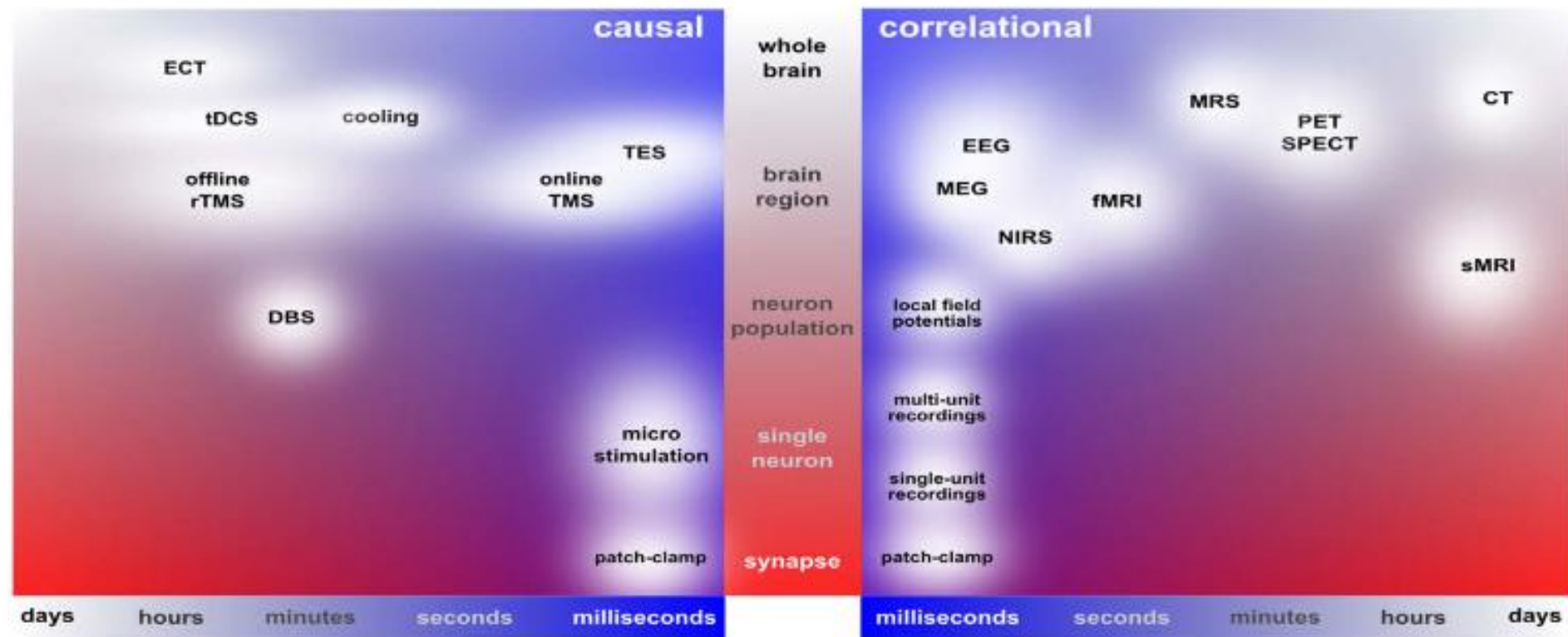
Principal experimental approaches using NTBS



Neuroimaging and electrophysiological techniques for combination with NTBS



Temporal and spatial resolution of neurostimulation and neuroimaging/electrophysiological techniques



Neuroimaging and electrophysiological techniques may inform NTBS about...



Bergmann et al. 2016 Neuroimage

Where to stimulate?

Determine **target site & device position/orientation** for stimulation based on...



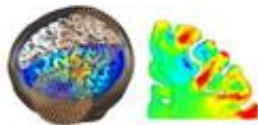
functional localizer



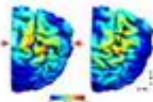
source localization



individual gyral anatomy



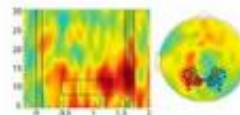
local strength of electric field



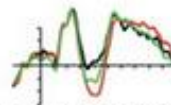
local direction of current flow

When to stimulate?

Determine **target onset/time window** relative to task or spontaneous event for stimulation based on...



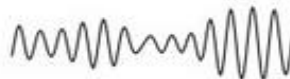
induced power



latency of evoked responses



oscillatory phase



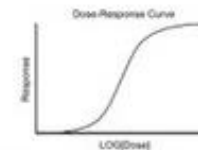
oscillatory power



occurrence of specific events

How to stimulate?

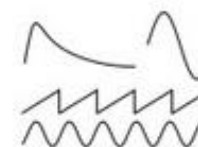
Determine **specific parameters** for stimulation such as...



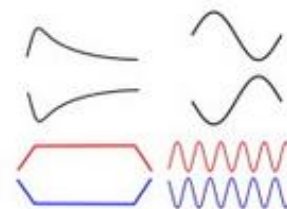
stimulation intensity



stimulation frequency



pulse/wave form



polarity

Neuroimaging and electrophysiological techniques as readouts of NTBS effects

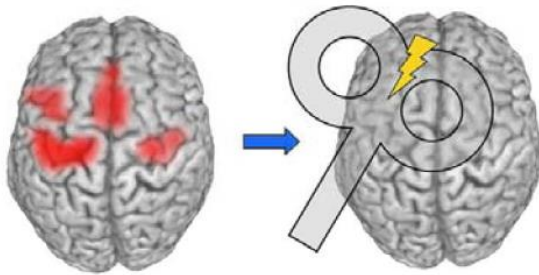


TMS		TCS	
Offline	Online	Offline	Online
fMRI <ul style="list-style-type: none"> • cTBS of left IFG → Task-related BOLD response (Hartwigsen et al., 2013) • cTBS to left anterior PFC → task-related BOLD response (Volman et al., 2011) 	<ul style="list-style-type: none"> • 2 Hz and 10 Hz rTMS of M1 → rCBF during blocks with CASL (Moisa et al., 2008) • 9 Hz rTMS bursts of FEF → TMS-related BOLD-response (Ruff et al., 2006) 	<ul style="list-style-type: none"> • Anodal TDCS of M1 → functional connectivity (graph theoretical analysis) in resting state BOLD (Polania et al., 2011) 	<ul style="list-style-type: none"> • Anodal/cathodal TDCS of M1 → BOLD-signal change during 20s TDCS blocks with or without fingertapping (Antal et al., 2011)
PET <ul style="list-style-type: none"> • 1 Hz rTMS of M1 → rCBF $H_2^{15}O$ (Siebner et al., 2003) • 10 Hz rTMS trains of DLPFC → dopamine [^{11}C]raclopride (Strafella et al., 2001) 	<ul style="list-style-type: none"> • 1–5 Hz rTMS of M1 → rCBF $H_2^{15}O$ (Siebner et al., 2001) • Burst-TMS FEF → rCBF $H_2^{15}O$ (Paus et al., 1997) 	<ul style="list-style-type: none"> • Anodal/cathodal TDCS of M1 → rCBF $H_2^{15}O$ (Lang et al., 2005) 	<ul style="list-style-type: none"> • Anodal/cathodal TDCS of M1 → task-related change in rCBF $H_2^{15}O$ (Paquette et al., 2011)
MRS <ul style="list-style-type: none"> • Anodal/cathodal/sham TDCS of M1 → GABA (Kim et al., 2014) 	<p>Limited sensitivity of MRS necessitates temporal averaging which complicates the assessment of online effects.</p>	<ul style="list-style-type: none"> • anodal/cathodal TDCS of M1 → GABA & Glx (Stagg et al., 2009) 	<p>Limited sensitivity of MRS necessitates temporal averaging which complicates the assessment of online effects.</p>
NIRS <ul style="list-style-type: none"> • 1 Hz rTMS of M1 → HbO_2/HHb at contralateral M1 (Chiang et al., 2007) 	<ul style="list-style-type: none"> • Single-pulse TMS at M1 → HbO_2 directly under the TMS coil (Noguchi et al., 2003) 	<ul style="list-style-type: none"> • Anodal/sham TDCS of prefrontal cortex → HbO_2 at the stimulation site (Merzagora et al., 2010) 	<ul style="list-style-type: none"> • TRNS of left DLPFC → HbO_2/HHb/HbT at LPFC directly under the TCS electrodes (Snowball et al., 2013)
EEG <ul style="list-style-type: none"> • PAS of M1 → spindle density and SWA during subsequent NREM sleep (Bergmann et al., 2008) • 1 Hz rTMS to V1 → VEP amplitude (Bohotin et al., 2002) 	<ul style="list-style-type: none"> • EEG-triggered single-pulse TMS of M1 during sleep slow oscillation up- vs. down-states → TEP (Bergmann et al., 2012) • Single- and paired-pulse TMS after pharmacological intervention → TEP (Premoli et al., 2014a, 2014b) 	<ul style="list-style-type: none"> • TACS at IAF of occipital cortex → posterior alpha power (Neuling et al., 2013; Zaehle et al., 2010) 	<ul style="list-style-type: none"> • 10 Hz TACS of occipital cortex → alpha power, frequency and phase (Helfrich et al., 2014)
MEG <ul style="list-style-type: none"> • cTBS of FEF → attentional parieto-occipital alpha and gamma power modulation (Marshall et al., 2015b) 	<p>Technically not feasible because (i) TMS coil does not fit into MEG helmet and (ii) TMS pulse would probably destroy MEG sensors</p>	<ul style="list-style-type: none"> • Anodal/sham TDCS to M1 → swallowing-related oscillatory power changes (Suntrup et al., 2013) • TACS at 10 Hz of primary sensorimotor cortex → cortico-muscular coherence (Wach et al., 2013) 	<ul style="list-style-type: none"> • Anodal TDCS of M1 → motor task-related beta power desynchronization^(n.s.) (Soekadar et al., 2013) • Anodal/cathodal TDCS of occipital cortex → visual stimulus-induced gamma power synchronization and alpha power desynchronization (Marshall et al., 2015a)

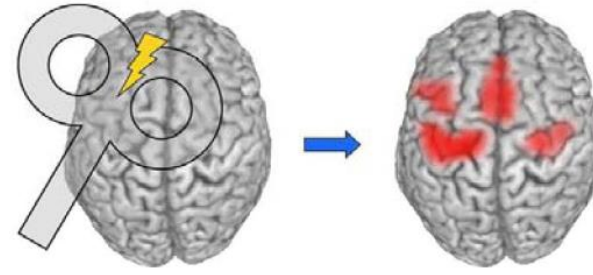
Combining NTBS and imaging



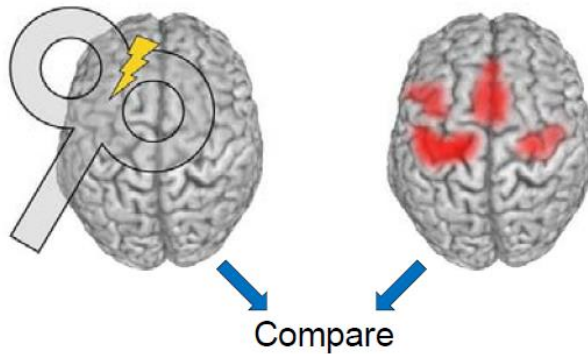
Offline: Stimulation after neuroimaging



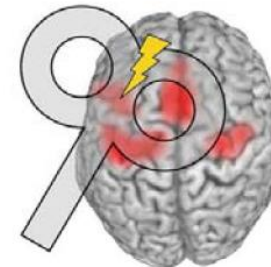
Offline: Stimulation before neuroimaging



Offline: Correlational approach



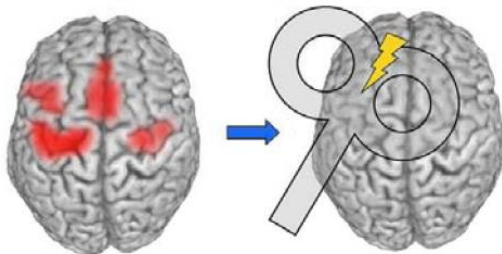
Online: Stimulation during neuroimaging



1. Localization of target areas

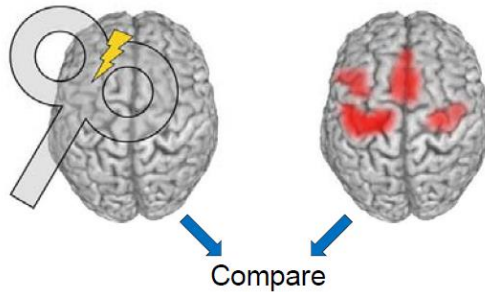


Offline: Stimulation after neuroimaging



2. Links between structure and function

Offline: Correlational approach



Journal of Alzheimer's Disease 48 (2015) 251–260
DOI 10.3233/JAD-150067
IOS Press

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Distinct Pattern of Gray Matter Atrophy in Mild Alzheimer's Disease Impacts on Cognitive Outcomes of Noninvasive Brain Stimulation

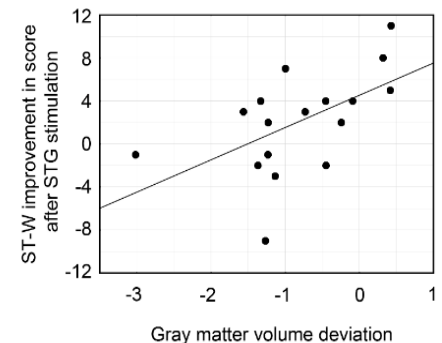
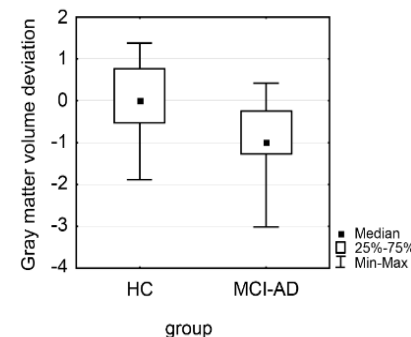
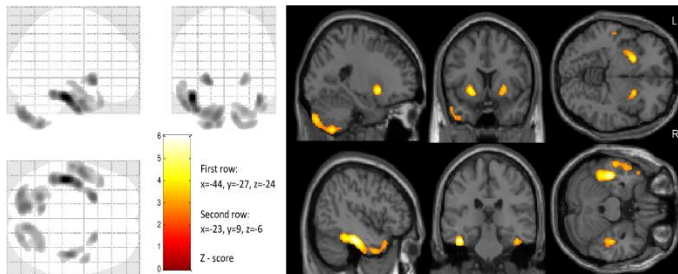
Lubomira Anderkova^{a,b}, Ilona Eliasova^{a,b}, Radek Marecek^{a,b}, Eva Janousova^c and Irena Rektorova^{a,b,*}

^aApplied Neuroscience Research Group, Central European Institute of Technology, Masaryk University (CEITEC MU), Brno, Czech Republic

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^cInstitute of Biostatistics and Analyses, Faculty of Medicine, Masaryk University, Brno, Czech Republic

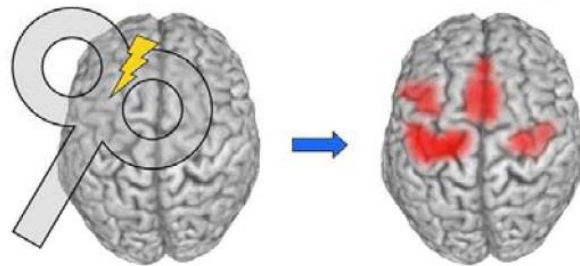
- correlation of atrophy and TMS-induced changes
- Source based morphometry
- N=17 (MCI-AD) + 17 HC
- Mann-Whitney U test, Spearman Rank-Order Correlation



3. Exploring neuroplasticity and reorganization after NTBS



Offline: Stimulation before neuroimaging



Study: Brain plasticity, compensatory patterns and their modulation by noninvasive brain stimulation

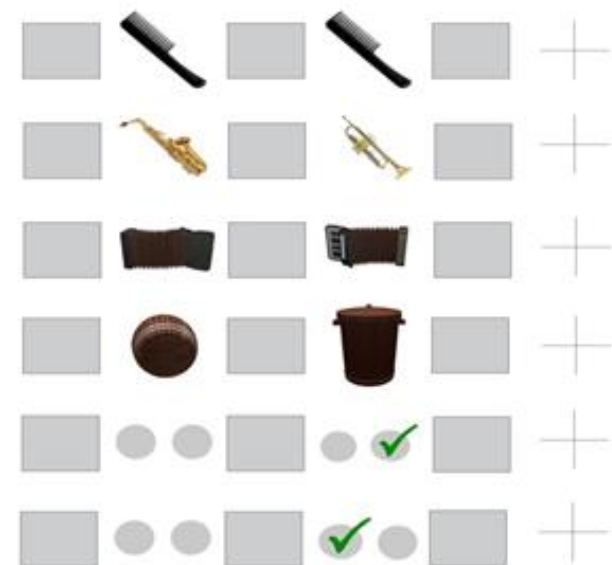
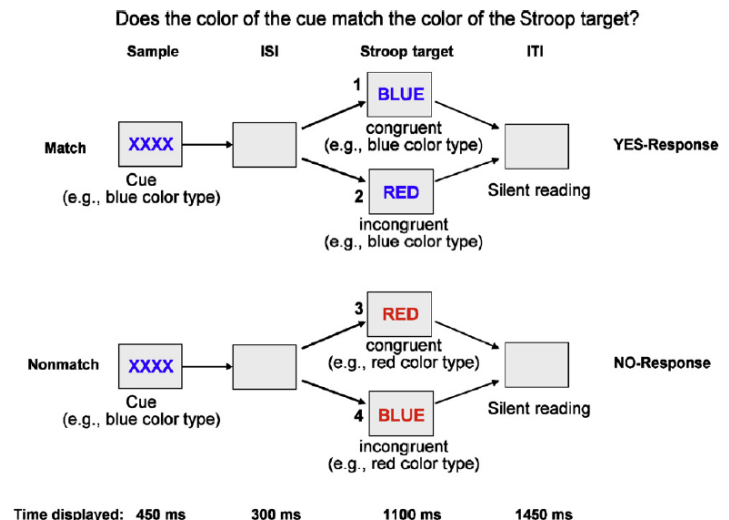
Agency for the Czech Republic health research
AZV, 1. 4. 2016 – 31. 12. 2019

rTMS-fMRI: 80 subjects.. MCI-AD, HC (HY, HA)

6 sessions, 3 stimulation sites

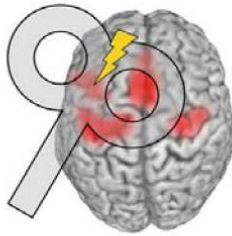
cTBS a iTBS

fMRI: cognitive task: ± 15 min, resting state: 7 min
blood samples for genetic tests



4. Direct/Causal proof of connectivity

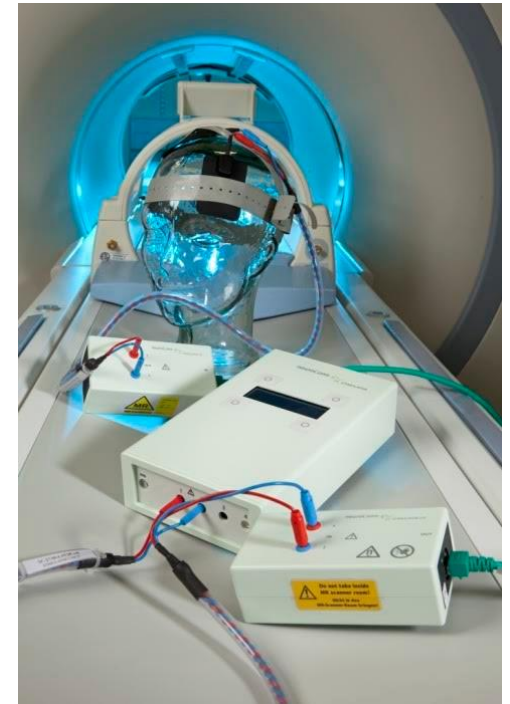
Online: [Stimulation during neuroimaging](#)



An effect of noninvasive brain stimulation on brain plasticity (rTMS/ tDCS/ tACS – fMRI human studies)

Monika Pupíková

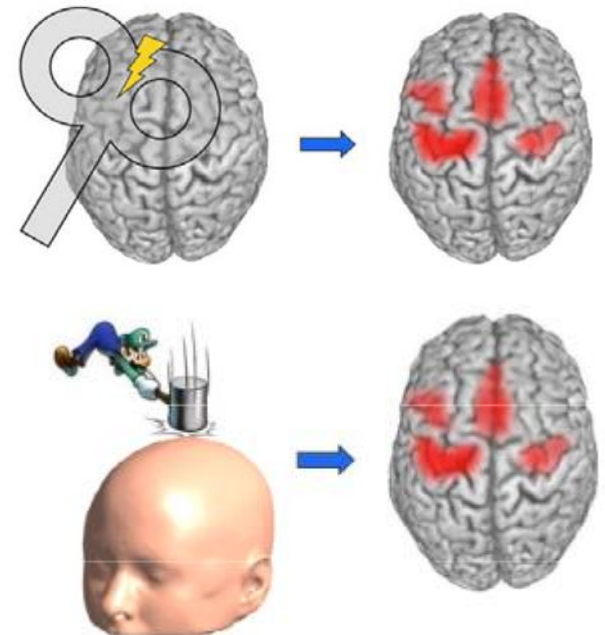
Patrik Šimko



Offline approach – methodological aspects

- Generally easy to handle
- Less methodological challenges as NTBS and imaging are separated in time (or space)
- Practical hurdle: imaging as quick as possible after stimulation
- Limited time for testing (effects gone after about 30 minutes)
- Comparison to sham: rule out unspecific effects, problems with mimicking the real stimulation

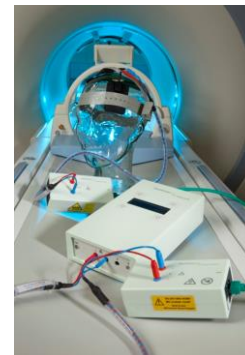
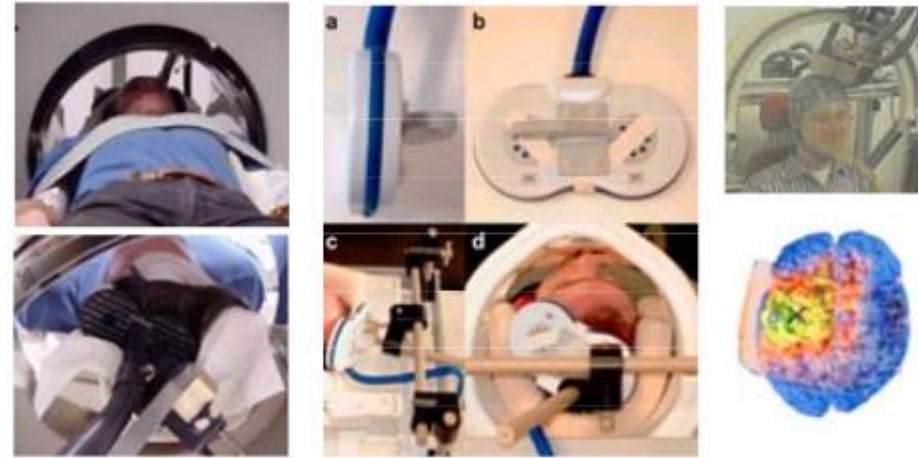
Offline: Stimulation before neuroimaging



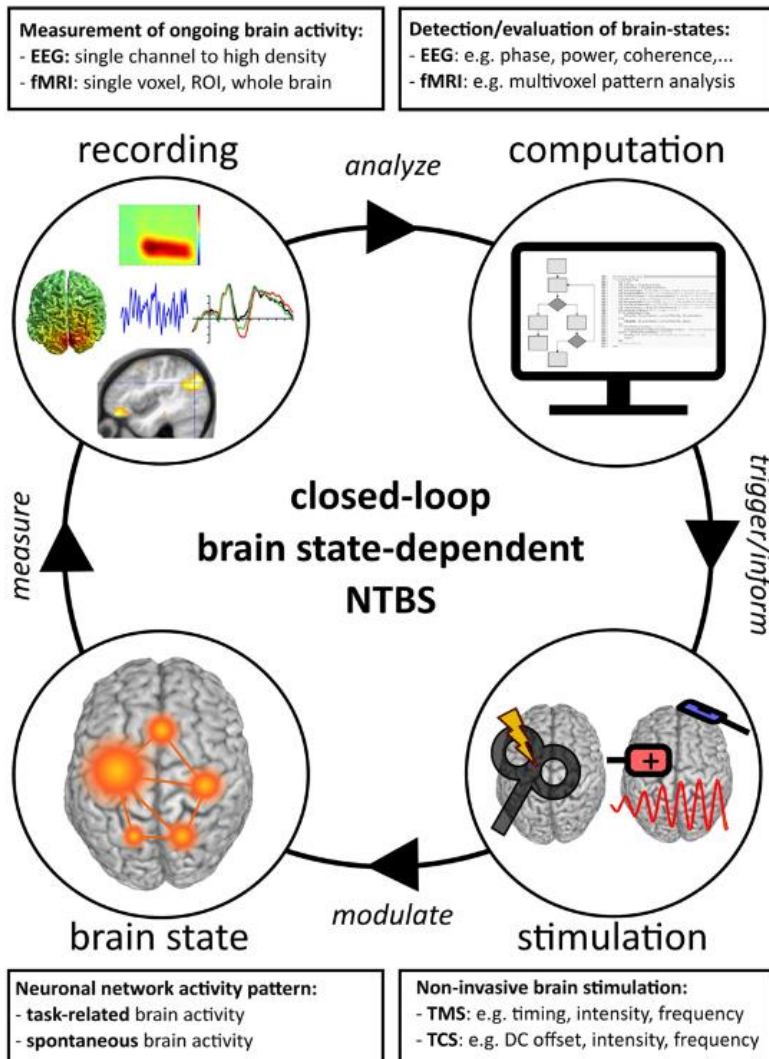
Online approach – methodological aspects



- Methodologically and technically demanding
- Practice hurdle: artifacts
- Auditory and somatosensory co-activations (control condition)
- Complex set-ups and needs for special compatible materials



Future perspectives



Closed-loop application
and tailored therapeutical
interventions

Thank you for your attention

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