Local Immediate Versus Long-Range Delayed Impact Of rTMS On The Visual Attention Network

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Introduction

Network integrity and interhemispheric inhibition in the parietal cortex are linked to healthy control of visual selective attention (Kinsbourne, 1977; Battelli et al., 2001; Baldassarre et al., 2014)

Repetitive inhibitory TMS (rTMS) disrupts the balance of interhemispheric neural activity and commensurately impairs visual tracking (Plow et al., 2014)

The impact of rTMS on visual performance may be delayed as late as 30 minutes following stimulation (Agosta et al., 2014)

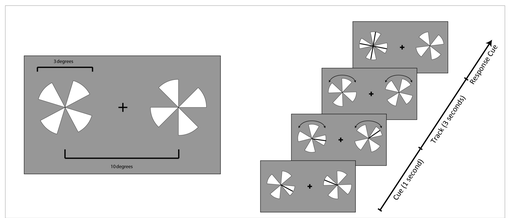
Approach

Procedure:

- N = 7
- Two sessions, counterbalanced
  - ➢ rTMS (15 min 1Hz), or
  - ➢ sham (15 min sham)
- TMS delivered to left IPS
- TMS is offline (no task)
- Subjects tracked during fMRI scans
  - ➢ Each scan 12 min

Tracking task:

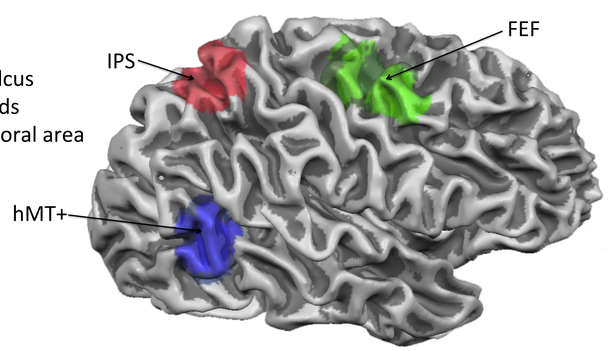
- Subjects monitored two cued spokes of a rotating pinwheel
- 4AFC probe after 3 sec rotation



fMRI analysis:

- Data preprocessing in Brain Voyager
- Bilateral ROIs identified in each subject, tracking - rest activity (TMS and sham)
- Functional connectivity = Pearson's r computed using BOLD timeseries

IPS: Intraparietal sulcus
FEF: Frontal eye fields
hMT+: middle temporal area



Questions

Goal: To measure changes in functional connectivity (FC) in a simplified model of three brain regions in the dorsal attention network engaged by visual tracking: the intraparietal sulcus (IPS), frontal eye fields (FEF) and human MT+ (hMT+)

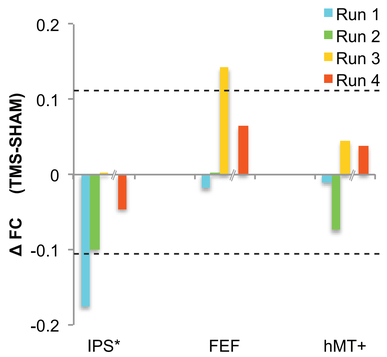
1. What is the impact of rTMS on functional connectivity?
2. How do those changes unfold over time?
3. How are those FC dynamics linked to performance on a sustained attention task?

Results

ΔFC = Change in functional connectivity following rTMS as compared to sham

- Dashed lines denote statistical significance, as computed by a bootstrap Monte Carlo procedure
- Note: *indicates stimulated region (left IPS)

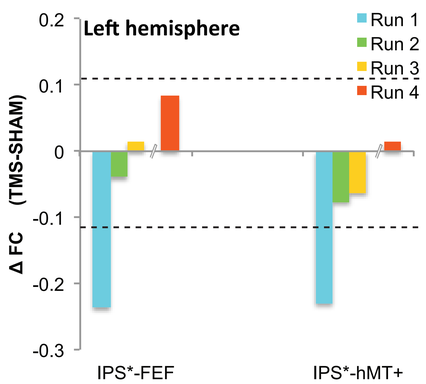
*Inter*hemispheric Functional Connectivity across time



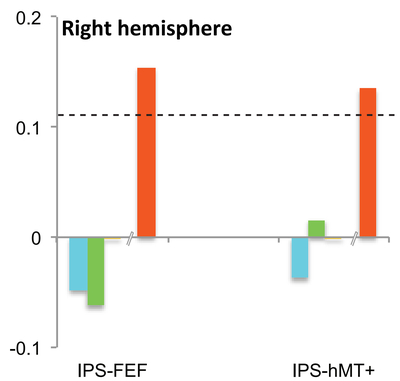
Results:

1. rTMS significantly ***decreased*** FC between left and right IPS, with recovery 20 min post-stimulation.
2. rTMS significantly ***increased*** FC between left and right FEF 30 minutes after stimulation.
3. rTMS over IPS did ***not*** impact left and right hMT+ connectivity.

*Intra*hemispheric Functional Connectivity across time



Results: rTMS significantly ***decreased*** interregional connectivity with the stimulation site, with recovery 20 min following the end of stimulation.

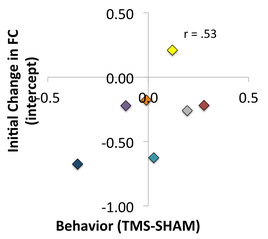


Results: rTMS significantly ***increased*** interregional FC in the unstimulated hemisphere approximately 48 minutes following stimulation.

Results

Relationship between impact of rTMS and recovery: individual subjects

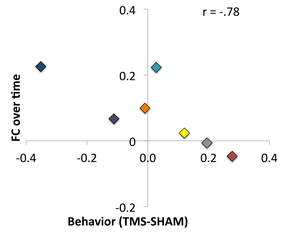
Initial impact

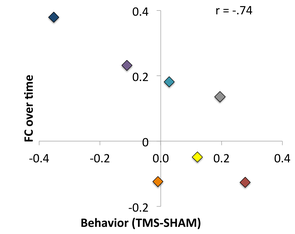


IPS homotopic connectivity vs behavior

- Subjects most impacted by rTMS directly after stimulation were most impaired in tracking and had the most dynamic recovery (not shown)

Recovery





IPS homotopic connectivity vs behavior:

- Those subjects with greatest dynamic recovery were the most impaired in tracking. These are the subjects where the rTMS really changed FC.

IPS*-hMT+ (left hemi) vs behavior:

- The impact of rTMS on functional connectivity dynamics spread within the stimulated hemisphere.

Conclusions

Inhibitory rTMS over left IPS induced widespread changes in the FC of the dorsal attention network.

The **immediate decreases** in functional connectivity

1. homotopic at the IPS stimulation site
2. Inter-regional to the stimulation site (IPS*-FEF and IPS*- hMT+)
3. Strongly correlated with tracking scores

Delayed increases in functional connectivity:

1. Homotopic FEF approximately 36 min following stimulation, consistent with
   - Agosta et al. (2014) finds peak impact of 1Hz offline rTMS on right parietal patients 30 min following stimulation
   - Hubl et al. (2006) reports delayed peak impact of theta burst rTMS over FEF at 25 min post-stimulation
2. Inter-regional to the stimulation site (IPS*-FEF and IPS*-hMT+) approximately 50 min following stimulation

References and Acknowledgments

Agosta, S. *et al.* Contralesional rTMS relieves visual extinction in chronic stroke. *Neuropsychologia* 62, 269–276 (2014).
Battelli, L. *et al.* Unilateral right parietal damage leads to bilateral deficit for high-level motion. *Neuron* 32, 985–995 (2001)
Baldassarre A *et al.* Large-scale changes in network interactions as a physiological signature of spatial neglect. *Brain*137:3267-83 (2014).
Kinsbourne M. Hemi-neglect and hemisphere rivalry. *Adv Neurol* 18, 41-49 (1977).
Plow, E. B. *et al.* The compensatory dynamic of inter-hemispheric interactions in visuospatial attention revealed using rTMS and fMRI. *Front Hum Neurosci* 8, 226 (2014).
Hubl, D. *et al.* Time course of blood oxygenation level–dependent signal response after theta burst transcranial magnetic stimulation of the frontal eye field. *Neuroscience* 151, 921–928 (2008).

Acknowledgments: LB was funded by the Autonomous Province of Trento, Call "Grandi Progetti 2012", project "Characterizing and improving brain mechanisms of attention – ATTEND.