Evaluation of the contributions of the frontal and posterior parietal cortices in spatial working memory with repetitive transcranial magnetic stimulation

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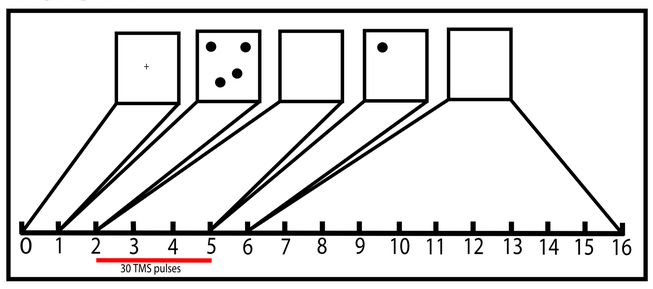
Introduction

- Working memory refers to the ability to maintain information in an active state when it is no longer present in the environment.
- The relative contributions of the dorsolateral prefrontal cortex (dlPFC) and posterior cortical areas to the retention of information in spatial working memory are the focus of considerable interest and debate (e.g., Goldman-Rakic & Leung, 2002; Curtis & D'Esposito, 2003).
- We tested the neccesity of the dlPFC, frontal eye fields (FEF) and 2 posterior areas for the retention of spatial information in working memory by targeting each region with high frequency repetitive transcranial magnetic stimulation (rTMS).
- rTMS allows for within-subject comparison of performance with and without disruptive rTMS applied to the area in question (Pascual-Leone et al., 2000).

Subjects & Methods

- 50 right-handed healthy subjects participated.
- 1st session - Screening and Training
  - Subjects were trained on the task to achieve an accuracy of at least 70%.
- 2nd session - MRI
  - High-resolution anatomical volumes acquired for all subjects.
- 3rd session - rTMS
  - Subjects completed 4 blocks of the task for each brain area targeted with rTMS.

Task

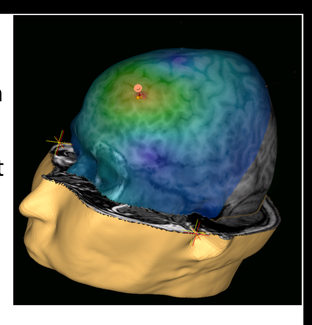


- Target: four circles (1 degree of visual angle in diameter) presented at random locations, one in each quadrant of the screen.
- Probe: required Y/N recognition decision; matched a target location with p=0.5; invalid probes were offset from the nearest target location by an average of 3.08 (S.D. = 0.4) deg. along one of the 8 cardinal or ordinal axes.

Targets of rTMS

- **Experiment 1** (30 subjects): rTMS was applied to the dlPFC, superior parietal lobule (SPL), and as a control , the post-central gyrus (PCG).
  - rTMS was applied to the left hemisphere in18 subjects, and the right hemisphere in 12 subjects.
- **Experiment 2** (20 subjects): rTMS was applied to the FEF, intraparietal sulcus (IPS) and the PCG.
  - 10 subjects were stimulated in the left hemisphere, 10 in the right hemisphere.
- The order of region to which rTMS was applied was counterbalanced accross subjects.

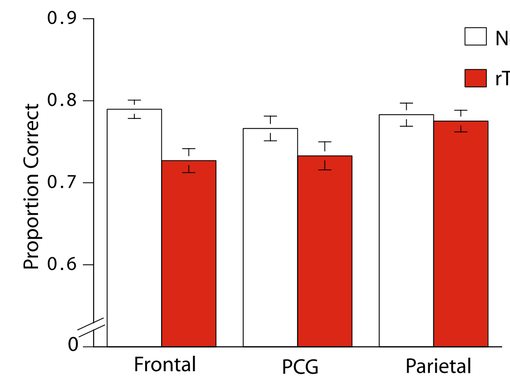
rTMS



- TMS pulses were delivered via Magstim Standard Rapid (Magstim Co., Whitland, UK) 70 mm air-cooled figure-eight coil.
- Each subject's head was co-registered with his/her MRI using eXimia NBS frameless stereotaxy navigation sytem (Nexstim, Helsinki, Finland).
  - Targets of rTMS guided by individual subject's anatomy.
- rTMS (10 Hz, 110% MT, 3 seconds) coincided with the delay period on 50% of the trials (randomly determined order).
  - Stimulation intensity was corrected for scalp-to-cortex distance using eXimia NBS's calculation of induced electric field potential.

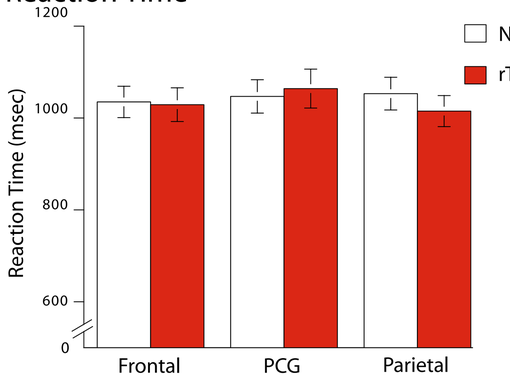
Results

All Subjects (N=50): Accuracy



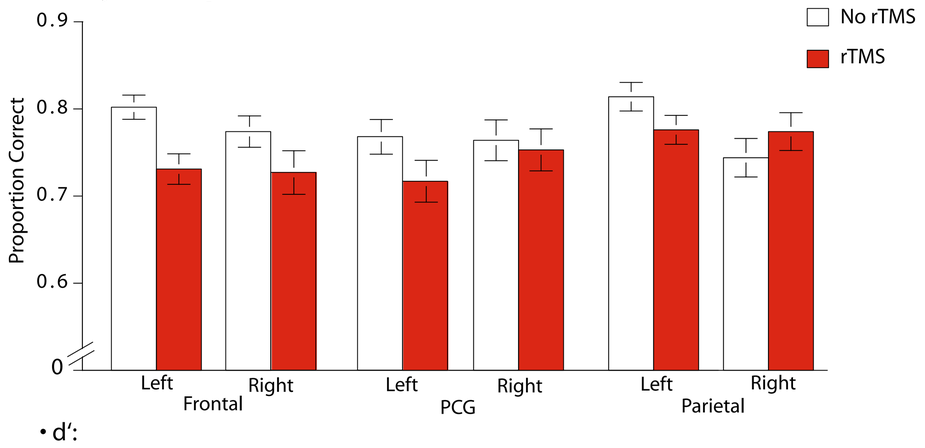
- d':
  - Main effect of rTMS [$F(1,49)=14.74$; $p<0.001$].
    - d' *decreases* with rTMS ($p<0.001$).
  - Brain Area x rTMS interaction [$F(2,98)=3.21$; $p<0.05$].
  - However, neither area is different from the PCG.
- Criterion *decreases* with rTMS:
  - Main effect of rTMS [$F(1,49)=4.40$; $p<0.05$].

Reaction Time

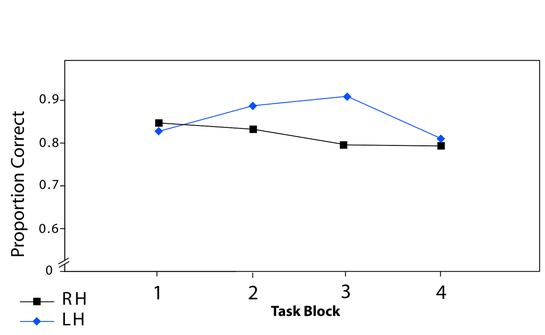


- Reaction Time:
  - Brain Area x rTMS interaction [$F(2,98)=3.33$; $p<0.05$].
  - rTMS of posterior brain areas *decreases* reaction time ($p<0.001$).

rTMS by hemisphere stimulated

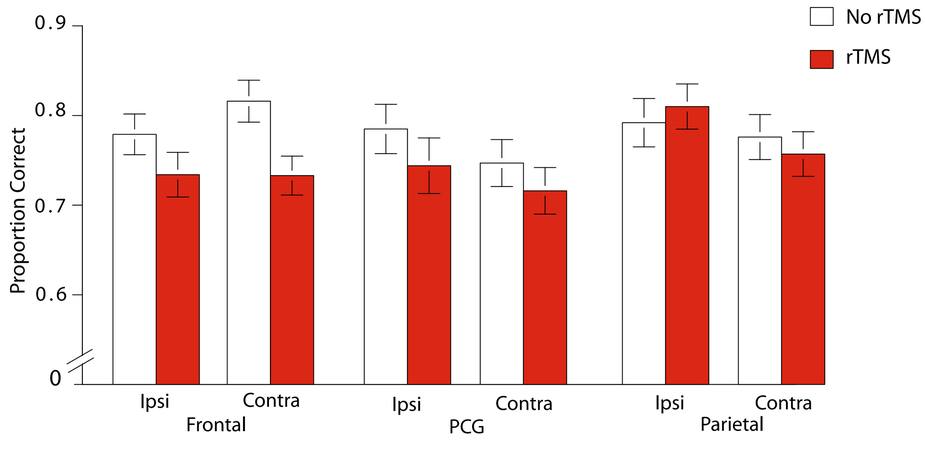


- d':
  - Hemisphere x rTMS interaction ($F(1,49)=4.90$; $p<0.05$).
    - rTMS of the left hemisphere *decreases* d' a greater amount than does rTMS of the right hemisphere ($p<0.05$).
- No rTMS x Hemisphere interaction with Criterion or reaction time.



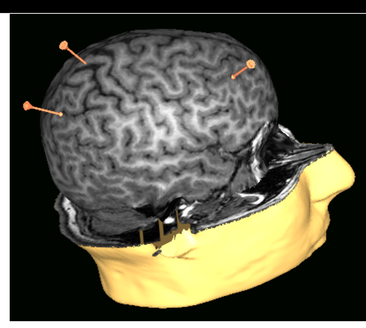
- Analysis of non-stimulated trials by block reveals:
  - Marginal main effect of Hemisphere [$F(1,49)=3.00$; $p=0.09$].
  - Main effect of Block [$F(3, 144)=2.74$; $p<0.05$].
  - Block x Hemisphere interaction [$F(3,144)=3.37$; $p<0.05$].

Visual Field Effects

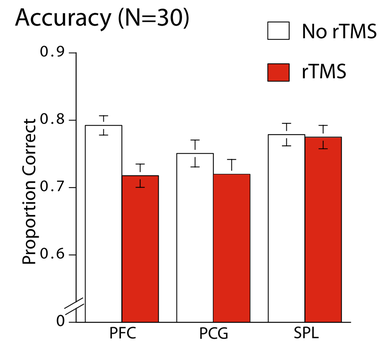


- Accuracy for probes that appeared in the visual hemifield contralateral to rTMS was lower.
  - Main effect of visual hemifield [$F(1,49)=3.42$; $p=0.07$].

Experiment 1

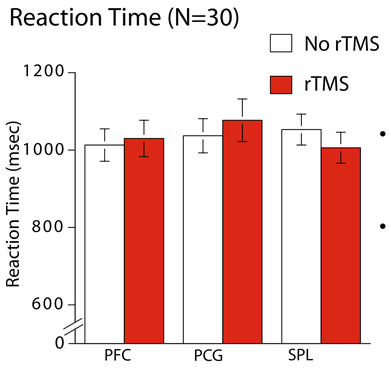


Accuracy (N=30)



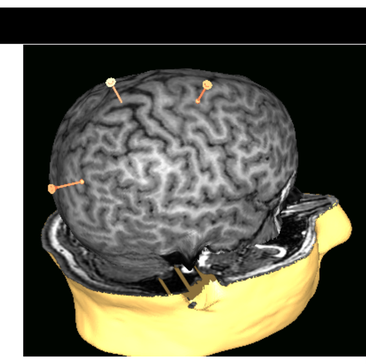
- Main effect of rTMS [$F(1,29)=10.08$; $p<0.005$].
- Brain Area x rTMS interaction [$F(2,58)=4.00$; $p<0.05$].
  - However, neither area is significantly different from the PCG.

Reaction Time (N=30)

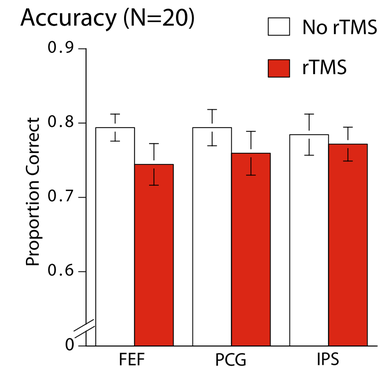


- Brain Area x rTMS interaction [$F(2,58)=9.06$; $p<0.001$].
- rTMS of SPL decreased reaction time compared to PCG ($p<0.001$).

Experiment 2

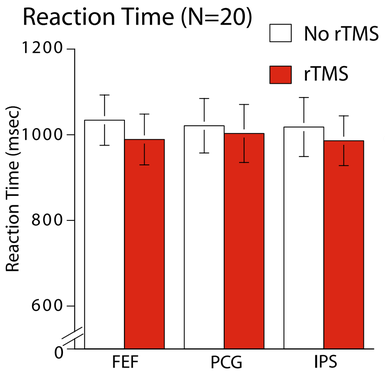


Accuracy (N=20)



- d': Main effect of rTMS [$F(1,19)=4.83$; $p<0.05$], but no significant interactions.
- Criterion: Main effect of rTMS[$F(1,19)=5.92$; $p<0.05$], but no significant interactions.

Reaction Time (N=20)



- Trend towards a main effect of rTMS decreasing reaction time (p=0.09).

Conclusions

- No evidence for a role of dlPFC in spatial working memory storage.
- Privaleged role for parietal cortex in spatial working memory.
  - rTMS has paradoxical region-specific effects on working memory, with rTMS of the parietal cortex making responses faster and leaving accuracy relatively unchanged.
- Spatial working memory is supported by a broadly distributed cortical network.
  - rTMS has a global effect of decreasing accuracy and making subjects more likely to give a *Yes* response.