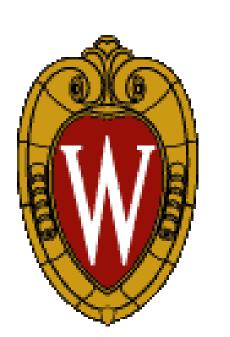


Effect on spatial working memory of repetitive transcranial magnetic stimulation of the dosolateral prefrontal cortex and superior parietal cortex



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Introduction

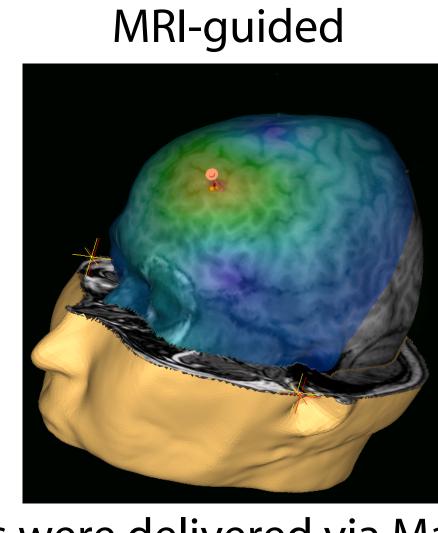
- Working memory refers to the ability to maintain information in an active state when it is no longer present in the environment.
- The relative contributions of the dorsolateral prefrontal cortex (dIPFC) and posterior parietal cortex (PPC) to the retention of information in spatial working memory are the focus of considerable interest and debate (e.g., Goldman-Rakic, 1987; Curtis and D'Esposito, 2003).
- We tested the neccesity of the dIPFC and PPC for the retention of spatial information in working memory by targeting these two regions 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).

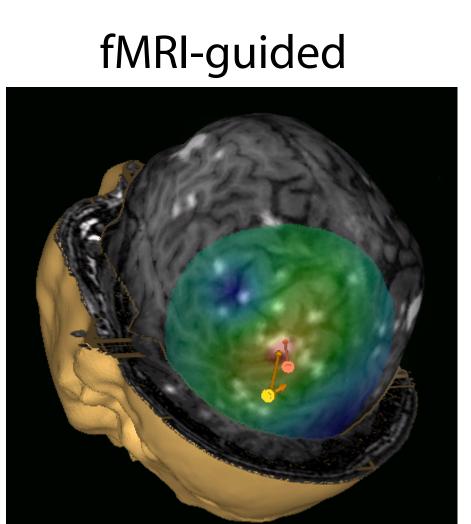
Subjects & Methods

- 25 right-handed healthy subjects (mean age = 23 years, S.D.=5.3); passed psychiatric screening.
- 1st session Screening and Training Subjects were trained on the task to achieve an accuracy of at least 75%.
- 2nd session MRI
- High-resolution anatomical volumes acquired for all subjects.
- For 7 subjects, fMRI of task performance also acquired.
- 3rd session rTMS Subjects performed 4 blocks of the task for each brain area stimulated: middle frontal gyrus of the dIPFC, superior parietal lobule (SPL) of the PPC, and a region of post-central gyrus (PCG) that served as a stimulation control area.

- High-resolution anatomical T1-weighted images (248 slices, 0.5 mm x 0.5 mm
- For 7 participants, a gradient echo, echoplanar sequence was used to measure
- Maps of delay-period activity were merged with the anatomical image and used to guide rTMS.

TMS





- TMS pulses were delivered via Magstim Standard Rapid (Magstim Co., Whitland, UK) 70 mm air-cooled figure-eight coil.
- Each subject's head was coregistered with his/her MRI using eXimia NBS frameless stereotaxy navigation sytem (Nexstim, Helsinki, Finland).
 - MRI-guided study rTMS guided by anatomy.

fMRI Results

Delay-period evoked activity

in a representative subject.

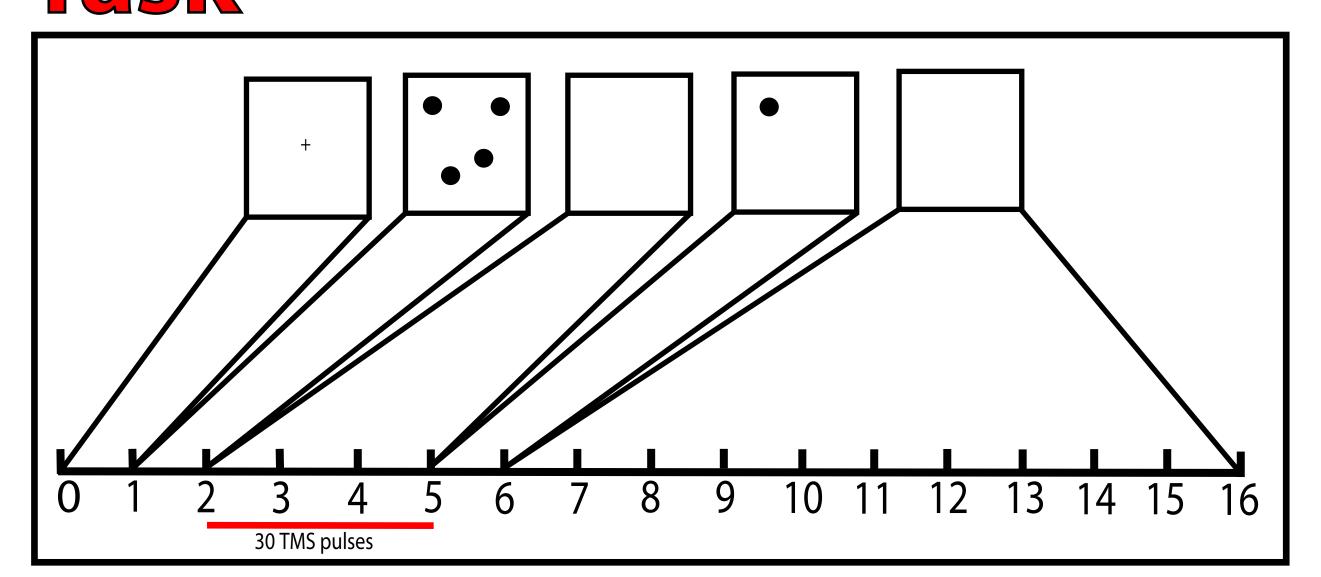
rTMS applied during the

Time (sec)

delay period.

- fMRI-guided study rTMS targeted delay-period activity.
- 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.
- The order of region to which rTMS was applied was counterbalanced accross subjects.
- 17 subjects were stimulated in the left hemisphere (5 fMRI-guided), 8 in the right hemisphere (2 fMRI-guided).

Task

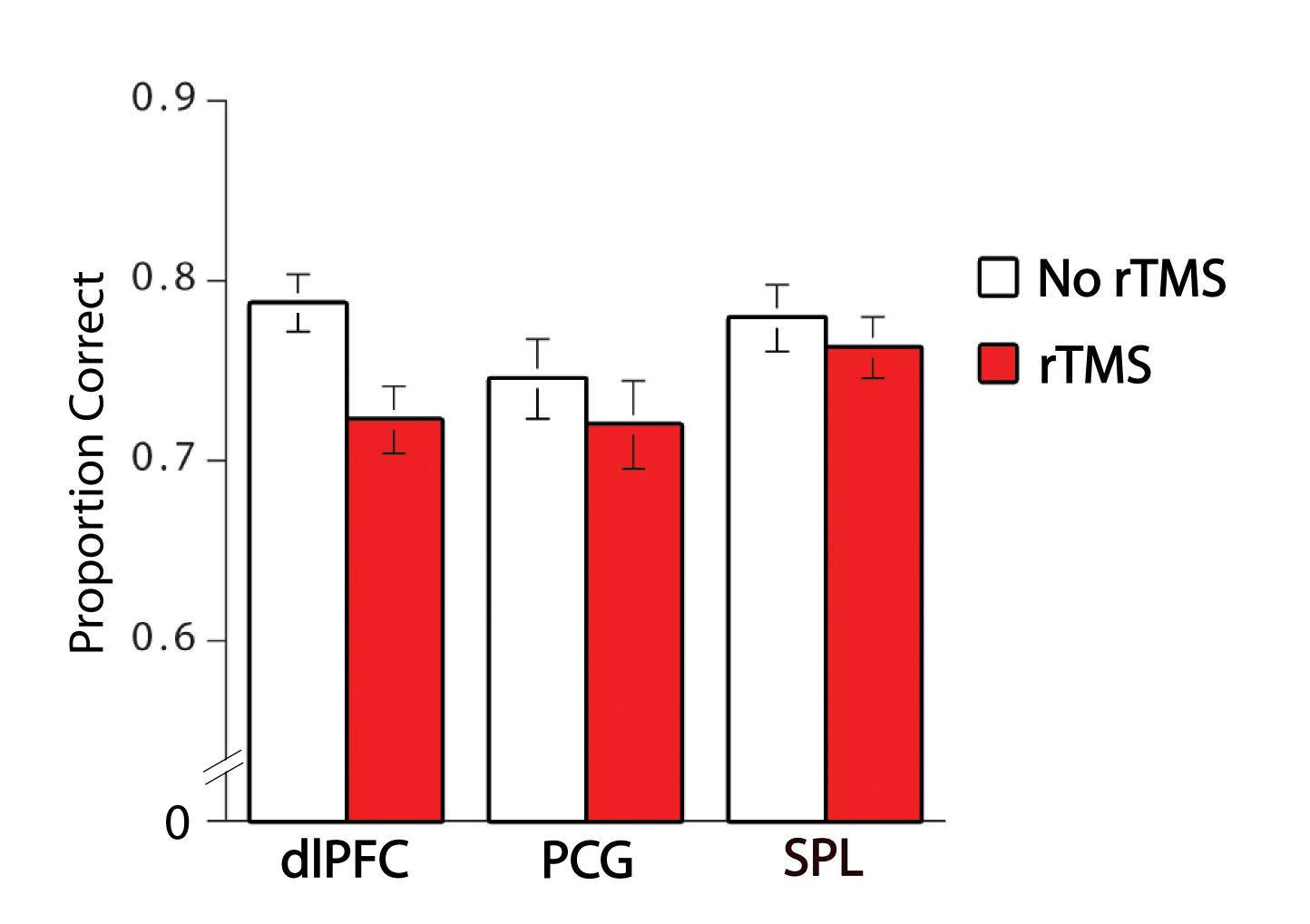


- Target: four circles (1 degree of visual angle in diameter) presented at random locations, one in each quadrant of the screen.
- Probe: required Y/N recognition decision; matched a target location with p=0.5; invalid probes were offset from the nearest target location by an average of 3.08 (S.D. =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

- MRI data was acquired on a 3T scanner (GE Signa VH/I).
- x 0.8 mm) were obtained for all participants.
- the BOLD response while performing the delayed-recognition task.

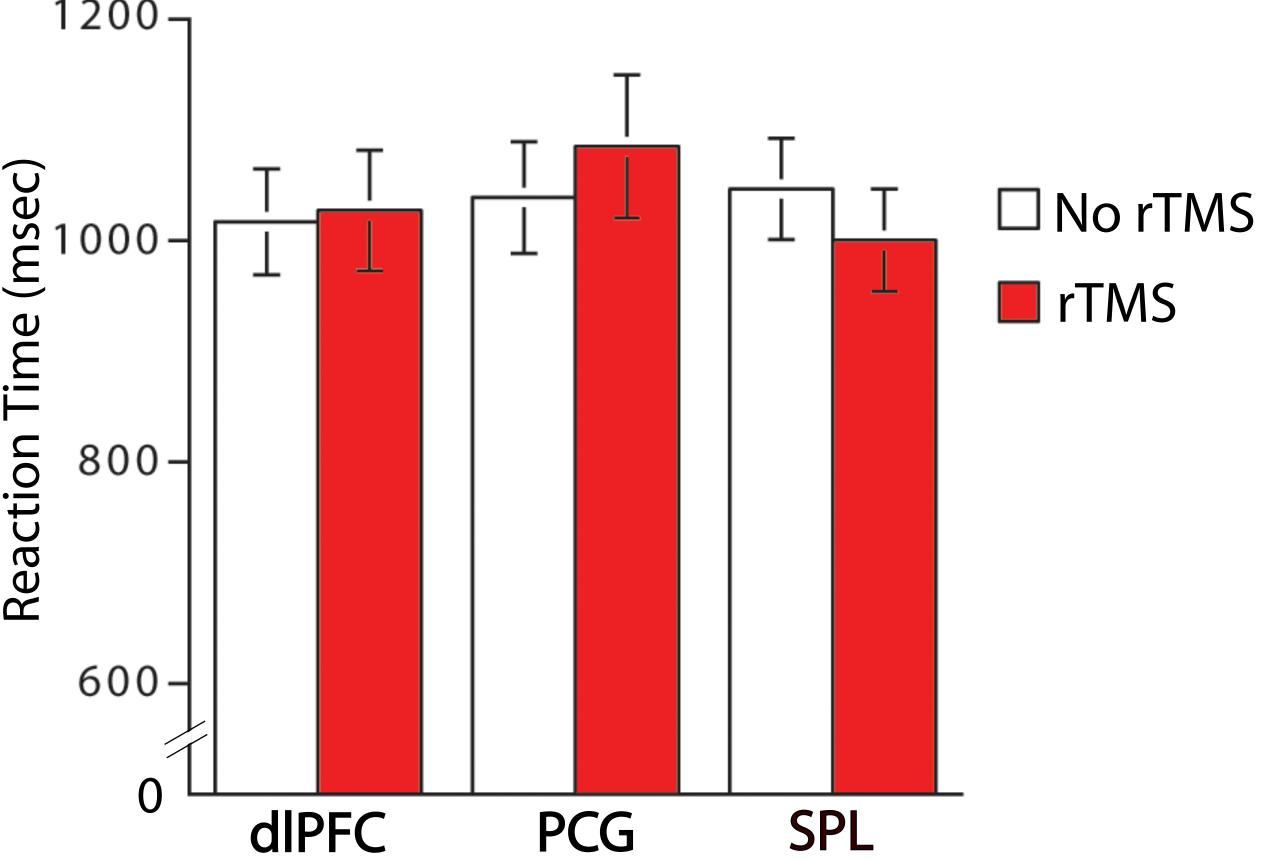
TMS Results

All Subjects (N=25) - Accuracy:



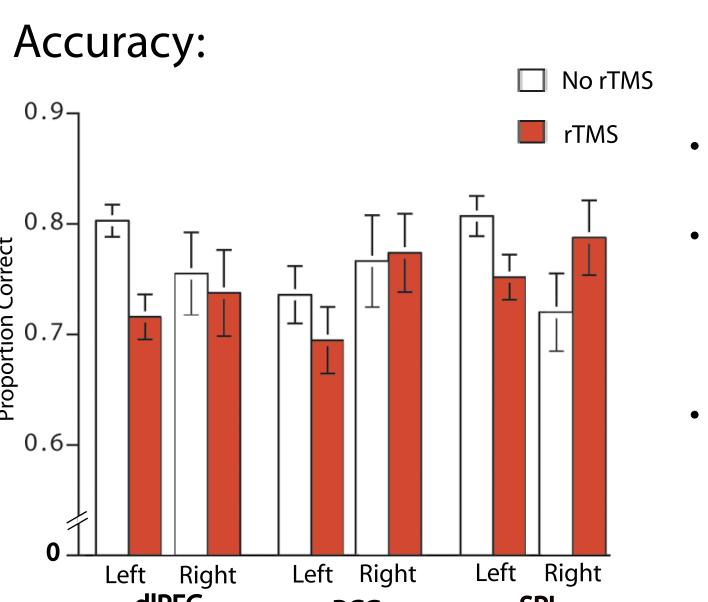
- Repeated measures ANOVA on accuracy: TMS (rTMS, no rTMS) x Brain area stimulated (dIPFC, PCG, SPL):
 - No main effect of area of stimulation [F(2,48)=1.87, n.s.].
 - A main effect of stimulation [F(1,24)=7.96, p=0.01].
- No interaction of Brain area xTMS [F(2,48)=1.35, n.s.].
- Pairwise comparison of dIPFC vs. PCG (x TMS) also nonsignificant [t(24)=-1.23,
- Signal detection analysis did not change results.
- Repeated measures ANOVA on d'revealed only a main effect of stimulation [F(1,24)=7.97, p=0.01].
- Repeated measures ANOVA on criterion revealed no significant effects.

All Subjects (N=25) - Reaction time:

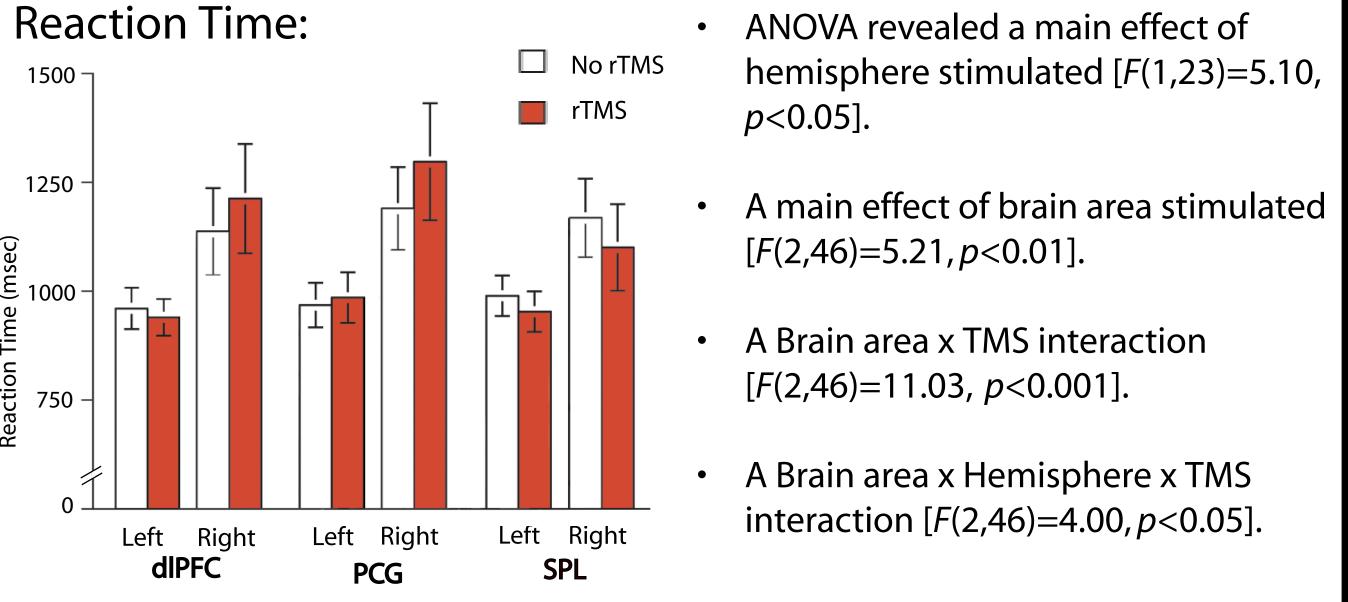


- Repeated measures ANOVA on reaction time:
- A borderline main effect of Brain area [F(2,48)=2.63, p=0.08].
- No main effect of stimulation [F(1,24)=0.03, n.s.].
- A reliable Brain area x TMS interaction [F(2,48)=7.87, p=0.001].
- Pairwise comparison of SPL vs. PCG (x TMS) was significant [t(24)=-3.33, *p*<0.005].
- Additional pairwise comparison of SPL confirmed that rTMS decreased reaction time [t(24)=-2.37, p<0.05].
- A comparison of MRI-guided and fMRI-guided stimulation revealed no differences on accuracy and reaction time.

Effect of TMS by hemisphere stimulated



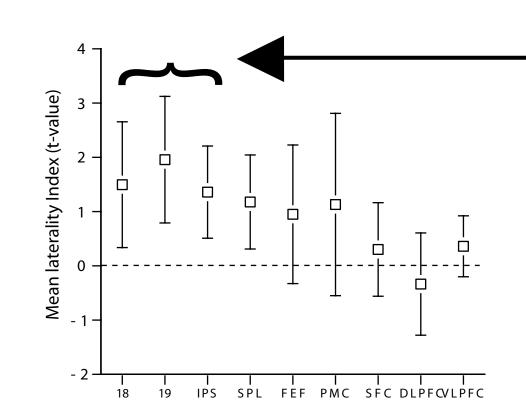
- No main effects of hemisphere stimulated, brain area stimulated, or
- Significant interaction of TMS x hemisphere stimulated [F(1,23)=12.32,



- ANOVA revealed a main effect of hemisphere stimulated [F(1,23)=5.10,
- [F(2,46)=5.21, p<0.01].
- A Brain area x TMS interaction [F(2,46)=11.03, p<0.001].
- A Brain area x Hemisphere x TMS interaction [F(2,46)=4.00, p<0.05].

Conclusions

- No evidence of regionally specific effect of rTMS on accuracy.
- Perhaps rTMS targeting of a more posterior region of the dorsal stream would affect accuracy.



Postle et al. (2004) assesed laterality of spatial delayperiod activity as an index of attention-based rehearsal, and found a posterior-to-anterior gradient of attentional effects in the dorsal stream.

- rTMS-related decrease in reaction time in SPL did not reflect a trade-off with accuracy or a change in criterion.
 - --> a priming effect?
 - (e.g., rTMS may facilitate access to the stored information that is necessary for the memory-guided decision and response)

References

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