Pre-registration: Effects of rhythmic TMS on visuospatial working memory capacity

Background:

The capacity of the Working Memory (WM) has been found to be limited to about 4 to 6 items. The theta-gamma-coupling theory proposes, that this is due to the nesting of fast gamma brain oscillations, each representing one item, into slower theta oscillations, binding them together during the retention interval. (Lisman & Jensen, 2013; for discussion see Sauseng et al., 2019) According to this theory the number of gamma cycles nested into one theta wave is the limiting factor of the WM capacity. Recent studies tested this by using tACS stimulation to manipulate the frequency of the theta wave. The results of these studies were mixed, but all at least showing a trend supporting the theory. (Bender et al., 2019; Vosskuhl et al., 2015; Wolinski et al., 2018) As tACS stimulation is limited in its spatial precision it might be that it not just stimulated brain areas associated with WM but distributed cortical regions and subcortical structures, confounding the results. Therefore we decided on testing the theory with a similar experiment, but using transcranial magnetic stimulation (TMS) to be able to focus stimulation exclusively on the right parietal cortex. We hypothesise that parietal TMS applied in a slow theta frequency during retention leads to a higher WM capacity contralateral to the TMS and applying TMS in a faster theta frequency shows the opposite effect.

Methods & Materials

Participants

We will test healthy, young participants between 18 and 35 years. Left- and righthanded as well as men and women will be tested. Excluded are colourblind people, since the visual task requires ability to distinguish colours. A standard TMS-screening will be undertaken beforehand to be able to exclude people who might be at risk having severe side effects from the TMS.

Recent studies found different effects for the interaction of condition and hemifield. (Bender et al., 2019; Wolinski et al., 2018) The mean of in these experiments found effects was taken for a power analysis using More Power. A 2x2 ANOVA analysis with eta2=0.219, alpha=0.05 and power of 0.8 suggested a total sample size of 30 participants. A one-sided paired t-Test power analyses using an effect size of d=0.44 (Wolinski et al., 2018) suggested a total sample size of 34 people. To reach a power of 0.8 in all the planned statistical analyses the latter sample size plus a buffer of 4 people results in 38 participants that will need to be tested.

Experimental Paradigm

A visual delayed match to sample task will be run. The task starts with a fixation cross on the screen. (19-inch CRT View Sonic G90fB monitor, resolution of 1024 x 768, 100 Hz refresh rate, placed approximately 80 cm from the observer.) In each trial sets of coloured squares will be presented on

both sides of the cross (100ms). A beforehand arrow (200ms) indicates if the right or left squares should be memorised. This is followed by a retention interval of 1900ms, after which a set of squares is shown again on screen for 2000ms. The participant has to decide if the colours of presented squares on the cued side are the same or different than before by pressing the left or right button of the mouse. Each trial is followed by a 5750ms to 5850ms long inter-trial interval. The visual load between the trials will range from 4 to 6 items. Each trial is altogether 10.000ms long. Figure 1 shows the temporal structure of the task.

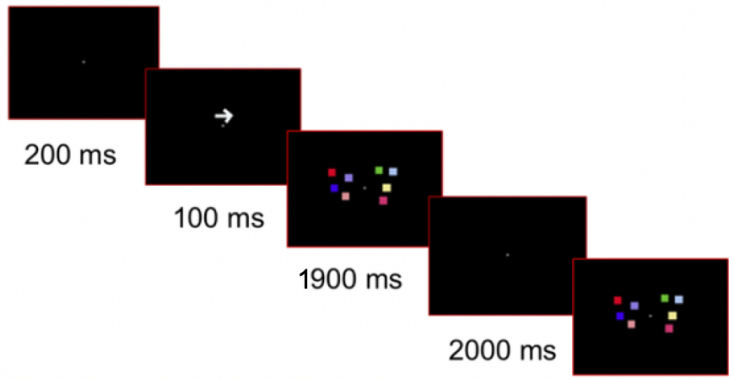


Fig. 1: Temporal structure of the delayed match to sample task

TMS parameter

TMS will be applied over the Intraparietal Sulcus (P4 according to the EEG 10-20 system) during the retention interval of each trial using a PowerMAG 100 research TMS stimulator with a double coil PDM 70 by Mag&More®.

The retention interval showing just the fixation cross on screen starts with a 300ms buffer, following the TMS stimulation applying 6 pulses in either 4Hz, 7Hz or 5.5Hz (baseline) frequency.

Due to different speed of the pulses the stimulation will last for either 1500ms, 858ms or 1092ms. The retention interval will be 1900ms long in every trial, consequently the buffer at the end ranges from 100ms up to 762ms.

Experimental Procedure

After participants filled out the screening form and signed the informed consent, the individual motor threshold of each participant is found by applying TMS over the hand area of the motor cortex. The applied intensity of stimulation will be low in the beginning and increased until the fingers twitch. Intensity will be decreased again until twitch is no longer found in 5/10 pulses. Stimulation in the experiment will be performed on the 80% level of this individual motor threshold.

Participants will perform two practice blocks of the delayed match to sample task of 16 trials each. One without TMS stimulation and the following one with TMS stimulation to get to know the task as well as the feeling of performing it during stimulation.

After this the experiment will start. 4 blocks of 60 trials will be presented. (each block takes 10min, resulting in 40min and 240 trials in total.) In each trial another frequency of TMS pulses will be applied randomised to avoid sequence effects. (Software used conducting the stimulus presentation is Presentation 0.71 by Neurobehavioural Systems, Inc.)
Between each block participants can take a break for several minutes.

Statistical Analysis

The 5.5Hz baseline corrected K-values for each participant will be calculated for both the 4Hz and 7Hz stimulation condition. (The K-value is a standardised measure for WM capacity, defined as K = S * (H – F), where H is the hit rate, F the false alarms and S the set size e. g. number of items in the trial.) A repeated measure 2x2 ANOVA with the factors hemifield (left, right) and stimulation frequency (4Hz, 7Hz, baseline corrected) will be used to analyse the interaction between hemifield and condition.
When this interaction is significant, one-tailed, paired t-Tests will be performed testing the baseline corrected K-values for both 4Hz and 7Hz stimulation condition against 0.
It is expected that the ANOVA shows an interaction between hemifield and condition and that the t-Test for the 4Hz-stimulation shows a significantly positive effect, while the t-Test for the 7Hz-stimulation shows a significantly negative effect.

References:

Bender, M., Romei, V., & Sauseng, P. (2019). Slow Theta tACS of the Right Parietal Cortex Enhances Contralateral Visual Working Memory Capacity. *Brain Topography*, *32*(3), 477–481. https://doi.org/10.1007/s10548-019-00702-2

Lisman, J. E., & Jensen, O. (2013). The Theta-Gamma Neural Code. *Neuron*, *77*(6), 1002–1016. https://doi.org/10.1016/j.neuron.2013.03.007

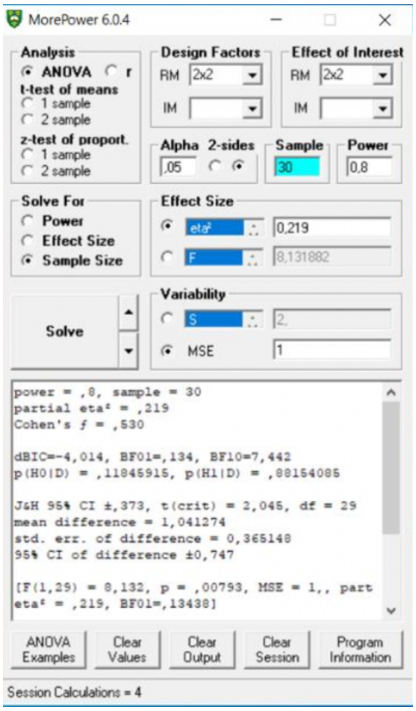
Sauseng, P., Peylo, C., Biel, A. L., Friedrich, E. V. C., & Romberg-Taylor, C. (2019). Does cross-frequency phase coupling of oscillatory brain activity contribute to a better understanding of visual working memory? *British Journal of Psychology (London, England: 1953)*, *110*(2), 245–255. https://doi.org/10.1111/bjop.12340

Vosskuhl, J., Huster, R. J., & Herrmann, C. S. (2015). Increase in short-term memory capacity induced by down-regulating individual theta frequency via transcranial alternating current stimulation. *Frontiers in Human Neuroscience*, *9*, 257. https://doi.org/10.3389/fnhum.2015.00257

Wolinski, N., Cooper, N. R., Sauseng, P., & Romei, V. (2018). The speed of parietal theta frequency drives visuospatial working memory capacity. *PLoS Biology*, *16*(3), e2005348. https://doi.org/10.1371/journal.pbio.2005348

Planning of sample

For ANOVA using More Power:



For t-Tests using R:

```
> pwr.t.test(power= 0.8, sig.level = 0.05, d = 0.44, type = "paired", alternative= "greater")

     Paired t test power calculation

              n = 33.33001
              d = 0.44
      sig.level = 0.05
          power = 0.8
    alternative = greater

NOTE: n is number of *pairs*
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