## BOOSTING WORKING MEMORY CAPACITY BY STRENGTHENING THE OSCILLATORY FUNCTIONAL FRONTOPARIETAL PATHWAY

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**Background:** Oscillatory brain activity serves long-range networks communication including the fronto-parietal network, involved in cognitive control functions such as working memory (WM).

**Aims:** Here we implemented and validated for the first time a novel information-based Transcranial Magnetic Stimulation (TMS) protocol to selectively enhance frequency-tuned long-range communication within the fronto-parietal network and impact WM performance in a frequency specific fashion.

**Method:** A paired TMS protocol, namely, frequency-tuned cortico-cortical paired associative stimulation (ccPAS), was applied to the right frontal and parietal nodes of the fronto-parietal network, to induce Hebbian-like plasticity to 180 healthy volunteers. In four groups (30 participants each), the stimulation could follow a fronto-parietal or a parieto-frontal direction with an interpulse interval set to a timing corresponding to the duration of each individual alpha (8-14Hz) or theta (4-7Hz) oscillatory peak. As a control, one group (N=30) received no stimulation (sham) while another group (N=30) received simultaneous stimulation unable to induce Hebbian plasticity. Electroencephalographic (EEG) fronto-parietal functional connectivity was measured before and after ccPAS, both during resting state and WM performance.

**Results:** EEG results showed enhanced fronto-parietal alpha-band connectivity following fronto-parietal alpha-tuned-ccPAS, both at rest and during task execution, but not following the opposite parieto-frontal direction or sham. This effect was frequency specific as no modulation was observed for control frequency bands, i.e., theta. Conversely, we found no effect after theta-tuned ccPAS, independently of the stimulation direction. Lastly, no effect was found after simultaneous stimulation. At the behavioural level, fronto-parietal alpha-tuned ccPAS induced an enhanced performance for visual stimuli ipsilateral to the stimulation site, compared to sham. Performance of all the other groups did not significantly differ from sham.

**Conclusions:** Here we demonstrated that alpha-tuned timing and direction of stimulation are critical in modulating long-range alpha-phase coherence between the stimulated areas. Furthermore, we provide direct evidence of oscillatory functional relevance. Specifically, we show the causal involvement of alpha rhythms in the top-down suppression of irrelevant items with a concurrent release of resources to facilitate memorization of the relevant ones.

**Keywords:** Working memory, Brain oscillations, Electroencephalography, Transcranial magnetic stimulation, Functional connectivity

## **Publications:**

- 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. <u>https://doi.org/10.1007/s10548-019-00702-2</u>
- Cooke, J., Poch, C., Gillmeister, H., Costantini, M., & Romei, V. (2019). Oscillatory properties of functional connections between sensory areas mediate cross-modal illusory perception. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 39(29), 5711–5718. <u>https://doi.org/10.1523/JNEUROSCI.3184-18.2019</u>
- Pietrelli, M., Zanon, M., Làdavas, E., Grasso, P. A., Romei, V., & Bertini, C. (2019). Posterior brain lesions selectively alter alpha oscillatory activity and predict visual performance in hemianopic patients. *Cortex*, *121*, 347–361. https://doi.org/10.1016/j.cortex.2019.09.008
- Chiappini, E., Borgomaneri, S., Marangon, M., Turrini, S., Romei, V., & Avenanti, A. (2020). Driving associative plasticity in premotor-motor connections through a novel paired associative stimulation based on long-latency cortico-cortical interactions. *Brain Stimulation*, *13*(5), 1461–1463. https://doi.org/10.1016/j.brs.2020.08.003
- Di Luzio, P., Borgomaneri, S., Sanchioni, S., Tessari, A., & Romei, V. (2021). Exposure to first-person shooter videogames is associated with multisensory temporal precision and migraine incidence. *Cortex*, *134*, 223–238. https://doi.org/10.1016/j.cortex.2020.10.009
- Ellena, G., Starita, F., Haggard, P., Romei, V., & Làdavas, E. (2021). Fearful faces modulate spatial processing in peripersonal space: An ERP study. *Neuropsychologia*, 156, 107827. <u>https://doi.org/10.1016/j.neuropsychologia.2021.107827</u>
- Fotia, F., Cooke, J., Van Dam, L., Ferri, F., & Romei, V. (2021). The temporal sensitivity to the tactile-induced double flash illusion mediates the impact of beta oscillations on schizotypal personality traits. *Consciousness and Cognition*, *91*, 103121. <u>https://doi.org/10.1016/j.concog.2021.103121</u>
- Trajkovic, J., Di Gregorio, F., Ferri, F., Marzi, C., Diciotti, S., & Romei, V. (2021). Resting state alpha oscillatory activity is a valid and reliable marker of schizotypy. *Scientific Reports*, *11*(1), 10379. <u>https://doi.org/10.1038/s41598-021-89690-7</u>
- Tarasi, L., Trajkovic, J., Diciotti, S., di Pellegrino, G., Ferri, F., Ursino, M., & Romei, V. (2022). Predictive waves in the autism-schizophrenia continuum: A novel biobehavioral model. *Neuroscience and Biobehavioral Reviews*, 132, 1–22. https://doi.org/10.1016/j.neubiorev.2021.11.006
- Tarasi, L., Magosso, E., Ricci, G., Ursino, M., & Romei, V. (2021). The Directionality of fronto-posterior brain connectivity is associated with the degree of individual autistic traits. *Brain Sciences*, *11*(11), 1443. <u>https://doi.org/10.3390/brainsci11111443</u>
- Di Gregorio, F., Trajkovic, J., Roperti, C., Marcantoni, E., Di Luzio, P., Avenanti, A., Thut, G., & Romei, V. (2022). Tuning alpha rhythms to shape conscious visual perception. *Current Biology*, *32*(5), 988-998.e6. <u>https://doi.org/10.1016/j.cub.2022.01.003</u>
- Trajkovic, J., Di Gregorio, F., Marcantoni, E., Thut, G., & Romei, V. (2022). A TMS/EEG protocol for the causal assessment of the functions of the oscillatory brain rhythms in perceptual and cognitive processes. *STAR Protocols*, *3*(2), 101435. https://doi.org/10.1016/j.xpro.2022.101435
- Bertaccini, R., Ellena, G., Macedo-Pascual, J., Carusi, F., Trajkovic, J., Poch, C., & Romei, V. (2022). Parietal alpha oscillatory peak frequency mediates the effect of practice on visuospatial working memory performance. *Vision*, *6*(2), 30. https://doi.org/10.3390/vision6020030
- Gillmeister, H., Succi, A., Romei, V., & Poerio, G. L. (2022). Touching you, touching me: Higher incidence of mirror-touch synaesthesia and positive (but not negative) reactions to social touch in Autonomous Sensory Meridian Response. *Consciousness and Cognition*, *103*, 103380. <u>https://doi.org/10.1016/j.concog.2022.103380</u>
- Di Luzio, P., Tarasi, L., Silvanto, J., Avenanti, A., & Romei, V. (2022). Human perceptual and metacognitive decision-making rely on distinct brain networks. *PLoS Biology*, *20*(8), e3001750. <u>https://doi.org/10.1371/journal.pbio.3001750</u>

- Di Gregorio, F., Petrone, V., Casanova, E., Lullini, G., Romei, V., Piperno, R., & La Porta, F. (2023). Hierarchical psychophysiological pathways subtend perceptual asymmetries in neglect. *NeuroImage*, 270, 119942. https://doi.org/10.1016/j.neuroimage.2023.119942
- Trajkovic, J., Di Gregorio, F., Avenanti, A., Thut, G., & Romei, V. (2023). Two oscillatory correlates of attention control in the alpha-band with distinct consequences on perceptual gain and metacognition. *The Journal of Neuroscience*, *43*(19), 3548–3556. https://doi.org/10.1523/JNEUROSCI.1827-22.2023
- Tarasi, L., Borgomaneri, S., & Romei, V. (2023). Antivax attitude in the general population along the autism-schizophrenia continuum and the impact of socio-demographic factors. *Frontiers in Psychology*, 14, 1059676. <u>https://doi.org/10.3389/fpsyg.2023.1059676</u>

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