# Neural bases of time processing: Combining neuroimaging techniques and clinical evidence

## ABSTRACT:

**Background**
There is growing interest in understanding cognitive mechanisms and neural bases of our sense of time. Despite the large amount of evidence, nevertheless, a number of open questions remains about the mechanisms by which our brain measures time.

**Aim**
The present project aimed at identifying whether there is a core mechanism for timing processes. Specifically, we investigated which brain areas subserve such mechanism, and their functional role.

**Methods**
1. High-density EEG study
2. rTMS study
3. EEG-TMS study
4. Clinical studies

**Results**
High-density EEG study - Brain source analysis of S1- and ISI-related ERP activity revealed activation of sensorial cortical areas and the supplementary motor area (SMA), respectively. We suggest that this area is the major cortical generator of the temporal CNV reflecting an automatic, action-independent mechanism underlying temporal expectancy.
rTMS study - The results showed that frontal TMS produced differential effects as a function of type of cuing. In symbolic cuing, TMS on either left or right frontal site (vs. sham) increased temporal orienting effects by reducing reaction times invalid trials. In rhythmic cuing, however, frontal TMS did not influence performance.
EEG-TMS study - Our results confirmed the reliability of the TMS-evoked N100 as a marker of cortical inhibition and provide insight into the neuromodulatory effects of 1-Hz rTMS.
Clinical studies - On-line comparison process between the two time intervals, reflected by the P1-P2 and LPCt amplitude and morphology, was impaired in patients with Parkinson's disease and support the presence of a deficit of memory for time in such clinical population.

**Conclusions**
Specific ERP components were shown to index processing of short interval durations. Our findings support the involvement of contingent negative variation (CNV) observed in frontal regions in time processing. Remarkably, the neural generators of the temporal CNV

have been located in the SMA. We may consider the CNV as an index of memory and decision. Furthermore, our researches show a role of both left and right DLPFC in the ability for temporal orienting. In patients with Parkinson's disease ERPs results suggest that the on-line comparison process between two different time intervals was distorted. This result support the presence of a deficit of memory for time in such clinical population.

**Keywords**
Time processing, High-density EEG, TMS, Parkinson Disease

## Published Work:

Cappon, D., D'Ostilio, K., Garraux, G., Rothwell, J. C., & Bisiacchi, P. (2016). Effects of 10Hz and 20Hz transcranial alternating current stimulation on automatic motor control. *Brain stimulation*. doi: 10.1016/j.brs.2016.01.001

Cappon, D., Jahanshahi, M., & Bisiacchi, P. (2016). Value and efficacy of transcranial direct current stimulation in the cognitive rehabilitation: A critical review since 2000. *Frontiers in Neuroscience, 10*, 157. doi: 10.3389/fnins.2016.00157

Cona, G., Bisiacchi, P., Scarpazza, C., & Sartori, G. (2016). Effects of cue focality on the neural mechanisms of prospective memory: A meta-analysis of neuroimaging studies. *Scientific Reports, 6*, 25983. doi: 10.1038/srep25983

Mioni, G., Grassi, M., Tarantino, V., Stablum, F., Grondin, S., & Bisiacchi, P. S. (2016). The impact of a concurrent motor task on auditory and visual temporal discrimination tasks. *Attention, Perception, & Psychophysics, 78*(3), 742-748. doi: 10.3758/s13414-016-1082-y

Cappon, D., D'Ostilio, K., Garraux, G., Rothwell, J. C., & Bisiacchi, P. (2015). Cortical modulation of automatic facilitation and inhibition by 10hz and 20hz transcranial alternating current stimulation *Brain stimulation, 8*(2), 356-357. doi: 10.1016/j.brs.2015.01.149

Cavazzana, A., Penolazzi, B., Begliomini, C., & Bisiacchi, P. (2015). Neural underpinnings of the "agent brain": New evidence from transcranial direct current stimulation. *European Journal of Neuroscience, 42*(3), 1889–1894. doi: 10.1111/ejn.12937

Cona, G., Arcara, G., Tarantino, V., & Bisiacchi, P. (2015). Does predictability matter? Effects of cue predictability on neurocognitive mechanisms underlying prospective memory. *Frontiers in Human* Neurosciences, *9*:188. doi: 10.3389/fnhum.2015.00188

Cona, G., Kliegel, M., & Bisiacchi, P. (2015). Differential effects of emotional cues on components of prospective memory: An ERP study. *Frontiers in Human Neuroscience*, *9*:10. doi: 10.3389/fnhum.2015.00010

Cona, G., Scarpazza, C., Sartori, G., Moskovitch, M., & Bisiacchi P. S. (2015). Neural bases of prospective memory: A meta-analysis and the "Attention to Delayed Intention" (AtoDI) model. *Neuroscience & Biobehavioral Reviews, 52,* 21-37.doi: 10.1016/j.neubiorev.2015.02.007

Mento, G., Tarantino, V., Vallesi, A., & Bisiacchi, P. (2015). Spatiotemporal neurodynamics underlying internally and externally driven temporal prediction: A high spatial resolution ERP study. *Journal of Cognitive Neuroscience, 27*(3), 425-439. doi:10.1162/jocn_a_00715

Bisiacchi, P., Cona, G., Tarantino, V., Schiff, S., Montagnese, S., Amodio, P., & Capizzi, G. (2014). Assessing inter- and intra-individual cognitive variability in patients at risk for cognitive impairment: The case of minimal hepatic encephalopathy. *Metabolic Brain Disease, 29*(4), 945-953. doi: 10.1007/s11011-014-9529-0

Casula, E., Tarantino, V., Basso, D., Arcara, G., Marino, G., Toffolo, G., Rothwell, J. C., & Bisiacchi, P. (2014). Low-frequency rTMS inhibitory effects in the primary motor cortex: Insights from TMS-evoked potentials. *NeuroImage, 98*, 225-232. doi: 10.1016/j.neuroimage.2014.04.065

Cavazzana, A., Begliomini, C., & Bisiacchi, P. (2014). Intentional binding effect in children: Insights from a new paradigm. *Frontiers in Human Neurosciences, 8*:651. doi: 10.3389/fnhum.2014.00651

Correa, Á., Cona, G., Arbula, S., Vallesi, A., & Bisiacchi, P. (2014). Neural dissociation of automatic and controlled temporal preparation by transcranial magnetic stimulation. *Neuropsychologia, 65*, 131-136. doi: 10.1016/j.neuropsychologia.2014.10.023

## Researcher's Contacts:

Patrizia S. Bisiacchi
Full Professor
Psychobiology & Psychological Physiology
Department of General Psychology
University of Padova
Via Venezia 8
35121 Padova
Italy

Tel. 0039 49 8276609
http://lcnl.psy.unipd.it/