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**Introduction** The Bereitschaftspotential (BP) is a slow ERP associated with motor preparation<sup>1</sup>, starting 1-3s before movement onset, peaking on central scalp electrodes<sup>2</sup> and originating in the left SMA. The brain network underlying BP time course is still unclear. Possibly, a different organization within the premotor or parietal regions in the EEG  $\beta$  and  $\gamma$  bands functional networks occurs<sup>3</sup>, but conclusive evidence is missing.

Recently, TMS-EEG integrated systems have been used to probe connectivity changes among different cognitive states<sup>4</sup>, allowing to measure cortical excitability and functional connectivity of a target region. Here, we recorded TMS evoked-potentials (TEP) stimulating the left-SMA before the onset of stimuli requiring motor responses in order to assess if and how cortical excitability and functional connectivity of this region change as the BP increases.

## Materials and methods

**TMS parameters:** Stimulation timing was set, according to the BP time course, at two SOAs: -700 ms (early BP) or -300 ms (late BP) from stimulus onset (90 trials per condition). Single pulse TMS was delivered over the SMA (2 sessions) or V2 (2 sessions) inducing an estimated electric field of 100 V/m computed on TMS hotspot by the NBS system (Eximia, Nexstim).

**EEG recording:** 60-channels EEG was recorded with a sample-and-hold system, 1450Hz sampling rate, noise masking applied.

**Analyses of Cortical excitability:** Cluster based analysis comparing within stimulation site TEPs amplitude in the two SOAs.

**Functional connectivity:** Whole-head WPLI in  $\theta$ ,  $\alpha$ ,  $\beta$ ,  $\gamma$  bands.

**Participants:** Fourteen healthy participants (8 females, mean age=24,3y, SD=2.2y)

**Design:** Five TMS-EEG recordings of 180 pulses each were acquired in one experimental session.

**Experimental task:** Go/No-Go task (50% ratio)<sup>5</sup>.

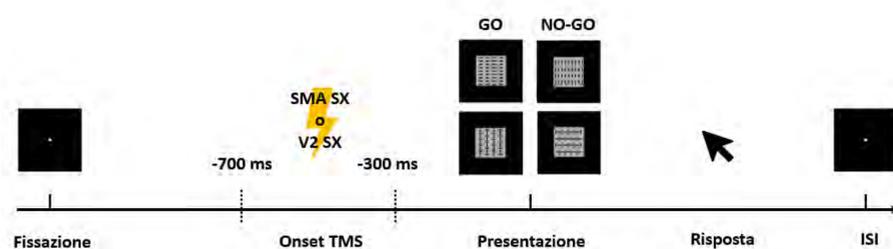


Fig. 1: Experimental timeline

## Results

**TMS Evoked Potentials** A TEP component peaking 45ms after TMS pulse was significantly greater when TMS was applied over SMA at -300ms SOA compared to -700ms SOA. Targeting V2 induced no difference in cortical excitability between the SOAs.

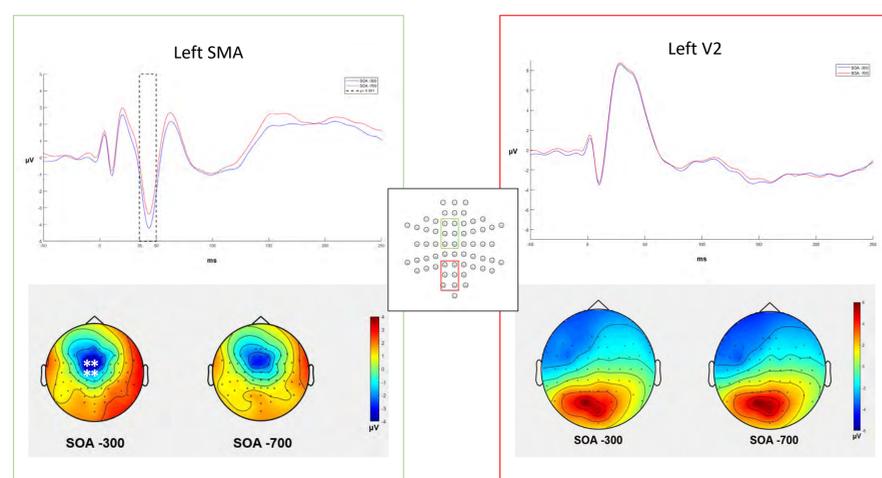


Fig. 2: TEPs recorded from the SMA cluster (green box, upper line) and from the V2 cluster (red box upper line) in the two SOAs conditions. Bottom lines: scalp topographies of the component peaking around 45ms from TMS onset. White asterisks indicate significant differences.

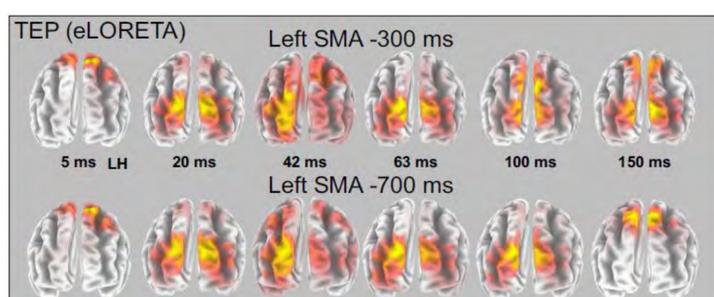


Fig. 3: Source reconstruction of TEPs time-course in the two SOAs conditions when stimulating the left SMA. Activity spreads from TMS hotspot to several connected cortical sites. Differences are prominent from 42ms post TMS.

## Functional Connectivity

At -300ms from stimulus onset  $\gamma$ -band network in fronto-central areas was greater compared to -700ms SOA.

$\beta$  band network was wider, and did not differ between SOAs

Targeting the left V2 at -300ms SOA triggered a wide  $\theta$  band network between occipital and frontal regions compared to -700ms SOA.

$\beta$  band network did not differ between SOAs

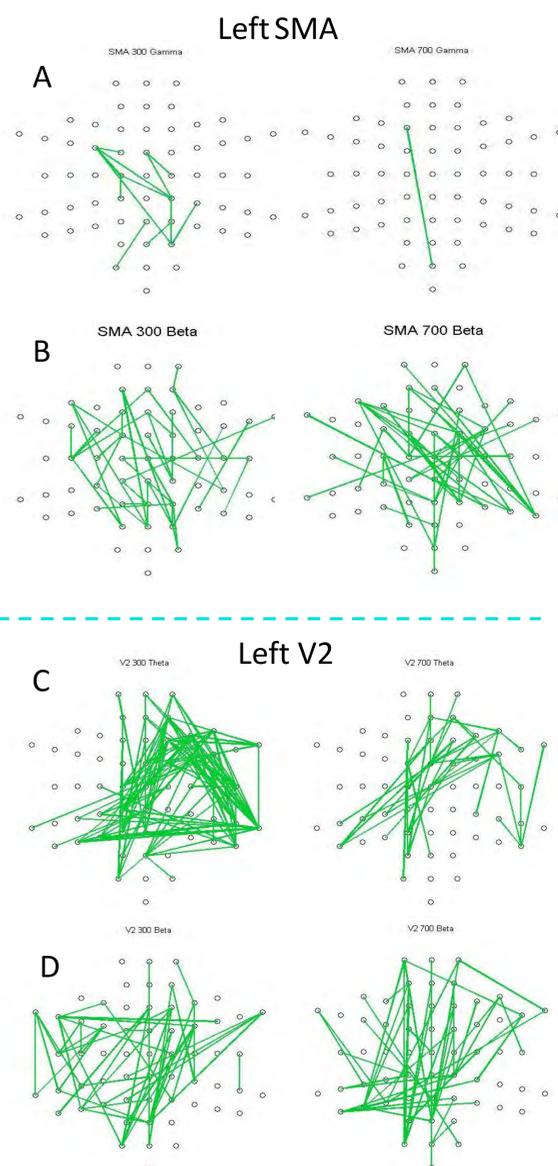


Fig. 4: Functional connectivity in the gamma (A) and beta (B) bands triggered when stimulating the left SMA, and in the theta (C) and beta bands with TMS over the left V2

**Discussion** The BP is a complex event, whose time-course includes different functional meanings. As it reaches its peak, SMA activity increases, as indexed by a greater response to TMS and from the source reconstruction. This greater activity reflects an increased connection between the SMA and premotor and motor regions, as a greater  $\gamma$  band connectivity was found in late compared to early BP. This indicates a gradual specialization of the activity of the SMA in building a voluntary motor act. Conversely, bottom up activity increases after V2

stimulation at late BP stages, as indicated by  $\theta$  band connectivity modulation.  $\beta$  band connectivity, instead, did not change neither according to TMS site, nor to TMS SOA. This is possibly due to its role in proactive attentional control.

**References** <sup>1</sup>Shibasaki H, & Hallett M (2006) Clin neurophys; <sup>2</sup>Di Russo et al. (2017) Neurosci & Biobehav Rev; <sup>3</sup>Kim et al. (2017) Front hum neurosci; <sup>4</sup>Pisoni et al. (2018) Neuroimage; <sup>5</sup>Bianco et al. (2017) Neuroscience.