

User Research

On the combination of EEG transcranial magnetic stimulation

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A great advantage of EEG is the ability to acquire simultaneous measurements of activity in the entire brain, thus providing a broader picture of the cortical responses during a task execution or a given state of the subject (i.e., physiological or pathological). Nevertheless, as all neuroimaging techniques, EEG has its limitations. It only identifies correlational links between brain activity and behaviour/state. Combining two different methods, such as transcranial magnetic stimulation (TMS) and EEG, has the advantage of overcoming this limitation, thereby supplementing the information provided by correlational analysis with a technique that can establish a causal link between brain function and behaviour. The combination of TMS with EEG provides unique information on cortical reactivity and connectivity and is a powerful tool to directly investigate the effects induced by TMS on brain activity (1, 2). Co-registration also allows to study the TMS evoked activity from silent brain areas, so it theoretically extends our possibilities to spatially and functionally characterize complex brain networks (2, 3). Finally, TMS EEG co-registration can be used to infer the role of specific brain activity (4). Nevertheless, even after the introduction of recording systems which can work in high magnetic field, preventing saturation of the amplifiers, TMS-EEG co-registration may be technically challenging (5). We still miss crucial information about what the best technical conditions to record such a signal are and, above all, how long the TMS-induced artifact lasts. In this vein, we conducted a study (6) to provide experimental data about the artifact duration and to investigate the influence of some parameters on TMS-EEG co-registration.

To better characterize the artifacts and to exclude any cortical responses, a phantom 'head' was employed and then compared to the results obtained from a knee stimulation (a model with skin properties similar to the scalp but without cortical responses) and a cortical stimulation.

EEG signal was acquired with BrainAmp 32 MR plus or BrainAmp DC, with a resolution of 0.1, band-pass filtered at 0.01–1000 Hz and sampled at 5000 Hz. The artifact shape and duration induced by

different types of Magstim stimulator (monophasic, biphasic with four boosters, and biphasic with single power supply module), four figure-of-eight coils (standard 50-70 mm, custom 25-70 mm), intensities (ranging from 10% to 100% of the stimulator output) and frequencies (single pulse, 5 Hz and 20 Hz) was compared.

Most of the sessions were recorded from TMS-compatible sintered Ag/AgCl electrodes (EasyCap GmbH, Herrsching, Germany) i.e., rings of 2 mm thickness, with inner and outer diameters of 6 mm and 12 mm, respectively. Moreover to verify whether the electrodes shape is able to modify the artifacts features, some electrodes had a 2 mm slit in the ring or the slit closed by means of silicone. Additional recordings were done with small sintered Ag/AgCl disks that were 1 mm thick and 3 mm in diameter, mounted in an elastic cap (EasyCap GmbH, Herrsching, Germany).

Our main result indicates that, regardless to the above cited parameters, TMS induced artifact always lasted about 5 ms (5–5.6 ms). When the knee was stimulated, we found an induced artifact comparable in length to that evoked by the stimulation of the phantom. Finally, when cortical stimulation was compared to the other models, a similar time-course was found up to 5 ms. Interestingly, differences just appeared at about 5 ms after the TMS pulse when the EEG signal went back to baseline for all conditions with exception of the cortical stimulation in which two additional deflections appeared at 6 and 8 ms.

Besides the above described TMS-artifact, several milliseconds after TMS pulses, the signal was contaminated by a coil-recharge-artifact that was present with biphasic stimulators, but not with the monophasic one. Its amplitude was constant ($\pm 12 \mu\text{V}$), while its latency increased with the increase of the power strength, i.e., from 8 to 70 ms.



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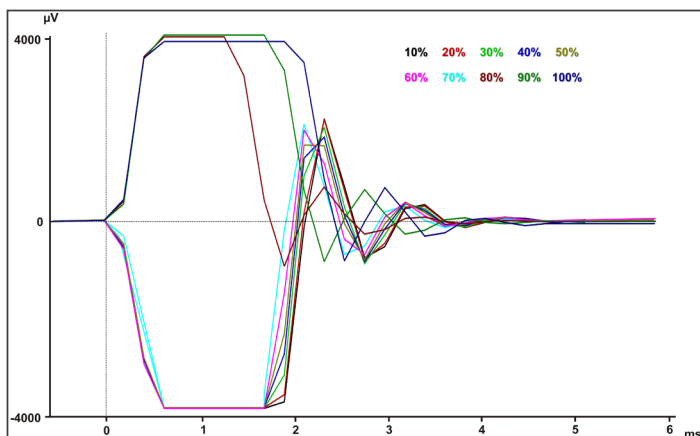


Figure 1. Effect of stimulus intensity (from 10 to 100% of MSO) on the artifact length. Each line represents the average of 100 stimuli.

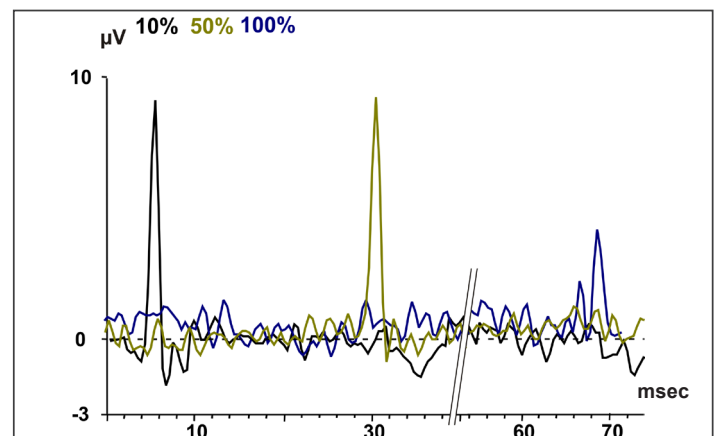


Figure 2. Amplitude and latency of the later artifact in the EEG signal as a function of stimulus intensity (% of MSO).

These data were collected using an EEG recording system that allows continuous data recording without saturation of the signal and does not require pinning the preamplifier output to a constant level during TMS delivery. In such a way, we were able to follow the signal evolution even in a time window usually left out for technical reasons. We also verified that high frequency TMS was not able to induce any modulation of the artifact amplitude or duration per se. Because of this, no summation of the induced artifacts was found.

Nevertheless, the artifact induced by the TMS pulse is not the only problem. We also found that the wires should be arranged in an orientation away from the coil or coil cable, regardless of where stimulation takes place on the head. The reorientation of the wires before stimulation can therefore help to record cleaner signals. The impedance values also play an important role in the artifact contamination, as we found that for high values (about 20 k Ω) signal recovering time was slower (15–20 ms) and artifact amplitude was more than two times the amplitude than the lower impedance condition (0–3 k Ω). To avoid additional noise it should also be useful to hold the lower surface of the coil approximately 1 mm from the stimulating electrodes.

It is important to consider that TMS is also inducing non specific or indirect responses in the brain, which may influence the EEG recording (2). These non specific, task unrelated contaminations consist of auditory responses (due to the coil click); of somatosensory

responses (mostly due to trigeminal afferents or afferent responses after motor cortex stimulation); of muscular responses (because of eye blink startle reflexes, eye movements induced by the coil click, or peripheral muscular contractions due to peripheral stimulation). Also, general arousal due to TMS or auditory inter-sensory facilitation by the coil click might be present. Other challenges come from the stimulator recharging artifacts which in some cases could overlap real cortical responses, even if it is clearly visible as a short transient response, with fixed latencies and that correlate with stimulation intensity. All these effects should be eliminated or masked whenever possible. In instances where this is not possible, these artifacts should, as part of the experimental design, be reproduced in separate conditions (i.e., via control stimulation at appropriate sites), and their effects should be taken into account during data analysis.

A critical point is the choice of the acquisition parameters. We suggest using a high sampling rate, 5000 Hz and a low pass filter at 1000 Hz. Lower sampling rate or filters will cause a rippling of the signal, an increase in the duration and therefore will limit the possibility of getting information from the first milliseconds after the pulse. In conclusion data suggest that it is possible to analyze the TMS evoked response starting from 5 ms after the pulse onset. The capability of combining EEG with TMS represents an important innovation that will open new frontiers in the field of basic and clinical neuroscience. ●

References

- 1) S. Komssi, S. Kahkonen (2006) *The novelty value of the combined use of electroencephalography and transcranial magnetic stimulation for neuroscience research. Brain Res Rev* 52, 183–92.
- 2) C. Miniussi, G Thut (2009) *Combining TMS and EEG offers new prospects in cognitive neuroscience. Brain Topogr* doi: 10.1007/s10548-009-0083-8.
- 3) P. Taylor, V Walsh, M Eimer (2008) *Combining TMS and EEG to study cognitive function and cortico–cortico interactions. Behav Brain Res* 191, 141–14.
- 4) G. Thut, C. Miniussi (2009) *New insights into rhythmic brain activity from TMS-EEG studies. Trends Cogn Sci* 13, 182–9.
- 5) C. Bonato, C. Miniussi, P.M. Rossini (2006) *Transcranial magnetic stimulation and cortical evoked potentials: a TMS/EEG coregistration study. Clin Neurophysiol* 111, 699–1707.
- 6) D. Veniero, M. Bortoletto, C. Miniussi (2009) *TMS-EEG co-registration: On TMS-induced artifact. Clin Neurophysiol* 120, 1392–1399.