

Did you know...!?

Combining EEG with Transcranial Magnetic Stimulation (2)

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Introduction

This review is the second instalment in a series on combined electroencephalography and transcranial magnetic stimulation (EEG-TMS). The first part discussed the fundamental principles and properties of TMS, and the conceptual grounds motivating combining it with other methods (see also [1-4]). Having discussed the ‘whys’, we now cover the ‘hows’: the recording, analysis and interpretation of EEG-TMS data. To acquire the optimal EEG-TMS recordings requires setting up and tweaking several different aspects of the TMS and EEG hardware and software, and each of these is an active research area, going through continual development and refinement. Having acquired clean data, a substantial other field of interest is the development of the best procedure for analysing it.

Data Acquisition

Initially, a TMS pulse represented a considerable obstacle to those wishing to record a clean EEG signal from nearby EEG electrodes. The problem is that magnetic pulses from TMS can interfere not only with brain activity but also with any electronic equipment in the immediate proximity e.g. the set-up required for recording that brain activity. In the past, an unchecked TMS pulse would overload normal neurophysiological apparatus for several seconds. What is needed is some means of preventing the amplifier from being saturated by the sudden surge which the TMS pulse induces in the electrodes and leads. Since it was first demonstrated that it is possible to protect an EEG amplifier from the TMS pulse so that veridical data can be recorded from a full cap of electrodes within milliseconds of the TMS pulse [5], there are now several solutions available for dealing with and limiting the effect of TMS on the EEG. One solution is to ‘clamp’ or ‘sample and hold’ the amplifier – essentially this is akin to switching the EEG amplifier away from the circuit connecting it to the EEG electrodes so that the amplifier is protected from the surge of current which TMS induces in the electrode and leads. Another approach is to use an amplifier with a large dynamic range such that the TMS pulse does not lead to such saturation (e.g. the BrainAmp DC), and then explicit clamping is unnecessary. Either of these approaches reduces the effect of TMS to very brief spike, referred to as an ‘artifact’ in the data, lasting milliseconds, rather than seconds. Naturally the nature of this artifact – its length and profile – is being researched extensively, to which we now turn.

Limiting the Artifact

Veniero et al. recently characterised the early part of the TMS artifact by comparing the effects of TMS on EEG on the head with two ‘phantom’ controls [6], one on the knee, and the other on a melon. In addition to showing that the spike was similar across these preparations, this enabled demonstrating a secondary artifact which

can occur when TMS machines recharge (this recharging artifact occurred reliably at particular times for particular intensities). Again an alternative approach is to use TMS pulses or machines that do not recharge during the interval of the interest. There are particular settings to the EEG recording which can also maximise EEG quality – in particular using a high sampling rate and sensitivity to characterise the artifactual spike and also to apply as little filtering as possible: filters could interact with the spike in the data to produce a ripple lasting on the order of the seconds. It is also important to prevent any movements of the TMS coil on the head on or relative to the electrodes because this will naturally lead to disturbances in the signal, as would occur with any physical contact with the EEG electrodes. There are also developments in EEG placement which can limit the TMS-EEG artifact: a tiny (and very short) needle has been used to mini-puncture the skin of the scalp and shown to reduce the amplitude and width of the TMS artifact in the EEG, compared to the conventional ‘rubbing’ method of EEG preparation [7].

Data Analysis

One way to remove the spike of the artifact from the data is simply to excise it out of the data and replace the deleted section with either an interpolated, generated or repeated data-set: alternatively, recent developments in software are investigating automated source approaches to TMS artifact reduction [8]. An additional and very important source of artifact is quite apart from that caused by the mechanical or electrical effect on the wires or electrodes: rather this stems from the activation by TMS of the muscular tissue of the scalp. This brief contraction leads to the ‘knocking’ or ‘tapping’ sensation which experimental participants report during TMS. This is naturally vital to be controlled for in all TMS studies, let alone TMS-EEG studies: usually by comparing TMS over an active site of interest to a control site. This also controls for the acoustic stimulation that accompanies TMS – a loud click. The muscular activation however presents a different challenge to EEG recording. To address this, developments in EEG analysis are tackling how to separate out the EMG caused by the muscle activation after TMS, which is especially apparent within the first 50 ms and if stimulating through the jaw muscles near Broca’s area, and also from premotor cortex [9, 10].

Data Interpretation

Given the ERP elicited by the TMS pulse – the TMS-evoked potential or TEP – the next question is what exactly it represents. The TEP presumably reflects some of the neural correlate of perceiving the TMS pulse – for example the click [11]. This means that, as



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with TMS studies of behaviour, EEG-TMS studies need to compare TMS over one site with either a different site and/or a different experimental condition in order to control that some part of the elicited EEG response is driven by the neural representation of the somatosensory or acoustic TMS artifact. The TEP is increasingly being demonstrated to be highly reliable but also extremely sensitive. For example, TEPs are broadly consistent across sessions a week apart [12]. At the same time the TEP is sensitive to stimulation intensity and coil angle [13]. Changes in the orientation with which the coil is held can lead to drastic effects on the TEP e.g. comparing the results of holding the coil at different orientations varying by 90 degrees, over the same primary motor site [14]. The TEP amplitude scales with intensity and varies across area (e.g. M1 vs PFC) [15]. Given this sensitivity it is logical to ask what the resolution of TMS-EEG is. Given that the TMS pulse peaks within approximately 100 microseconds and EEG sampling rates of at least 5000 Hz being simply ‘another setting’ of the amplifier, then the temporal resolution seems initially extremely

high. In practice there is a theoretical caveat to note, being that normally changes in the EEG (whether in the time or frequency domain) need to exceed a certain magnitude to become statistically significant. Some of these measures, such as time-bin averages in ERP or frequency decompositions in EEG, need to be evaluated over a period of several data-points. In addition a latency of a change in the EEG between two conditions only represents the upper bound of the time at which neural activity between two conditions ‘truly’ differed: a change could have occurred earlier and yet not been detectable by EEG. The immediate spatial resolution of TMS is often quoted as being of the order of millimetres given, for example, the change in position that can elicit or fail to elicit phosphenes or motor evoked potentials. There are now of course a collection of different approaches to boosting the spatial resolution of EEG. In the long run, experimental design is likely to have the greatest role in the spatial or temporal resolution of the method used, and so it may be sensitive to think of ‘cognitive resolution’ as has been suggested with TMS [16]. ●

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