MEP-ART: A system for real-time feedback and analysis of transcranial magnetic stimulation motor evoked potentials

Margaret Skelly*, Brain Plasticity and NeuroRecovery Laboratory, Louis Stokes Cleveland Veterans Affairs Medical Center, Cleveland, OH, USA

Ahlam Salameh, Brain Plasticity and NeuroRecovery Laboratory, Louis Stokes Cleveland Veterans Affairs Medical Center, Cleveland, OH, USA

Case Western Reserve University School of Medicine, Cleveland, OH, USA

Case Western Reserve University Department of Biomedical Engineering, Cleveland, OH, USA

Jessica McCabe, Brain Plasticity and NeuroRecovery Laboratory, Louis Stokes Cleveland Veterans Affairs Medical Center, Cleveland, OH, USA

Svetlana Pundik, Brain Plasticity and NeuroRecovery Laboratory, Louis Stokes Cleveland Veterans Affairs Medical Center, Cleveland, OH, USA

Case Western Reserve University School of Medicine, Cleveland, OH, USA

Dear Editor:

Transcranial magnetic stimulation (TMS) of primary motor cortex (M1) is commonly used to evaluate functional integrity of the corticospinal tract (CST). TMS-elicited motor-evoked potentials (MEPs) recorded with electromyography (EMG) have been used to measure excitability of the corticospinal motor pathway [1]. The quality of recorded MEP data can be enhanced by real-time feedback of baseline EMG activity, visualization of MEPs, and online analysis during the TMS session [2]. Several open source TMS analysis toolboxes exist [3–6]. Although the existing tools are very useful, limitations in their functionality remain. For example, several toolboxes are limited to analyzing data after the TMS recording session, when it is too late to address the factors that lead to poor quality of the recorded data or insufficient collection of MEP data [3–5]. While one toolbox provides online data processing, the analysis is limited to the MEP recruitment curve (MEP-rc) only.

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*Corresponding author. Louis Stokes Cleveland VA Medical Center, 10701 East Blvd (Research 151-W), Cleveland, OH, 44106, USA

mxs70@case.edu (M. Skelly).

Author contributions

MS and SP designed the toolbox. MS wrote the toolbox code. MS, AS, and JM wrote the manuscript. All authors discussed and revised the manuscript.

Declaration of interest

None.
Therefore, to address these limitations we have developed a comprehensive, modular, open-source toolbox to record and analyze MEP data in real time during the TMS recording session (Fig. 1A).

MEP-ART (MEP Analysis in Real Time) is an open source MATLAB-based toolbox available at https://github.com/Pundik-BPNR-Lab/MEP-ART. MEP-ART is designed to perform real-time data analysis by: 1) providing continuous visual feedback of EMG activity; 2) monitoring stimulator output (SO); 3) displaying and recording EMG at the time of stimulation; and, 4) extracting and processing MEP amplitude in an analysis module. The analysis modules include: 1) MEP-rc fitting; 2) short interval intracortical inhibition (SICI) and intracortical facilitation (ICF) display; and, 3) EMG averaging.

Visualization and recording of EMG and MEPs with immediate analysis provides real-time quality assurance. Live analysis of data allows for assessment of data quality and informs the user whether collection of additional data is warranted.

**Technical features**

- MEP-ART consists of three apps run in three separate instances of MATLAB: 1) Activity Monitor (ActMon) (Fig. 1B); 2) Display Data (DispData) (Fig. 1C); and 3) Magnetic Stimulator Monitor (MagSpy) (Fig. 1D). The analysis modules (Fig. 1E) are run within DispData. Communication among the apps is achieved using memory-mapped files, a mechanism where apps can map part of their memory to a location in a shared file.

- Magnetic stimulator: The code currently operates with Magstim 200\textsuperscript{2} (and BiStim\textsuperscript{2}) (Magstim Inc., Eden Prairie MN). Brainsight neuronavigation (Rogue Research Inc., Montreal, Canada) is connected via a serial cable to the Magstim. Brainsight continuously queries Magstim’s status. Magstim’s response is returned to Brainsight and sent to MagSpy (Fig. 1D) via a custom-made serial splitter and serial-to-USB cable. MagSpy continuously reads the SO and relays it to other modules. Magstim generates a trigger pulse at the time of stimulation that is sent to the EMG recording system.

- EMG system: BrainAmp ExG (Brain Vision LLC, Morrisville, NC) is used for collecting EMG with up to 8 channels. The system and accompanying software amplify and display EMG; the data along with the trigger pulse from the stimulator are then streamed to the Activity Monitor (ActMon) (Fig. 1B).

- EMG visualization: ActMon provides continuous feedback of EMG activity to assist the subject with maintaining a desired EMG level. When ActMon detects a trigger, it relays EMG data to the MEP Display (DispData) (Fig. 1C). DispData shows EMG data within a specified (customizable) window. It displays the baseline EMG level, whether it is in the target range, the MEP amplitude (measured as the difference between the maximum and minimum signal within the adjustable timeframe after the stimulus), and a checkbox indicating if the data is to be included in analysis.
Analysis module selection (Fig. 1E): Information from DispData and MagSpy are relayed to a selected analysis module (Fig. 1F–H). There are three analysis modules.

1. Recruitment curve fitting module: MEP amplitude from DispData is plotted against SO from MagSpy.

A Boltzmann sigmoid function is fitted to the recorded MEPs:

$$\text{MEP}(S) = \text{MEP}_{\text{min}} + \frac{\text{MEP}_{\text{max}} - \text{MEP}_{\text{min}}}{1 + e^{m(S_{50} - S)}}$$

where $S$ is SO, $\text{MEP}_{\text{max}}$ and $\text{MEP}_{\text{min}}$ are the maximum and the minimum asymptotes, $m$ is the maximum slope which occurs at $S_{50}$, the inflection point between $\text{MEP}_{\text{max}}$ and $\text{MEP}_{\text{min}}$. The display includes the curve’s parameter estimates, their confidence intervals, curve fit $R^2$, and the area under the curve. The display of datapoints and the estimated curve assist in determining what additional SO levels may improve curve fit.

2. SICI/ICF analysis module: MEP amplitude from DispData is plotted in 3 columns depending upon the stimulus being delivered: test stimulus, SICI, or ICF. The 98% confidence intervals surrounding the mean value of each stimulus type facilitate the operator in determining if enough data have been recorded.

3. EMG averaging module: DispData window contains a checkbox to indicate if the displayed trial of data should be included in analysis. The operator can scroll through trials and select/unselect trials. Selected trials are shown (light lines) with their average (bold line) in the averaging module.

Data saving and offline re-analysis: EMG data for each stimulus is saved in csv files along with the SO and whether it was selected or unselected to include in the analysis. The datapoints used in each analysis module and analysis results are saved in csv and text files. The software includes an offline application to read, display, and analyze the data using the same real-time analysis modules. During analysis, whether offline or online, individual datapoints can be unselected and excluded from analysis as needed.

In summary, we have developed a real-time MEP recording and analysis system. The continuous EMG activity indicator, MEP data display, and three analysis modules provide real-time feedback during the data recording session. This feedback helps identify EMG artifacts, ensure appropriate SO levels are employed, and verify if enough data are recorded. The result is a more efficient and higher quality TMS/MEP data collection experiment.

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Fig. 1. MEP-ART implementation overview. A – TMS data collection setup. Subject has EMG electrodes on the lower limb connected to the EMG system. The TMS Power Level or stimulator output (SO) is sent to the computer running Brainsight neuronavigation software and MEP-ART. The TMS Trigger pulse is sent to the EMG System that relays it along with the EMG Data Stream to the MEP-ART Computer. B – Activity Monitor (ActMon) displays the real-time EMG activity level of a selected EMG channel. The goal/desired EMG level (horizontal bold line) and allowable range (dashed lines) are displayed. The color of the vertical bar changes from yellow and orange when activity is below range to green when in range and purple and red when above range. EMG activity is root mean squared value averaged over a moving 0.5 s window. C – Display Data (DispData) plots the EMG time course for a stimulus pulse. The time displayed before and after the stimulus are editable. Draggable green vertical lines delineate the time interval to use for determining MEP amplitude (red, upper right). Pre-stimulus EMG level is in the lower left of the axes. The lower left of the figure window contains buttons to scroll through previous trials and a checkbox to select/unselect trials to include in analysis, used most intensively in conjunction with the Averaging Module. D – MagSpy displays SO. E – Arrows indicate how data flows from ActMon to DispData and from MagSpy to an Analysis Module. F – Recruitment Curve fitting module plots SO vs MEP amplitude; datapoints (blue) and curve fit (red). The sigmoid function parameter estimates are listed and displayed graphically; $S_{50}$ is a star on the x-axis, 95% confidence intervals of MEPmin and MEPmax are short horizontal lines on the left and right edges of the y-axis. The curve fit’s $R^2$ value and area under the curve are
also listed. G – SICI/ICF Module plots MEP amplitude for 3 conditions: Test Stimulation (TS), SICI, and ICF. Mean value (solid line) and 98% confidence intervals (dashed lines) are shown. The number of stimuli per condition is listed along with the TS and conditioning stimulus (CS) SO levels. H – Averaging Module plots the time course of EMG relative to the stimulus trigger (time = 0 ms). The mean at each time point of individual (gray) trials forms the average (blue) line. Number of trials averaged is listed.