Brain Stimulation 12 (2019) 192–194

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Novel tools for rapid online data acquisition of the TMS stimulus-response curve

Dear Editor,

A change in the input-output relationship between transcranial magnetic stimulation (TMS) intensity and the motor evoked potential (MEP) may be used as a marker for neuroplasticity [1–3]. Traditionally, stimulus response (SR) curve data are acquired using 3–10 stimulation intensity bins determined *a priori* as a percentage of the resting or active motor threshold, with 5–20 stimuli/bin and inter-stimulus intervals (ISI) ranging from 3 to 10 s. Data acquisition often exceeds 10 min, and therefore curves can be susceptible to changes in corticospinal excitability as a result of attention, drowsiness and emotional state [4–7]. Previously, we demonstrated that reliable SR curve data can be acquired in less than 4 min but the technique was inaccessible to most researchers [8]. Here, we describe and validate a freely available tool, implemented in Signal 7.0 (Cambridge Electronic Design, Cambridge) and MATLAB. that controls the stimulator and provides online feedback to the user in order to reduce the risk of acquiring poor quality or insufficient data to construct the curve.

The general concept for SR curve data acquisition is illustrated in Fig. 1a. A serial port connection allows communication with, and control of, the stimulator. The tools were designed to work with Magstim stimulators, although they can be adapted to work with other stimulators. Communication via the serial port allows the software to receive information about the current status of the stimulator, and to arm/disarm the stimulator, and to set the stimulation intensity. Direct feedback about the EMG recordings and the SR curve are provided to the user after each stimulation.

The MATLAB graphical user interface (GUI) is illustrated in Fig. 1b (left). All data acquisition (e.g. sample frequency, pre/post trigger time, background EMG alert threshold etc.) and stimulator settings (e.g. ISI, maximum step increase) can be defined in the GUI settings menu. User controlled pushbuttons start and stop stimulation and save acquired data. The minimum ISI is restricted to 1.5 s to allow the GUI to refresh and to facilitate smooth serial port communication between the PC and stimulator. Stimulation intensity is determined randomly by the software to a value that is set by minimum and maximum slider bars. This value can be adjusted 'on the fly'. This allows the user to concentrate on specific areas of the curve (e.g. near the motor threshold) should this be desired, and to control the presentation of succesive high intensity stimuli in order to prevent changes in corticospinal excitability due to anticipation [9]. After each stimulus, the GUI is updated to display the current EMG trace and SR curve. Background RMS EMG is calculated and the user is alerted if an *a priori* threshold is exceeded. The MEP_{pp} amplitude is extracted between two user-defined cursors superimposed on the EMG trace.

The essential features of the MATLAB GUI were also implemented in a Signal 7.0 script (Fig. 1b - right). Whilst the stimulus intensity is calculated automatically by the script, the main difference from the MATLAB GUI is that stimulator is triggered manually through a popup window. The user has the option to change the stimulation intensity range via this popup window. The script is freely available through http://ced.co.uk/downloads/scriptsigcont. Both implementations were validated in 10 participants, with the study approved by the University of East Anglia Faculty of Medicine and Health Sciences Research Ethics Committee (2017/18–97) and performed in accordance with the Declaration of Helsinki.

EMG was acquired from the first dorsal interosseous (FDI) muscle. EMG was amplified (500-1k) and analogue filtered (20–1000 Hz) before sampling (5000 Hz) and storage. Magstim stimulators were used to deliver TMS over the primary motor cortex using a standard figure-of-8 coil. Stimuli were delivered to site producing the largest MEP (motor hotspot). Coil position and orientation were monitored using frameless stereotaxy.

SR curves were acquired using both the traditional and rapid method. For the traditional method, data was collected using fixed stimulation intensity bins determined based on the participant's resting motor threshold (RMT). Stimuli were administered at ten different intensities from 0.8 to 1.7*RMT, an ISI of 3–5 s and with 20 stimuli per bin. Fig. 2a shows a representative data set acquired rapidly using the GUI alongside data acquired in the same participant using the traditional approach. The curves collected using the GUI required on average 64 ± 12 stimuli (96 ± 18 s, 66–116 s). All but one of the acquired curves could be well fitted using the Boltzmann sigmoid (all $r^2 > 0.7$; on average: $r^2 = 0.87 \pm 0.12$).

In addition, the script was tested with two Magstim stimulators: the Magstim Rapid^2 and Magstim 200^2. Fig. 2a shows the curves when Signal was used to acquire an SR both using the traditional and rapid method. Fig. 2b shows a representative data set acquired rapidly using Signal 7.0 for both a Magstim 200^2 as well as a Magstim Rapid^2 stimulator. The curves were collected with on average 72 ± 22 stimuli (233 ± 80 s, 115–405 s). All but two of the acquired curves could be well fitted using the Boltzmann sigmoid (all $r^2 > 0.7$; on average: $r^2 = 0.87 \pm 0.12$).

In summary, we have introduced two scripts, one written in MATLAB and one for the CED Signal 7.0 software, to rapidly acquire data for the SR curve using Magstim TMS stimulators. High quality SR curve data were successfully acquired with these scripts. Both implementations automate communication with the TMS stimulator and provide immediate online feedback of the EMG/MEP

https://doi.org/10.1016/j.brs.2018.09.015
1935-861X/

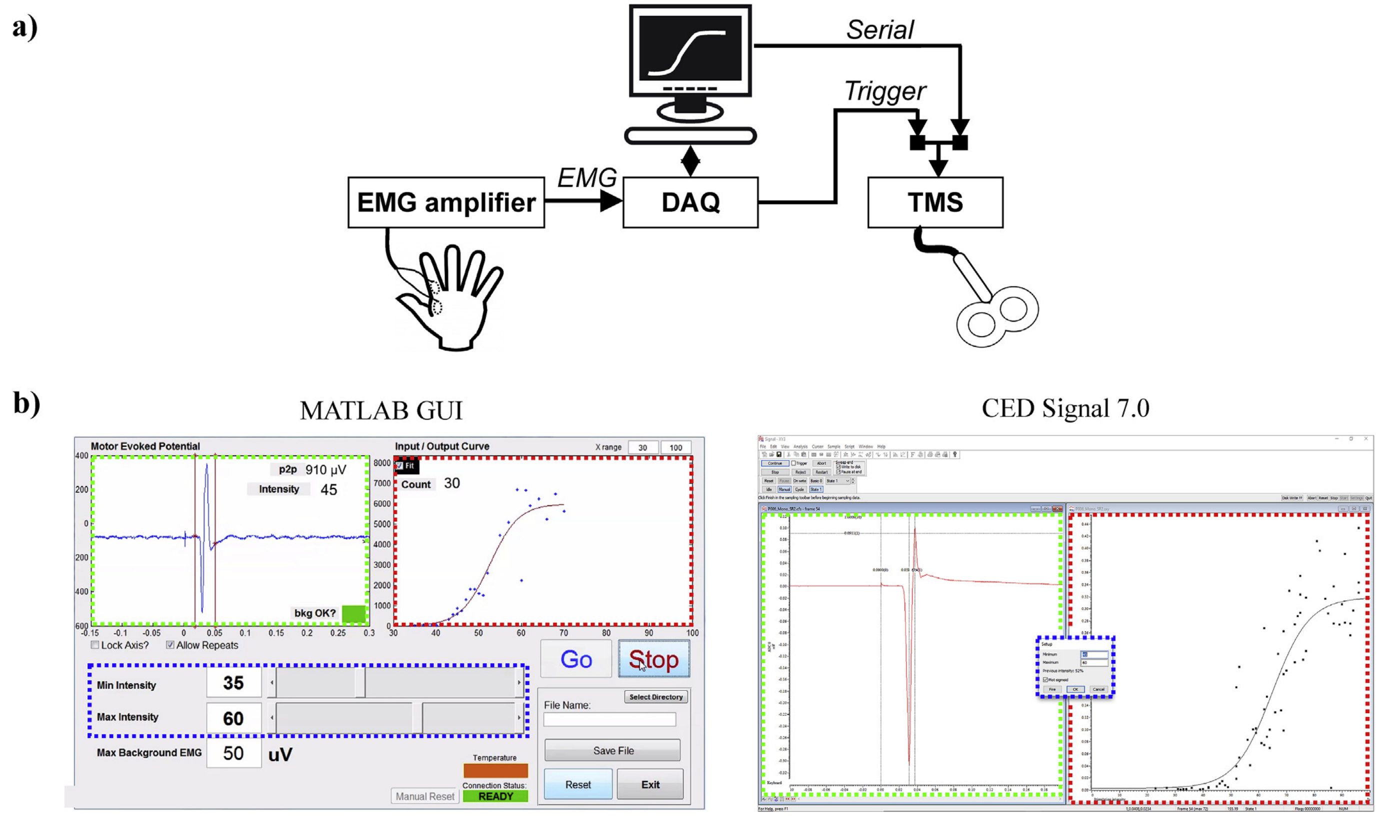

Fig. 1. (a) The setup during data acquisition of the SR curve using the MATLAB GUI. A data acquisition board (DAQ) is connected to the PC to acquire EMG data and to trigger the TMS stimulator via digital TTL signal. Communication with the stimulator to control its settings and receive status information is achieved via the PC's serial port (RS232). (b) The MATLAB GUI (left) and Signal CED script (right) for rapid acquisition of the SR curve are illustrated. The GUI is updated after each stimulus to display the EMG record (green outline). Moveable cursors define the window in which the MEP_{pp} is determined. MEP_{pp} is displayed in the top right corner of this window together with the stimulus intensity (910μV and 45%, respectively in this example). Background EMG prior to the stimulus artefact is analysed and a warning displayed in the lower right corner of this window if the RMS EMG crosses the threshold set with the Max Background EMG input box (50μV in this example). The updated SR curve is displayed in the right window (red outline) by plotting stimulation intensity vs. MEP_{pp} amplitude. The Boltzmann curve fit (red line) is superimposed over the updated MEP_{pp}—stimulus intensity data set. Stimulation intensity for the next stimulus is controlled via slider bars (blue outline). Stimuli are automatically delivered at a rate that can be defined in the GUI settings. The CED Signal script includes the most critical functions required for rapid acquisition of the SR curve. Similar to the MATLAB GUI, this script updates the most recent EMG record (green outline) and the resulting SR curve (red outline). It identifies the stimulus artefact and the peak and trough of MEP without the need to user input in order to automatically calculate MEP latency and MEP_{pp}. Stimulation intensity is controlled via the setup dialog box (blue outline). When the user presses the 'Fire' button, a command is sent to the stimulator via the serial port to set the stimulation intensity at a random value between the minimum and maximum values defined in this dialog box, a TTL trigger is then sent via the DAQ the generate the magnetic stimulus. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

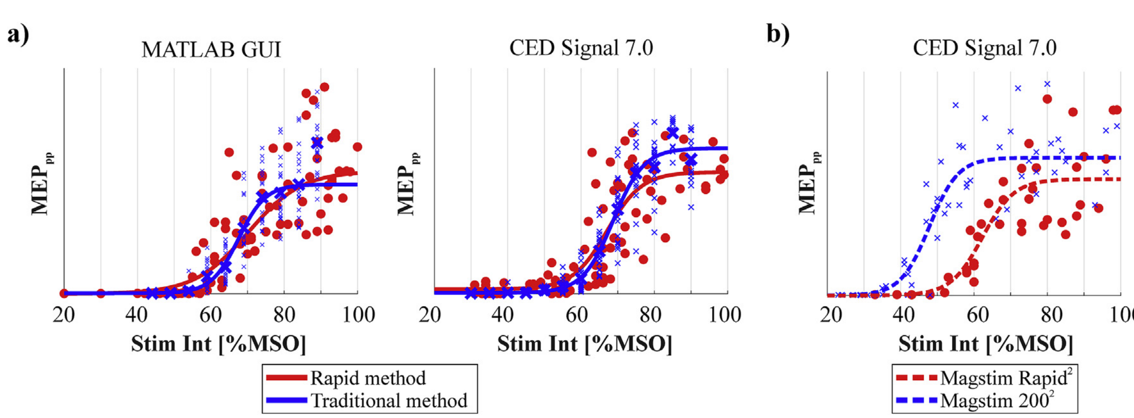

Fig. 2. (a) SR curves obtained using the traditional method (blue lines and crosses) and rapid acquisition method (red lines and dots) with the MATLAB GUI (left) and CED Signal 7.0 (right). The large blue x's highlight the mean MEP amplitude at each stimulation intensity for the traditional method. (b) SR curves obtained using the CED Signal script with two different Magstim stimulators (Magstim Rapid^2, red dashed line and dots; Magstim 200^2, dashed blue line and crosses).

and SR curve. This provides the user a platform to tailor data acquisition to the individual and to stop data acquisition when a satisfactory SR curve has been acquired. This negates the need for post-acquisition analysis of a fixed number of stimuli, thus eliminating the chance of administering too few or too many stimuli. Whilst the specific setup described here uses Magstim stimulators, this setup can be adapted for use with any TMS stimulator that can be externally controlled. We believe this is a valuable and clinically feasible method for rapid SR curve acquisition.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of interest

TP is employed by Cambridge Electronic Design Ltd. MvdR and MJG developed the concept and the. MATLAB GUI. TP coded the Signal 7.0 script. MvdR, TP and MG recorded the data. MvdR analysed the data. MvdR and MG wrote the manuscript with critical feedback from TP.

References

[1] Carroll TJ, Riek S, Carson RG. Reliability of the input-output properties of the cortico-spinal pathway obtained from transcranial magnetic and electrical stimulation. J Neurosci Methods 2001;112(2):193–202.
[2] Devanne H, Lavoie BA, Capaday C. Input-output properties and gain changes in the human corticospinal pathway. Exp Brain Res 1997;114(2):329–38.
[3] Rossini PM, Burke D, Chen R, Cohen LG, Daskalakis Z, Di Iorio R, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. Clin Neurophysiol 2015;126(6):1071–107.
[4] Kamke MR, Ryan AE, Sale MV, Campbell ME, Riek S, Carroll TJ, et al. Visual spatial attention has opposite effects on bidirectional plasticity in the human motor cortex. J Neurosci 2014;34(4):1475–80.
[5] Kiers L, Cros D, Chiappa KH, Fang J. Variability of motor potentials-evoked by transcranial magnetic stimulation. Electroencephalogr Clin Neurophysiol 1993;89(6):415–23.
[6] Rosenkranz K, Rothwell JC. The effect of sensory input and attention on the sensorimotor organization of the hand area of the human motor cortex. J Physiol 2004;561(Pt 1):307–20.
[7] Tormos JM, Canete C, Tarazona F, Catala MD, Pascual-Leone Pascual A, Pascual-Leone A. Lateralized effects of self-induced sadness and happiness on corticospinal excitability. Neurology 1997;49(2):487–91.
[8] Mathias JP, Barsi GI, van de Ruit M, Grey MJ. Rapid acquisition of the transcranial magnetic stimulation stimulus response curve. Brain Stimul 2014;7(1):59–65.
[9] Moller C, Arai N, Lucke J, Ziemann U. Hysteresis effects on the input-output curve of motor evoked potentials. Clin Neurophysiol 2009;120(5):1003–8.

Mark van de Ruit
Department of Biomechanical Engineering, Delft University of Technology, Delft, the Netherlands

Tom Pearson
Cambridge Electronic Design Ltd., Cambridge, UK

Michael J. Grey*
Acquired Brain Injury Rehabilitation Alliance, School of Health Sciences, University of East Anglia, Norwich Research Park, Norwich, NR4 7TJ, UK

* Corresponding author.
E-mail address: m.grey@uea.ac.uk (M.J. Grey).

17 September 2018
Available online 2 October 2018