NeuroImage 153 (2017) 307–318

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Automatized set-up procedure for transcranial magnetic stimulation protocols

S. Harquel[a,b,c,d,*], J. Diard[a,b], E. Raffin[a,c], B. Passera[a,b], G. Dall'Igna[e,c], C. Marendaz[a,b], O. David[a,c], A. Chauvin[a,b]

[a] Univ. Grenoble Alpes, F-38000 Grenoble, France
[b] CNRS, UMR 5105, Laboratoire de Psychologie et de Neurocognition, LPNC, F-38000 Grenoble, France
[c] INSERM, U1216, Grenoble Institut des Neurosciences, GIN, F-38000 Grenoble, France
[d] CNRS, INSERM, UMS 3552, IRMaGe, F-38000 Grenoble, France
[e] Pôle de Psychiatrie et Neurologie, Centre Hospitalier Universitaire Grenoble Alpes, F-38000 Grenoble, France

ARTICLE INFO

Keywords:
Robotized TMS
Hotspot hunting
Cortical excitability
MEP
Motor mapping

ABSTRACT

Transcranial Magnetic Stimulation (TMS) established itself as a powerful technique for probing and treating the human brain. Major technological evolutions, such as neuronavigation and robotized systems, have continuously increased the spatial reliability and reproducibility of TMS, by minimizing the influence of human and experimental factors. However, there is still a lack of efficient set-up procedure, which prevents the automation of TMS protocols. For example, the set-up procedure for defining the stimulation intensity specific to each subject is classically done manually by experienced practitioners, by assessing the motor cortical excitability level over the motor hotspot (HS) of a targeted muscle. This is time-consuming and introduces experimental variability. Therefore, we developed a probabilistic Bayesian model (AutoHS) that automatically identifies the HS position. Using virtual and real experiments, we compared the efficacy of the manual and automated procedures. AutoHS appeared to be more reproducible, faster, and at least as reliable as classical manual procedures. By combining AutoHS with robotized TMS and automated motor threshold estimation methods, our approach constitutes the first fully automated set-up procedure for TMS protocols. The use of this procedure decreases inter-experimenter variability while facilitating the handling of TMS protocols used for research and clinical routine.

1. Introduction

Transcranial Magnetic Stimulation (TMS) is a non-invasive brain stimulation technique (Barker et al., 1985; Hallett, 2000). Applied alone or coupled with other neuroimaging techniques (Bestmann and Feredoes, 2013), its application are now numerous in both fundamental (Rogasch and Fitzgerald, 2013; Bortoletto et al., 2015) and clinical research (Ragazzoni et al., 2013; Lefaucheur et al., 2014; Lefaucheur and Picht, 2016).

In order to standardize procedures and consequently reduce inter-subject variability in response to TMS, the field has recently embraced major technological evolutions. Neuronavigation systems dedicated to TMS (Herwig et al., 2001) significantly improved its spatial precision and reproducibility (Julkunen et al., 2009; Weiss et al., 2013) and TMS-robotized systems enabled the automation of coil positioning (Finke et al., 2008; Kantelhardt et al., 2009; Ginhoux et al., 2013). In addition to improving spatial precision and reproducibility compared to manual positioning (Ginhoux et al., 2013), robotized TMS paves the way for new acquisition protocols, such as automated cortical mapping procedures (Harquel et al., 2016a). It is thus likely that the future of TMS resides in the full automation of protocols, partly enabled by robotics.

Every TMS protocol begins by a mandatory set-up procedure, which aims at defining the stimulation intensity to be employed on the cortical target (Rossi et al., 2009; Herbsman et al., 2009; Wassermann and Epstein, 2012). This intensity has to be defined specifically for each subject because it depends on individual neuroanatomy. The procedure consists in assessing the resting (or active) motor threshold (rMT, or aMT) by measuring the muscular activity evoked by the stimulation of the motor hotspot (HS) over the primary motor cortex (M1). Stimulation intensities are then most often expressed as a percentage of this threshold, in order to conform to safety guidances and to standardize stimulation power between subjects (Herbsman et al., 2009).

* Correspondence to: Laboratoire de Psychologie et de Neurocognition, CNRS UMR 5105, Université Grenoble Alpes, BSHM, BP47, 38040 Grenoble Cedex 9, France.
E-mail addresses: sylvain.harquel@univ-grenoble-alpes.fr (S. Harquel).

http://dx.doi.org/10.1016/j.neuroimage.2017.04.001
Received 16 November 2016; Accepted 1 April 2017
Available online 05 April 2017
1053-8119/

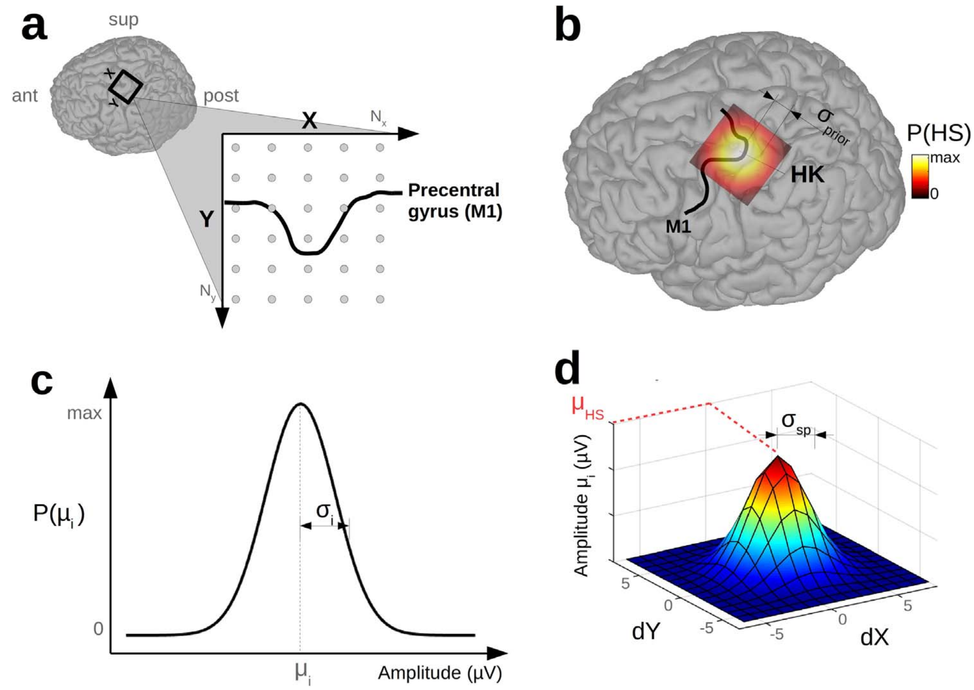

Fig. 1. Main components and hypotheses of the AutoHS model. a: stimulation grid used for hunting and for expressing point coordinates. b: Probabilistic prior concerning *HS* position, centered on the hand knob of the primary motor cortex M1 (precentral gyrus). c: Probability distribution of MEP amplitudes, estimated on *N* EMG recordings. d: MEP mean amplitude (μ_i) modulation as a function of the distances *dX* and *dY* between S_i and *HS* along the X and Y-axis respectively.

Depending on its definitions (Meincke et al., 2016), the HS corresponds to the cortical target over M1 where TMS evokes the lowest MT (Rossini et al., 1994), or the largest motor evoked potentials (MEPs) on the targeted muscle (van de Ruit et al., 2015). While efficient automated MT estimation methods have already been developed and are used since then (Awiszus, 2003; Awiszus and Borckardt, 2011), it is not the case for HS hunting. In practice, the HS position is manually set by experienced practitioners, even though Meincke et al. (2016) recently developed the first automated HS hunting procedure using the mapping of MTs. This method appeared to be effective in automatically assessing the HS position, and producing insightful data for motor mapping protocols. However, its substantial duration (over one hour) prevents its practical use in clinical settings and in most TMS experiments. Although quicker (about ten minutes), manual set-up procedures also have limitations: i. they represent an additional source of inter-experimenter variability (Gugino et al., 2001; Cincotta et al., 2010; Sollmann et al., 2013), ii. they require well-trained TMS practitioners, and iii. they rely on the observation of MEP mean amplitudes which are highly variable (Wassermann, 2002; Jung et al., 2010).

In order to overcome these limitations, we propose here an automated HS hunting procedure (AutoHS) based on a Bayesian model. AutoHS aims at localizing the HS in a faster, more reliable and more reproducible way compared to a manual HS hunting performed by TMS experimenters. The present paper describes how we implemented HS hunting in a Bayesian model, and how we tested our method on virtual data and validated it against manual HS hunting performed by four TMS experts on 19 healthy volunteers. We finally discuss our method and its relevance for progressing towards fully automated set-up procedures for TMS protocols.

2. Materials and methods

We describe first the Bayesian model of AutoHS in detail and second the experimental procedure used to test and compare AutoHS to manual methodology. Throughout this work, the targeted muscle for the HS hunting procedure is the first interosseous muscle (FDI).

2.1. Bayesian model of AutoHS

2.1.1. Overview

AutoHS is a probabilistic procedure, as is classical in the domain of multisensor data fusion in robotics (Bessière and Lebeltel, 2008). Its objective is to estimate the HS position, using the history of stimulated sites and recorded MEP amplitudes.

AutoHS is built in two steps, applying the Bayesian programming methodology (Bessière et al., 2013). The first step consists in defining the joint probability distribution over five variables, including the HS position. From this joint probability distribution, the second step consists in applying Bayesian inference, so as to compute the probability distribution over HS positions, conditioned on previous observations. This procedure is complemented by a “smart” prospective method, that considers the most promising next cortical position to be stimulated, in terms of information gain (Baek et al., 2016), in order to find the HS as fast as possible. AutoHS automatically stops and settles on the HS position once enough information has been gathered.

The method was implemented using Matlab (The Mathworks Inc., USA) and was run concurrently with the neuronavigation and the EMG recording systems. The default values of the model variables used in this work are reported throughout this section. These values have been estimated during pre-tests conducted on real motor mapping datasets not shown in this report. Their robustness are discussed later (see Discussion).

2.1.2. Model description

The structure of the Bayesian model is defined by specifying the joint probability distribution over the five following variables.

HS represents the spatial position of the HS. The model makes the assumption that the 3D stimulation space can be projected to a 2D stimulation grid placed on the scalp surface over the motor cortex (Fig. 1a). *HS* is thus a two dimensional