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Automatized Procedure to Shape a Regional Personalized Electrode for Transcranial Electrical Stimulation

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Abstract

Objective: The purpose of this study is to obtain/create/develop an automatized procedure to personalize electrodes for transcranial electrical stimulation (tES) using individual brain magnetic resonance images (MRI). The electrode thus matches the individual cortical folding of the whole body bilateral primary somatosensory cortex (S1RePE). The selection of a specific regional brain target is a crucial part of any neuromodulation intervention, which is a promising tool in the enhancement of recovery from neurological or psychiatric damages.

Methods: By employing highly standardized MRI analysis software, we developed an automatized procedure for S1RePE shaping. We applied this procedure in 14 healthy people and assessed the accuracy of the procedure by comparing the automatized S1RePE with that which was manually traced in individual brain 3D MRI.

Results: In all subjects, the automatic and manual procedures were highly consistent, with mean Euclidean distance of 2.3 mm and mean intra-class correlation 0.995.

Conclusion: We successfully developed an automatized procedure, which is simpler, more replicable and requires less time than the procedure used up to this point in shaping S1RePE.

Significance: We provide an automatic procedure using the individual cerebral MRI exam to shape a tES personalized electrode that matches the individual cortical folding. This automatic procedure can be adapted to any cortical region in the case that a specific cortical sulcus demarcates it.

Introduction

Recent multidisciplinary neuroscientific work has led to the parceling of the human cerebral cortex into a mosaic of several distinct areas. Advances in the analysis of 'structural' and 'functional' connectivity using powerful noninvasive neuroimaging methods are yielding intriguing insights about brain circuits, their variability across individuals, and their relationship to behavior. In parallel, neuromodulation techniques are emerging as promising tools in modifying the behavior and reaction of subjects to neurological and psychiatric damage. Neuromodulation refers to a class of non-invasive techniques capable of inducing changes in neuronal excitability – which is defined as the change in response to the same input - and includes two subgroups based on their respective stimulating mechanisms: transcranial magnetic stimulation (TMS) and transcranial electrical stimulation (tES) [1]. In the transcranial direct current stimulation (tDCS), which is a type of tES, low-intensity direct currents flow across two or more electrodes placed on the scalp. Applied for a few minutes, tDCS can induce neuronal excitability changes that persist for minutes to hours and, if repeated for days, can last weeks or months. The potential of selecting a specific regional target is a crucial step that requires the proper integration of 'structural' and 'functional' knowledge about the brain. We developed a procedure that personalizes the tES electrode to fit the individual cortical folding of the target area. We observed that the personalized electrode is more efficacious than one that is not personalized in its capacity to modify the neuronal excitability of the entire extended area via tES. We observed efficacy against multiple sclerosis (MS) fatigue when we utilized this electrode in a tDCS treatment aimed at compensating for the alterations typical of the network imbalances found in the brains of these patients. To be specific, we adapted a tDCS intervention, known to improve endurance to fatigue in healthy subjects, to fatigued people with MS [2]. We considered the following indications present in literature:

1) An impaired functional interplay between parietal sensory and frontal motor areas may be at the origin of MS fatigue, and tDCS is able to improve parieto-frontal functional connectivity.

2) Primary motor cortex (M1) is often too excitable in fatigued people with MS.

3) Primary somatosensory cortex (S1) displays signs of lower excitability in MS patients.

4) The symptoms in MS typically involve the lower as well as the upper limbs.

5) No evidence of mono hemispheric prevalence regarding MS fatigue currently exists.

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Considering these notions together, we created a whole body bilateral S1 electrode to enhance the excitability of this area and sustain the S1-M1 projection without directly enhancing M1 excitability. The personalized whole body bilateral S1 electrode fits the personal S1 cortical folding using the individual brain MRI (S1RePE) [3-5].

Here, we present an automatized procedure that begins with brain magnetic resonance images (MRI) of each person, and then obtains/produces/reveals his/her electrode shape, fitting his/her central sulcus projection on the scalp.

Methods

Experimental

We included 14 volunteers (10 females, 4 males; age range 25-56 years), from whom we collected signed informed consent forms for participation in the study as approved by the Ethics Committee of 'San Giovanni Calibita' Fatebenefratelli Hospital. Each subject underwent a structural brain MRI exam with a 1.5 T scanner (Achieva, Philips Medical Systems, Best, The Netherlands) that provided a 33 mT/m gradient amplitude, online 2D/3D geometric distortion correction and a standard quadrature head coil. The acquisition protocol consisted of one 3D high-resolution anatomical sequence empirically optimized to increase grey/white matter image contrast (T1-weighted Turbo Field Echo TR/TE/FA=9.5 ms/4 ms/8°; 2562 matrix resulting in an in-plane resolution 0.98 × 0.98 mm, slice thickness 1.2 mm, 160 coronal contiguous slice).

Automatic S1RePE procedure

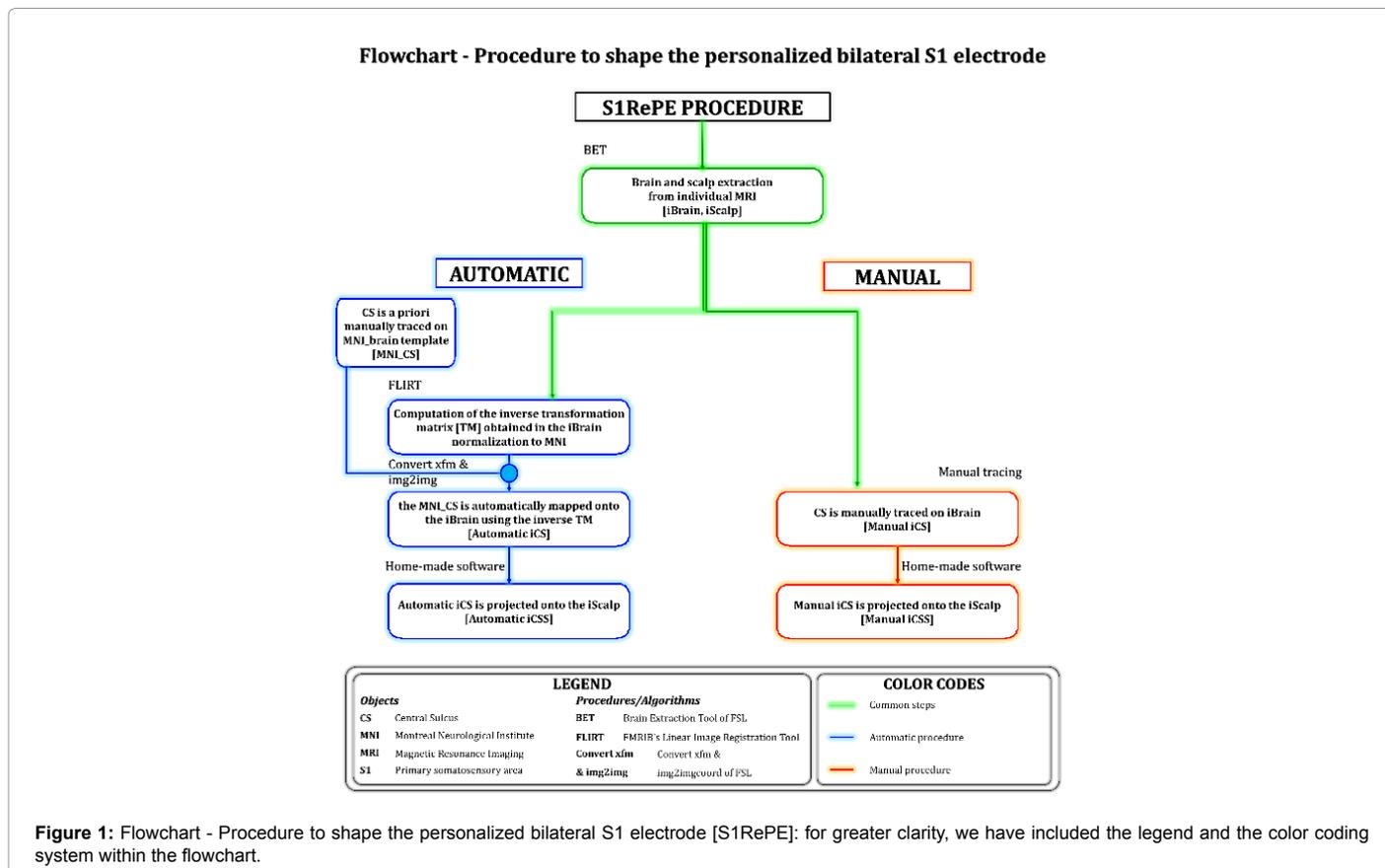The automatic process to shape the personalized S1 electrode (Figure 1) consisted of the following steps:

- On the standard MNI152_T1_1mm_brain MR template we traced the central sulcus manually selecting one point in the middle of the pre- and post-central sulcus walls in the 123 sagittal slices passing across the template central sulcus, resulting in a set of 123 points. These traced CS points span from the Sylvian sulcus of the left hemisphere to the same sulcus of the right hemisphere (MNI_CS);

- Scalp and brain tissues were segmented from individual original MRIs (iMRI) using the Brain Extraction Tool (BET) of FSL (iBrain and iScalp);

- iBrain images were spatially normalized in respect to the standard MNI152_T1_1mm_brain MR template by means of the FMRIB's Linear Image Registration Tool (FLIRT) and the related transformation was saved as a matrix (TM);

- The 123 MNI_CS points were automatically mapped onto the iMRI of each subject using the inverted spatial normalization matrix [TM-1, convert xfm and img2img] to obtain the 123 points on iMRI (Automatic iCS);

- We projected the Automatic iCS onto the external surface of the 3D iScalp using a homemade software (Automatic iCSS).

S1RePE were made out of parallelograms of 2 cm in width, starting from Cz, and approximately the same length in the left and right hemispheres.

Evaluation of the automatic iCSS identification

To evaluate the ability of this automatic procedure to shape S1RePE,

Figure 1: Flowchart - Procedure to shape the personalized bilateral S1 electrode [S1RePE]: for greater clarity, we have included the legend and the color coding system within the flowchart.

we compared the 123 Automatic iCSS points with those obtained by manually tracing the central sulcus on individual MRIs projected on the scalp (Fig. 1 right, Manual iCSS) [6-8].

Two independent researchers selected every sagittal image where the central sulcus appeared on the individual segmented brain and memorized one point (x,y,z) for each slice. Accordingly, the number of points of Manual iCSS varied across subjects between a minimum of 102 and a maximum of 117. We projected the Manual iCS onto the external surface of the 3D iScalp using the same software that was used for the Automatic procedure (Manual iCSS).

We quantified the accuracy of the Automatic iCSS identification as the point-to-point Euclidean distance to the Manual iCSS set and the Intra-Class Correlation (ICC) between Automatic iCSS and Manual iCSS [8-10] (Figure 2).

Results

We verified that the distributions of the Euclidean distances and ICCs between Automatic iCSS and Manual iCSS did not differ from a Gaussian (Shapiro-Wilk test >.400 consistently). Thus, we calculated the individual average across the point-to-point distances of the two Manual and Automatic sets (about 102-117 points; Table 1). All subjects displayed a low Euclidean distance which resulted 2.3 mm in average, low varying intra-individually (mean standard deviation 2.2 mm). The high consistency of the two Automatic iCSS and Manual iCSS sets appeared in the high intra-class correlation ranging from 0.990 to 0.999, resulting 0.995 in average (Table 1).

Discussion

The main achievement of our work is the newfound capacity, given the individual anatomical cerebral MRI, to produce personalized electrodes for transcranial electrical stimulation, which fit the individual cortical folding of the predetermined target, through an automatized procedure. We implemented all steps of the procedure according to widely used standards and well-tested software for the processing of standard magnetic resonance images. The main innovation is the identification of the individual central sulcus. We inversely transform in the individual brain MRI space the central sulcus identified once for all on the MNI template [11-15].
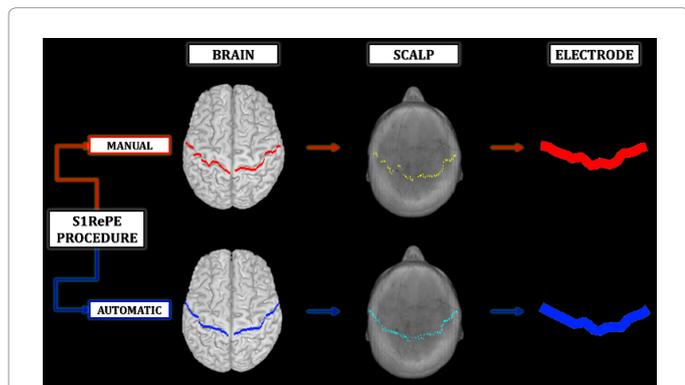

Figure 2: CS shape traced on iBrain and iScalp in Manual and Automatic S1RePE procedures. The personalized bilateral S1 electrode (S1RePE) obtained by Manual (upper row) or Automatic (lower row) procedure: the individual central sulcus, either traced manually in in individual brain MRI or retro-projected from MNI template traced once for all (first column), projected on the individual scalp (second column) to shape S1RePE (third column).

Subject	Number of points	Mean distance [mm]	Distance SD [mm]	ICC [dimensionless]
S1	109	3.3	2.3	0.998
S2	115	1.4	1.8	0.999
S3	102	3.1	2.9	0.99
S4	114	2.9	2.2	0.996
S5	112	1.7	1.9	0.992
S6	117	2.7	2.3	0.993
S7	109	1.6	1.9	0.993
S8	116	3.1	3.2	0.994
S9	115	2.5	2.5	0.997
S10	113	2.1	1.7	0.995
S11	117	1.6	1.8	0.998
S12	106	1.7	1.8	0.993
S13	113	2.7	2.1	0.996
S14	117	2.2	2.7	0.997
Mean	112.5	2.3	2.2	0.995
Min	102	1.4	1.7	0.99
Max	117	3.3	3.2	0.999

Table 1: Automatic Icss Vs. Manual Icss Comparison.

For each subject, individual number of points of the two Automatic iCSS and Manual iCSS sets. Between the Automatic iCSS and Manual iCSS points: the mean and standard deviations (SD) of the point-to-point distances and the intra-class-correlation (ICC).). In the last three rows, mean, minimum (Min) and maximum (Max) across the 14 subjects.

This automatized procedure offers multiple advantages with respect to the manual one:

1) A significant reduction of the electrode preparation execution time: in fact, while the central sulcus manual tracing requires 1-1.5 hours when done by an intermediate experienced operator, the present automatic procedure lasts about 10-15 minutes;

2) No need for the subject/patient to be present in the laboratory, thus avoiding a further trip to the treatment environment in addition to the tES sessions;

3) No need for a neuronavigation system to shape the electrode;

4) The reduction of the potential for inter-subject and intra subject variability in electrode shape as a result of variations in the expertise of the researcher or technician who conducts it.

As noted in the introduction, we developed the whole body bilateral S1 electrode personalization aimed at remedying the neuronal activity alterations underlying multiple sclerosis fatigue. A successful clinical study indicates that this issue deserves further attention. Electrode personalization is necessary when the target of stimulation is an extended region. In fact, through an experimental trial, in which we targeted bilateral M1 as a simple-to-test region by transcranial magnetic stimulation (TMS) protocol, we observed that the personalized electrode in particular, as opposed to a non-personalized one, induced an efficacious neuromodulation of the whole body representations in both hemispheres. In other terms, while neuromodulation of the lower limbs representation with both the personalized and non-personalized electrodes ensured the proper execution of the two stimulation blocks, proper neuromodulation of upper limb representations was achieved only through use of the personalized one. Thus, we conclude that the need for personalizing the electrode geometry emerges when we target an extended region, to the order of 5-10 cm from the centering point (in our case, hand representation from the central Cz position), as

bilateral S1 or M1 areas devoted to the whole body representation [13].

A key step in the present procedure is the identification of the sulcus that demarks the target area on the MNI model, retro transforming it onto individual MRIs by the inversion of the matrix, which is calculated to normalize individual MRI space into the MNI model. We evaluated the accuracy of this procedure and observed errors to the order of 2-3 mm with respect to the manual tracing executed by two independent MRI analysis experts. This procedure can by simply exported to other extended cortical targets, such as most bilateral associative cortices. While, in the case of the central sulcus, our procedure proved to be very appropriate, for other more variable sulci, different brain normalization procedures that take into account all cortical folding should be evaluated. Furthermore, our procedure will be useful in cases where a more rounded shape region, like the dorsolateral prefrontal cortex – typical of many psychiatric and neurological interventions – is the target, but the neuromodulatory effects on nearby cortical regions must be limited. Definitely/Certainly, further investigation through tES studies - experimental and simulative, employing realistic head models - will enhance knowledge about the degree to which efficacy is dependent upon the reference electrode and personalized electrode positioning. In the present investigation, we used 1.5T 3D high-resolution MRI cerebral images. In other tests performed, which we have not included in the present study due to their small number and lack of homogeneity, we developed the complete procedure starting from lower resolution images. This was done so that we could determine the minimal requirement to apply the proposed automatic procedure 3D anatomical MRI with voxels smaller than 5 mm of slice thickness and in-plane resolution better than 3 x 3 mm, as typical of clinical MRIs. The procedure does not require a predetermined direction of the exam, as we were able to obtain the personalized electrode starting from axial, sagittal and coronal acquired images. We decided to identify the transformation matrix as that which would normalize the individual brain to the MNI brain model (MNI152_T1_1mm_brain), but other templates may be used as well [15].

Conclusion

We provided an automatic procedure, which, from the individual cerebral MRI exam, produces the shape of the personalized electrode to target a neuromodulation intervention on whole body bilateral primary somatosensory cortex. We can simply export this process to any extended cortical region in the case that a specific cortical sulcus demarcates it.

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