Optimizing fMRI Techniques for Post-stroke Motor Rehabilitation: Preliminary Protocol Standardization

Abigail Miranda-Hernández[1], José Carlos López-Mata[2], Gabriel Valadez-Roque[3], and Luis Jimenez-Angeles[1](✉)

[1] Departamento de Ingeniería en Sistemas Biomédicos, DIMEI-Facultad de Ingeniería UNAM, Ciudad de México, Mexico
luis.jimenez@ieee.org
[2] Laboratorio de Neuroimagenología, Departamento de Ingeniería Eléctrica, Universidad Autónoma Metropolitana, Ciudad de México, Mexico
[3] División de Rehabilitación Integral, Instituto Nacional de Rehabilitación "Luis Guillermo Ibarra Ibarra", Ciudad de México, Mexico

Abstract. This paper presents preliminary results of the standardization for the acquisition of fMRI scans for post-stroke motor rehabilitation in the MRI service of the Mexican National Institute of Rehabilitation. fMRI scans of 9 healthy volunteers (30.22 $\pm$ SD 3.41 years) with no prior history of neurological or psychiatric disorders were acquired while they performed a motor paradigm that included tasks of action observation plus motor execution (AOME) and action observation plus motor imagery (AOMI) for fist and finger tapping. Our findings revealed that the primary cortical surfaces (precentral gyrus, postcentral gyrus, supplementary motor area, and premotor cortex) had a functional gradient with higher values for AOME and lower values for AOMI, which is in line with existing literature, indicating that this standardized approach can be beneficial for routinely carrying out post-stroke motor rehabilitation research projects.

Keywords: fMRI · standardization · post-stroke · motor imagery

1 Introduction

Biomedical Engineers (BME) study the physics of magnetic resonance imaging (MRI), the hardware, software and understand the clinical relevance of MRI. In a multidisciplinary field, BME are responsible for the development of new types of imaging [1], improve the image quality [2], reduce imaging artifacts and acquisition times [3], all with the goal of maximizing the clinical utility of MRI techniques. In this work BME students worked alongside psychologists, radiologists, and technicians on a global project aimed at refining a protocol for motor rehabilitation using functional MRI (fMRI).

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Numerous studies have highlighted the potential benefits of Motor Imagery (MI, dynamic processes whereby actions are mentally generated and unfold over time without physical movement execution) and Action Observation (AO, dynamic mental processes that represent action content and are triggered when observing other's actions); as strategies for aiding post-stroke motor rehabilitation [4–8]. However, the combination of Action Observation and Motor Imagery (AOMI) produces increased activity in motor-related brain areas compared with AO or MI alone. AOMI involve greater neural activity in the caudal supplementary motor area (SMA), left precentral gyrus, basal ganglia, and cerebellum compared with AO, and the bilateral cerebellum and precuneus compared with MI [9,10]. These findings indicate that AOMI may be more effective in enhancing motor function during post-stroke rehabilitation. fMRI has proven to be useful for monitoring post-stroke rehabilitation because it has valuable characteristics for both clinical and research applications. However, in MRI facilities with initial experience in hardware and software, there is a continuous need for methodological improvements to ensure the validity and reliability of studies, as errors, variations, or inconsistencies are often observed, which have an impact on obtaining reliable results, and the design of the paradigm is a key factor in optimizing these parameters [11]. Therefore, the contribution of BME expertise and skills are crucial in optimizing the time spent on selection and interviews with patients, reducing the acquisition time of fMRI, programming and validating the paradigm task, and achieving functional results in line with those reported in the literature.

This paper reports on the initial validation of the paradigm task as a means of obtaining functional outcomes comparable to those reported in the literature for healthy volunteers, with the aim of using fMRI studies as a monitoring tool for post-stroke motor rehabilitation in the MRI service of the Mexican National Institute of Rehabilitation.

2 Methods

2.1 Participants

Nine healthy participants (5 women) with an average age of 30.22 $\pm$ SD 3.41 years (range: 26–36 years) were selected. The participants had no history of neurological or psychiatric disorders and provided written consent to participate in the study. The participants were enrolled through direct invitation. Interested subjects voluntarily attended a brief interview at the MRI service to perform a series of psychological tests, verify the inclusion and exclusion criteria, sign a letter of informed consent if they were met and participate in a training session. The inclusion criteria were: ages between 25 and 40 years; dexterous (Edinburgh Inventory $\geq$ 10); between 9 and 18 years of schooling; Kinaesthetic and Visual Imagination Questionnaire R (KVIQ) test $\geq$ 3 and Perceived Stress Control Questionnaire (PCE)$\leq$ 13. The exclusion criteria were: structural brain lesions (insults, dysplasias or tumors); systemic or chronic disease; claustrophobia; contraindication to MRI procedure (prostheses, pacemakers, valves, etc.). The elimination criteria were: voluntary abandonment; excessive motion that produces artifacts during MRI acquisition and loss or deterioration of subject information.

2.2 Training Session

Subjects who met the selection criteria were scheduled for a training session where they performed the following tasks: 1) opening and closing the fist (fist AOME), 2) joining and separating the tips of the thumb and index finger (finger tapping AOME), 3) imagined opening and closing the fist (fist AOMI), and 4) imagined joining and separating the tips of the thumb and index finger (finger tapping AOMI). Subjects had to synchronize their perfomance with a short video (30 s) of the expected task with 1 Hz frequency presented at the begining of each trial. The video also included a 1 Hz beat to facilitate syncronization. The approximate duration of the training session was 12 min, in addition to the time used for explanation.

2.3 fMRI Paradigm

On the day following the training session, MRI images were acquired while participants performed the trained tasks. A block design paradigm was employed (5 blocks for Rest and 5 blocks for Task), each lasting 30 s (10 volumes, TR = 3 s) while the subjects were shown the indications and videos of the tasks to be performed as well as the beginning and end of the activation periods. The basic structure of the paradigm is illustrated in Fig. 1. Each paradigm was presented separately by randomizing the order of exposure, and the tasks were randomized to avoid carryover and interaction effects.

2.4 fMRI Acquisition and Preprocessing

The MRI equipment was synchronized to a laptop computer via an event synchronizer device designed specifically for this research. The objective of this device was to synchronize the electrical pulses from the MRI equipment with the stimulation paradigm controller software (PsychoPy v3.0) to start the sequences of each trial. Anatomical and functional images were acquired using a Philips Magneto Ingenia 3 Tesla with a standard 16-channel head antenna. For functional MRI, a whole-brain echo planar imaging (EPI) sequence with the following parameters was used: Repetition Time (RT) = 3000 ms, Echo Time (ET) = 36 ms, acquisition matrix = 80×95 voxels, Field of View (FOV) = 190×230 mm, Flip Angle (FA)= $90°$, slices = 40, slice thickness = 4 mm, inter-slice gap = 0 and 4000 volumes over the experimental scan time of 5 min. Functional image preprocessing and analysis were conducted using the FMRIB Software Library (FSL, FLIRT version 6.0). The Brain Extraction Tool (BET) was applied to each structural image from the command line before preprocessing and for functional

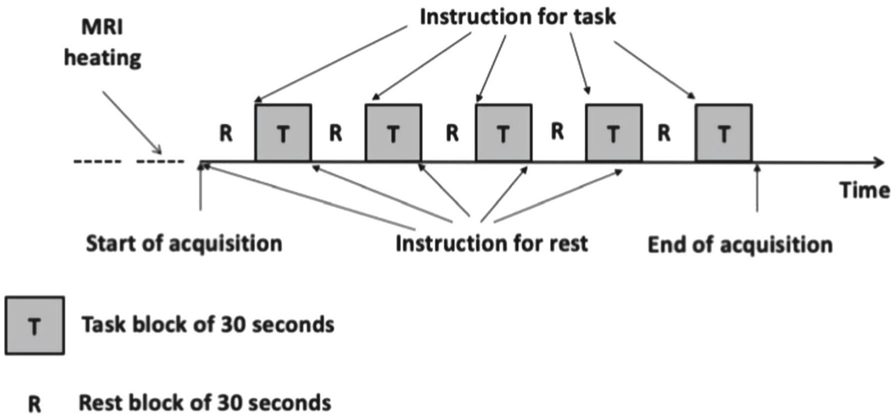

Fig. 1. The basic structure of the paradigm execution during fMRI scanning. The Task and Rest blocks were composed of five blocks, each lasting 30 s (10 volumes, TR = 3 s). The entire paradigm was carried out for each condition (fist AOME, fist AOMI, finger tapping AOME, and finger tapping AOMI).

data with the BET option within the Prestats module of FEAT. The rest of the preprocessing steps (motion correction, slice-timing correction, smoothing, registration, and normalization) were performed using the FEAT GUI with the default options. To correct for motion, each volume from the BOLD images was first rigidly registered to the middle volume using a normalized correlation cost function and linear interpolation (MCFLIRT12 tool). After spatial smoothing with a 5 mm FWHM, registration and normalization were performed using the default linear registration method with full search and 12 degrees of freedom.

2.5 Functional Analysis

The first-level analysis was performed using a general linear model (GLM), and the contrast images were computed for the following conditions: fist AOME, fist AOMI, finger tapping AOME and finger tapping AOMI. On the second level analysis, we used separated models to compute the main effect between conditions by conducting one-sample t-tests with the respective first-level contrast images (Fist AOME > AOMI, Finger tapping AOME > AOMI, Fist AOME > Finger tapping AOME, and Fist AOMI > Finger tapping AOMI) on whole brain level concerning all clusters considering a p-value below 0.05 as significant. As results the cluster sizes higher than 20 voxels, the coordinates of the cluster peaks as well as further relevant local maxima within these clusters are reported.

3 Results and Discussions

3.1 Differences and Similarities Between Fist AOME and AOMI

Figure 2 shows the functional analysis of the Fist AOME, Fist AOMI, and Fist AOME > Fist AOMI in the cluster coordinates [–44 –18 54]. This cluster caused a considerable rise in the left-sided BOLD signal of the precentral and postcentral gyrus, as well as the premotor cortex and supplementary motor area (PM+SMA). The voxel volume in AOME was significantly larger than AOMI in the precentral gyrus (3357 vs. 82), postcentral gyrus (3190 vs. 81), and PM+SMA (1739 vs. 17). The contrast to Fist AOME > AOMI shows a significant decrease in voxel volume across all structures while preserving the proportions as seen in AOME. These findings indicate that Fist AOME and AOMI involve the same cortical areas but differ in their volume sizes, and that Fist AOMI can be beneficial for post-stroke motor rehabilitation. Our results are consistent with those reported by Chepurova et al. [12] which verified the activation of primary motor cortex (M1, situated in the precentral gyrus) during both active and passive hand movements. They monitored the brain activity of the motor cortex while the participants performed independent (active) and assisted (passive) fist opening and closing tasks. During active movement, the contralateral M1 showed slightly more activation and there were also some overlapping

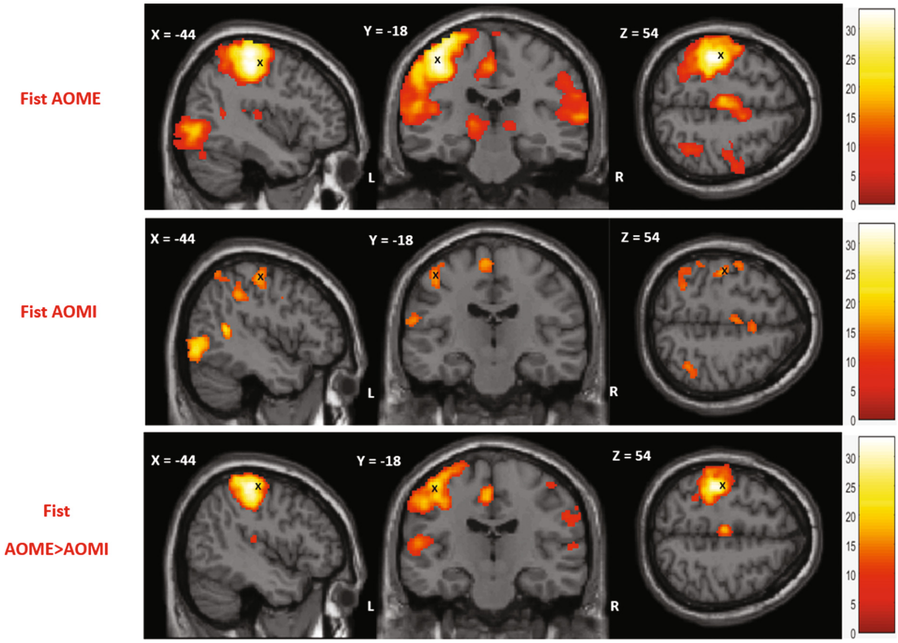

Fig. 2. T-maps showing group brain activation related to the fist condition: AOME, AOMI and AOME>AOMI.

activity in the contralateral primary somatosensory cortex (S1, located in the postcentral gyrus). The authors conclude that the fist opening and closing task is successful in stimulating M1 and S1, even with the help of assisted movement, making it a viable option for patients with paresis.

3.2 Differences and Similarities Between Movement and Imagined of Finger Tapping

Figure 3 shows the functional analysis of the Finger tapping AOME, Finger tapping AOMI, and Finger tapping AOME > Finger tapping AOMI in the cluster coordinates [–44 –18 54]. As in Fist analysis, Finger tapping caused a significant increase in the left-sided BOLD signal of the precentral and postcentral gyrus, as well as in PM+SMA. The voxel volume in AOME was significantly bigger than AOMI in the precentral (1171 vs. 201), postcentral gyrus (1574 vs. 50), and PM+SMA (634 vs. 89). The contrast to Finger tapping AOME > AOMI shows a significant decrease in voxel volume of precentral gyrus (337) and PM+SMA (24) but a lesser change in postcentral gyrus (673).

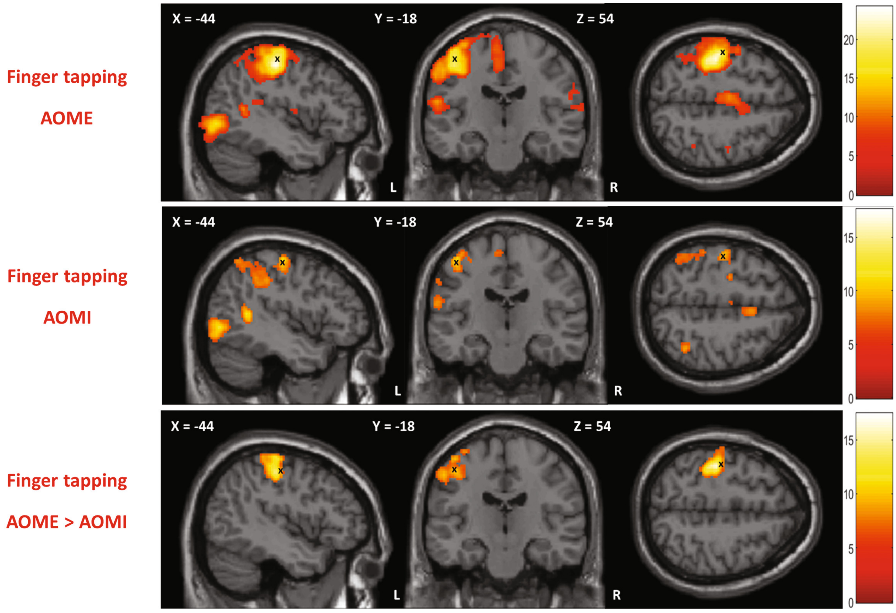

Fig. 3. T-maps showing group brain activation related to the finger tapping condition: AOME, AOMI and AOME>AOMI

These findings are in line with those of Rao et al. [13], who showed that basic free-frequency finger extension and flexion movements activate M1, and that complex finger tapping movements with the same fingers activate the contralateral (sometimes ipsilateral) M1, as well as both SMA and PM bilaterally.

They also showed that when the frequency of the movement is set to 2 Hz for complex movements, there is less intense activation (due to the lower frequency compared to free frequency movements) in the (M1), (SMA), (PM). Lastly, the authors discovered that during a first-person complex movement imagination task, the SMA is more active than the PM.

3.3 Differences and Similarities Between Fist and Finger Tapping in AOME and AOMI

Figure 4 shows the functional analysis of the Fist AOME > Finger tapping AOME and Fist AOMI > Finger tapping AOMI in the cluster coordinates [–44 –28 54]. Analyzing the sames structures in AOME contrast (first row) the voxel volume for precentral gyrus, postcentral gyrus and PM+SMA were 128, 411 and 9 voxels respectively. While non-significant differences were found for AOMI contrast (second row).

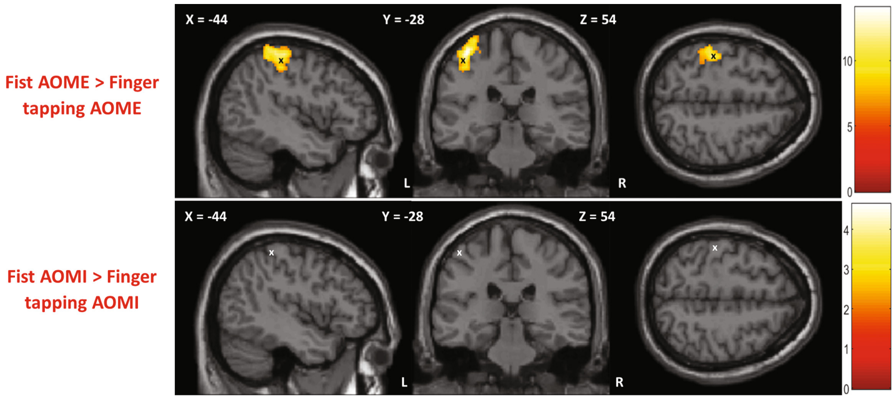

Fig. 4. T-maps showing group brain activation between Fist and Finger Tapping in AOME and AOMI.

Hanakawa et al. [14] reported similar results identifying common cortical brain areas that were activated during the Finger tapping AOMI and Finger tapping AOME tasks. The M1, dorsolateral premotor area in its caudal portion (PMdc) and supplementary motor area in its caudal portion (SMAc) were more active during movement execution than during imagination. Nevertheless, activation was equal in the rostral part of the dorsolateral premotor area (PMdr), ventral premotor area (PMv) and rostral part of the supplementary motor area (SMAr). Their findings suggest a functional gradient from more "executive" to more "imaginative" areas, which further corroborates Rao et al. [13], adding specificity to the neuroanatomy of equivalent activation.

4 Conclusions

The aim of this work was to provide an overview of the standardization process for the acquisition of fMRI studies as a monitoring tool for post-stroke motor rehabilitation in the MRI service of the Mexican National Institute of Rehabilitation. To this point, we have established a standard set of psychological tests and a pre-training protocol that is indicated to the subjects one day before the MRI images are taken. The connection between the MRI machine and the computer that displays the results of the motor paradigm has been established and standardized, making it possible for the service to routinely conduct this type of research. The motor paradigm designed with AOME and AOMI motor tasks of fist and finger tapping showed that, in a control group of healthy volunteers, the primary cortical surfaces (precentral gyrus, postcentral gyrus, SMA, and PM) had a functional gradient from executive to imaginative surfaces (AOME > AOMI), which is in line with the literature. In future work, we will assess the efficiency (time/effect) of the training processes and performance of motor tasks, and a linguistic processing paradigm will be included to evaluate the accuracy (percentage) of motor and linguistic tasks during image acquisition, and analyze the overall brain BOLD signal intensity during motor and linguistic processing tasks.

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