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ABSTRACT

Brain–computer interfaces (BCI) decode user's intentions to control external devices. However, performance variations across individuals have limited their use to laboratory environments. Handedness could contribute to these variations, especially when motor imagery (MI) tasks are used for BCI control. To further understand how handedness affects BCI control, performance differences between two monozygotic twins were analysed during offline movement and MI tasks, and while twins controlled a BCI using right-hand MI. Quantitative electroencephalography (qEEG), brain structures' volumes, and neuropsychological tests were assessed to evaluate physiological, anatomical and psychological relationships with BCI performance. Results showed that both twins had good motor imagery and attention abilities, similar volumes on most subcortical brain structures, more pronounced event-related desynchronization elicited by the twin performing non-dominant MI, and that this twin also obtained significant higher performances with the BCI. Linear regression analysis implied a strong association between twins' BCI performance, and more pronounced cortical activations in the contralateral hemisphere relative to hand MI. Therefore, it is possible that BCI performance was related with the ability of each twin to elicit cortical activations during hand MI, and less associated with subcortical brain structures' volumes and neuropsychological tests.

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KEYWORDS Motor imagery; hand orthosis; BCI; electroencephalography; handedness

Introduction

Brain-Computer Interfaces (BCI) are systems which allow users to control external devices by decoding their intentions from neurological sources

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such as the electroencephalogram (EEG). In order for EEG-based BCI systems to decode users' intentions, the EEG signal must be acquired, pre-processed, and processed through temporal and spatial digital filters. Afterwards, a processing stage allows specific task-related features to be extracted and classified. Following task classification, communication with an external device, such as a computer monitor, or a robot, allows control of the device using user's intentions (Wolpaw, Birbaumer, McFarland, Pfurtscheller, & Vaughan, 2002). Performance with a BCI is often measured as the percentage of user's attempts or trials for which the BCI correctly identified commands prompted by the user. Most BCI provide performance feedback to the user, with visual and somatosensory feedbacks being the most commonly reported (King et al., 2014; Kondo, Saeki, Hayashi, Nakayashiki, & Takata, 2015). BCIs have a wide range of applications including entertainment (Kerous, Skola, & Liarokapis, 2018), neuromarketing (Morin, 2011), wheelchair control (Ron-Angevin et al., 2017), and neurorehabilitation (Soekadar, Birbaumer, Slutzky, & Cohen, 2015). For users to achieve control of a BCI, a strategy or paradigm must be performed to generate EEG patterns from which intentions can be recognized. Although several BCI paradigms are currently used, motor imagery (MI) has the advantage that it does not require an external stimulus and, has shown potential for BCIs aimed for neurorehabilitation (Alonso-Valerdi, Salido-Ruiz, & Ramirez-Mendoza, 2015).

MI is the mental rehearsal of a movement, for example, hand or feet, without performing the actual movement (Jeannerod & Decety, 1995; Pfurtscheller & Neuper, 2001). Several studies featuring advanced imaging techniques have shown that MI-related cortical activations are similar to those observed when actual movement is performed (Carrillo-de-la-Peña, Galdo-Álvarez, & Lastra-Barreira, 2008; Kraeutner, Gionfriddo, Bardouille, & Boe, 2014; Rodriguez, Llanos, & Sabate, 2009). Before movement-related tasks, such as hand MI, a decrease in EEG power relative to a reference or baseline period can be observed in alpha and beta bands (known as Event-Related Desynchronization, or ERD), as described by Pfurtscheller and da Silva (1999). During voluntary hand movement, it has been reported that alpha ERD can be elicited in the contralateral hemisphere, and that after movement, the central area can exhibit alpha Event-Related Synchronization (increased power relative to a reference period) (Pfurtscheller & da Silva, 1999). In addition, after 1 s of terminating a movement task, beta ERS can also be observed (Pfurtscheller & da Silva, 1999). Furthermore, hand MI has been reported to elicit mu ERD in the cortical hand representation area contralateral to the task (Pfurtscheller, Brunner, Schlögl, & da Silva FH, 2006). In healthy subjects, it has been observed that right- and left-hand MI can elicit contralateral desynchronization and/or synchronization similar to activations observed when right- and left-hand movements are performed (Carrillo-de-la-Peña et al., 2008; Kraeutner et al., 2014). However, in some cases, MI elicits ipsilateral or bilateral activations (Pfurtscheller & da Silva, 1999; Cantillo-Negrete, Gutiérrez-Martínez, Flores-Rodríguez, Cariño-Escobar, & Elías-Viñas, 2014).

Despite the promising applications of BCI systems, most of them are still restricted to universities and laboratory environments, since not all target users will be able to achieve control of the system (Edlinger, Allison, & Guger, 2015). Some reasons for this, include high variability between EEG signals from different users (Kang, Ojha, Lee, & Lee, 2017; Meyer, van Oort, & Barth, 2013), between EEG signals of same users recorded at different time periods (Cajochen & Dijk, 2003; Peterson & Harmon-Jones, 2009), gender differences (Cantillo-Negrete, Gutierrez-Martinez, Carino-Escobar, Carrillo-Mora, & Elias- Vinas, 2014; Duregger et al., 2007), users' inability to correctly perform the targeted BCI paradigm (Edlinger et al., 2015; Vuckovic & Osuagwu, 2013), spatial ability (Jeunet, Jahanpour, & Lotte, 2016), ability to perform mental and movement tasks (Friedrich, Neuper, & Scherer, 2013; Lotte, Larrue, & Mühl, 2013), feedback type (Lotte et al., 2013), task's instructions (Lotte et al., 2013), and handedness (Kasuga et al., 2015; Willems, Toni, Hagoort, & Casasanto, 2009; Zhang, Yuan, Huang, Yang, & Chen, 2014). Some studies have reported that subjects performing MI of their dominant or non-dominant hand can also affect their ability to elicit MI-related patterns. Willems et al. described differences in functional Magnetic Resonance Images (fMRI) between right and left-handed healthy subjects while performing hand MI tasks, specifically in the contralateral pre-motor and motor cortex. Compared with ipsilateral, contralateral activations were stronger if subjects performed MI of their dominant hand (Willems et al., 2009). Another study using fMRI showed higher Blood Oxygen Level Dependent (BOLD) power changes in healthy subjects with right-handedness while performing a left-hand MI task, compared to right-hand MI. This implied that right-handed healthy subjects recruited more nerve cells for performing left MI (Zhang et al., 2014). Also, Kasuga et al. reported differences in ERD elicited by MI from the dominant and non-dominant hand of healthy subjects, after transcranial direct current stimulation was applied to the dominant contralateral primary motor cortex. Subjects showed increased ERD during dominant hand MI, and only a small ERD increase during non-dominant hand MI, after the stimulation procedure (Kasuga et al., 2015). Therefore, BCI control with dominant or non-dominant hand MI tasks could affect users' performance with these systems.

Several BCIs described in the literature, especially those proposed for neurorehabilitation, use hand MI as control scheme (Ang et al., 2014; Cantillo-Negrete, Carino-Escobar, Carrillo-Mora, Elias-Vinas, & Gutierrez-Martinez, 2018; Ono et al., 2014; Várkuti et al., 2012). It is reasonable to assume that hand dominance could affect BCI performance, since studies have observed differences in MI patterns associated with hand dominance (Kasuga et al., 2015; Willems et al., 2009; Zhang et al., 2014). However, to the authors' knowledge, there are no studies reporting how hand dominance is related to BCI performance. Such studies could be useful for BCI design considerations, such as MI strategies, and could provide more information for BCI systems aimed for neurorehabilitation; since patients often have paralysis of one side of the body (hemiparesis) and are unable to move the hand contralateral to their affected brain hemisphere (Katzan, 2017). Therefore, some patients will have paralysis in their non-dominant hand, and their ability to control a BCI could be different from patients with paralysis in their dominant hand.

The goal of the present study was to analyse if dominant or non-dominant hand MI tasks could have an effect regarding BCI performance in a case study of discordant handedness. For this purpose, two users with similar environmental and genetical backgrounds, such as a pair of monozygotic twins with discordant hand dominance, were recruited and attempted to control a BCI. To test BCI performance under different feedback conditions, visual and somatosensory feedbacks were provided by means of a simulated virtual hand, and by a robotic hand orthosis, respectively. Brain Magnetic Resonance (MR), quantitative EEG, neuropsychological tests, and classification accuracy were analysed to assess anatomical, physiological, psychological, and BCI performance differences between the twins, respectively, and to analyse possible relationships between BCI performance with the other variables. It was hypothesized that the twin attempting to control the BCI system using dominant hand MI would achieve a higher performance, due to having the advantage of using the dominant hand for controlling the system.

Materials and methods

Subjects

Two female monozygotic twins with discordant handedness were recruited, age 24 at the time of the study, without any reported prior neurological conditions. An Edinburgh handedness inventory, adapted for Spanish-speaking populations, was used to test hand dominance (Oldfield, 1971). The subscales of digit detection and visual detection of the NEUROPSI Attention and Memory were used to evaluate attentional processes (Ostrosky-Solis, Gomez-Perez, Ardilla, Rosselli, & Matute, 2003). The complete version of the MI ability test known as Kinesthetic and Visual Imagery Questionnaire (KVIQ) was applied to both subjects (Malouin et al., 2007). The KVIQ is comprised by 17 items for the visual scale, and 17 items for the Kinesthetic scale. Subjects were asked to evaluate the clarity of the visual image (visual scale) or the intensity of sensations associated with their MI. Rating of each item is performed using a 5-point ordinary scale. Average values computed for Visual and Kinesthetic scales are presented for each twin. Both twins signed an informed consent approved by the ethical commission of the National Institute of Rehabilitation in Mexico City.

Magnetic resonance and volumetric analysis of brain structures

Volumes of twins' brain structures were compared in order to assess if anatomical brain asymmetries, were present between twins, and to assess relationships between brain structures' volumes and BCI performance. Image sequence was acquired using a 64 channels head coil (Siemens Skyra 3.0T, Erlangen, Germany). The anatomical scan collected 192 slices with $1 \times 1 \times 1.2$ mm voxel size, repetition time and echo time (TR/TE) were of 2050/2.43 ms, slice thickness 1.2 mm, field of view (FOV) 256×256, and matrix 256×256.

The volumetric analysis of brain structures was performed for each twin using FreeSurfer software (Reuter, Schmansky, Rosas, & Fischl, 2012). After automatic segmentation, the estimated total intracranial volume, total grey matter volume, total white matter volume, and white and grey matter per hemisphere volumes were computed. Subcortical brain structures' volumes were also computed. Percentage differences between twins' brain structures, regarding right and left hemispheres, and between the dominant hemispheres of each twin, were calculated for comparison purposes.

Experimental paradigm

Each twin participated in four sessions during four consecutive days at the same hour. The first two sessions, session 1 and 2, were calibration sessions; each one comprised by 60 trials of right-hand movement (RIGHTM), 60 trials of left-hand movement (LEFTM), 60 trials of right-hand MI (RIGHTMI), and 60 trials of left-hand MI (LEFTMI). Each run was comprised by 10 RIGHTM and 10 LEFTM trials or by 10 RIGHTMI and LEFTMI trials randomly presented to the subjects to prevent habituation. Therefore, in total, 120 trials were acquired for LEFTMI, 120 for RIGHTMI, 120 for LEFTM, and 120 for RIGHTM tasks. For each trial, a modified Graz paradigm was used to present visual cues to the subject (Pfurtscheller & Neuper, 2001). Each trial lasted 8 s and started with a white cross displayed on the computer's screen, 2 s later a short warning tone was reproduced. In this period subjects were instructed to rest with eyes open looking at the cross (REST condition). After the 3rd second, the cross was replaced by an arrow pointing at the right or left direction. This instructed the subject to perform either RIGHTM or LEFTM for movement runs, or RIGHTMI or LEFTMI for MI runs. The arrow lasted 1.5 s on the screen and afterwards disappeared leaving a black background for 3.5 s while subjects continued performing MI. In calibration sessions, at the 8th second of the trial, a blue screen appeared instructing the subject to relax and blink (relaxation period), this period lasted between 3 and 5 s to prevent habituation. For each trial, extracted EEG data were comprised by 3 s of REST, and 3 s of RIGHTM, LEFTM, RIGHTMI or LEFTMI. In order to calibrate the BCI system only REST, and RIGHTMI time intervals were used. For quantitative EEG analysis, data from REST, movement, and MI trials were used. In the last two sessions, session 3 and 4, subjects attempted to control the BCI system through visual and somatosensory feedback. In each session, each subject performed 120 trials. On session 3, the first 60 trials were comprised by visual feedback and the last 60 trials by somatosensory feedback; in the fourth session, the first 60 trials were comprised by somatosensory feedback and the last one, by visual feedback. The differences between offline and online analysis were that the online trials were only comprised by RIGHTMI and had a feedback interval from the trial's 8th second until the 12th second, and the relaxation period started after this interval. Offline and Online trials' structures can be observed in Figure 1.

For MI tasks, subjects were instructed to imagine the feeling of closing and opening their hands by recalling such sensation of movement from hand movement tasks. For offline tests, it was confirmed that the twins performed correctly right or left MI, by asking them to say the word "left" or "right" at the end of each trial (at a time in which EEG features were not extracted). Twins

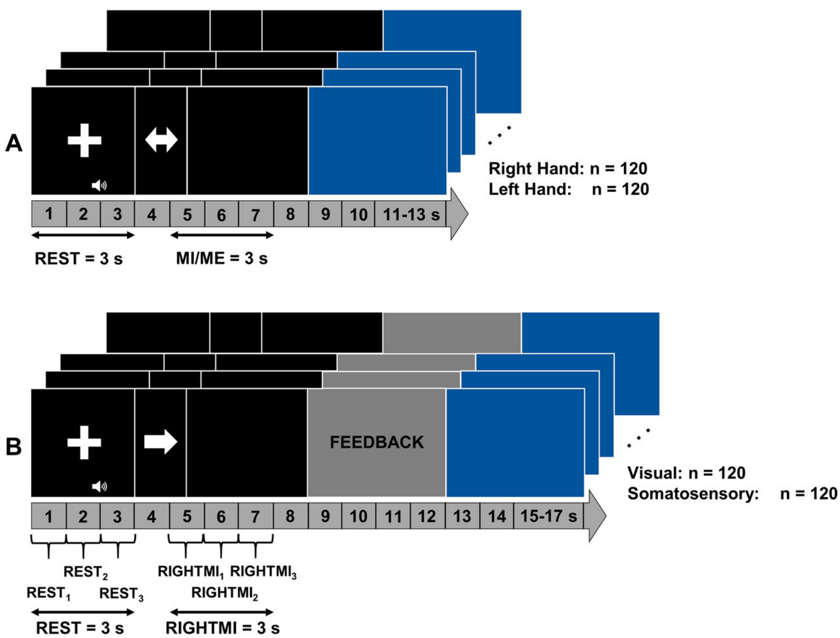

Figure 1. (A) Offline trials' time structure. (B) Online trials' time structure with two types of feedback. Number of trials (*n*) for every analysis is shown.

were asked to depict how they performed MI at the end of each offline and online run, stating they have attempted MI as instructed.

EEG acquisition

A 24-bit amplifier, g.USBamp from g.tec, was used for EEG recordings. A total of 11 EEG channels were acquired over the sensorimotor cortex according to the international 10–20 system (Cz, C3, C4, Pz, P3, P4, Fz, F3, F4, T3, and T4) using active electrodes at a 256-Hz sampling rate. The right earlobe was used as reference electrode and ground electrode was located at the AFz position.

BCI system

The BCI system was comprised by the previously described EEG amplifier, a processing stage implemented in a PC, and a feedback strategy. The processing stage was encompassed by pre-processing, feature extraction, feature selection, and classification of EEG signals (Cantillo-Negrete et al., 2018). In order to set up the processing stage for BCI online control (calibration), offline EEG data from 120 trials of REST and RIGHTMI were inputted into a training algorithm. This algorithm first performed a temporal filtering of the EEG data to obtain six frequency sub-bands, 4 Hz broad, and 1 Hz overlapping. The filtered bands comprised mu and beta (8–12, 12–16, 16–20, 20–24, 24–28, and 28–32 Hz). Afterwards, a 60-Hz band-stop filter was applied to each filtered band. Temporal filters were FIR of 20th order. After temporal filtering was performed, spatial filters were applied to each frequency sub-band using the Common Spatial Patterns algorithm (CSP) (Ang, Chin, Wang, Guan, & Zhang, 2012; Ramoser, Muller-Gerking, & Pfurtscheller, 2000). CSP extracted features were selected with the Particle Swarm Optimization (PSO) algorithm (Carino-Escobar, Cantillo-Negrete, Vazquez, & Gutierrez-Martinez, 2016). Selected CSP features were used for Linear Discriminant Analysis (LDA) classification between the resting state (REST) and right-hand MI (RIGHTMI). Therefore, after the calibration phase of the processing stage, CSP coefficients for spatial filtering, and LDA coefficients for classification were computed. During online BCI control non-overlapped 1-s windows of EEG data were spatially filtered in selected frequency bands obtained for each twin in the calibration phase. Afterwards, these filtered 1-s windows were classified as REST or as RIGHTMI. Feedback was provided only if two or more of the three 1-s windows that comprised RIGHTMI (from the 4th to the 7th second), were correctly classified. Two different types of feedback could be given to the subjects, visual or somatosensory. Visual feedback was given in the form of a virtual right hand which finger's opened and closed simulating a grasping action. Somatosensory feedback was comprised by a robotic hand orthosis (Cantillo-Negrete, Carino-Escobar, Elias-Vinas, & Gutierrez-Martinez, 2015; Martinez-Valdes et al., 2014), which provided passive flexion followed by extension movement of the right-hand's fingers, thus allowing the user to perform a grasping action. Figure 2 shows the BCI system.

Offline and online quantitative EEG measurement

Power features were extracted using time–frequency analysis by convoluting complex Morlet wavelets with Gaussian shapes. Analysis was performed in a frequency range from 8 to 30 Hz with a 0.5 Hz resolution; and from 0 to 8 s (the complete trial) with steps of 50 ms. ERD/ERS were computed with respect to baseline for movement and MI offline trials, in alpha (8–13 Hz) and beta (14–32 Hz) bands. ERD/ERS was also computed with respect to baseline for online RIGHTMI, for visual and somatosensory feedbacks, in alpha and beta. Topographic brain maps were computed for the averaged data of 11 EEG channels (Cz, C3, C4, Pz, P3, P4, Fz, F3, F4, T3, and T4) from offline and online sessions. For offline measurements, sets of brain maps were computed using averaged alpha and beta ERD/ERS across trials with RIGHTM and LEFTM data (from 4 to 7 s of each trial), and another set of brain maps using RIGHTMI, and LEFTMI data (from 4 to 7 s of each trial). For online measurements a set of brain maps were computed with averaged ERD/ERS computed from RIGHTMI time intervals from all trials, for visual and somatosensory feedbacks. For comparison purposes all maps were calculated

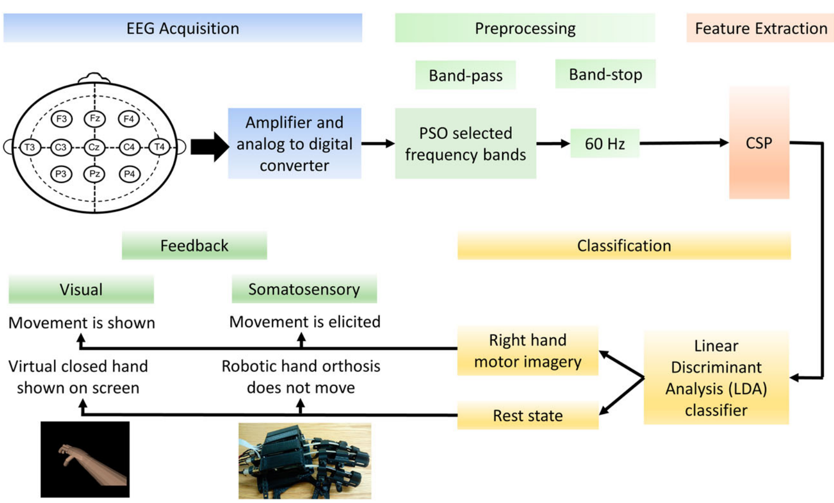

Figure 2. BCI system. The online phase of the BCI processing stage is depicted.

using the same ERD/ERS scale. Figure 2 shows the methodology for offline and online data processing.

Online BCI performance

For online BCI performance assessment, the number of correctly classified trials was computed for the 120 trials recorded for each subject (sessions 3 and 4), separately for visual or somatosensory feedbacks. This was done by using the three classification outputs during each second of the REST condition and the three outputs during the MI. Therefore, for each trial, %CA (percentage of classification accuracy) was computed using Equation (1), as follows:

$$\%CA = \frac{(REST_1 + REST_2 + REST_3) + (RIGHTMI_1 + RIGHTMI_2 + RIGHTMI_3)}{6} \times 100. \tag{1}$$

With REST and MI having a value of 1 if the LDA classifier of the BCI processing stage correctly classified a time window of EEG processed data, and 0 if the classification was incorrect for that time window. The sub-index of REST and MI show which of the three analysed time windows was classified (for example, 1 for the first processed time window). The output of this equation is an ordinary variable, which can be equal to 100%, 83.3%, 66.66%, 50%, 33.3%, 16.6%, and 0%. This value is the %CA for each trial. After computing the %CA, a trial was regarded as correct if the value of a %CA was higher than the practical level of chance (56.2%), computed as stated by Muller-Putz et al. (2008). Comparisons were computed between the Right-Handed Twin's (RTWIN) and the Left-Handed Twin's (LTWIN) number of correct trials expressed as percentage (%CT) for the visual and somatosensory feedback conditions.

Statistical analysis

For the KVIQ questionnaire significant differences between RTWIN's and LTWIN's scores for the visual and kinesthetic scales were assessed using a Mann–Whitney *U* test ($\alpha = 0.05$) after testing for a non-Gaussian distribution using a Lilliefors normality test.

For offline and online qEEG measurements differences between the RTWIN's and LTWIN's ERD/ERS were computed using the Friedman test ($\alpha = 0.05$), after testing a non-Gaussian distribution using a Lilliefors normality test. Post hoc comparisons were performed using Mann–Whitney *U* tests with the Bonferroni correction.

For BCI performance the number of correct and incorrect trials were a dichotomous variable, therefore, Chi-Squared tests ($\alpha = 0.05$) for independence, with Bonferroni correction, were used to assess statistically significant distribution differences between RTWIN's and LTWIN's, separately for visual and for somatosensory feedbacks. Post Hoc statistical power ($\alpha = 0.05$) was computed using the g*power software (Faul, Erdfelder, Lang, & Buchner, 2007, 2009), considering the 120 acquired values of number of correct and incorrect trials per twin.

Associations between twins' BCI performance with visual and somatosensory feedback, with KVIQ results, subcortical structures' volumes, and ERD/ERS were assessed using a stepwise multiple linear regression analysis (Draper & Smith, 1998). The kinesthetic and visual scores of the KVIQ, subcortical structures' volumes with a percentage difference higher than 10% between twins, and median ERD/ERS channels which presented significant differences during MI throughout online BCI control, were inputted into the linear model. Stepwise regression allowed to test which variables could potentially predict BCI performance variability. Cross-validation and permutation tests were applied to assess the regression model's stability and reliability (Draper & Smith, 2014). A leave-one-out cross-validation was performed, and the root mean squared error (RMSE) was computed. The permutation test was comprised by performing the regression of all possible permutations of the dependent variable (%CT) and computing the *p*-values of the statistic. Afterwards, the *p*-values were ordered, and the proportion of these values lower than the confidence level of .05 was set as the significance value for assessing the reliability of the obtained model (Nyblom, 2015).

Results

Volumetric analysis of brain structures

Table 1 shows brain structures' volumes computed for each twin. Total intracranial volume was 1.5% higher for the RTWIN. Twins' dominant hemispheres' cortical white and grey matter volumes differed in less than 10%. RTWIN's brain structures with percentage differences higher than 10% compared to LTWIN's were the Left Accumbens area and the Central Corpus Callosum. LTWIN's brain structures with percentage differences higher than 10% compared to RTWIN's were the Left cerebellum white matter, the Left and Right Lateral Ventricles, the 3rd and the 4th ventricle. The brain structure that showed the highest percentage difference between twins was the Right Inferior Lateral Ventricle, which had a larger volume in the LTWIN. Also, when comparing brain structures' volumes relative to twins' handedness, the structures that showed differences higher than 10% were the lateral ventricle, inferior lateral ventricles, and the Pallidum, with the LTWIN presenting higher volumes in these structures.

Table 1. Brain structures volumes.

Brain structures (mm^3)	RTWIN (mm^3)	LTWIN (mm^3)	RTWIN vs. LTWIN percentage difference (%)
Brain Segmentation Volume	1,154,764	1,156,160	−0.1
Brain Segmentation without Ventricles	1,143,021	1,140,547	0.2
Left Hemisphere cortical grey matter volume	241,350	238,467	1.2
Right Hemisphere cortical grey matter volume	246,486	240,668	2.4
Total cortical grey matter volume	487,836	479,136	1.8
Left Hemisphere cortical white matter volume	226,075	229,943	−1.7
Right Hemisphere cortical white matter volume	231,269	232,909	−0.7
Total cortical white matter volume	457,344	462,853	−1.2
Subcortical grey matter volume	59,512	59,396	0.2
Total grey matter volume	656,972	646,123	1.7
Left Lateral Ventricle	3,997	5,522	**−27.6**
Left Inferior Lateral Ventricle	215	322.6	**−33.4**
Right Lateral Ventricle	3,317	4,492	**−26.2**
Right Inferior Lateral Ventricle	102	377	**−72.9**
3rd Ventricle	566	662	**−14.5**
4th Ventricle	963	1,106	**−12.9**
Left Cerebellum White Matter	14,188	16,724	**−15.2**
Left Cerebellum Cortex	53,563	52,970	1.1
Right Cerebellum White Matter	14,398	15,273	−5.7
Right Cerebellum Cortex	55,577	53,686	3.5
Left Pallidum	1,256	1,378	−8.9
Right Pallidum	1,380	1,512	−8.7
Left Caudate	4,048	4,237	−4.5
Right Caudate	3,894	3,996	−2.6
Left Putamen	6,147	6,197	−0.8
Right Putamen	5,455	5,553	−1.8
Left Accumbens area	690	572	**20.6**
Right Accumbens area	661	656	0.8
Posterior Cerebral Callosum	950	959	−0.9
Posterior Middle Corpus Callosum	429	466	−7.9
Central Corpus Callosum	906	766	**18.3**
Anterior Middle Corpus Callosum	697	652	6.9
Anterior Corpus Callosum	1,080	1,109	−2.6
Dominant Hemispheres’			
Cortical grey matter volume	241,350	240,668	0.3
Cortical white matter volume	226,075	232,909	−3.0
Dominant Lateral Ventricle	3,997	4,492	**−12.4**
Dominant Inferior Lateral Ventricle	215	377	**−75.3**
Dominant Cerebellum White Matter	14,188	15,273	−7.6
Dominant Cerebellum Cortex	53,563	53,686	−0.2
Dominant Pallidum	1,256	1,512	**−20.4**
Dominant Caudate	4,048	3,996	1.3
Dominant Putamen	6,147	5,553	9.7
Dominant Accumbens area	690	656	4.9
Estimated Total Intracraneal Volume	1,433,153	1,411,375	1.5

Notes: RTWIN’s volume differences with respect to LTWIN’s are expressed as percentages. Positive values show higher volumes for RTWIN and negative values indicate higher volumes for LTWIN. Differences higher than 10% are shown in bold.

Neuropsychological tests

Table 2 shows the results of the tests performed on both twins. The Edinburgh Handedness Inventory showed that the RTWIN had the highest score for right-hand dominance, while the LTWIN had the highest score for left-hand dominance.

During the neuropsychological assessment, the participants were alert and oriented in time and space. They were able to attend to the stimulus of interest and ignore the irrelevant ones. In addition, they could stay concentrated on the task for a long time without being distracted. No history for major psychiatric or neurological disorders, as well as for drug or alcohol dependency, prior and after to the study, was observed during the assessment.

The KVIQ test showed that both twins had moderate to moderately high visual and kinesthetic imagery abilities. For the visual scale, no significant differences ($p < .05$) were found between RTWIN's and LTWIN's scores. However, for the kinesthetic scale, significant ($p < .05$) differences were found between RTWIN's and LTWIN's scores, with the RTWIN having higher scores compared to the LTWIN.

Offline quantitative EEG measurements

Figure 3 shows topographic brain maps plotted with ERD/ERS obtained during offline movement trials. EEG channels with statistically significant ERD/ERS differences ($p < .05$) between RTWIN and LTWIN are shown, for alpha and beta frequency bands and for RIGHTM and LEFTM tasks (with comparisons between dominant vs. dominant and non-dominant vs. dominant hemispheres of the twins).

During movement, ERD was observed in twins' ipsilateral and contralateral central EEG channels (C3 and C4) in both alpha and beta. In alpha, RIGTHM

Table 2. Results of the neuropsychological assessment of both twins.

	Edinburgh handedness inventory			
Measurement	RTWIN		LTWIN	
Total	100%/100% Right-handed		100%/100% Left-handed	
Test	NEUROPSI Attention and Memory			
Subject	RTWIN		LTWIN	
Visual detection total	24/24		23/24	
Digit detection	10/10		10/10	
Measurement	Kinesthetic and Visual Imagery Questionnaire (KVIQ)			
	RTWIN		LTWIN	
	Visual	Kinesthetic*	Visual	Kinesthetic*
Total average (*SD*)	4.2/5 (±0.8)	4.4/5 (±0.8)	3.7/5 (±0.9)	3.5/5 (±1.2)

Notes: The Edinburgh Handedness Inventory and NEUROPSI show the total scores of each twin. The KVIQ shows the average total of visual and kinesthetic scales' scores and their standard deviations, "*" shows that statistically significant differences ($p < .05$) were observed between twins' visual or kinesthetic scores. The maximum magnitude of each scale is shown to the right of each of the twin's scores.

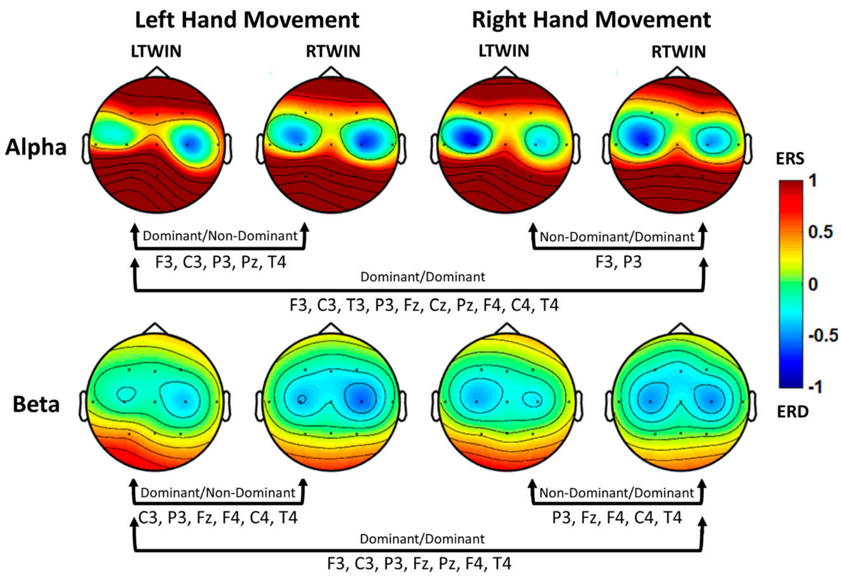

Figure 3. Topographic brain maps computed from movement tasks in offline sessions. RTWIN's and LTWIN's ERD/ERS are shown. Blue and red tones show a decrease or increase in power, respectively, during movement tasks (4–7 s) compared to the REST period (0–3 s). EEG channels' that presented significant differences after multiple comparison correction are shown under the connecting lines.

presented less differences between twins' cortical activations, with no significant differences observed in the central areas. Dominant hand movement tasks presented the most differences regarding cortical activation regions, in both alpha and beta. The channel C3 presented significantly different ERD/ERS between twins across more comparisons (dominant vs. non-dominant in alpha and beta, and in beta for the dominant vs. dominant comparison).

Figure 4 shows topographic brain maps for ERD/ERS information extracted during offline MI trials. EEG channels with statistically significant differences between ERD/ERS values for RTWIN and LTWIN are shown, for alpha and beta frequency bands and, for RIGHTMI and LEFTMI conditions.

During MI, ERD was observed in twins' ipsilateral and contralateral central EEG channels (C3 and C4) in both alpha and beta. RIGTHMI observed in alpha and beta was the task which presented less differences between twins' cortical activations, with no significant differences observed in any region. Central regions' activations (C3 and C4) were significantly different between twins across more comparisons (LTWIN dominant vs. RTWIN non-dominant in alpha and beta, and LTWIN dominant vs. RTWIN dominant in alpha), with the LTWIN presenting more pronounced ERD across these comparisons.

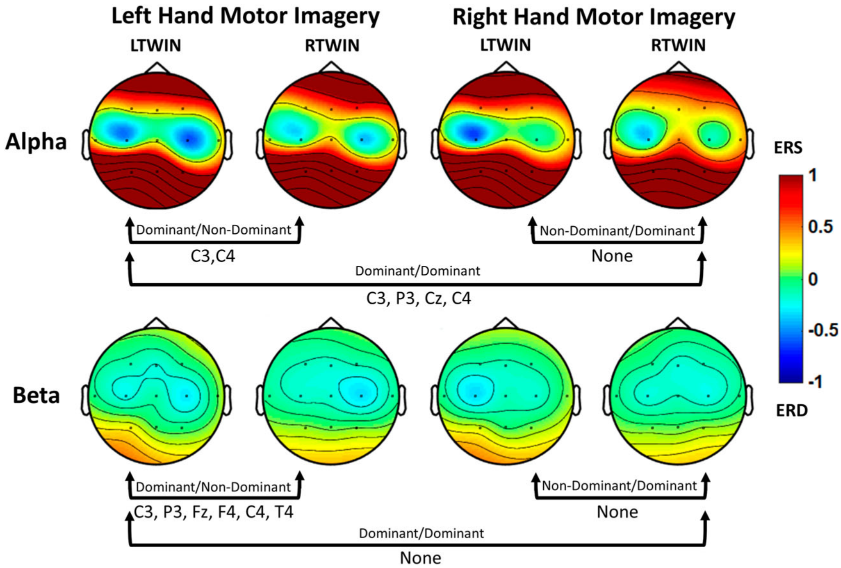

Figure 4. Topographic brain maps computed from MI task in offline sessions. EEG channels' significant differences after multiple comparison correction are shown.

Online quantitative EEG measurements

Figure 5 shows topographic brain maps for ERD/ERS information extracted from online RIGHTMI trials. EEG channels with statistically significant ERD/ERS differences between RTWIN and LTWIN are shown for alpha and beta frequency bands, and for visual and somatosensory feedbacks.

During online RIGHTMI with both visual and somatosensory feedbacks, C3 was the only central channel for which significant different ERD/ERS were observed. Compared to the RTWIN dominant MI, LTWIN non-dominant MI presented more pronounced beta ERD in C3 with the visual feedback, and the LTWIN also presented more pronounced alpha and beta ERD in C3 with the somatosensory feedback.

BCI performance

Selected CSP filters used for feature extraction of the RTWIN's RIGHTMI, were comprised by four pairs of filters, with two filter pairs for extracting EEG features from 8 to 12 Hz, one pair for 16–20 Hz, and one pair for the 24–28 Hz band. For LTWIN's RIGTHMI, CSP filters were comprised by five pairs, with three filter pairs for 8–12 Hz, one pair for 16–20 Hz and one pair for 28–32 Hz. Table 3 shows the number of correct and incorrect trials computed for visual and somatosensory feedbacks. Percentage of correct trials are also

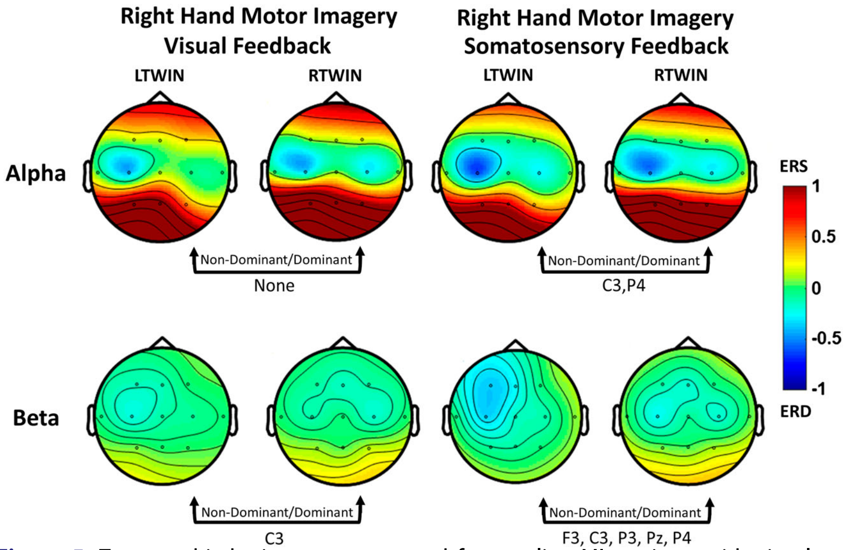

Figure 5. Topographic brain maps computed from online MI sessions, with visual and somatosensory feedback. Blue and red tones show a decrease or increase in power, respectively, during RIGHTMI tasks (4–7 s) compared to the REST period (0–3 s). EEG channels' significant differences, after multiple comparison correction are shown.

stated. With the visual feedback, LTWIN's number of correct trials was significantly ($p < .05$) higher than RTWIN's. With the somatosensory feedback LTWIN's number of correct trials was also significantly ($p < .05$) higher than RTWIN's. Statistical power computed for the tests between RTWIN and LTWIN with visual and somatosensory feedbacks were of 91% and 94%, respectively.

The cross-validation tests showed that the regression models with lower *p*-values were the ones that associated a more pronounced beta ERD in C3, with higher BCI performance, and the models' coefficients ranged from −1.21 to −1.52. The RMSE of the models' predictions with the cross-validation analysis

Table 3. Results of BCI performance.

	Visual		Chi-squared test for visual	Somatosensory		Chi-squared test for somatosensory
	RTWIN	LTWIN		RTWIN	LTWIN	
Number of incorrect trials	61	43	$p < .05$	31	14	$p < .05$
Number of correct trials	59	77		89	106	
Percentage of correct trials	49.2%	64.2%		74.2%	88.3%	

Notes: Number of incorrect, correct, and percentage of correct trials computed for RTWIN and LTWIN for somatosensory and visual feedbacks are shown. The *p*-values of comparisons between RTWIN and LTWIN number of correct trials with both feedbacks are shown.

was of 6.2. The permutation test implied that a p-value lower than .0206, was necessary to assess the reliability of the linear model at a .05 confidence level. Equation (2) shows the linear model computed using the whole dataset with the lowest p-value, as recommended by Draper and Smith (2014). The model had a statistical significance of $p = .008$ for prediction of twins' BCI performance variability (adjusted $R^2 = 0.97$)

$$\%CT = -(1.3[-1.8, \ -0.7])\,(C3_{\beta}) + 49.2, \tag{2}$$

where %CT is the percentage of correct trials for online BCI performance as observed in Table 3. $C3_{\beta}$ is the median ERD/ERS in the beta frequency of the left central EEG channel, computed from twins' online sessions during RIGHTMI. The model's only coefficient was −1.3, while its confidence interval ranged from −1.8 to −0.7 (shown in brackets) is zero non-inclusive, suggesting that beta ERD in C3 is relevant for prediction of %CT. The model implied that a more pronounced beta ERD in C3 (a negative value of C3 is equivalent to ERD) during RIGHTMI, can be associated with a higher BCI performance with both feedbacks. The intercept term of 49.2 indicates that if the twins did not elicit beta ERD/ERS in C3, then only a 49.2% of trials would be correctly recognized by the BCI processing stage, which is below the practical level of chance. Since the obtained model had a significance ($p = .008$) lower than the required by the permutation test ($p = .026$), it could be inferred that the model was reliable for predicting %CT.

Discussion

Total intracranial (1.5%), brain segmentation (0.12%), and grey matter volumes (1.67%) did not differ considerably between both twins since this difference was lower than the ones reported by Pol et al. (2002); if mean differences of total intracranial volume (1.79%), brain segmentation (1.08%) and grey matter (2.28%) are computed from their observations between pairs of female monozygotic twins. Twins' dominant hemisphere's cortical volumes did not differ considerably, therefore, it can be implied that twins' dominant motor regions had similar anatomic features. The subcortical structures that presented the most pronounced differences between twins were the ventricles. Although it has been hypothesized that asymmetries in ventricles structures' volumes can be related with handedness (Erdogan, Dane, Aydin, Özdikici, & Diyarbakirli, 2004), a lack of such association has also been suggested (Guadalupe et al., 2017), and the precise functions of these structures are still not completely understood (Mortazavi et al., 2014). Furthermore, regression analyses implied that none of the subcortical brain structures that presented asymmetries between twins could be associated with BCI performance. Therefore, it can be suggested that twins' BCI performance differences were not likely related with anatomical brain asymmetries between twins.

Twin's discordant handedness was confirmed by the Edinburgh inventory. The KVIQ questionnaire's scores seem to imply that both twins have an average to above-average ability to perform visual and kinesthetic MI. However, RTWIN's scores were significantly higher than LTWIN's for the kinesthetic scale and were not significantly different for the visual scale. This suggested that RTWIN had more ability to perform kinesthetic MI than LTWIN and, that both twins have the same ability to perform visual MI. Offline and online quantitative EEG measurements seem to confirm that both twins do have the ability to elicit ERD on central EEG channels. In case of the online measurements, ERD was also observed for both visual and somatosensory feedbacks. However, BCI performance measurements show that LTWIN's performance was higher than RTWIN, for both visual and somatosensory feedbacks, which is contrary of what could be expected from the KVIQ scores. This could be explained by the moderate and weak correlations found between KVIQ scores and performance using a MI-based BCI, reported by Vuckovic and Osuagwu (2013). In addition, Rimbert et al. reported a lack of association between a MI questionnaire and hand MI-based BCI performance (2019). Therefore, the present study further implies that subjective questionnaires such as the KVIQ, cannot accurately predict MI-based BCI performance.

Offline and online qEEG measurements showed that twins elicited activations over the sensorimotor cortex during movement and hand MI tasks. These activations are the most reported during hand movement-related tasks, which implied that twins could elicit activations associated with hand movement or MI. During twins' dominant hand movement tasks, activation differences between twins were observed among most cortical regions. However, during dominant hand MI tasks, activations' differences were observed in a lower number of regions. This could imply that handedness affected cortical activations in a smaller degree during MI tasks compared to movement tasks, in the observed monozygotic twin model. This is in line with the observations of Shironouchi et al. reporting more pronounced corticospinal excitability effects of movement compared to MI in healthy subjects (2019). Also, the fact that twins' left sensorimotor regions presented significant different cortical activations across most comparisons must be emphasized. This suggested that the dominant hemisphere of the RTWIN and non-dominant of the LTWIN elicited different cortical activations among tasks, which could be expected from discordant handedness. However, unlike the expected scenario, in which the RTWIN should have shown more pronounced contralateral cortical activations during dominant MI tasks compared to the LTWIN (while this twin performed non-dominant MI tasks), the LTWIN had more pronounced activations. A possible explanation for this could be that some left-handers develop, due to environmental pressure, better coordination of their non-dominant upper limb compared to right-handers, as hypothesized by Przybyla et al. (2012). Another possibility, in case of online tests, is that the LTWIN cortical activations were reinforced in a greater degree by the visual and somatosensory feedback provided by the BCI system, since feedback has shown to aid users in generating more pronounced cortical activations in alpha and beta during MI (Cantillo-Negrete, Carino-Escobar, Carrillo-Mora, Barraza-Madrigal, & Arias-Carrión, 2019; Gomez-Pilar, Corralejo, Nicolas-Alonso, Álvarez, & Hornero, 2016; Neuper, Scherer, Wriessnegger, & Pfurtscheller, 2009).

Online BCI performances showed that for both visual and somatosensory feedbacks LTWIN's performances were significantly better than RTWIN's. This was unexpected, and contrary to the hypothesis of the RTWIN achieving higher performances, since the BCI was driven by RIGHTMI, the non-dominant hand of LTWIN. A possible reason for these differences in performance could be implied by the linear model that best fitted BCI performance. The model implied a strong association between beta activations in LTWIN non-dominant hemisphere, and RTWIN dominant hemisphere, with BCI performance. The model's reliability was tested, and is in line with the study of Blankertz et al., which also suggested a predictor of MI-based BCI performance, that associated more pronounced ERD in the contralateral somatosensory cortex regions during hand movement-related tasks, with higher BCI accuracies in a large sample of healthy subjects (2010). In addition, in the present study the other studied variables derived from MI questionnaires, subcortical structures' volumes, and ERD in alpha or in other regions in beta, did not contributed to improving the model's prediction of BCI performance. Therefore, although an association between brain structures and different regions' activations in alpha and beta could still be possible, at least with the studied twin model, BCI performance seemed to be mostly associated with beta activations in the sensorimotor area. On the other hand, performance of both twins using the visual feedback was lower than with the somatosensory feedback. This could have been caused by the closer resemblance of somatosensory feedback to real movement, which could have helped the twins generate more pronounced ERD activations than with visual feedback. Vukelic and Gharabaghi also reported higher performances with somatosensory feedback in a hand MI-based BCI compared to visual feedback, in a sample of healthy subjects (2015).

The present study has limitations that must be acknowledged. Firstly, since only a right-hand orthosis was available for the study, RIGHTMI was evaluated during online BCI control, while the effects of the LTWIN performing dominant hand MI and the RTWIN non-dominant hand control were not online assessed. Although offline comparisons between LTWIN dominant MI and RTWIN non-dominant MI suggested somatosensory cortex activation differences between twins, the lack of online comparisons during this condition does not allow to further confirm these observations during online BCI control. Furthermore, this limitation of the study design did not allow to assess the relationship between cortical activations during twins' left-hand MI with BCI performance, which could have provided more insights of the role of handedness in BCI control with the studied twin model. Also, a higher sample of twin pairs would be needed to further evaluate the effects of handedness in the performance of a MI-based BCI. In addition, although the twin model allows to reduce variability between individuals, it does not guarantee an absence of individual differences in cortical activations caused by factors such as motor learning. These individual differences could have contributed to the observed asymmetries in cortical activations and BCI performances between twins. Finally, the limited time window of the experiment, 2-day sessions of online control, could be too small to assess the effect of BCI feedback and training, in left and right handers' ability to elicit cortical activations during hand MI, since higher degrees of control and changes in cortical activations during MI have been previously reported within longer BCI training sessions (Carino-Escobar et al., 2019; Irimia, Ortner, Poboroniuc, Ignat, & Guger, 2018).

To the authors' knowledge, this is the first study reporting BCI performances, qEEG measurements, neuropsychological tests and brain volumes between hand discordant monozygotic twins. BCI performance differences suggested that in the analysed case study, the twin driving the system with non-dominant MI achieved higher accuracy. This was probably associated with more pronounced cortical activations in the non-dominant hemisphere of this twin during MI. Therefore, BCI performance could be more associated with laterality-related physiological asymmetries, compared to results of subjective tests for MI assessment and anatomical brain asymmetries.

Conclusions

The present work analysed a case study of discordant handedness and its effect in BCI performance using hand MI. Results showed, that in the analysed case study, hand dominance was a feature that did not limited BCI performance, since the twin with handedness opposite to the hand MI required to control the system, achieved better performances. This was attributed to a higher ability of the left-handed twin in eliciting more pronounced cortical activations in central EEG channels during hand MI. Although the present study's limitations, such as it being a case study, does not allow to infer general conclusions of the role of handedness in BCI performance, these observations justify and could provide a starting point for further research.

Compliance of ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author, JCN. The data are not publicly available due to data containing information that could compromise the privacy of research participants.

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