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Neural Organization of Externally and Internally Guided Motor Learning in Left-Handed Individuals as a function of Language Lateralization

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Abstract

Execution of overlearned and well-established motor sequences tends to co-lateralize with language. To determine whether this relationship extends to novel motor learning, the present study explored the neural substrates of internally and externally guided novel motor sequence execution. Ninety-eight left-handed participants (62 typical and 36 with atypical language lateralization) underwent functional magnetic resonance imaging while performing a newly designed Motor Sequence Execution task comprising internally and externally guided novel movement conditions. To assess the relationship between language lateralization and motor learning, language lateralization was assessed using a visually presented Verb Generation task to obtain individual Lateralization Indexes. Whole-brain analyses characterized task-related activation and differences between participants with typical and atypical language lateralization. Compared with rest, both motor conditions recruited bilateral motor, parietal, supplementary motor, anterior cingulate, and cerebellar regions. Direct comparison revealed greater involvement of parietal, supplementary and lateral premotor regions during internally guided sequences, whereas externally guided sequences preferentially recruited primary sensorimotor, occipitotemporal, angular gyrus, and frontal pole regions. Importantly, atypical language lateralization was associated with greater right-hemisphere recruitment during externally guided motor learning, including the right angular gyrus, precuneus, and lateral occipital cortex, whereas no significant group differences were observed for internally guided sequences. These findings suggest that the relationship between language and motor organization depends on the demands of motor learning. Externally guided novel movements may particularly reveal hemispheric reorganization in individuals with atypical language lateralization, consistent with models proposing partially mirror-like organization of cognitive functions across the hemispheres.

INTRODUCTION

One of the most consolidated findings in neuropsychology is the lateralization of cognitive processes across the two brain hemispheres (Vingerhoets et al., 2013). Greater task performance has been suggested to be associated with increased lateralization (Groen et al., 2012; Sheehan and Mills, 2008). While language and praxis are typically lateralized in the left hemisphere, spatial processing, face recognition, and emotional processing are typically lateralized in the right hemisphere (Gerrits et al., 2020). However, not all individuals follow this pattern. For language processing, the presence of atypical lateralization (either right-hemispheric or bilateral) has been described as more prevalent in left-handed individuals (22–24%; Pujol et al., 1999; Mazoyer et al., 2014). Atypical lateralization is not limited solely to language and has been reported for different cognitive processes, such as visuospatial processing (Villar-Rodríguez et al., 2024b), face recognition (Gerrits et al., 2020) or inhibitory control (Villar-Rodríguez et al., 2024a), highlighting the complex interactions involved in the establishment of functional specializations during human brain development.

Gerrits's (2024) Segregation Bias Theory can currently be regarded as the most explicative framework to understand the reorganization of cognitive functions in individuals with typical and atypical language

lateralization. Similar to the segregation mechanism proposed in Kosslyn's causal hypothesis, this theory posits a general bias in functional lateralization whereby each individual has a high probability of allocating different cognitive functions to opposite hemispheres, as described in the preceding paragraph. This functional segregation bias, which favors the pattern of hemispheric organization most commonly observed in the general population. Much less frequently, other individuals—most of whom are left-handed—exhibit a reversed typical functional segregation bias. This bias simultaneously shifts cognitive functions toward the opposite hemisphere to the one favored in the typical pattern, thereby substantially increasing the probability of developing a fully or almost fully mirrored cerebral organization. Nevertheless, because each cognitive function has a different probability of becoming lateralized, neither bias invariably produces a single cerebral configuration. Instead, both can give rise to individual patterns that deviate to varying degrees from their corresponding prototypical organization (Gerrits et al., 2020). This is because the emergence of a given cerebral configuration depends not only on probabilistic biases but also on the interaction of those biases with genetic predispositions, patterns of brain connectivity and experiential factors (Gerrits et al., 2024).

In the case of higher-order motor functions such as praxis, several studies have reported findings consistent with this model. In an early investigation, patients with epilepsy completed language and praxis tasks during the intracarotid sodium amobarbital (Wada) test. Language lateralization was found to be a stronger predictor than handedness of the hemisphere dominant for praxis (Meador et al., 1999). Accordingly, left-handed patients with left-hemisphere language dominance made errors when pantomiming actions following transient inactivation of the left hemisphere. Subsequent studies examined healthy participants using praxis tasks and functional magnetic resonance imaging (fMRI). Vingerhoets et al. (2013) found complete co-lateralization of language and praxis in all 20 participants: 10 with typical and 10 with atypical language lateralization, with each group comprising one right-handed, one ambidextrous, and eight left-handed individuals. This procedure was subsequently replicated in substantially larger samples, yielding similar group-level findings but lower individual rates of co-lateralization (Gerrits et al., 2020; Króliczak et al., 2021). Thus, although language and praxis exhibit a high degree of co-lateralization at the group level, individual cases occur in which the two functions are lateralized to opposite hemispheres or one of them is represented bilaterally, as predicted by Gerrits's (2024) model.

Taken together, these studies indicate that praxis is highly likely to be lateralized to the language-dominant hemisphere, even though individual dissociations occur. Motor praxis can be defined as the capacity to perform learned, complex gestures that is, to generate, coordinate, and execute acquired intentional motor programs. These programs do not consist merely of reflexive movements; rather, they represent motor skills consolidated through learning, repetition, and social transmission, particularly in the case of symbolic gestures and conventional signs (Ewen et al., 2016; Goldenberg, 2014). Praxis develops over many years, and its neural substrates are primarily associated with left-hemisphere frontoparietal regions, including the angular and supramarginal gyri, premotor cortex, and inferior frontal cortex (Johnson-Frey et al., 2005). Whereas motor praxis relies on well-established actions routinely performed in everyday life, executing novel motor programs in unfamiliar situations requires the

acquisition of new motor skills that do not depend on prior overlearning. These skills are acquired through motor learning, which entails developing task-specific movement patterns, integrating sensory information, and gradually optimizing motor commands. Compared with praxis, motor learning is less closely associated with language and depends on more dorsal frontoparietal regions (Hardwick et al., 2013). Moreover, several studies have demonstrated that some forms of motor learning may remain preserved in patients with apraxia, supporting a partial dissociation between the two processes (Dovern et al., 2011; Willms et al., 2021).

In the present study we employed fMRI to better understand lateralization of motor learning processes in a sample of left-handed individual classified as a function of language lateralization. Unlike overlearned motor programs, the establishment and refinement of these movement representations is essential for these new motor programs to be executed with proficiency (Krakauer et al. 2019). This kind of movement execution can be guided through external or internal cues. In the former, motor actions are driven "online" by environmental sensory cues, requiring the integration of this information through the particular involvement of a frontoparietal network (Gowen & Miall, 2007) and other areas such as middle and inferior temporal cortex, left occipito-parietal cortex, posterior cingulate gyrus and medial ventral prefrontal areas, but notably not the basal ganglia (Jenkins et al. 2000). While the lateral premotor cortex activity has been more closely linked to externally guided motor outputs, SMA specializes in internally monitored innovative actions (Mushiake et al., 1991; Wessel et al., 1997) in which basal ganglia do play a role. The study of Jenkins et al. (2000) identified the DLPFC, parietal areas as well as insular cortex as regions more closely linked to innovative self-initiated movements in comparison to triggered actions using PET. To study motor functioning, these studies used commonly employed tasks such as tool pantomimes and finger-tapping tasks. These tasks are varied and differ in complexity, ranging from single-finger tapping to complex unimanual or bimanual sequences. While motor praxis can be assessed through the execution of a repeatedly rehearsed motor sequence, the study of motor learning processes requires the execution of internally and externally guided motor sequences that are new to the participant.

Following Jenkins´ experiment, we will use a visual version of a fMRI Motor Sequence Execution Task (MSE) which included 2 conditions, an IG sequence condition (IG) and an externally guided sequence condition (EG) with innovative sequences for the subject. Our main objective was to assess how each of these motor processes relate to language lateralization, measured using a Verb Generation (VG) task. In addition, we aimed to explore potential differences in lateralization between distinct motor learning processes, IG learned movement and EG learned movement. Based on recent findings from our group and on Gerrits´ Segregation Bias Theory, we hypothesized that motor learning would co-lateralize with language, such that individuals with Typical Language Lateralization would exhibit left-lateralized frontoparietal brain areas, whereas individuals with Atypical Language Lateralization would exhibit a more right-lateralized pattern. Finally, we predicted that these associations would be stronger in individuals with more extreme patterns of language lateralization.

METHODS

Participants

Ninety-eight left-handed participants (62 typical and 36 atypical) of ages ranging from 17 to 42 years old (M = 23.95; SD = 5.16) and Edinburgh Handedness Inventory (EHI; Oldfield, 1971) values (M = 42.67; SD = 5.21) were included in the study. EHI scores resulted of the sum of the scores of 10 items ranging from 1 (“only right”) to 5 (“only left”), with higher total scores indicating a greater left-hand preference. An additional measure, the Laterality Quotient (LQ) ranged from − 100 (total left-handed preference) to 100 and derived from EHI scores. Every participant met the following eligibility criteria: a) being at least 16 years old; b) self-reporting to write mainly with their left hand and a score above 32 on the EHI; c) absence of clinically relevant hearing or vision loss and absence of diagnosed neurological or psychiatric disorders. The experimental procedure was performed entirely in accordance with the guidelines and regulations approved by the Research Ethics Committee (CEISH/89/2024) of Jaume I University. All participants were informed about the objectives of the study and their right to withdraw from the study at any time through a written informed consent. Descriptive data for all participants are publicly available at repository.

Functional Magnetic Resonance (fMRI) procedure

Acquisition

Both structural data and functional MRI sequences were acquired using a 3T General Electric Signa-Architect scanner at the ASCIRES-Castellón clinic. We employed a similar protocol described in Villar-Rodríguez et al. (2024b) to assess hemispheric dominance for language. A 3D structural image was acquired using a T1-weighted magnetization gradient-echo sequence (TR/TE = 8.4/3.3 ms; flip angle = 12º; matrix = 512 x 512 x 384; voxel size = 0.47 x 0.47 x 0.5 mm). A T2-weighted gradient-echo echo-planar imaging (EPI) was used for functional tasks. A total of 144 volumes were obtained per participant with axial orientation for VG and the parameters were: TR/TE = 2500/23.5 ms; flip angle = 70°; matrix = 64 × 64 × 40; voxel size = 3.75 × 3.75 × 3.75 mm. 252 volumes were acquired in the case of MSE and the parameters were: TR/TE = 2000/23.5 ms; flip angle = 80°; matrix = 64 × 64 × 40; voxel size = 3.75 × 3.75 × 3 mm. In addition, we acquired reference field maps (gradient-echo EPI, GRE; 6 volumes) with identical geometry (same FOV, slice thickness, matrix, and TR/TE) but with the phase-encoding direction reversed (reverse phase-encoding polarity) relative to the main acquisition. This procedure, specified in the protocol through the pepolar option, enables voxel displacement mapping and correction of susceptibility-induced geometric distortions during fMRI preprocessing.

Verb Generation Task and Language Lateralization Analysis

Language lateralization was established as described in Villar-Rodríguez et al. (2024b) through a block fMRI-adapted visually presented VG task. During the activation condition participants say out loud the first verb that comes to their mind for each of the presented nouns while in the control condition, pairs of

letters are read when these appeared in the screen. The task consisted of 12 blocks (6 activation and 6 control) of 30 s of duration each during 6 minutes. Participants were instructed to minimize articulation as much as possible to reduce head movements during scanning. E-Prime 3.0 software (Schneider et al., 2012) and MRI-compatible googles (VisuaStim Digital, Resonance Technology Inc.) were used for task administration and stimulus presentation, respectively.

The Laterality Index (LI) was obtained using the bootstrap method implemented in the LI-toolbox for SPM12 (Wilke and Lidzba, 2007). LI was obtained from the proportion of differences in terms of activation between right and left subject´s brain hemispheres using the following formula: [(L-R)/(L + R)] * 100. The ROI for LI was composed by *pars triangularis* and *pars opercularis* of the inferior frontal gyrus, inferior frontal gyrus. The ROI mask was defined using the maximum probability Harvard-Oxford atlas (Frazier et al., 2005; Desikan et al., 2006; Makris et al., 2006; Goldstein et al., 2007) and then fitted to our functional images with the mask-preprocessing step of the LI-toolbox. LI values range from + 100 (totally left functionally lateralized) to -100 (totally right functionally lateralized). Following Mazoyer´s Gaussian Model, Participants with values above 40 (LI > 40) were categorized as typical while values below 40 (LI < 40) were categorized as atypical (Mazoyer et al., 2014). Individual Lis for each participant can be accessed in repository.

Motor Sequence Execution Task

To assess motor learning a Motor Sequence Execution Task was designed consisting of 3 conditions: 2 activation conditions (IG sequence condition and EG sequence condition) and a control condition (absence of movement). There were 7 blocks of 24 seconds each for both activation conditions and 14 rest blocks of 12 seconds with the following fixed nonrandomized sequential order: Control-IG-Control-EG. Each stimulus presented on the screen lasted for 1000 ms. The task was performed exclusively with the left hand. For both activation conditions each left hand finger except the thumb was assigned a given number (1 was considered the little finger and 4 the index finger) and this assignation lasted throughout the entire task, regardless of the condition. To minimize movement, subjects were instructed before entering the scanner to maintain their arms in a 90º position moving exclusively their fingers during activation conditions, being able to relax them during the control block.

For the IG Sequence condition, participants were instructed the tapping sequence order a week before the fMRI session and were told to practice it during 10 minutes at least 5 different days during the week. To prove that participants were performing the training correctly, it was asked them to submit a 3-minute video doing the learned movement sequence two days before the scanning session. An additional verification to determine whether the subject knew the sequence was made before performing that same tapping sequence inside the scanner. The visual stimulus (0 and 9) shown on the screen marked the pace in which participant had to tap with their left thumb to perform the following practised sequence: 2-4-1-3-4-2-3-1-4-3-2-1. In the EG condition, a specific random number sequence of numbers appeared on the screen with a frequence of 1 second per stimulus. The participant had to follow the externally driven sequence by tapping with their thumb the corresponding finger to match each

appearing number (see Fig. 1). The task was administered using E-Prime 3.0 software (Schneider et al. 2012) and presented through MRI-compatible googles (VisuaStim Digital, Resonance Technology Inc.).

Image Processing

Functional images were processed with the Statistical Parametric Mapping software package (SPM12; Welcome Trust Centre for Neuroimaging, London, UK). The followed preprocessing pathway included: (a) aligning the functional data to the AC-PC plane by using the anatomical image; (b) head motion correction, with realigning and reslicing the functional images to the mean functional image; (c) susceptibility distortion correction using the HySCO module, based on pairs of images acquired with reversed phase-encoding directions (pepolar acquisition); (d) initial segmentation of the anatomical image and bias correction; (e) creation of a corrected anatomical image using the Image Calculator (ImCalc) restricted to brain tissue; (f) coregistration of the corrected anatomical image to the mean functional image; (g) segmentation of the coregistered anatomical image to derive deformation fields; (h) spatial normalization of the HySCO-corrected functional images to the MNI space (voxel size: 3 × 3 × 3 mm; 4th-order interpolation); and (i) spatial smoothing with a 4 mm full-width-at-half-maximum (FWHM) Gaussian kernel for the VG task to preserve spatial specificity in language areas and a 6 mm FWHM for the motor task to improve signal-to-noise ratio and sensitivity in broader sensorimotor activations. The BOLD (Blood-Oxygen-Level-Dependent) signal was estimated by convolving each task´s block with the canonical hemodynamic response function (HRF). Six motion realignment parameters were included as nuisance regressors in the GLM and a high-pass filter (128 s) was applied to the contrast image to consider low-frequency drifts.

Statistical Analysis

Voxel-wise whole-brain activations during MSE tasks were extracted to analyse the relation between language lateralization and motor learning. One-sample *t*-tests were carried out to explore the activation pattern of the whole sample (N = 98). Voxel-wise two-sample *t*-tests were also conducted to explore differential activation between language groups across MSE task conditions. Both, one-sample and two-sample t-tests were thresholded at a voxel-wise significance level of $P < 0.001$, with cluster-level family-wise error (FWE) correction applied at $P < 0.05$.

RESULTS

IG and EG innovative motor sequences rely, respectively, on dorsal and ventral areas related to motor learning

To verify which areas were directly involved in each of the motor conditions of the MSE task, a whole-brain one sample *t* test was conducted for both ‘IG sequence > control’, ‘EG sequence > control’ contrasts. Both tests revealed wide activations including bilateral motor areas and cerebellum, with local maximas in the right motor areas and left Cerebellum. This pattern was expected as participants who performed this motor task were left-handed. Results of the ‘IG sequence > control’ showed 3 significant

clusters voxel-wise threshold of $p < .001$ with cluster-level family-wise error correction (FWEc: $p<.05$; Table 1a). In the case of 'EG sequence > control' contrast, 2 significant clusters with the same conditions were obtained (FWEc: $p<.05$; Table 1b). Activation distribution for both conditions is shown in Fig. 2.

Table 1
List of cluster-corrected significant brain activations for each of the contrasts between conditions of the MSE task

	BA	Cluster Extent (k)	MNI Space			t-value
			x	y	z	
a) IG > Control						
Right Precentral Gyrus	4	8812	39	-16	50	21.41
Left Cerebellum	-	941	-18	-52	-28	20.65
Left Frontal Pole	45	67	-42	38	14	4.41
b) EG > Control						
Right Precentral Gyrus	4	5333	39	-16	50	21.78
Left Cerebellum	-	2736	-21	-49	-28	20.12
c) IG > EG						
Posterior Division Right Supramarginal Gyrus	40	2922	42	-43	41	11.60
Paracingulate Gyrus	24	4291	3	29	35	11.56
Posterior Division Cingulate Gyrus	-	178	-3	-25	23	7.49
Cerebellum	-	246	3	-46	-25	7.41
Intracalcarine Cortex	17	330	-9	-85	2	4.68
d) EG > IG						
Inferior Division Right Lateral Occipital Cortex	19	1358	39	-88	-4	13.84
Inferior Division Left Lateral Occipital Cortex	19	1411	-39	-85	-7	12.17
Left Postcentral Gyrus	4	380	-54	-13	50	9.07
Left Frontal Pole	9	951	-12	47	35	9.02
Posterior Division Cingulate Gyrus	26	395	-3	-46	26	7.65
Right Postcentral Gyrus	3	484	45	-22	59	6.76
Anterior Division Right Middle Temporal Gyrus	-	138	63	-7	-19	6.22

a), b), c) and d) correspond to the IG > Control, EG > Control, IG > EG and EG > IG contrasts, respectively, in the whole sample. e) and d) refer to IG > Control and EG > IG contrasts in the Atypical > Typical comparison

	BA	Cluster Extent (k)	MNI Space			t-value
			x	y	z	
Right Insular Cortex	48	130	39	-13	14	5.97
Left Angular Cortex	48	102	-36	-16	8	5.35
Anterior Division Left Middle Temporal Gyrus	21	158	-60	-7	-22	5.16
Left Postcentral Gyrus	2	104	-21	-40	62	4.81
e) EG > Control (Atypical > Typical)						
Right Angular Gyrus	39	123	48	-61	35	4.46
f) EG > IG (Atypical > Typical)						
Superior Division of the Right Lateral Occipital Cortex	39	163	45	-70	35	5.93
Right Precuneus	7	2736	12	-64	35	4.92

a), b), c) and d) correspond to the IG > Control, EG > Control, IG > EG and EG > IG contrasts, respectively, in the whole sample. e) and d) refer to IG > Control and EG > IG contrasts in the Atypical > Typical comparison

To further study whether any brain region was more closely related to one type of movement or other, two one sample *t* tests were performed (one for 'IG sequence > EG sequence' contrast and another for the opposite contrast. Again, a voxel-wise threshold of $p < .001$ with cluster-level family-wise error correction (FWEc: $p<.05$) was employed. Five significant clusters resulted of the first contrast while EG movements in comparison with IG ones evoked 11 significant clusters. Results appear on Table 1c, Table 1d and Fig. 3.

Both IG and EG innovative motor processing shifts its lateralization in relation to language lateralization

To test whether language lateralization affects the lateralization of new motor sequences processing, two sample *t* tests between participants with typical and atypical language lateralization were also carried out. A voxel-wise threshold of $p < .001$ with cluster-level family-wise error correction (FWEc: $p<.05$) was used. In the 'EG sequence > control' contrast, compared with the typical group, the atypical group showed significantly greater activation in the Right Angular Gyrus (Table 1e; Fig. 4a). No significant differences in Typical>Atypical in that contrast were found with the same statistical threshold. In addition, in the 'IG sequence > control' contrast, none of the differences in activation between both groups survived cluster-level FWE correction.

We finally performed another two-sample *t* test to compare both language lateralization groups using the contrast between the two motor conditions. Two clusters resulted significant using a voxel-wise

threshold of $p < .001$ with cluster-level family-wise error correction (FWEc: $p<.05$). Specifically, increased activations in ALL participants in comparison to TLL subjects was found in the Superior Division of the Right Lateral Occipital Cortex and in the Right Precuneus (Table 1f; Fig. 4b). In the opposite direction (TLL > ALL), no cluster-corrected statistical differences were found.

DISCUSSION

The present study was designed to test the hypothesis that left-handers with atypical language lateralization recruit right frontoparietal motor regions for the control of motor learning more than those with typical language lateralization. To this end, two groups of left-handers with typical and atypical language lateralization performed two motor learning tasks under IG and EG conditions. At the whole-group level, the results were consistent with previous studies, especially with Jenkins et al. 2000, showing greater involvement of occipitotemporal and anterior frontal regions during the EG task, and greater activation of posterior frontal and parietal regions during the IG task. Importantly, the between-group comparison revealed greater involvement of the right precuneus and right supramarginal gyrus in left-handers with atypical language lateralization during the EG motor task. These findings therefore suggest that atypical language lateralization is associated with greater recruitment of right parietal regions during the initial stages of motor learning, extending previous findings from studies of praxis (Vingerhoets et al., 2013).

The current study aimed to identify the most relevant brain regions to the execution of different types of novel motor sequences, which rely on motor learning and may involve internally and externally guided movements (Bera et al., 2021). Before interpreting the results, it is important to clarify the differences between the two conditions. The IG condition required five days of prior practice, with performance on the day of the fMRI session being verified by requiring participants to perform the task perfectly before entering the scanner. Although the task was performed at a pace indicated by external stimuli that signaled when a response should be initiated, the response itself was internally generated. In contrast, the EG task was not practiced beforehand and therefore involved the acquisition of a completely novel motor sequence.

The neural results indicate a substantial overlap between the two conditions when each was contrasted with the motor-rest condition. Previous studies have highlighted the importance of temporal sequencing, and specifically whether the sequence is determined by external stimuli or generated internally by the individual, in distinguishing between different types of motor tasks (Ariani et al., 2015). When contrasted with rest, both conditions activated bilateral motor, parietal, supplementary motor area (SMA), anterior cingulate, lateral premotor, and cerebellar regions (see Fig. 2). Despite these common activations, a distinct cortical pattern differentiating the two motor conditions was observed. The direct comparison between the two motor conditions showed that, although IG novel movements were associated with activation of a common network including parietal, premotor, SMA, and posterior frontal regions, the EG condition preferentially recruited occipitotemporal regions, primary sensorimotor cortex, the left angular gyrus, and the frontal pole. Despite some methodological differences and the fact that previous studies

have primarily examined right-handed participants, these findings are largely consistent with those reported in previous research (Jenkins et al., 2000).

First, greater SMA activation was observed for the IG condition than for the EG condition, consistent with previous findings (Mushiake et al., 1991; Wessel et al., 1997). Contrary to the greater lateral premotor activation for the EG condition suggested by previous neurophysiological studies (Mushiake et al., 1991), our results showed greater lateral premotor activation during the IG condition, in agreement with the findings of Jenkins et al. (2000). This discrepancy with previous neurophysiological studies may be explained by the fact that the internally guided condition also involved external stimuli and is more extensively practiced. Two additional activations were observed for the EG condition relative to the IG condition: bilateral primary sensorimotor cortex and the left angular gyrus. The greater involvement of primary sensorimotor cortex likely reflects the greater motor response demands associated with the EG condition. The recruitment of the left angular gyrus, in contrast, may reflect greater demands on visuomotor integration during the initial stages of motor learning, when participants must continuously integrate the visual information specifying the required response with its corresponding motor output. Beyond the motor regions, the EG condition during this novel motor learning task also recruited two additional regions that may be particularly relevant to the demands of the task. First, bilateral fusiform activation may reflect the processing of the numerical stimuli indicating which response should be performed, suggesting greater reliance on visual processing of the response cues. Second, activation of the frontal pole may be related to the increased cognitive demands associated with acquiring a novel motor sequence, potentially reflecting greater involvement of anterior prefrontal regions in the monitoring and control of ongoing learning (Jueptner et al., 1997). Overall, the activation patterns observed in the two conditions are consistent with our predictions and with the proposed distinction between internally and EG motor learning.

The exploration of lateralization patterns was carried out by comparing groups with typical versus atypical language lateralization, with the latter including right-lateralized and bilateral participants. The results showed that the areas most relevant to the execution of EG novel motor sequences were more active in the right hemisphere in participants with atypical than typical language lateralization. Specifically, the right angular gyrus showed significant activation in the EG > rest contrast, whereas the right precuneus and right lateral occipital cortex were significant in EG > IG. All three associative regions appear to be crucial for the EG condition. The angular gyrus plays a role in the multisensory integration processes required to translate external visual information into an appropriate motor response (Block et al., 2013). Such integration is required to produce the correct finger tap in response to the information presented on the screen. The significant posterior activation pattern in the EG > IG contrast is consistent with this interpretation and may reflect the greater visuospatial and visuomotor demands involved in translating online visual cues into appropriate motor responses rather than executing previously rehearsed motor sequences. The lateral occipital cortex may contribute to the perceptual and action-related processing of external stimuli (Astafiev et al., 2004; Ogawa & Inui, 2009), whereas the precuneus may support the visuospatial transformations and sensorimotor integration required to guide movement according to those stimuli (Hackney et al., 2015).

A clear lateralization pattern was not observed for the IG condition. This difference between the two conditions may suggest that differences in hemispheric lateralization are particularly evident during the early stages of motor learning, when the functional relationships between parietal, premotor, and primary motor regions are being established within the motor network. In contrast, such differences may become less apparent once the task has been extensively practiced and its control becomes more internally driven.

In this regard, it is worth noting that pantomimes, which involve well-established and extensively practiced motor skills involving tool use, have also been shown to recruit the right hemisphere to a greater extent in atypical than in typical left-handers (Vingerhoets et al., 2013). Taken together, these findings suggest that EG motor learning may be associated with a greater involvement of right-hemisphere motor regions in left-handers with atypical language lateralization. This pattern would be consistent with models of atypical brain organization proposing that functional development may occur probabilistically in a mirror-like fashion across the two hemispheres (Gerrits, 2024).

In summary, the present study introduces two conditions for studying how novel motor sequences are executed using fMRI. For the first time, a cortical configuration was identified in which a more dorsal and premotor activation pattern was associated with IG movements, whereas ventral areas primary motor regions and the frontal pole were associated with EG movements. The lateralization analysis revealed that only the EG condition clearly shifted with atypical language lateralization, consistently with results obtained with pantomimes.

Declarations

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Data repository

The data used in this study has been deposited in repository and is freely available for replication: https://figshare.com/s/c9bde3e1922010e33ada

Ethics approval

All methods were carried out in accordance with guidelines and regulations approved by the Research Ethics Committee of Jaume I University (reference number: CEISH/89/2024).

Consent to participate

Written informed consent was obtained from all participants, following a protocol approved by Jaume I University, and they received monetary compensation for their participation.

Consent to publish

The authors affirm that every participant provided informed consent for the publication of data.

Generative IA and AI-assisted technologies statement

During the preparation of this work, the authors used ChatGPT (OpenAI) solely to assist with language editing. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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Author Contribution

M.BP. and C.CM. contributed to the study conception and design, material preparation, and data collection. C.CM also supervised the data analysis process. C.A. contributed to the study conception and design and the study funding. J.GM. contributed to the analysis of data and wrote the first draft of the manuscript. All authors commented on previous versions of the manuscript, read and approved the final manuscript.

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Data Availability

The data used in this study has been deposited in repository and is freely available for replication: https://figshare.com/s/c9bde3e1922010e33ada

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29. Statements & Declarations

Figures

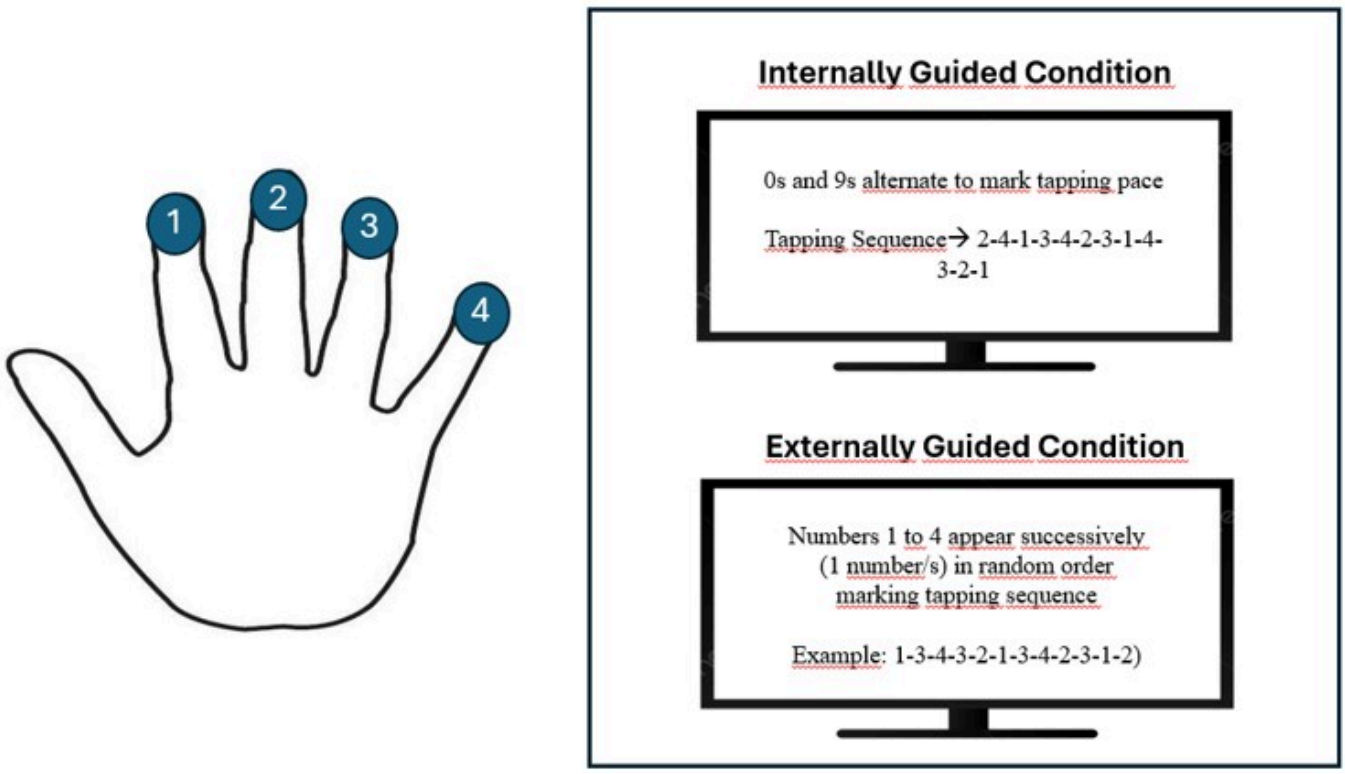


Figure 1

Graphical explanation of the IG and EG conditions of the Motor Sequence Execution Task

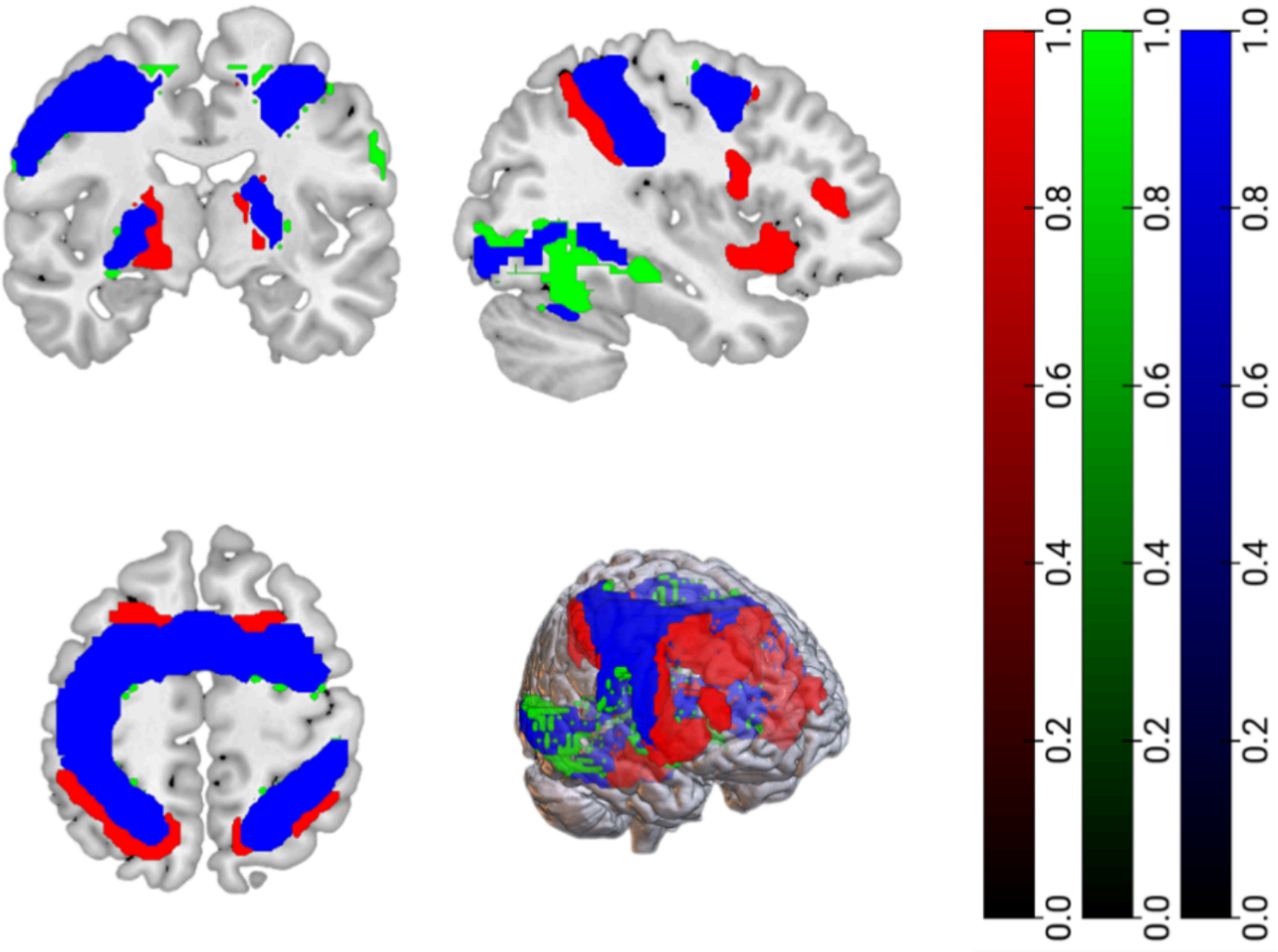


Figure 2

Activation distribution for the MSE task for the whole sample. Red represents IG>Control contrast; green shows EG>Control contrast. Overlap is shown in blue. Color bars express t-values

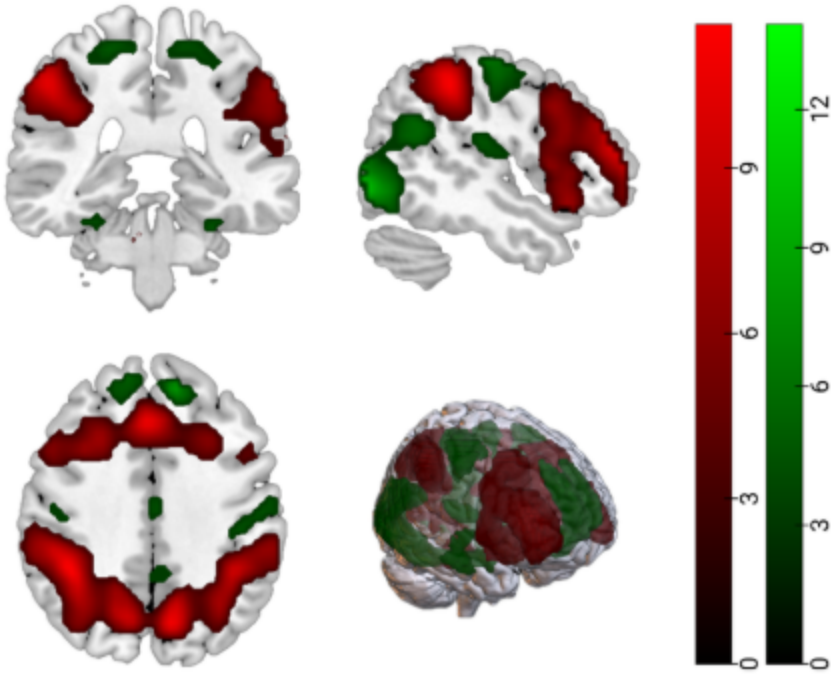


Figure 3

Activation distribution for the MSE task for the whole sample. Red represents IG>EG contrast; green shows EG>IG contrast. Color bars express t-values

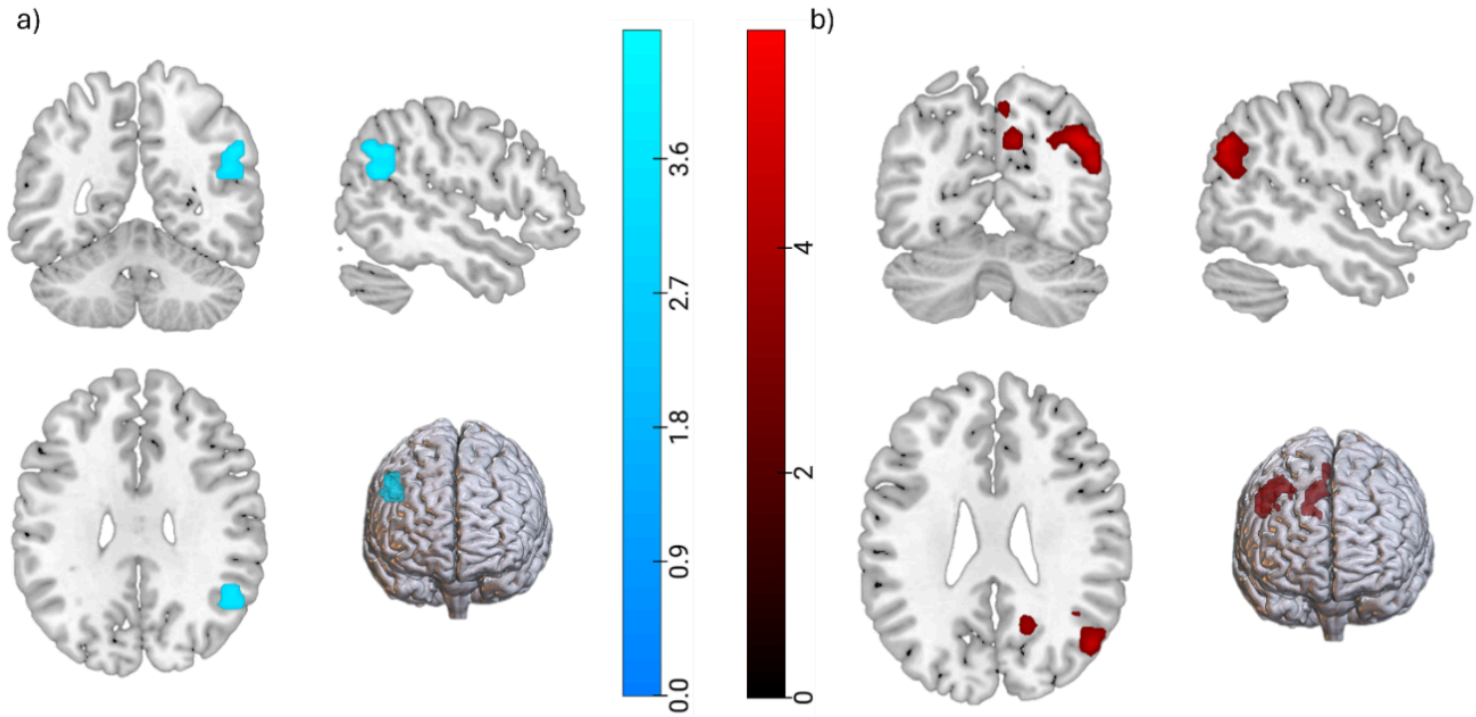


Figure 4

Differential results between both language lateralization groups for the MSE task. a) represents the comparison Atypical > Typical in the EG > Control contrast. b) represents the Atypical > Typical

comparison in the EG>IG contrast. Color bars express t-values