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RESEARCH ARTICLE

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Mapping brain structure and function in professional fencers: A model to study training effects on central nervous system plasticity

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Abstract

Brain magnetic resonance imaging (MRI) studies have shown different patterns of structural and functional reorganization in high-level athletes compared with controls, but little is known about their relationship with interlimb coordination mechanisms. To this aim, we investigated brain structural and functional differences in high-level fencers compared with nonathlete controls and the MRI substrates of interlimb coordination in elite athletes. Fourteen right-handed male fencers (median age = 22.3 years) and 15 right-handed age- and sex-matched healthy subjects (median age = 22.4 years) underwent structural and functional MRI acquisition during the execution of cyclic bimanual-movements as well as during in-phase and antiphase hand/foot-movements of the dominant-right limbs. No between-group differences were found in gray matter volumes and white matter architecture. Active-fMRI showed that controls versus fencers had higher activations in parietal and temporal areas during bimanual-task; whereas fencers versus controls had higher activations in the basal ganglia. During in-phase task, controls versus fencers showed higher activation of right cerebellum, whereas fencers had higher activity mainly in frontal areas. The functional-connectivity (FC) analysis showed that fencers versus controls had an increased FC between left motor cortex and fronto-temporal areas as well as bilateral thalami during the different tasks. Intensive and prolonged fencing activity is associated with brain functional changes mainly involving frontal regions related to high-level motor control and planning of complex tasks. These modifications are likely to reflect an optimization of brain networks involved in motor activities, including interlimb coordination tasks, occurring after intensive training.

KEYWORDS

athletes, functional MRI, motor coordination, MRI, neuroplasticity

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1 | INTRODUCTION

Coordination of different limb segments is essential for many activities of daily living, including manipulating objects, playing sports, and musical instruments, each requiring the ability to produce specific patterns of interlimb coordination. Hence, the study of coordination mechanisms is of particular interest for gaining insight into the organization of voluntary movements (Baldissera et al., 1991; Rocca et al., 2007). Complex coordination skills are also considered in the study of higher cognitive functions (e.g., attentional processes). Limb-segment coordination may be investigated through the study of interlimb coordination tasks, which informs about normal motor function and has great importance for understanding many neurological disorders affecting motor coordination. Therefore, it might help developing novel rehabilitation interventions (Handelzalts et al., 2019; Rocca et al., 2019).

Magnetic resonance imaging (MRI) techniques have been widely used to investigate brain structural and functional correlates of experience-induced neuroplasticity in healthy individuals (Tardif et al., 2016). These aspects have been also analyzed in musicians and athletes, who are considered among the best examples of neuroplastic adaptation due to their high motor-skill demand. During the interlimb coordination task of in-phase and anti-phase bimanual movements, "musically naïve" subjects had increased functional MRI (fMRI) activation in several brain regions compared with concert pianists, suggesting that the latter had higher efficiency of cortical and subcortical systems for bimanual movement control (Haslinger et al., 2004). Other studies in musicians showed an enlargement of cortical finger representations, an increased size of the corpus callosum and structural modifications of motor and cerebellar regions (Hutchinson et al., 2003; Schlaug et al., 1995). After 40-h golf practice, a significant decrease of neuronal recruitment in the right and left dorsal premotor cortex was found while mentally rehearsing a swing in golf novices but not in a control group (Bezzola et al., 2012).

Structural MRI studies in athletes demonstrated several differences of gray matter (GM) morphology and white matter (WM) architecture between competitors and noncompetitors in a given discipline and the occurrence of longitudinal structural changes following training. Skilled-golfers had larger fronto-parietal GM volumes and lower fractional anisotropy (FA) values in regions closer to the corticospinal tract compared with less skilled-golfers (Jancke et al., 2009), while basketball players showed an increased cerebellar volume, probably caused by continual practice of complex motor skills, compared with controls (Park et al., 2009). After a 40-h golf practice, an increased GM volume was found in fronto-parietal cortices only in golf novices and it was positively associated with training intensity (Bezzola et al., 2011).

Despite these findings, the MRI substrates of interlimb coordination have been only marginally evaluated (Debaere et al., 2001). Aim of this study was to investigate differences in brain GM morphology, WM architecture and patterns of functional recruitment during interlimb coordination in high-level fencers compared with nonathlete controls. Among sport activities, fencing requires high-level physical abilities (Tsolakis et al., 2010), important perceptual and psychological demands (Roi & Bianchedi, 2008), as well as fast responses and inhibitory abilities (Di Russo et al., 2006). It also requires an optimal level of interlimb coordination; in fact, it requires asymmetrical motor skills, with a prevalence of the dominant side. For example, during the lunge, the ipsilateral upper and lower limbs need to be spatially and temporally synchronized in order to reach the target (hand-foot in-phase movement). This feature of fencing let us to hypothesize that fencers could show a specific pattern of activation of the brain areas and neural circuits involved in interlimb coordination. In line with this, a recent review on 37 studies summarized the biomechanics of fencing, and it showed that elite fencers exhibited optimized sequential coordination of upper and lower limb movements, compared with novice fencers and controls (Chen et al., 2017). This resulted in improved action execution and higher forward linear velocity. Against this background, to explore brain structural and functional MRI differences in high-level fencers compared with nonathlete controls and the possible MRI substrates of interlimb coordination in elite athletes, we compared cortical activation patterns in elite fencers and nonathletes during the execution of three different types of coordination movements (i.e., cyclic in-phase and antiphase flexion-extension of the right hand and foot, and cyclic antiphase flexion-extension of both hands).

2 | METHODS

2.1 | Subjects and functional evaluation

We recruited 29 right-handed and right-footed (Oldfield, 1971) young healthy male subjects: 14 elite fencing athletes (median age = 22.3 years; interquartile range [IQR] = 20.1, 23.5) and 15 age-matched controls (median age = 22.4 years; IQR = 20.8, 24.7 years). Data on sport activities and medical status were recorded.

Fencers had to meet the following criteria: (1) being members of "Federazione Italiana Scherma"; (2) holding the sword exclusively with their right hand; (3) fencing experience lasting at least 10 years and a training frequency of ≥6 h per week or, for athletes with a fencing experience of at least 6 years, a training of ≥8 h per week; (4) regularly participating in national and/or international championships.

Control subjects could practice various sports at a non-professional level, but none of them should have had experience in fencing, neither at competitive or amateur level. The maximum training intensity allowed was 6 h per week.

For both groups, exclusion criteria were: (1) a history of serious medical, neurological or psychiatric illness, (2) muscle, joint or bone injuries of the upper or lower limbs, and (3) intake of psychotropic drugs or alcohol abuse.

Motor function assessment was performed for all subjects at the time of MRI acquisition using the nine-hole peg test

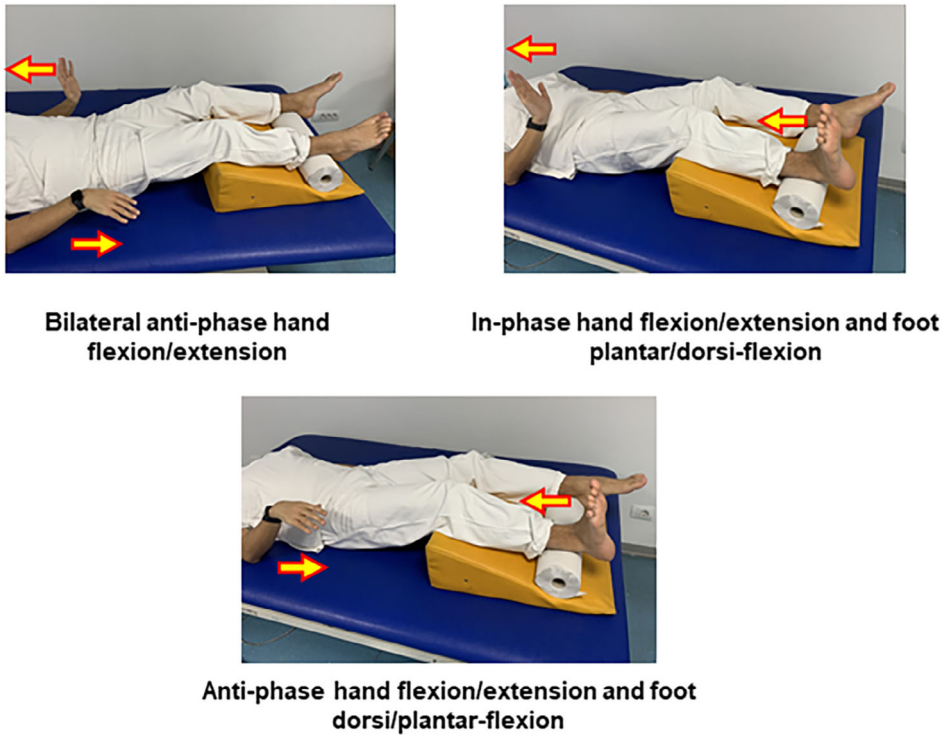

FIGURE 1 Set-up of active fMRI tasks: (a) bimanual anti-phase task; (b) right-limb in-phase task; and (c) right-limb anti-phase task

(9HPT) and the maximum finger-tapping frequency (FT) in 30 s. Each test was administered twice for both hands and then averaged.

Institutional Review Board of the IRCCS San Raffaele Scientific Institute provided ethical approval and written informed consent from each subject was obtained prior to study enrolment.

2.2 | MRI acquisition

In all subjects, using a 3.0 Tesla Philips Intera scanner (Philips Medical Systems, Eindhoven, The Netherlands), the following brain MRI scans were acquired: (a) dual-echo turbo spin echo (TR/TE = 2599/16–80 ms, echo train length = 6; flip angle = 90°, matrix size = 256 × 256, FOV = 240 × 240 mm^2, 44 axial 3 mm thick slices); (b) three-dimensional (3D) T1-weighted fast field echo (TR/TE = 25/4.6 ms; flip angle = 30°; matrix size = 256 × 256; FOV = 230 × 230 mm^2; 220 contiguous, axial slices with voxel size = 0.89 × 0.89 × 0.8 mm); (c) pulsed-gradient spin-echo EPI (TE/TR = 80/8283.2 ms; acquisition matrix size = 96 × 96; FOV = 240 mm^2; 55 contiguous, 2.3 mm thick axial slices) with SENSE (acceleration factor = 2) and diffusion gradients applied in 35 noncollinear directions. Two optimized b factors were used for acquiring diffusion weighted images (b1 = 0, b2 = 900 s/mm^2); (d) T2*-weighted single-shot EPI sequence during the performance of three coordination tasks (TE = 35 ms, flip angle = 85 ms, matrix size = 128 × 128, FOV = 240 mm^2, TR = 3.0 s). During each functional scanning run, 60 sets of 30 axial slices, parallel to the AC-PC plane, with a thickness of 4 mm, covering the whole brain were acquired.

For all scans, the slices were positioned to run parallel to a line that joins the most infero-anterior and infero-posterior parts of the corpus callosum.

Dual-echo scans were analyzed to exclude the presence of macroscopic brain lesions.

2.3 | FMRI tasks and design

During the fMRI tasks, subjects lied supine in the scanner, with a cushion under the flexed knees to ensure free ankle flexion-extension. The upper limbs were extended along the trunk and the distal part of each arm was supported by two roper pillows to enable free movement of the wrist. To further minimize hand movements, two additional cushions were placed upon the prone forearms. Wrists and feet were positioned in nonferromagnetic orthosis to allow experimenters to control the extent of movements (Figure 1). To avoid visual guidance, subjects were blind-folded.

Subjects were instructed to perform three different tasks: (1) bilateral cyclic anti-phase flexion-extension of the hands; (2) unilateral in-phase flexion-extension of the right hand and foot; and (3) unilateral anti-phase flexion-extension of the right hand and foot.

During the right-limb in-phase coordination pattern, upper and lower limbs moved in the same direction (i.e., hand flexion and foot plantar flexion or hand extension and foot dorsal-flexion). During the right-limb anti-phase coordination pattern, the segments were moved in opposite directions (i.e., hand flexion was combined with foot dorsal-flexion or vice versa for the unilateral pattern; while hand flexion was combined with the extension of the contralateral hand for the bilateral pattern).

Right hand-foot coordination movements were paced by a metronome at 1 Hz, whereas bilateral hand-hand coordination movements were paced at 1.8 Hz frequency. These speed rates ensured that all subjects (fencers and controls) could perform in-phase and anti-phase movements without phase shift. These frequencies were selected after a preliminary analysis of a group of healthy subjects, who did not take part to the present study (data not shown), in order to have similar between-subject task performance.

Before performing the study, outside the magnet, subjects were trained to perform the tasks until they could make the movements in a relaxed manner to avoid intra-session learning effects and to obtain similar motor performance between groups while in the scanner.

FMRI was acquired using a block design (ABAB), where six periods of activation were alternated with six periods of rest, each period of activation and rest including five measurements. The subjects were scanned while performing the three tasks previously described, split into three different runs, randomized among subjects. During the active phases of each run, each subject was instructed to perform only a specified movement, while during the rest phase the subjects lied supine with prone forearms along their side. During fMRI acquisition the subjects were monitored visually by an observer to ensure accurate task performance and to check for additional movements (e.g., mirror movements).

2.4 | Voxel-based morphometry

Voxel-based morphometry, as implemented in SPM12 (www.fil.ion.ucl.ac.uk/spm/), was used to map the differences in regional GM volumes between the two study groups. The 3D T1-weighted images were used for a group-wise alignment: first, the images were segmented into different tissue types via the Segmentation routine in SPM12 (Ashburner & Friston, 2005). Then, GM and WM segmented images of all subjects, in the closest possible rigid-body alignment with each other, were used to produce GM and WM templates and to drive the deformation to the templates. At each iteration, the deformations, calculated using the Diffeomorphic Anatomical Registration using Exponentiated Lie algebra (DARTEL) registration method (Ashburner, 2007), were applied to GM and WM, with an increasingly good alignment of subject morphology, to produce templates. Finally, an affine transformation that maps from the population average (DARTEL Template space) to MNI space was calculated. GM maps were spatially normalized, modulated and smoothed with an 8 mm Gaussian kernel. Regional between-group differences in GM volumes were assessed using the general linear model and the theory of Gaussian fields (Friston et al., 1995). To limit the analysis to the GM, an inclusion mask obtained from the GM DARTEL Template, transformed to the MNI space, smoothed, and thresholded at 0.5, was used.

2.5 | Tract-based spatial statistic

Diffusion-weighted images were corrected for distortions induced by the eddy currents and for head movements, and transformed to MNI space (http://white.stanford.edu/mrdiff/). Then, using the FMRIB's Diffusion Toolbox (FDT tool, FSL 5.0.5, http://www.fmrib.ox.ac.uk), the diffusion tensor (DT) was estimated in each voxel by linear regression (Basser et al., 1994) and fractional anisotropy (FA) maps derived. Tract-based spatial statistic analysis was used for voxelwise analysis of whole brain WM DT MRI measures (http://www.fmrib.ox.ac.uk/fsl/tbss/index.html/). In detail, individual FA images were nonlinearly registered to the FMRIB58_FA atlas (Rueckert et al., 1999) provided within FSL, and averaged. The resulting mean FA image was thinned to create a WM tract "skeleton", which was thresholded at a FA > 0.2 to include only WM voxels. Individual subjects' FA values were projected onto this group skeleton by searching perpendicular from the skeleton for maximum FA values. Maximum FA values were chosen in order to restrict analysis to the center of WM tracts (where maximum FA values are found), rather than considering voxels at the edge of tracts, which may suffer from partial volume effects.

Tract-based spatial statistic (TBSS; Smith et al., 2006) was used to map WM microstructural differences between the two study groups. Voxel-wise differences of FA values between fencers and controls were tested using a permutation method (the "Randomize" program within FSL) (Nichols & Holmes, 2002). The number of permutations was set at 5000 and threshold-free cluster enhancement option was used (Smith & Nichols, 2009).

2.6 | FMRI analysis

FMRI data were analyzed using the SPM12 software. Prior to statistical analysis, all images were realigned to the first one to correct for subject's motion, spatially normalized into the Montreal Neurological Institute (MNI) space, and smoothed with a 10 mm 3D Gaussian filter. None of the subjects was excluded from the analysis because of motion, since the maximum cumulative translation was <1.5 mm and the maximum rotation was <0.3° for all of them. Changes in blood oxygenation level dependent (BOLD) contrast associated with the performance of the motor tasks were assessed on a voxel-by-voxel basis using the general linear model (Friston et al., 1995) and the theory of Gaussian fields (Worsley & Friston, 1995). Specific effects were tested by applying appropriate linear contrasts. Significant hemodynamic changes for each contrast were assessed using *t* statistical parametric maps (SPMt). The activations during the performance of the different tasks and the comparisons between the different tasks were investigated using a random-effect linear models and one-sample or two-sample *t* test, as appropriate.

2.7 | Voxel-wise analysis of functional connectivity of the motor cortex

To assess the functional connectivity (FC) between functionally related anatomical structures, task related fMRI time series were processed in two steps: first, a region-of-interest (ROI), serving as a seed region for correlation, was selected, then a correlation analysis

TABLE 1 Main demographical and clinical characteristics of the two study groups

	Fencers ($n = 14$)	Controls ($n = 15$)	p value
Age (years)	22.3 (20.1, 23.5)	22.4 (20.8, 24.7)	.70
Professional activity (years)	13.0 (11.0, 14.0)	–	–
Training duration (hours/week)	9.0 (8.5, 12.0)	–	–
Right 9HPT (s)	18.4 (17.6, 20.2)	17.5 (16.8, 19.3)	.70
Left 9HPT (s)	20.2 (18.9, 21.9)	19.6 (18.8, 20.3)	.73
Right FT (taps in 30 s)	145 (137, 157)	138 (124, 144)	.07
Left FT (taps in 30 s)	135 (123, 147)	131 (122, 144)	.73

Note: Data reported as median and interquartile range.
Abbreviations: FT, finger tapping; 9HPT, nine-hole Peg Test.

between this seed region and all the remaining voxels of the brain was performed. Using rest software (http://resting-fmri.sourceforge.net/), time series (including both rest and active periods for each motor task) were extracted on the normalized and smoothed images form each subject from a spherical volume (radius, 5 mm) within a priori defined cluster centered at the most significant activated voxels in the left-motor cortex (MC; corresponding to hand-motor area). The location of the cluster in the left-MC was defined, for each individual, on the single-subject SPMt thresholded at $p < .001$ for unilateral in-phase flexion-extension of the right-hand and foot task. The value of the SPMt statistic associated with these voxels was taken as a measure of the activity level of each subject. FC was investigated by assessing the correlation between the left MC and any other voxel of the brain using SPM software. This allowed us to obtain a spatial map of correlation with the left MC for each subject involved in the study.

2.8 | Additional statistical analyses

Demographic and clinical variables were compared between the two groups using Mann–Whitney *U* test.

Structural and functional MRI results were assessed using random-effect linear models, age-adjusted, $p < .05$, family-wise error (FWE)-corrected at voxel-wise level. For explorative purposes, results were also tested at $p < .001$, uncorrected (cluster extent [kE] = 10).

For active fMRI scans, a 2 × 2 factorial analysis (group × task) was performed to investigate the interactions between groups (fencers vs. controls) and tasks (bimanual antiphase vs. right-limbs antiphase movements, right-limb antiphase vs. in-phase movements).

3 | RESULTS

3.1 | Subjects

Table 1 summarizes the main demographic and behavioral characteristics of the two study groups. The groups did not differ for age, 9HPT and FT performances.

3.2 | Structural MRI analysis

No abnormalities were detected on brain dual-echo scans acquired from all the subjects. VBM and TBSS analyses showed no regional GM volume or WM FA differences between the two study groups.

3.3 | Functional MRI: analysis of activation

During fMRI acquisition, all the subjects performed the tasks correctly and no additional movements were noted.

3.3.1 | Bimanual anti-phase hand-hand coordination movements

Compared with fencers, controls had more significant activation of the left inferior temporal gyrus and left middle cingulum ($p < 0.05$, FWE, Table 2 and Figure 2). At uncorrected threshold, a more significant activation of the left middle temporal gyrus, right supramarginal gyrus, left cerebellar lobule III, right inferior temporal gyrus, right middle frontal gyrus, left medial superior frontal gyrus, and right inferior parietal lobule was also found in controls versus fencers (Table S1). Compared with controls, fencers had more significant activation of the right pallidum ($p < .05$, FWE, Table 2 and Figure 2) and, at uncorrected threshold, of the left postcentral gyrus (Table S1).

3.3.2 | Right in-phase hand-foot coordination movements

Compared with fencers, controls had more significant activation of the right cerebellar lobule VI ($p < .05$, FWE, Table 2 and Figure 2). The opposite comparison showed that fencers had more significant activation of the bilateral middle frontal gyrus ($p < .05$, FWE, Table 2 and Figure 2). At uncorrected threshold, fencers also showed a more significant activation of the right precentral gyrus, left postcentral, left superior temporal gyrus, and left inferior frontal gyrus (Table S1).

TABLE 2 Significant results of between-group comparisons during active fMRI tasks ($p < 0.05$, family-wise corrected for multiple comparisons)

	Anatomical areas	BA	MNI coordinate (x, y, z)	*T* value	kE
Bimanual anti-phase task					
Controls > fencers	Left inferior temporal gyrus	20	−48, −22, −18	4.70	54
	Left middle cingulum	–	0, −36, 40	4.34	31
Fencers > controls	Right pallidum	–	20, −4, 6	4.44	30
Right-limb in-phase task					
Controls > fencers	Right cerebellar lobule VI	37	34, −52, −26	4.47	95
Fencers > controls	Left middle frontal gyrus	46	−34, 16, 38	4.39	37
	Right middle frontal gyrus	6	28, 6, 50	4.29	85

Abbreviations: BA, Brodmann area; fMRI, functional magnetic resonance imaging; kE, cluster extent; MNI, Montreal Neurological Institute.

3.3.3 | Right anti-phase hand-foot coordination movements

At corrected threshold, no significant differences of fMRI activation were detected between groups. At uncorrected threshold, compared with fencers, controls had more significant activation of the right cuneus (Table S1).

3.3.4 | Group × task interaction

Compared with controls, fencers showed higher activation of bilateral middle frontal gyrus (left: MNI-coordinates = −40, 18, 36; *T* value = 3.54, $p < .001$, kE = 19; right: MNI-coordinates = 44, 36, 32; *T* value = 3.86, $p < .001$, kE = 20) during right-limb in-phase versus antiphase movements. No interaction was found between bimanual antiphase versus right-limb antiphase movements.

3.4 | Functional MRI: analysis of left MC FC

Table 3 and Figure 3 summarize the patterns of left MC FC during the three tasks and the results of between-group comparisons.

3.4.1 | Bimanual anti-phase hand-hand coordination movements

Compared with controls, fencers had higher FC between the left MC and the bilateral thalami and right parahippocampal gyrus ($p < .05$, FWE). At uncorrected threshold, they also showed higher FC between the left MC and right middle occipital gyrus (Table S2).

3.4.2 | Right in-phase hand-foot coordination movements

Compared with controls, fencers had higher FC between the left MC and the right middle frontal gyrus ($p < .05$, FWE). At uncorrected threshold, fencers also showed higher FC between the left MC and left inferior frontal gyrus and left superior temporal gyrus (Table S2).

3.4.3 | Right anti-phase hand-foot coordination movements

At corrected threshold, no significant FC differences were detected between groups. At uncorrected threshold, compared with controls, fencers had an increased FC between the left MC and right supramarginal gyrus (Table S2).

4 | DISCUSSION

By applying a multimodal MRI approach, in this study we aimed to assess whether brain structure and function are influenced by intensive training in a highly coordinated sport like fencing. We chose top-level fencers since these athletes are highly trained to finely coordinate their ipsilateral upper and lower limb during a fencing action called "lunge." Accordingly, their evaluation may allow to investigate the neural correlates of interlimb coordination in elite athletes. We expected that they were likely to show different brain morphology or patterns of neural activation compared with nonathletes during the execution of different interlimb coordination tasks.

Interestingly, while no significant difference between fencers and controls was observed in terms of regional GM volumes and WM microarchitecture, fMRI analyses showed that, independently from the task performed, fencers had a different recruitment of cortical and subcortical areas compared with controls, possibly promoted by their intense, specific and asymmetric motor training.

During bimanual anti-phase task, compared with fencers, controls activated areas distributed throughout the temporo-parietal lobes, which have been identified as part of the circuits generally activated during such kind of activities (Duque et al., 2010; Lin et al., 2017) and are involved in attentional, visuospatial and coordination functions. Additionally, although not surviving correction for multiple comparisons, controls activated more than fencers other brain regions such as the cerebellum and the fronto-parietal cortices, which have previously

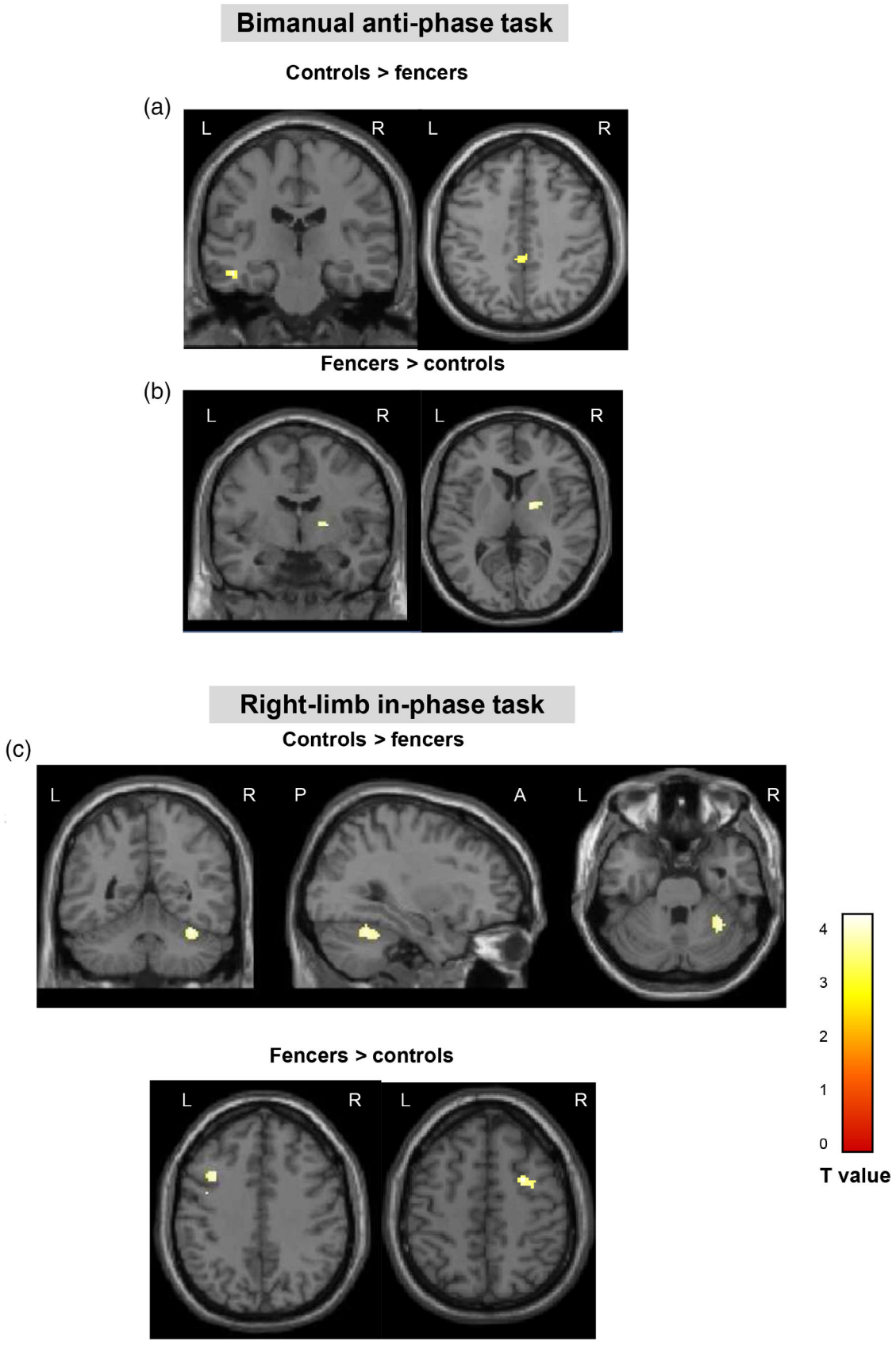

FIGURE 2 Random effect analysis showing, on a high-resolution T1-weighted image in the standard SPM space (neurological convention) regions of relative higher fMRI activations in: (a) controls > fencers and (b) fencers > controls during the performance of a bimanual anti-phase task; regions of relative higher fMRI activations in: (c) controls > fencers and in (d) fencers > controls during the performance of right-limb in-phase task. All comparisons are reported at $p < .05$, family-wise error corrected, and color-coded for t values. A, anterior; L, left; R, right; P, posterior

TABLE 3 Brain regions with significantly different FC with the left primary hand motor cortex between fencers and controls ($p < 0.05$, family-wise corrected for multiple comparisons)

	Anatomical areas	BA	MNI coordinate (x, y, z)	*T* value	kE
Bimanual anti-phase task					
Fencers > controls	Right thalamus	–	8, −16, 10	4.99	211
	Left thalamus		−6, −12, 10	4.75	
	Right parahippocampal gyrus	36	30, −14, −28	4.96	37
Right-limb in-phase task					
Fencers > controls	Right middle frontal gyrus	8	30, 8, 54	5.60	142

Abbreviations: BA, Brodmann area; FC, functional connectivity; kE, cluster extent; MNI, Montreal Neurological Institute.

shown to be involved in interlimb coordination (Debaere et al., 2001; Haslinger et al., 2004; Lin et al., 2017). The opposite comparison showed that fencers had higher activations in the right pallidum (i.e., basal ganglia). This region has a relevant role in sensorimotor function and motor control, and its functional modifications might suggest a recruitment optimization of areas involved in keeping the hands synchronized with auditory stimulation (Jantzen et al., 2005). Enhanced basal ganglia activity in initiating anti-phase hand movements has been related to their role in selecting specific actions and inhibiting competing ones (De Luca et al., 2010).

During right-limb in-phase movements, compared with fencers, controls showed an increased activation of the right cerebellum; conversely, fencers showed an increased activity mainly in bilateral middle frontal areas. It is tempting to speculate that intensive motor training might result in an imbalance in the cerebro-cerebellar interactions between pre-motor regions and the dentate nucleus (Grimaldi & Manto, 2012). In particular, fencers recruited cerebral areas involved in top-down control and planning of more skilled sport gestures (Di Russo et al., 2006; Xu et al., 2016), probably because the right hand-foot coordination pattern was a fully automatized task for them and their goal was to perform the movement in the best and more precise way as possible. On the other side, controls recruited the right cerebellum, a crucial area in early motor skill learning (Spampinato & Celnik, 2017), which ensures an online and feed-forward control on motor action especially for fast coordinate and not automatized movements (Pisotta & Molinari, 2014). This is also in line with a previous study showing right anterior cerebellar activations in a small group of healthy subjects performing in-phase wrist/ankle movements (Debaere et al., 2001).

The involvement of frontal regions in fencers reinforces the concept that athletes' skills are mediated not only by pure motor performance but also by a relevant cognitive component (Bezzola et al., 2012; Yarrow et al., 2009). Similar considerations have been reported by Scharfen and Memmert, who observed positive associations between specific motor skills and attentive as well as working memory functions in soccer players (Scharfen & Memmert, 2019).

During right-limb anti-phase movements, no area was significantly more activated in one group compared with the other one. It is likely that, for a more complex coordination pattern, only minimal differences exist among the two groups probably because fencers are used to perform in-phase movements (i.e., lunges) during their daily sportive practice and the anti-phase pattern is less frequent during their training.

These considerations are also supported by the analysis of interaction between groups and the two right-limb tasks, although these results should be considered with caution, since they were obtained at uncorrected threshold. We observed that fencers had an increased activation of bilateral frontal areas compared with controls during in-phase movements. According to the previous hypotheses (Di Russo et al., 2006; Xu et al., 2016), there could be a more evident frontal modulation in fencers during familiar interlimb movements.

FC analysis further supported the theory that in fencers there is an enhanced activity of the cortical-basal ganglia loops. Our study showed that, compared with controls, during bimanual task fencers had an increased FC between the left MC and bilateral thalami and right parahippocampal gyrus. As suggested by Wei et al. in professional divers (Wei & Luo, 2010), a selective activation of parahippocampal areas may be related to imagery of professional skills. As a consequence, it is tempting to speculate that the increased FC between left MC and the right parahippocampal gyrus and right middle occipital gyrus in fencers could be related to their higher ability to imagine movements.

Moreover, during the right-limb in-phase movements, fencers showed an increased connectivity between the left MC and right middle frontal gyrus, regions involved, respectively, in auditory processes and inhibition of motor responses (Bueti et al., 2008; Swick et al., 2008).

Taken together, these results indicate that intensive fencing activity over a long time period, through the development of sport-specific abilities, is associated with changes in the functional interactions between motor-related areas, as occurring in other athletes, such as golfers (Bezzola et al., 2012).

Differently from previous investigations that have observed structural regional modifications of motor-related areas in the GM and WM following intensive and professional motor training (such as golf, basketball and athletics; Jancke et al., 2009; Park et al., 2009; Taubert et al., 2015), our analysis found no differences of structural MRI measures between fencers and controls. Several factors could contribute to explain, at least partially, our findings, including the different type of sport-activities considered, the relatively small sample size and a high interindividual variability, which could reduce the ability to detect subtle changes. In particular, Del Percio et al. (2008)

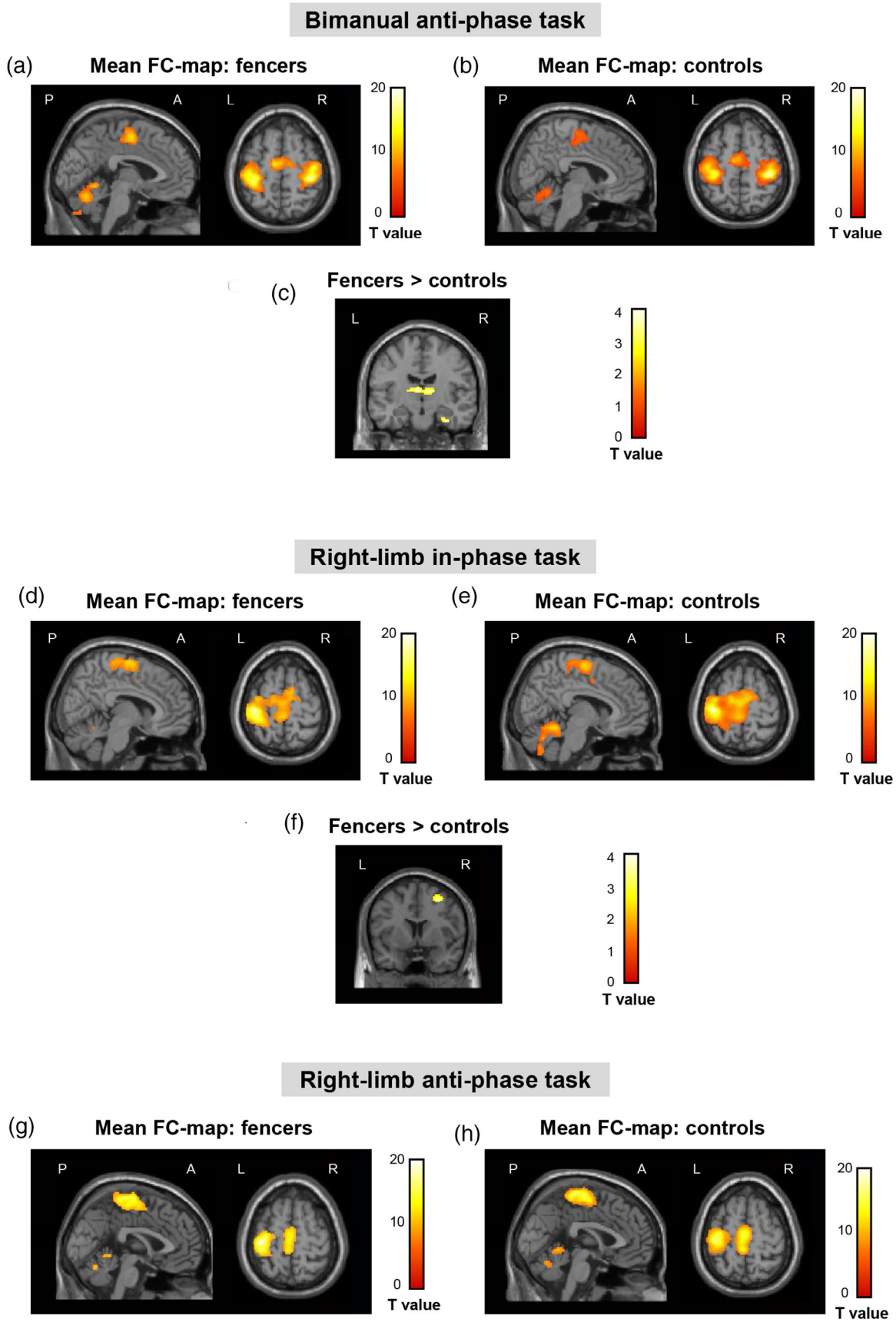

FIGURE 3 Random effect analysis showing, on a high-resolution T1-weighted image in the standard SPM space (neurological convention): mean FC-maps of (a) fencers and (b) controls as well as (c) regions of relative increased FC in fencers > controls, during bimanual anti-phase task; mean FC-maps in (d) fencers and (e) controls, as well as (f) increased FC in fencers > controls during the performance of right-limb in-phase task; mean FC-maps in (g) fencers and (h) controls. Mean FC-maps and between-group comparisons are reported at $p < .05$, family-wise error-corrected, and color-coded for t values. A, anterior; L, left; P, posterior; R, right

demonstrated that the "neural efficiency" hypothesis (which states that cortical activity is spatially focused in "experts") does not fully accounts for the organization of motor systems in top-level athletes, which would depend on several factors, including the side of movement and kind of athletes.

Clearly, our study is not without limitations and the results should be cautiously interpreted, especially those obtained using an uncorrected threshold. Specific behavioral measures of bimanual or interlimb coordination, as evaluated in previous studies with different populations (Haslinger et al., 2004; Jantzen et al., 2005; Wenderoth & Bock, 2001; Zanone & Kelso, 1992), were not available for our subjects. Accordingly, it was not possible to evaluate bimanual or interlimb coordination performances and their associations with specific brain structural and functional MRI measures. This may challenge the interpretation of fMRI differences between fencers and controls. Despite this, elite fencers are characterized by optimized coordination of limb movements that result in improved performances (Chen et al., 2017). Several brain regions found to be differently activated in fencers compared with controls in our study have been found to be involved in interlimb coordination tasks in previous studies (Debaere et al., 2001; Haslinger et al., 2004; Lin et al., 2017). As a consequence, it is tempting to speculate that the functional MRI differences found during interlimb coordination task between fencers and controls might reflect functional adaptive processes associated with optimized motor performances.

As previously mentioned, the small sample size might have influenced the ability to detect GM and WM differences between the two study groups. However, even if the number of subjects may appear to be limited in light of current standards for MRI experiments, it is important to keep in mind the exceptionality of the athlete sample, as the number of top-level fencers is limited. Second, the inclusion of a neuropsychological assessment would have provided interesting information about elite athletes' performances. Moreover, the characteristics of fMRI acquisition do not allow to investigate more complex coordination tasks. Finally, the cross-sectional design does not allow to ascertain whether these brain changes are pre-exiting or result from a reshaping of brain networks by sports training.

5 | CONCLUSIONS

In conclusion, intensive and prolonged fencing activity seems to be associated with brain functional changes mainly involving motor and frontal regions related to high-level motor control and planning of complex tasks. These changes may reflect an optimization of brain networks involved in motor activities, including interlimb coordination tasks, occurring after long periods of high-level trainings. Further studies with larger sample sizes on professional athletes should be performed to corroborate the current findings.

CONFLICT OF INTEREST

Massimo Filippi is Editor-in-Chief of the Journal of Neurology and Associate Editor of Human Brain Mapping. The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Maria Assunta Rocca and Roberto Gatti contributed to the conception and design of the study. Claudio Cordani, Paolo Preziosa, Roberto Gatti, Carlotta Castellani, Massimo Filippi and Maria Assunta Rocca contributed to the acquisition and analysis of data. Claudio Cordani, Paolo Preziosa, Roberto Gatti, Massimo Filippi and Maria Assunta Rocca contributed to drafting the text and preparing the figures.

ETHICS STATEMENT

The study was approved from the Institutional Review Board of the IRCCS San Raffaele Scientific Institute.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

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