

Switching handedness: fMRI study of hand motor control in right-handers, left-handers and converted left-handers

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The purpose of this study was to investigate the differences in the brain organization of motor control in left- and right-handers and to study whether early left-to-right handwriting switch changes the cortical representation of finger movements in the left and right hemispheres. Echo-planar MR imaging was performed in 52 subjects: consistent right-handers (RH), consistent left-handers (LH), and subjects who had been forced at an early age to switch their left-hand preferences toward the right side. The scanning was performed during simple (flexion/extension of the index finger) and complex (successive finger-thumb opposition) tasks. Subjects performed the tasks using both the preferred and non-preferred hand. In right-handers, there was a general predominance of left-hemisphere activation relative to right hemisphere activation. In left-handers this pattern was reversed. The switched subjects showed no such volumetric asymmetry. Increasing levels of complexity of motor activity resulted in an increase in the volume of consistently activated areas and the involvement of the ipsilateral in addition to contralateral activations. In both right- and left-handers, movements of the preferred hand activated mainly the contralateral hemisphere, whereas movements of the non-preferred hand resulted in a more balanced pattern of activation in the two hemispheres, indicating greater involvement of the ipsilateral activations. Overall, this study shows that in both left- and right-handed subjects, the preferred hand is controlled mainly by the hemisphere contralateral to that hand, whereas the non-preferred hand is controlled by both hemispheres. The switched individuals share features of both left-handers and right-handers regarding their motor control architectures.

Key words: left-handedness, motor control, fMRI, brain plasticity, hemispheric asymmetry

INTRODUCTION

Hand preference is the most prominent behavioral expression of brain asymmetry in man. The majority (approximately 90%) of the human population is right-handed. Despite a long history of research on the neurobiological origin of handedness and common belief that it is strongly linked to the brain asymmetry (Grabowska et al. 1994), the neural correlates of hand preferences are still a matter of debate. The advances in functional neuroimaging techniques have allowed the cortical representation of movements to be mea-

sured directly. The neuroimaging studies that have focused on the brain correlates of hand preference have attributed this behavioral asymmetry to hemispheric lateralization of the cortical areas controlling motor function (Kim et al. 1993, Amunts et al. 1996, 2000, Dassonville et al. 1997, Kawashima et al. 1997, Singh et al. 1998, Volkman et al. 1998, Solodkin et al. 2001, Hlustik et al. 2002, Hervé et al. 2005, Verstynen et al. 2005, Klöppel et al. 2010, Rocca et al. 2008, Wu et al. 2008). There is, however, a lack of consistency in these authors' opinions as to the specific manifestation of handedness-related differences. Such differences have been found either in the localization, the volumes or the number of activated areas in the two hemispheres or in the specific presence of ipsilateral activation in the motor control of the preferred vs. non-preferred

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hand. Moreover, this ipsilateral activation pattern seems to be dependent on such features as movement complexity (Kim et al. 1993, Allison et al. 2000, Nirkko et al. 2001, Newton et al. 2005, Smith et al. 2006).

In their fMRI study Solodkin and coauthors (2001) found that, during the performance of a sequential finger movement task, left-handers tended to activate larger volumes in a greater number of association cortices and showed less lateralization than did right-handers. A subsequent report by the same authors revealed that right-handers had greater activation in the left premotor area for either hand, indicating a general dominance of the left hemisphere in motor function, whereas the left-handed group showed a predominance of activation in the premotor cortex contralateral to the moving hand (either left or right), indicating no such asymmetry (Hlustik et al. 2002). However, similar comparisons performed by Volkman and colleagues (1998) in a magnetoencephalographic study and by Dassonville and others (1997) in an fMRI study revealed that, in both right- and left-handers, the use of the preferred hand was associated with a greater volume of activation in the contralateral motor cortex.

Several papers have specifically focused on the ipsilateral activation issue based on the observation that in right-handers ipsilateral activation is characteristic of non-preferred (left) hand movements as opposed to preferred hand movements (Kim et al. 1993, Solodkin et al. 2001, Kobayashi et al. 2003, Gut et al. 2007, Wu et al. 2008). Singh and coauthors (1998) reported that right-handers showed greater activation of the ipsilateral hemisphere in the sensorimotor region for non-preferred (left) hand movements compared to ipsilateral hemisphere activation for preferred (right) hand movements; whereas, in left-handers, such asymmetry was not present. In line with those findings Gut and coworkers (2007) found in right-handed participants the advantage of ipsilateral activation during the left hand movements compared to the right hand movements.

Ipsilateral activation was also registered in left-handed individuals by Kawashima and others (1997), but the effects were present in the premotor and not the motor cortex and in the right and not the left hemisphere. Unfortunately, these data could not be contrasted with data from right-handers, as no appropriate control group was involved. Two other studies (Kim et al. 1993, Verstynen et al. 2005) pointed to similarities in the motor control of left- and right-handers: both

groups had stronger ipsilateral activations in the motor cortex of the left hemisphere compared to the right hemisphere. The only difference (revealed by Verstynen and coworkers in 2005) was that, in left-handers, the hemispheric asymmetries were less pronounced.

The divergence of the obtained results increases if one takes into account the type of motor tasks performed by the subjects in these studies. Specifically, it is not clear whether differences between left- and right-handers apply to motor behavior in general or are predominantly linked to more complex motor tasks involving sequential component in the movements. Using simple and complex movements, Solodkin and coauthors (2001) and Verstynen and colleagues (2005) found handedness-related differences only for complex tasks, however, differences have also been reported for relatively simple tasks (Volkman et al. 1998, Klöppel et al. 2007). These findings points to the importance of controlling for task complexity in future studies.

Questions about the brain correlates of motor control in case of forced right-handedness are another interesting issue concerning the effect of hand-preference on the organization of motor function in the brain. Many individuals, especially in older generation, report that they had experienced considerable pressure to switch their hand preference from left to right (Porac and Friesen 2000, Searleman and Porac 2001). Switch attempts may proceed either nearly free of problems and lead to a change in the child's hand preference for a wide range of everyday activities, including writing; or switch attempts may bring much difficulty and result in a switch of preferences for only few activities. These specific activities are likely to include the specific targets of forced right-handedness such as writing, drawing or eating.

Taken these facts together, the question follows whether early changes of hand preference behaviors due to environmental pressure exerted upon originally left-handed individuals lead to changes in brain organization toward a more "right-handed" brain, or do these people still preserve "left handed" brain features. The first possibility seems more plausible in light of many brain plasticity studies showing that the human brain is capable of substantial reorganization due to experience (Pascual-Leone et al. 2005), and sensorimotor training (e.g., Draganski et al. 2004). However, the latter possibility cannot be excluded because the lateralization of brain function seems to be strongly

genetically driven (Carter-Saltzman 1980, Annett 2002) and, thus, heavily dependent on innate factors. Whether the effectiveness of a hand-preference conversion process is somehow related to what happens in the brain is also extremely interesting. It could be predicted that individuals who were more resistant to the alteration of hand preference were also more resistant to reorganization of their brains as compared with the individuals who switched more successfully. In other words, the question is whether changes in the profile of behavioral preferences are reflected in the brain's functional organization patterns.

Studying individuals who underwent attempts to switch toward right handedness and comparing them with consistent left- and right-handers presents an unusual opportunity to gain a better insight into the mechanisms that, on the one side, determine the lateralization of function and, on the other side, are involved in brain plasticity. There are few functional or structural neuroimaging studies that investigated the neural correlates of switching handedness (Siebner et al. 2002, Klöppel et al. 2007, 2010). Siebner and coworkers (2002), performed fMRI study during writing with the dominant hand (i.e. the hand normally used for writing by the tested subjects). The results showed the predominance of activation in left parietal and premotor regions in right-handers, and more bilateral activation with some activation foci in the right hemisphere (particularly in premotor, parietal and temporal areas) in switched left-handers. Moreover, there was a relationship between the degree of left hand dominance and cerebral blood flow in these right hemisphere regions. In the same research the brain activation pattern was also studied in consistent left-handers; this pattern was characterized by a clear right hemisphere dominance (Siebner et al. 2002). The authors concluded that the presence of right-hemisphere activation in converted left-handers is the reflection of not complete left-to right shift in handedness and still present motor control exerted by the right hemisphere. The disadvantages of this experimental design were that the authors were neither able to compare brain activity during dominant and non-dominant hand movements (which, according to the previously mentioned papers, is critical for detecting hand preference-related differences), nor to make direct comparison between left- and right-hand writers as scanning in the two groups was performed for different hands.

In a more recent study Klöppel and colleagues (2007) studied the localization of movement related activity with fMRI while converted left-handers and age-matched groups of consistent left handers and right handers pressed a button with their right, left or both hands depending on which of three symbolic visual cues was presented. The authors have found two regions of increased activity in converted left-handers as compared to either consistent left-handers or right-handers: one in sensorimotor and premotor cortex in the left hemisphere and the other in inferior parietal cortex of the right hemisphere. The increased activation in the left hemisphere was interpreted as a consequence of educationally induced high daily practice in right hand writing of that originally left-handed group. The persisting activity in their right inferior parietal cortex was taken as evidence that the involvement of higher order associative areas in the originally dominant hemisphere is invariant and cannot be switched to the opposite hemisphere due to educational training. Importantly enough, this study did not consider the possible relationship between the ipsi- vs. contralateral activations and the handedness factor, neither it directly compared the activations in the two hemispheres elicited by either hand. Moreover, due to simplicity of the movement (just pressing a button), the task focused more on taking a decision which hand should be used, than on movement execution control itself. And this might require quite different neural circuits than finger tapping or writing used in previous studies.

This short review of the literature demonstrates that the existing data relating the functional brain architecture of motor function to handedness is highly inconsistent. The failure to obtain consistent findings in these studies can be attributed to several factors, with the heterogeneity of the left-handed groups, the low numbers of participating individuals and the selection of divergent motor tasks being the most likely sources of confusion.

In the present study we used two different unpracticed motor tasks, one simple and one complex, that have been most commonly used in previous research on the brain's representation of motor function and can be performed with either hand. This enabled us: (1) to relate our data to the existing literature on motor control, (2) to provide data for both preferred and non-preferred hand, and (3) to estimate the effect of task complexity on handedness-related differences in activation patterns. The volumes of activation in ipsilateral and contralateral hemispheres obtained in left-

handers as well as converted left-handers were compared to those obtained in right-handers who were tested in our previous study (Gut et al. 2007) using the same procedure and scanner.

The present study addressed the following questions: (1) what are the differences in the organization of motor control in the brain between left- and right-handers, (2) does motor task complexity influence those differences, (3) do early switch of hand preference, due to social pressure, leads to long-lasting changes in brain organization, and (4) does the organization of motor function patterns in the brain reflect handedness preference and performance?

These issues are interesting not only from theoretical point of view, but they also have clinical value. The knowledge on brain activation patterns in subgroups that differ in hand preference might help to make proper decisions as to which hand should be chosen for writing in individual cases in which the preference is not obvious and in those who have used the non-preferred hand for a long time after injury of the originally preferred hand.

METHODS

Subjects

Fifty-two healthy subjects (24 males and 28 females) between 17 and 36 years of age (mean = 22.1 years; SD = 5.3) participated in the study.

All participants were informed about the purpose of the study before giving their written consent. None of the participants had any contraindications to MRI. No participants reported neurological or psychiatric illnesses, learning disabilities, failures in elementary school or claustrophobia. The study protocol was approved by the Ethics Committee of Jagiellonian University.

Handedness assessment

To assess individual profiles of handedness we measured the direction and degree of hand preference in all subjects. For this purpose subjects completed the 10-point Edinburgh Handedness Inventory (Oldfield 1971). For each subject, a Handedness Preference Index (HPI) ranging from +100 for extreme right-handers to -100 for extreme left-handers was calculated (see Oldfield 1971).

The participants were divided into four groups: consistent right-handers (RH, $n=12$), consistent left-handers (LH, $n=17$), switched successfully (SS, $n=11$) and switched unsuccessfully (SU, $n=2$). The former two groups (LH and RH) consisted of subjects who reported consistent left- or right-hand preferences across their lives and no attempts at rightward shifts during childhood. All individuals in the group of consistent left-handers used their left hand for writing and had a handedness preference index (HPI) < 20. Individuals in the group of consistent right-handers used their right hand for writing and had a HPI > 20. The two latter groups (SS and SU) consisted of subjects who had been forced in childhood to switch their original left-hand preferences toward the right side resulting in the use of their right hands for writing. In all cases interviews provided detailed information about the conversion process. All unclear cases were excluded. The selection of subjects for either the SS or the SU group was based on their hand preference profile. Individuals showing the HPI > 20 (as in the RH group) were selected for the SS group, whereas the individuals showing the HPI < 20 (as in the LH group) were selected for the SU group. Following other studies (Annett 2002), we used the HPI score of 20 as the demarcation line between left- and right-handedness because it is thought that the brain organization of individuals with slight preferences toward the right side resembles that typical for left-handers rather than for right-handers. Thus, people with slight right preferences are, to some extent, considered to be left-handers who adapted their behavior to the demands of the right-shifted environment.

Brain imaging

The experimental paradigm consisted of two experimental runs that each contained 10 alternating blocks of 3 conditions: (A) a simple movement task (flexion/extension of the index finger), (B) a complex movements task (sequential opposition of the thumb to tips of other fingers in the order: 5, 4, 3, 2, 5, 4 and so on), and (C) a rest period (during which the subjects were required to remain still). Within each run, the blocks were repeated in the sequence CABABCABC. Each block lasted 15 s for a total 2 min 30 s per run. Within each run the tasks were performed either with the right or the left hand. The order of left and right hand runs was randomized across subjects. Movements were

self-paced at a rate of approximately 2 Hz, which was comfortable for subjects and easy to control. All subjects practiced the two tasks prior to scanning to ensure similar task execution. The onset of each of the different tasks was signaled by the presentation of one of three differently colored squares presented on a rear-projection screen visible to subjects through a system of mirrors mounted in the scanner. A white square indicated the rest condition, a red square indicated the simple movement condition and a blue square indicated the complex movement condition. The squares remained visible during each condition.

Before scanning the subjects were instructed how to react to each stimulus type that they would see on the screen. Stimuli were back-projected from a multi-media projector (Sony LCD Data Projector VPL-SC50, Tokyo, Japan) on a screen located approximately 3 meters away from the magnet.

The study was performed using a 1.5 T Signa Horizon MR system (General Electric Medical Systems, Waukesha, WI). The functional MRI images were acquired using an interleaved gradient-echo echoplanar (EPI) sequence sensitive to the blood oxygenation level dependent (BOLD) contrast with the following parameters: 3000/60 (repetition time ms/echo time ms), a 90° flip angle, a 18×13 cm field of view (FOV), a 96×64 matrix, and the number of excitations equal to one. In plane resolution was 1.41×1.41 mm. During each functional scanning session 50 sets of 10 contiguous, 7 to 10-mm-thick oblique sections were acquired, without any gap.

For each subject, all sections were set parallel to the axis connecting the anterior commissure and the caudal surface of the cerebellar tonsil and extended right up to the posterior midline boundary of the parietal lobe. The selected slice-thickness was adjusted to each subject's brain volume.

Coplanar, high-resolution structural MRI images were acquired for the same locations as the functional images using a Spoiled Gradient-echo (SPGR) sequence with the following parameters: 50/6 (repetition time ms/echo time ms), a 60° flip angle, a 18×13 cm FOV, a 256×256 matrix, and the number of excitations equal to two. In plane resolution was 0.86×0.86 mm. Depending on the subject, ten 7- to 10-mm-thick oblique sections were acquired, without any gap.

We made every effort to ensure subjects were as comfortable as possible to reduce head motion. Subjects were asked to refrain from any movements, not to

strain their muscles in any special way (except during the required motor tasks) and not to think about anything in particular while lying in the scanner. A standard radio-frequency (RF) head coil with foam padding to restrict head motion was used.

The fMRI experiment was preceded by training of the subjects' on the motor task. Special attention was given to teaching the subjects to pace their movements at approximately twice a second without any preceding cues. Thus, the task was highly automated before the start of the scanning procedure.

The images were first converted to the Analyze format with xmedcon (<http://xmedcon.sourceforge.net/>). The skull was then removed on the anatomical Analyze images with a probabilistic anisotropic diffusion and multi-scale watershed algorithm (Undeman and Lindeberg 2003).

Statistical analyses were performed with FSL 3.1 (FMRIB Software Library) (Smith et al. 2004). In the pre-processing step, the functional images were co-registered to the anatomical image. To remove low frequency artifacts, a high-pass temporal filter was applied to the functional images by using a straight line fitting with a cutoff at 45 s. Gaussian spatial smoothing with an FWHM kernel of 8 mm was carried out on the functional images to reduce noise. In the statistical analysis, linear contrasts on between conditions at the subject level were calculated in native subject space as a pre-step to the higher-level analyses.

Higher level group analyses were performed by first registering the subject-level contrast images to a reference brain in Talairach standard space (Roland and Zilles 1994); next FLAME (FMRIB's Local Analysis of Mixed Effects) was used on the contrast images to estimate the inter-subject random-effects. Each group's cross-subject variance was estimated separately. The statistical Z-images from the group analysis were thresholded at $z=3.3$ to obtain clusters. All clusters with a $P \leq 0.05$ were considered significant.

As a final step, the intersection volumes between significant clusters and cytoarchitecturally defined regions were calculated (Geyer et al. 1996, 1999, Schleicher et al. 1999).

Previous reports suggest that the localization of particular brain areas associated with motor function may vary across subjects (see Volkman et al. 1998 and Verstynen et al. 2005 for reviews) and that the particular regions need not to be the same size

Table I

Mean Handedness Preference Index (HPI) as assessed with Edinburgh Handedness Inventory

| GROUP | HPI | |
|--------------------|--------|------|
| | mean | SE |
| RH <i>n</i> =12 | 84.17 | 3.98 |
| LH <i>n</i> =17 | -73.53 | 8.31 |
| SU <i>n</i> =12 | -20.00 | 8.79 |
| SS <i>n</i> =11 | 56.36 | 5.76 |

(SE) Standard error

in the left and right hemispheres, especially when the sample varies in handedness profile (Amunts et al. 1996, 2000). Taking this variation into consideration, we decided rather to assess the general roles of left or right hemisphere in motor control by calculating the total volume of the activated areas in the left/right – contralateral/ipsilateral hemispheres. Thus, our strategy was to quantify hemispheric asymmetries in the spatial extent of hand representation by computing the volume of all significantly activated voxels in either hemisphere. These analyses were run in native subject space.

RESULTS

Behavioral data

Mean Handedness Preference Index (HPI) was calculated for each group of subjects and the mean index of handedness are presented in Table I.

Noticeably, both the consistent right-handed (RH) and the successfully switched (SS) groups had clearly positive HPI values indicating right-hand preferences in a large range of activities. Lower values of the index in the SS compared to the RH group indicate that the hand preference alteration was not complete, and some features of covert left-handedness persisted.

In both consistent left handed (LH) and unsuccessfully switched (SU) groups, the mean HPIs were nega-

tive, indicating the predominance of left-hand preferences for the majority of activities and thus an unsuccessful handedness switch in the SU group.

Imaging data

Localization of activation

The fMRI scans revealed a number of areas that were consistently activated during hand movements used in the study. Figure 1 illustrates the localization of significant activations in the four groups of subjects for simple and complex movements performed with the right or left hand. Significant group activations during simple movements were found in: precentral, postcentral, parietal superior, parietal inferior and supramarginal gyri, all exclusive to the hemisphere contralateral to the moving hand. For complex movements, activation covered much broader areas including the cerebral cortex (precentral gyrus, postcentral gyrus, supplementary motor area, insula, cingulum, parietal lobuli, supramarginal, superior and medial temporal gyri), subcortical areas (putamen, pallidum, the thalamus) in both the contralateral and ipsilateral hemispheres for either hand. In addition, cerebellar activations (mainly ipsilateral) were registered.

Volumes of hemispheric activation in relation to handedness and task complexity

Because the aim of the study was to determine whether the motor networks responsible for controlling left and right hand movements in the ipsilateral and contralateral hemispheres were asymmetrically activated and whether this effect depended on the hand preference and complexity of the task, the data were subjected to analysis of variance (ANOVA) that used group (RH, LH, SU and SS), movement complexity (simple/complex), hemisphere (ipsilateral/contralateral) and hand (left/right) as the main factors and the volume of activation as the dependent variable. This analysis revealed significant main effects of movement complexity ($F_{1,48}=116.59$; $P<0.01$) and hemisphere ($F_{1,48}=101.54$; $P<0.01$). The result of *t*-tests indicated a larger volume of activation during complex than simple movement task ($t_{51}=11.2$; $P<0.01$) and a larger volume of activation in the contralateral, compared to the ipsilateral hemisphere ($t_{51}=10.08$; $P<0.01$). Moreover, the analysis revealed three sig-

nificant interactions: movement complexity \times hemisphere ($F_{1,48}=12.42$; $P<0.01$), hand \times hemisphere \times group ($F_{3,48}=4.61$; $P<0.01$) and movement complexity \times hemisphere \times group \times hand ($F_{3,48}=5.06$; $P<0.01$). To investigate these interactions, two analyses of variance, separately for simple and complex tasks, using hemisphere (ipsilateral/contralateral), group (RH/LH/SS/US) and moving hand (left/right) as the main factors were conducted. Analysis of the simple movement task data revealed a significant effect of hemisphere ($F_{1,48}=86.23$; $P<0.01$), indicating larger activa-

tion in the contralateral, compared to the ipsilateral, hemisphere. No other factors or interactions reached significance. The same analysis performed for complex task showed a significant main effects of hemisphere ($F_{1,48}=74.94$; $P<0.01$, with larger contralateral activations) and a significant interaction of group \times hand \times hemisphere ($F_{3,48}=6.34$; $P<0.01$). As illustrated in Figure 2, during the complex movement task in the RH group, larger contralateral activations were elicited by right (preferred) hand movements than left (non-preferred) hand movements ($t_{11}=2.24$; $P<0.05$),

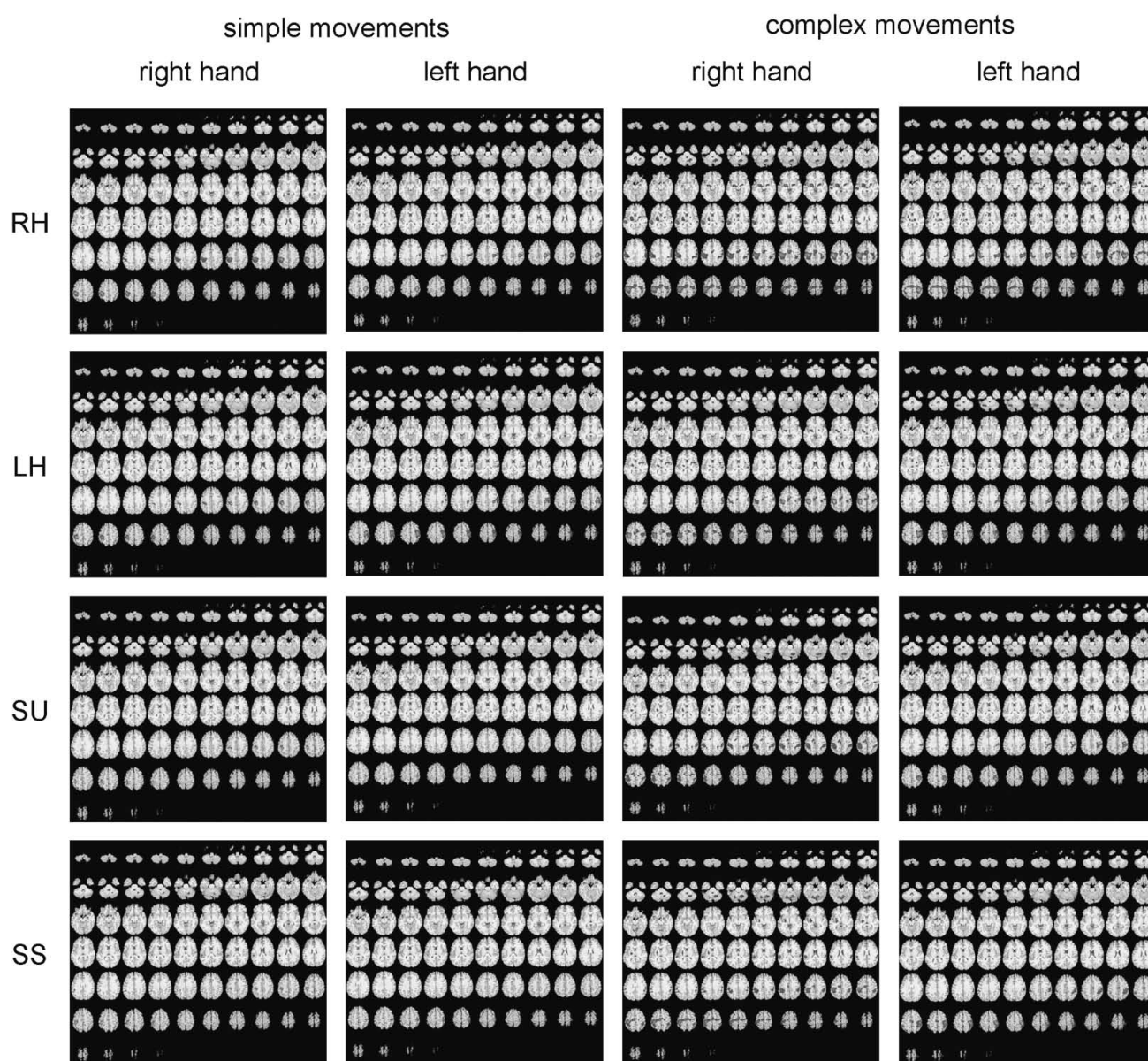


Fig. 1. Localization of significant activations in the RH, LH, SU and SS groups during simple and complex movements performed with either the left or the right hand.

whereas larger ipsilateral activations were elicited by left (non-preferred) hand movements than the right hand movements ($t_{11}=2.87$; $P<0.05$), both leading to greater total activation in the left hemisphere. The reverse pattern of activation emerged in the LH group: larger contralateral activations were elicited by the left (preferred) hand, and larger ipsilateral activations were elicited by the right (non-preferred) hand

(both leading to larger total activation in the right hemisphere, however the differences between hands were not significant for contralateral or ipsilateral activation volumes). In the two switched (SS and SU) groups the pattern of ipsilateral activations resembled those found in the RH and LH groups, respectively; whereas the contralateral activations for either hand did not differ from each other.

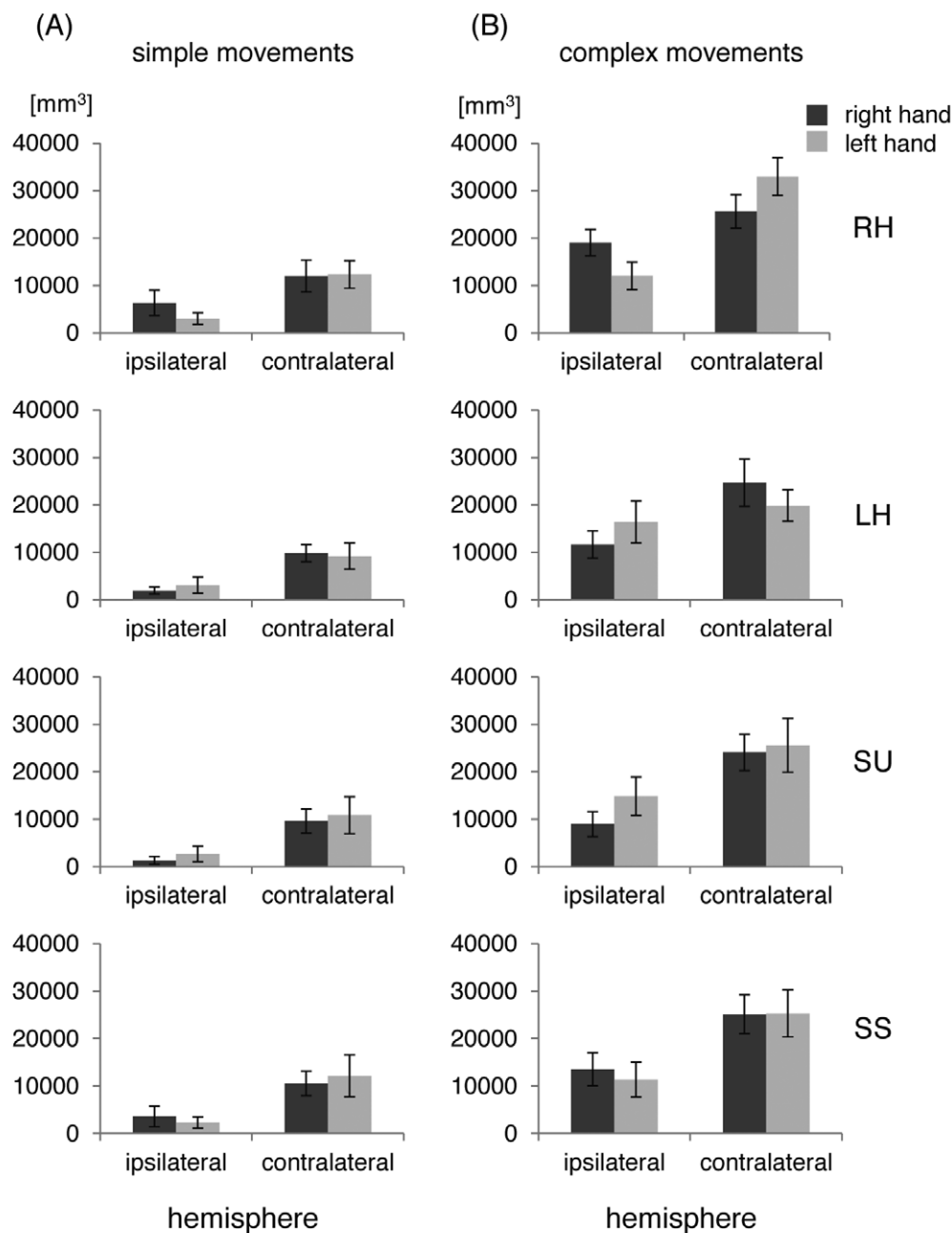


Fig. 2. Mean activation volumes in the ipsilateral and contralateral hemispheres for simple (A) and complex (B) movements performed with either the left or right hand in all groups of subjects.

To analyze a possible relationship between brain activation patterns and behavioral lateralization patterns, total volumes of activation in each hemisphere were correlated with HPI index (assessed by the Oldfield Inventory). Pearson correlation procedures for the entire sample of subjects (raw data from individual subjects from all four groups) revealed a significant positive correlation ($r=0.31$, $P<0.05$) between the HPI and the total amount of activation in the left hemisphere. No such relationship was found for the right hemisphere. Higher HPIs (i.e. stronger right hand preference) were associated with larger volume of activation in the left hemisphere. Separate analyses for the simple and complex movements revealed that this correlation was only significant for complex movements ($r=0.34$, $P<0.05$).

DISCUSSION

This study examined the volume of left and right hemisphere activations during hand movements in right-handers, left-handers and originally left-handed individuals who, during their childhood, received pressure to switch hand preference toward the right side. Our goal was to clarify issues related to the brain mechanisms of hand preference and, specifically, to investigate the effect of switching hand preferences on the organization of motor control in the brain. In contrast to previous studies, we controlled for the potential influences of several factors that are suspected to play a role in the brain activation pattern while subjects perform manual tasks: type of movement (simple vs. complex), hand performing the movement (preferred vs. non-preferred) and the activated hemisphere (ipsilateral vs. contralateral).

The most obvious finding of our study was that, for both hands and tasks, the contralateral activations were larger than the ipsilateral activations in all groups. This concords with several previous studies (Dassonville et al. 1997, Volkman et al. 1998, Hlustik et al. 2002) and could be related to the fact that most of the motor fibers cross within the pyramidal tract (Kuypers 1981, Nathan et al. 1990). Regarding the main question of the effect of hand preference on hemispheric asymmetry, our study revealed that both in left-handers and right-handers, movements of the preferred hand (right in RH and left in LH) produced larger contralateral activations than movements of the non-preferred hand. In contrast to this, movement of

the non-preferred hand, led to larger ipsilateral activations. Consequently, in right-handers there was a general predominance of left-hemisphere activation, whereas in left-handers there was a predominance of right-hemisphere activation; although in the latter case, the asymmetry was smaller.

Notably, these effects were specific to complex rather than simple tasks (during simple tasks the activations elicited by either hand were similar). This concords with the previous observations by Solodkin and coauthors (2001) and Verstynen and others (2005) who also found handedness-related differences only for complex tasks. Finding by Klöppel and colleagues (2007) that the cortical sensorimotor representation may depend on hand preference in simple bar pressing movements could be associated with the experimental procedure which differed considerably from that used in other studies. In this choice reaction time paradigm the subjects were expected to react with their left, right, or both hands depending on a presentation of one of three possible visual cues. This task might present special difficulty for the left-handers due to their problems with discrimination between the left and right directions. It seems plausible therefore, that the results obtained by Klöppel and coauthors (2007) are related to decisions regarding the hand choice rather than to monitoring the execution of an automatically performed bar pressing.

The finding that, in both the RH and LH groups, movements of the preferred hand lead to greater contralateral activation and movements of the non-preferred hand lead to greater ipsilateral activation implicates the existence of a common mechanism for motor control. It may consist in exerting the motor control by the dominant hemisphere not only over the contralateral (preferred) hand but also over the ipsilateral (non-preferred) hand. In contrast, the non-dominant hemisphere is involved mainly in the motor control of the contralateral (non-preferred) hand. In other words the preferred hand seems to be controlled mainly by the dominant hemisphere, while the non-preferred hand is controlled by both the dominant and non-dominant hemispheres as has already been suggested by Baraldi and others (1999).

The conclusion that in the right-handers the left hemisphere plays a dominant role in motor control is consistent with clinical evidence demonstrating that limb apraxia is more common after left hemisphere damage than after right hemisphere damage (Heilman

2000, Rinehart et al. 2009) and disrupts motor skills even when the left, ipsilesional hand is used by the patients (Haaland and Harrington 1996). This conclusion also conforms the anatomical data showing structural asymmetries in the central sulcus (larger surfaces of dorsolateral motor cortex in the dominant hemisphere) in right-handers and left-handers (White et al. 1994, Amunts et al. 1996, 2000, Klöppel et al. 2010, but see Hervé et al. 2005 for the contradictory results).

Interestingly, recent clinical study on right-handed patients with unilateral paretic stroke (Rinehart et al. 2009) provided further observation, which perfectly matches our findings. In this study the authors assessed the relative use of the right, left and both arms with wrist accelerometers. The study demonstrated that the use of the ipsilateral but not contralateral limb after unilateral stroke was influenced by hand preference: the right hemisphere damaged patients used their ipsilateral, right (preferred) limb more than the left-hemisphere damaged patients used their ipsilateral, left (non-preferred) limb and more than healthy right-handers. In other words the damage to the left hemisphere impaired the motor abilities of the left hand more than the damage to the right hemisphere impaired the motor abilities of the right hand. This might suggest that in right-handers the involvement of the left (dominant) hemisphere in ipsilateral (left hand) motor control is greater than the involvement of the right hemisphere in the ipsilateral (right hand) motor control.

This nicely concords our findings which showed the involvement of the left hemisphere in both the contralateral and ipsilateral motor control in right-handers. Those findings also agree to our conclusion that the right hemisphere in right-handers is mainly involved in the contralateral (left hand) control and thus, damage to this hemisphere does not have so much negative impact on the use of the right hand as does the damage to the left hemisphere on the use of the left hand. Those data also conform the general conclusion regarding the dominance of the left hemisphere in motor control in right-handers.

What could be the functional significance of relatively greater volume of activation in the hemisphere contralateral to the preferred hand? It is reasonable to assume that an increase in the volume of neural tissue engaged in a motor behavior may support the correct execution of that behavior. The expansion of hand

motor cortex in the hemisphere contralateral to the dominant hand may thus provide the neural substrate for the more efficient execution of the complex motor activities performed by this hand. The high proficiency in motor control of the hemisphere contralateral to the preferred hand may then be utilized during the execution of motor tasks not only by the preferred hand but also by the non-preferred one. The finding of higher volumes of activation in the hemisphere contralateral to the preferred hand in both right- and left-handers agrees with a few other functional imaging studies of right- and left-handers (Dassonville et al. 1997, Volkman et al. 1998, Hlustik et al. 2002, but see Kim et al. 1993 for contradictory results).

In the present study we also investigated the brain organization patterns of subjects who were originally left-handed, but at the age of 7, were switched to right-handedness. The results showed that switched participants shared features of both left-handers and right-handers. Therefore, it could be speculated that the brains of the originally left-handed subjects underwent plastic changes that consisted in reorganization of their motor function toward the “right-handed” brain. This reorganization, however, was not complete and showed persisting features of the “left-handed” brain. Interestingly, there was a correspondence between the amount of supposed brain reorganization and the degree to which the individuals changed their hand preferences toward the right side. Although the differences in brain activation in the two switched (SU and SS) groups were not statistically significant, it is worth noting that the activation patterns of their brains reflected the differences observed at the behavioral level: the SS group was more similar to the RH group, while the SU group resembled the LH group (at least when the pattern of ipsilateral activations was considered). In both groups of converted left-handers, however, the brain organization was more symmetrical than in the two consistent handedness groups.

It is a matter of debate whether the hemispheric asymmetry in cortical organization of motor function is a consequence of, or a cause of hand preferences. There are two contradictory explanations that should both be considered; different hand preferences may lead to differences in the amount of left and right hand training and, consequently, to differences in the cortical representation of each hand. It could also be argued that it is the primary difference in brain organization that constitutes the causal factor driving human handedness. The two

groups of SU and SS subjects might have been different from an early age as to their hand preference profiles. Their present brain organization patterns could, therefore, be a consequence of those early differences (Harris 1990). Leaving the solution of this chicken and egg problem to future research, we want to note that neither of the two switched groups (even the SS group) was able to conform fully to environmental demands and completely change their hand preferences to full right-handedness. Consequently, their HPIs were significantly lower than those of the group of consistent right-handers. This difference may reflect the importance of inherited factors in shaping brain architecture, which can only undergo plastic changes to a limited extent.

Similar conclusion was drawn by the authors of two previous studies performed on converted left-handers, using functional MRI (Siebner et al. 2002, Klöppel et al. 2007). The advantage of our study consists in testing the effects of handedness on brain activation pattern using separate recordings for hand and hemisphere (ipsilateral or contralateral to the moving hand). In the previous fMRI studies the authors either used the paradigm which did not allow for making such comparison (Siebner et al. 2002) or simply disregarded those factors (Klöppel et al. 2007) focusing on identification of brain regions where converted left-handers showed a consistent difference in task related BOLD signal across all movement conditions and hands. Such approach did not allow them to focus on the mechanisms which, as we have shown, may differ for ipsilateral vs contralateral activation patterns. The observation that in the two switched (SS and SU) groups it was the patterns of ipsilateral and not contralateral activation which resembled that found in the RH and LH groups might suggest that the ipsilateral motor representation is more prone to undergo reorganization due to educational training than the contralateral one. Testing this interesting possibility, however, requires more specific further investigation.

It is widely known that individual subjects, whether they are right- or left-handed, differ considerably as to their specific pattern of handedness. In this study, we attempted to directly relate behavioral differences (individual profiles of hand preference) to individual patterns of activation in the two hemispheres. In other words the question was whether individual patterns of organization of motor control in the brain constitute a continuum that corresponds directly with a continuum of individual patterns of hand preferences. Our data

revealed a significant correlation between total activation in the left hemisphere and the handedness preference index (HPI) that indicates that the stronger the right hand preference, the larger the total volume of activation in the left hemisphere. A similar relationship between hand preference index and the anatomical parameters has been demonstrated by Amunts and coauthors (1996, 2000) in the primary sensorimotor and by Klöppel and others (2010) in the left middle putamen.

CONCLUSIONS

To sum up, in both left- and right-handed subjects, the preferred hand is controlled mainly by the hemisphere contralateral to that hand, whereas the non-preferred hand is controlled by both hemispheres. The switched individuals share features of both left-handers and right-handers regarding their motor control architecture and hand preference profiles.

Increasing levels of complexity of motor activity results in an increase in the volume of consistently activated areas and the involvement of the ipsilateral in addition to contralateral activations, especially in the dominant hemisphere.

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