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Brain correlates of right-handedness

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Abstract. Recent development of neuroimaging techniques has opened new possibilities for the study of the relation between handedness and the brain functional architecture. Here we report fMRI measurements of dominant and non-dominant hand movement representation in 12 right-handed subjects using block design. We measured possible asymmetry in the total volume of activated neural tissue in the two hemispheres during simple and complex finger movements performed either with the right hand or with the left hand. Simple movements consisted in contraction/extension of the index finger and complex movements in successive finger-thumb opposition from little finger to index finger. A general predominance of left-hemisphere activation relative to right hemisphere activation was found. Increasing the complexity of the motor activity resulted in an enlargement of the volume of consistently activated areas and greater involvement of ipsilateral areas, especially in the left hemisphere. Movements of the dominant hand elicited large contralateral activation (larger than movements of the non-dominant hand) and relatively smaller ipsilateral activation. Movements of the non-dominant hand resulted in a more balanced pattern of activation in the two hemispheres, due to relatively greater ipsilateral activation. This suggests that the dominant (right) hand is controlled mainly by the contralateral (left) hemisphere, whereas the non-dominant hand is controlled by both left and right hemispheres. This effect is especially apparent during execution of complex movements. The expansion of brain areas involved in motor control in the hemisphere contralateral to the dominant hand may provide neural substrate for higher efficiency and a greater motor skill repertoire of the preferred hand.

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INTRODUCTION

The organization of motor system in humans follows the basic principle of contralateral control of distal movements. At the anatomical level this principle is reflected in almost complete crossing of corticospinal fibers which innervate distal muscles, including hand muscles. However, a specific feature of the human brain is that the two hemispheres are not symmetrical but are specialized in a number of functions, including the motor control of the two hands. Typical human right-handedness is considered a behavioral manifestation of that specialization. Nine of every 10 humans prefer to use their right rather than the left hand for the majority of manual activities (Perelle and Ehrman 1994). The question is how this right hand preference is reflected in the organization of the motor function in the brain.

Clinical evidence strongly supports the view that the two hemispheres contribution to motor control is not symmetrical. Damage to the left hemisphere cause more substantial motor deficits than does damage to the right hemisphere. Left hemisphere damage can impair the motor function of the ipsilateral left hand in addition to contralateral right hand (Haaland and Harrington 1996). Lesions leading to apraxia (a disorder of complex movement such as tool use or dressing) typically involve left frontal and parietal lobes and the underlying white matter (Alexander et al. 1992, Heilman 2000).

Recent development of neuroimaging techniques opened new possibilities to investigate the relation between handedness and brain functional architecture. In recent years several fMRI, PET, and magnetoencephalography experiments have been performed to study whether behavioral asymmetry (handedness) is associated with an asymmetry in activation of neural tissue in the two hemispheres. The outcomes of those studies, however, differ in several aspects, especially as regards activations ipsilateral to the moving hand. The majority of studies points to the existence of ipsilateral activation (Baraldi et al. 1999, Kim et al. 1993, Kobayashi et al. 2003, Singh et al. 1998, Verstynen et al. 2005, but see Colebatch et al. 1991 for a negative finding). However there is no agreement as to whether these activations are associated exclusively with higher order cortices or with primary motor cortex, and whether they are characteristic of the non-dominant hand or both hands.

Some authors report that hemispheric asymmetries in ipsilateral activations are present at the level of primary motor cortex (Babiloni et al. 2003, Kawashima et al. 1993, Kim at al. 1993). Others claim that the amount of activation in the ipsilateral motor cortex during left- or right-hand movements is similar (Volkmann et al. 1998) and attribute handedness to a possible hemispheric asymmetry of higher order motor cortices (premotor – Hlustik et al. 2002, Singh et al. 1998, or supplementary motor – Li et al. 1996). Still others do not find any ipsilateral activation in the primary sensorimotor cortex (Solodkin et al. 2001). Moreover, it is not clear whether asymmetries in activation elicited by dominant and non-dominant hand movements are present only during complex movements (Kim et al. 1993, Singh et al. 1998, Verstynen et al. 2005) or, as some papers suggest, constitute a more general feature also present during simple movements (Babiloni et al. 2003, Kawashima et al. 1997).

In our view, a possible source of inconsistency between studies is the common adoption of ROI (region of interest) methods for processing fMRI data in which volumes of activation within a priori defined brain regions, known to play a critical role in motor control, are estimated and then comparisons are being made between those values for regions localized in the left- and right hemispheres. However, as revealed by several studies, the precise localization of particular areas may vary across subjects (see Verstynen et al. 2005, Volkmann et al. 1998 for a review) and their anatomical size may not be the same in the left and right hemispheres (Amunts et al. 1996, 2000). Using ROI analysis may, thus, constitute a likely source of confusion, as it would run the risk of comparing regions that are functionally not quite equivalent in different individuals and different hemispheres. Having this in mind we decided in the present study not to perform ROI analyses, but to calculate total volume of the activated areas in the left/right-contralateral/ipsilateral hemispheres. Our strategy was, thus, to quantify hemispheric asymmetries in the spatial extent of hand representation by computing the volume of all significantly activated voxels in both hemispheres.

To be able to reconcile the divergent views as to the effect of task complexity on handedness-related differences in ipsi- and contralateral hemisphere activation patterns, we used two different (simple and complex) unpracticed tasks which could be performed with either hand and which were most commonly used in previous studies. This enabled us to relate our data to the existing literature.

METHODS

Subjects

Twelve adult subjects (mean age 24.3, SE 4.6; 6 males and 6 females) participated in the study. All reported consistent right-hand preference across their life and no rightward shift attempts in childhood. Their mean Handedness Preference Index (HPI) as assessed by the Edinburgh Handedness Inventory (Oldfield 1971) was 84.2 indicating strong right-handedness.

All participants were informed about the purpose of the study before giving their written consent. None had any contraindications to fMRI and none reported neurological or psychiatric illness, learning disability, failure in elementary school or claustrophobia. The study protocol was approved by the Ethics Committee of Jagiellonian University.

Materials and procedure

NEUROIMAGING DATA ACQUISITION

The experimental paradigm consisted of two experimental runs each containing 10 alternating blocks of 3 three tasks: (A) simple movement (flexion/extension of the index finger), (B) complex movements (sequential opposition of the thumb to tips of other fingers in order: 5, 4, 3, 2, 5, 4 and so on), (C) rest (which required the subjects to remain still). Within each run the blocks were repeated in a sequence CABCABCABC with 15 s per each block and 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 about 2 Hz which was comfortable for subjects and easy to control. Subjects were practiced in the two tasks prior to scanning to ensure similar task execution by all subjects. The onset of each of the different tasks was signaled by 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 a rest condition, a red square indicated simple movements and a blue one complex movements. The squares remained visible during each condition.

Before scanning the subjects were instructed how to react to each stimulus type they would see on the screen. Stimuli were back-projected from a multimedia projector (Sony LCD Data Projector VPL-SC50, Tokyo, Japan) on a screen located about 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: 3 000/60 (repetition time ms/echo time ms), a 90° flip angle, a 18 × 13 cm field of view (FOV), a 96 × 64 matrix, number of excitations, 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 always set parallel with the axis connecting the anterior commissure and the caudal surface of the cerebellar tonsil, and extended up to the posterior midline boundary of the parietal lobe. The selected slice thickness was adjusted for each subject's brain volume to keep the scanned brain area constant across all subjects.

The coplanar, high-resolution structural MRI images were acquired in the same locations as the functional images, using 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, number of excitations, 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.

Much effort was exerted to make the subject as comfortable as possible, so as to reduce head motion. The 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 thing about anything particular, while lying in the scanner. A standard radio-frequency (RF) head coil was used with foam padding to restrict head motion.

The fMRI experiment was preceded by subjects' training in the motor task. Special attention was given to teach them to pace their movements at approximately twice a second without any preceding cues. The task was thus highly automated before starting the scanning procedure.

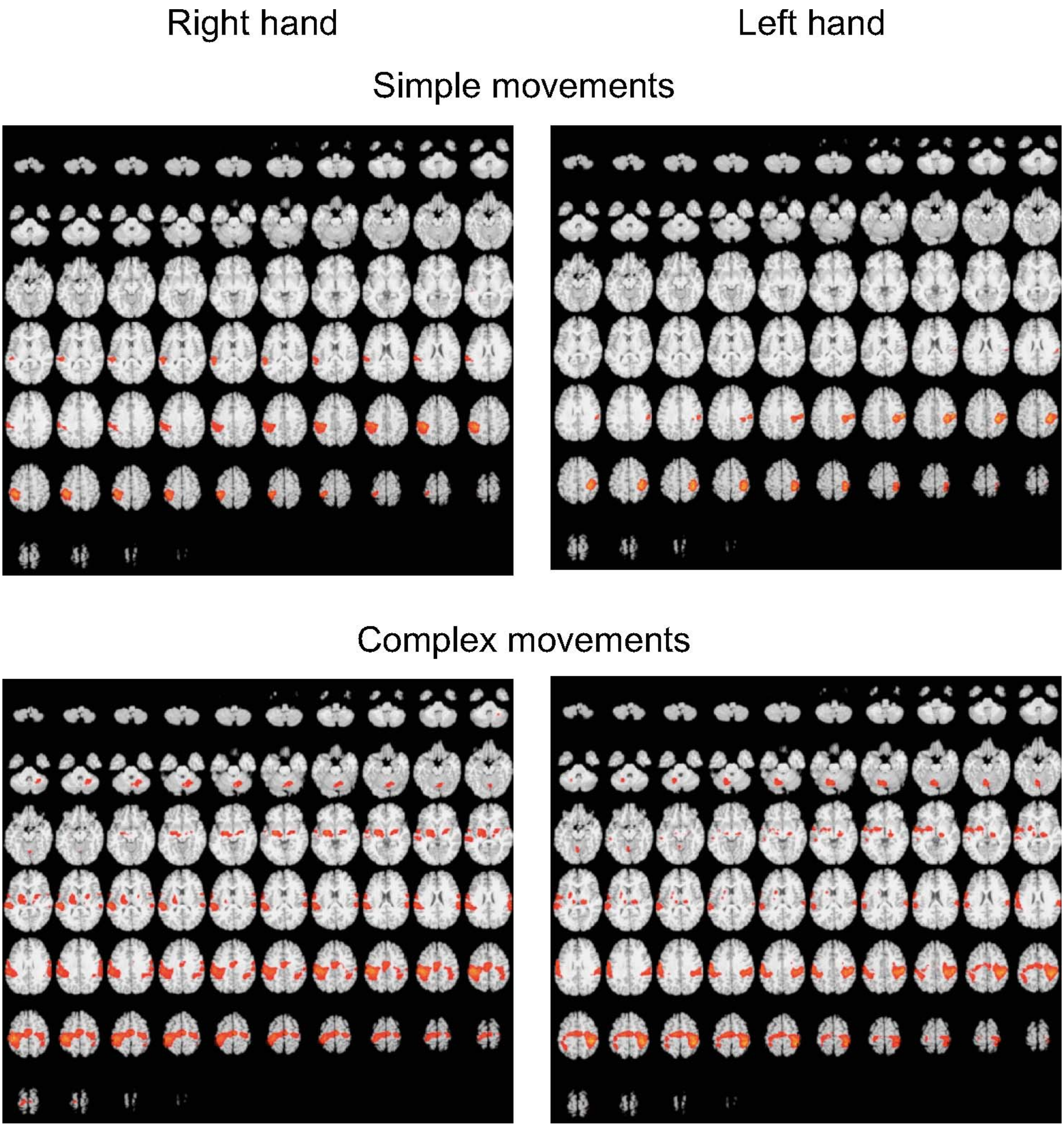

Fig. 1. Localization of significant activation during simple and complex movements performed with either the left or the right hand

PROCESSING OF THE FUNCTIONAL IMAGES

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

The statistical analyses were done using 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 artefacts, a highpass temporal filtering was applied on the functional images by using straight line fitting with a cutoff at 45 s. Gaussian spatial smoothing with a FWHM kernel of 8 mm was carried out on the functional images to reduce noise. In the statistical analysis, linear contrasts on between subjects conditions were calculated in native subject space (i.e., before transformation of images to the Talairach space) as a pre-step to the higher level analysis.

Higher level group analyses were performed by first registrating the subject level contrast images to a reference brain in Talairach standard space (Roland and Zilles 1994), then using FLAME (FMRIB's Local Analysis of Mixed Effects) on the contrast images to estimate the inter-subject random effects. The statistical Z-images from the group analysis were thresholded at z=3.3 to get clusters. All clusters with a $P \leq 0.05$ were considered significant.

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

RESULTS

Localization of activation

The fMRI scans revealed a number of areas that were consistently activated during finger movement. Figure 1 illustrates the localization of significant activations in the whole group of subjects for simple and complex tasks. Significant group activations during simple movements were found in: precentral, postcentral, parietal superior, parietal inferior and supramarginal gyri, contralateral to the moving hand. For complex movements activation covered much broader areas in the cerebral cortex including the precentral gyrus, postcentral gyrus, supplementary motor area, insula, cingulum, parietal lobuli, supramarginal, superior and medial temporal gyri subcortical areas (putamen, pallidum, thalamus) as well as both contralateral and ipsilateral cerebellar hemispheres for both hands.

Volumes of hemispheric activation

To study the effect of hand dominance on movement representation in the two hemispheres we calculated in each subject the volume of all significantly activated voxels in either cerebral hemisphere during left- or right hand movements for the simple and complex tasks. To preserve individual variation, these calculations run in native subject space. These data were subjected to a three factorial ANOVA with hand (dominant/non-dominant), hemisphere (ipsilateral/contralateral) and task (simple/complex) as the main factors. The results are presented in Table I.

Table I

The results of three factorial ANOVA with hand, hemisphere, and task as the main factors

	F	*P*
Task	26.230*	0.001*
Hand	0.085	0.776
Hemisphere	23.119*	0.001*
Task × hand	0.323	0.581
Task × hemisphere	10.850*	0.007*
Hand × hemisphere	15.951*	0.002*
Task × hand × hemisphere	17.296*	0.002*

(*) statistically signifcant

The analysis revealed significant main effects of task (with larger activations for complex task than for simple task) and hemisphere (with larger contralateral than ipsilateral activations). There were two 2-factorial interactions: hemisphere by hand and hemisphere by task. As illustrated in Fig. 2, bigger contralateral activations were elicited by right (dominant) hand movements, whereas bigger ipsilateral activations were elicited by left (non-dominant) hand movements. In consequence, differences in activation area between

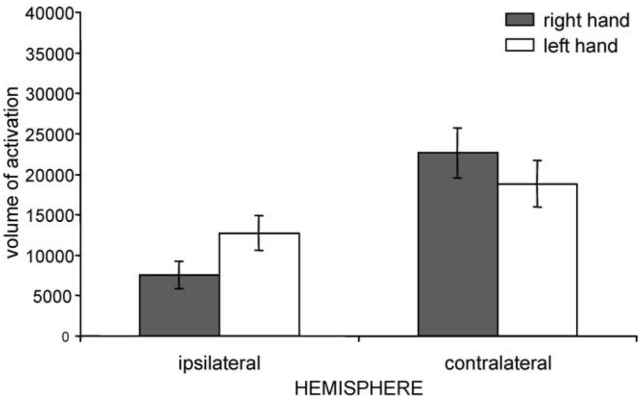

Fig. 2. Mean activation volumes (mm^3) in the ipsilateral and contralateral hemispheres for left- and right-hand movements

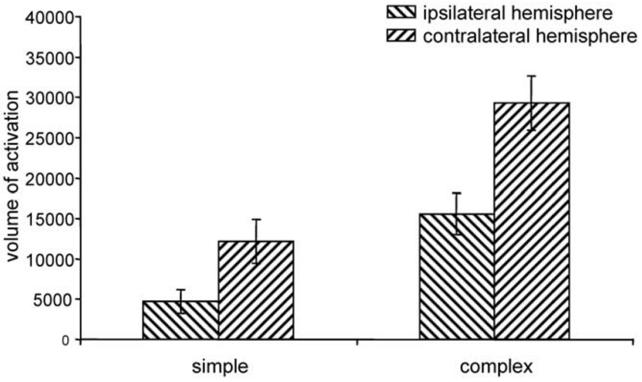

Fig. 3. The proportion of ipsilateral relative to contralateral activation in simple and complex tasks

the ipsilateral and contralateral hemispheres were more pronounced for the right hand than for the left hand. The hemisphere by task interaction (see Fig. 3) resulted from a relatively higher proportion of ipsilateral relative to contralateral activation in the complex task in comparison to the simple task. The ANOVA also revealed a significant 3 factorial interaction between hemisphere, hand and task (Fig. 4) which was due to different patterns of ipsilateral and contralateral activation for complex and simple movements. For complex movements contralateral activation was larger for the right hand whereas ipsilateral activations were larger for the left hand, both resulting in larger activation in the left hemisphere (F=15.951, P<0.002). For simple movement the contralateral activations were similar for the two hands, whereas ipsilateral activations were slightly larger for the left hand (insignificant difference).

DISCUSSION

The current experiment was designed to investigate whether hand preference has any association with the volume of activation in the two cerebral hemispheres during hand movements and whether the expected asymmetry in activation depends on the task complexity. The study provided the following main results:

First, for both hands and tasks, contralateral activation was larger than ipsilateral activation.

Second, the total volume of activation (in both hemispheres) elicited by the dominant (right) and non-dominant (left) hand was similar.

Third, a predominance of left-hemisphere activation over right hemisphere activation was observed. This resulted from both larger contralateral activation for the right (dominant) hand and from larger ipsilateral activation for the left (non-dominant) hand. It is worth noting that those effects were specific to the complex rather than the simple tasks. During the simple task activation in the two hemispheres did not differ.

Fourth, increasing the complexity level of motor activity resulted in an increase in the volume of consistently activated areas and greater ipsilateral activations, especially when the movement was performed with the non-dominant hand.

The finding of larger activations in the cerebral hemisphere contralateral to the moving hand, also found in previous studies (e.g., Dassonville et al. 1997, Volkmann et al.1998), can easily be attributed to contralateral cerebral organization of the primate motor system (due to crossing of pyramidal tract), where the

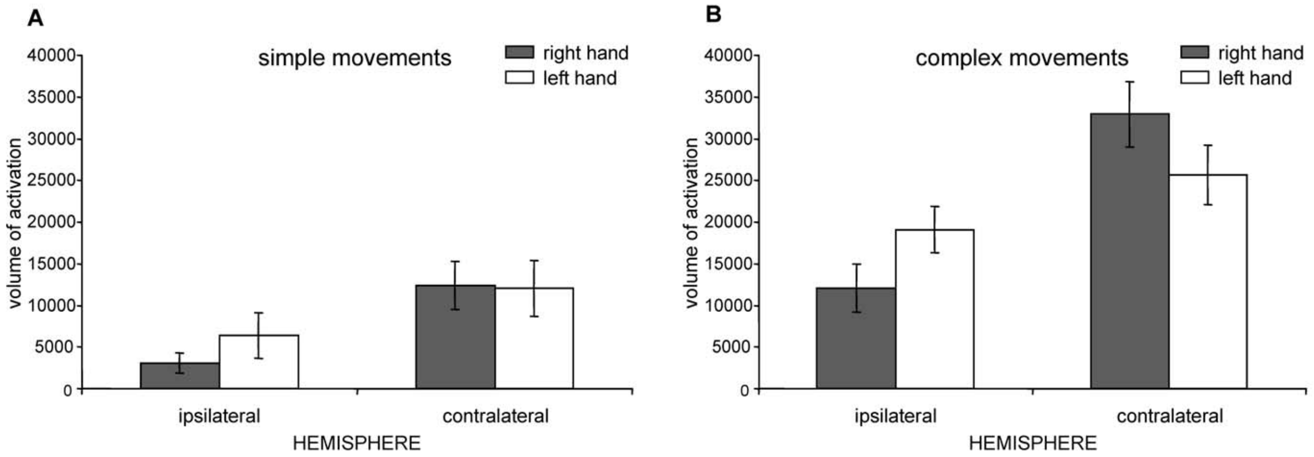

Fig. 4. The effect of task complexity on mean activation volume (mm^3) in the ipsilateral and contralateral hemispheres for left- and right-hand movements

right cerebral hemisphere controls movements of the left side of the body and the right cerebral hemisphere exerts control over the right side. It is also not surprising that complex tasks produced larger activations and involved higher association cortices, subcortical structures and the cerebellum in addition to sensorimotor areas (Roland and Zilles 1996, Solodkin et al. 2001).

However, the most important findings of the present study are those which showed that the activation pattern depended on whether subjects performed movement with their dominant or non-dominant hand. Interestingly, the effect of hand dominance was apparent only during complex movement. Our study revealed that the right-hand dominance is associated not only with larger activations contralateral to the dominant hand but also with larger activations ipsilateral to the non-dominant hand. This points to the importance of an ipsilateral component in the mechanisms underlying hand dominance. The finding, that ipsilateral activation is mainly present during performance of the complex rather than the simple task, and that hemispheric asymmetry for both contralateral and ipsilateral activation also depends critically on task complexity implies that the more complex the motor task, the greater the involvement of those mechanisms which regulate hand-dominance. This agrees with an intuitive view, that when a subject performs simple task he/she can do so with either hand, for example carrying a bag or handling an umbrella. However, when a more demanding (complex) task is performed, it is the right hand which is preferred. When a complex task is performed with the non-dominant hand, the involvement of ipsilateral structures (those specialized in motor control for the dominant hand), could be of special value. Indeed, it can easily be imagined that the poor motor abilities of the left hand require more support from the better "skilled" left hemisphere, than the better trained right hand from the less skilled right hemisphere. During simple motor tasks such left-hemisphere assistance is required less.

A general predominance of left-hemisphere activation relative to right hemisphere activation in right-handers was also found in previous studies (Babiloni et al. 2003, Dassonville et al. 1997, Hlustik et al. 2002, Verstynen et al. 2005, Volkmann et al. 1998), but those data were limited to particular motor cortices or particular tasks investigated. In our study we were able to compare directly the effects of task complexity by using both simple and complex tasks in the same subjects. The results showed that right-hand preference was reflected in leftward asymmetry of motor representation only during performance of complex motor tasks. These observations are in line with the idea that the expansion of activation area in the dominant hemisphere may provide extra space for the more efficient cortical encoding of a greater motor skill repertoire of the preferred hand (Volkmann et al. 1998).

Our finding that in right-handers ipsilateral activation was larger for the non-preferred (left) than for the preferred (right) hand, corroborates some other fMRI and PET studies (Babiloni et al. 2003, Kawashima et al. 1993, Kim et al. 1993). These studies demonstrated that right M1 and S1 areas were more activated during left rather than right hand movements, whereas such a difference was less evident in left M1 and S1. Other studies, however, imply that this asymmetry is characteristic of higher order cortices and not of primary sensorimotor cortex (Hlustik et al. 2002, Li et al. 1996, Singh et al. 1998). Babiloni and coauthors (2003) found an advantage of activation in the left SMA, but this activation was comparable during contralateral and ipsilateral movements. In our view, these discrepancies could result from differences in motor tasks used in those studies and, as we mentioned in the Introduction, from problems with correct identification (in ROI analysis) of particular brain areas due to inter-subjects and inter-hemispheric variance. Our research provides data explicitly showing that the entire volume of the ipsilateral activation was consistently greater in the left hemisphere as compared to the right, and that this effect was characteristic of complex rather than simple movements.

Interestingly, a recent study (Verstynen et al. 2005) which controlled for the complexity of task and the number of moving fingers showed that the ipsilateral activity in left motor cortex does not depend on the number of fingers involved in the task but, rather, on the complexity of the task. Based on this finding it could be supposed that in our study, where the two tasks differed both in the number fingers used and in task complexity, the later factor would be of primary significance for the consistently greater activation seen in the complex task condition. It might also be expected that the above-described differences would even be more pronounced for tasks of a very high level of complexity.

It remains unclear what causes the ipsilateral activation. The simplest hypothesis would attribute it to the existence of an ipsilateral uncrossed motor pathway. This hypothesis, however, can easily be rejected for at least three reasons. First, only 10% to 15% of pyramidal fibers are uncrossed (Kuypers 1981, Nathan et al. 1990) and thus they can not explain the massive ipsilateral activation seen during complex movements. Second, ipsilateral corticospinal fibers reach preferentially proximal, and not distal hand muscles (Colebatch and Gandevia 1989). Third, differences in ipsilateral activation for the dominant and non-dominant hand would require the unbalanced number of the uncrossed fibers for the two hands. This in turn would result in a clear hand-preferences in very young children. Developmental studies (Bishop 1990) provide concordant findings that this is not the case and that hand preference develops with age.

A more plausible hypothesis would be that the ipsilateral activation is due to callosal connections.

What could be their functional significance? Greater ipsilateral activation present in the hemisphere contralateral to the preferred hand could imply that this hemisphere exerts control not only over the contralateral (preferred) hand but also over the ipsilateral (non-preferred) hand. In contrast to this, the non-dominant hemisphere is involved mainly in the motor control of contralateral (non-preferred) hand movement. In other words, it seems, that the preferred hand is controlled mainly by the dominant hemisphere while the non-preferred hand by both hemispheres (Baraldi et al. 1999).

The view that in right-handers the left hemisphere supports the execution of complex movements of the non-dominant left hand is consistent with clinical evidence demostrating that damage to the left hemisphere leads to apraxia (Heilman 2000) and disrupts motor skills even when the left, ipsilesional hand is used (Haaland and Harrington 1996, Kimura 1977).

CONCLUSIONS

This study provided a very concise pattern of results which suggests that in humans handedness is reflected in hemispheric asymmetry in the volume of activated cortical area. Importantly, this asymmetry does not imply that the dominant hand produces more activation than the non-dominant hand. Rather, right-hand dominance is associated with larger activations in the left hemisphere that results from both larger contralateral activation for the right (dominant) hand and from larger ipsilateral activation for the left (non-dominant) hand. This points to the importance of an ipsilateral component in the mechanisms underlying hand dominance.

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