Hemispheric asymmetries in goal-directed hand movements are independent of hand preference

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Asymmetries in the kinematics and neural substrates of voluntary right and left eye–hand coordinated movements have been accredited to differential hemispheric specialization. An alternative explanation for between-hand movement differences could result from hand preference related effects. To test both assumptions, an experiment was conducted with left- and right-handers performing goal-directed movements with either hand paced by a metronome. Spatiotemporal accuracy was comparable between hands, whereas hand peak velocity was reached earlier when moving with the left compared to the right hand. The underlying brain activation patterns showed that both left- and right-handers activated more areas involved in visuomotor attention and saccadic control when using their left compared to the right hand. Altogether, these results confirm a unique perceptuomotor processing specialization of the left brain/right hand system that is independent of hand preference.

Introduction

When producing goal-directed eye and hand movements, a tight and consistent temporal and spatial coupling between the effectors is observed. In general, the eyes precede and pilot the hand to the target both in discrete and cyclical movements (Helsen et al., 1998a, 2000, 2010; Lavrysen et al., 2006, 2007). Behavioral and brain research has revealed consistent differences between left and right hand movements paired with eye movements in right-handers. For example, the right-hand advantage emerges as a shorter phase for making corrections at the end of the movement. This is typically expressed as a shorter time after peak velocity (i.e., the time to decelerate) when using the right compared to the left hand (Lavrysen et al., 2007; Roy et al., 1994). In our previous fMRI study with right-handers (Lavrysen et al., 2008), the differences found in left and right eye–hand coupling were attributed to functional specialization differences between the left and right hemisphere. Alternatively, they might simply be an expression of the reduced processing effort when using the well-trained preferred hand. Hence, left-handers would show the opposite pattern of behavioral and functional asymmetries. To differentiate between these two hypotheses, the present study extended the paradigm of Lavrysen et al. (2008) to a group of extremely lateralized left-handers. This group

has typically been neglected in the literature compared to the vast amount of publications that addresses right-handers.

With regard to movement control, the left side of the brain largely controls the right body side and vice versa. In addition, some specific functions are largely lateralized to one hemisphere (see Toga and Thompson, 2003 for a review) due to genetics and/or environmental influences (Goble and Brown, 2008). As a consequence of lateralization of function, it is suggested that performance of both hands differs because each hand has access to resources and capabilities of a different hemisphere. The unique role of each hemisphere in movement control has been studied in several paradigms (see Serrien et al., 2006 for a review). As an alternative to studying brain damaged patients (Haaland et al., 2004), paradigms using simple unimanual movements can be used to study hemispheric asymmetries, since these tasks predominantly address the contralateral hemisphere (Hausmann et al., 2004). The resulting differences in performance between the left and right hands are then most likely an expression of the functional capacities of the contralateral hemisphere. Examples of manual asymmetries that have been consistently found in behavioral research are reaction time advantages for the left hand and movement time advantages for the right hand in simple manual aiming (e.g., Carson et al., 1995; Elliott et al., 1995; Helsen et al., 1998b; Mieschke et al., 2001). Because the majority of studies only tested right-handed participants, some right-hand advantages might be explained by the large amount of practice of the preferred as compared to the non-preferred hand. Nevertheless, some differences cannot be explained by hand preference alone because they occur both in left- and right-handers, offering support for the
hemispheric specialization hypothesis (Boulinguez et al., 2001; Gonzalez et al., 2006; Hodges et al., 1997; Lavrysen et al., 2003).

In any case, functional specialization in motor control is quite complex and different task requirements or even strategies of the participants might require differential recruitment. In this regard, hand preference and other functional hemispheric specializations may coexist and even mask their expression in performance measures. This could be controlled by comparing left- with right-handed participants. Generally speaking, the majority of functional activation studies have only looked at right-handers when aiming or reaching with the preferred hand (for example, Astafiev et al., 2003; Beurze et al., 2007; Ellermann et al., 1998; Grafton et al., 1992; Prado et al., 2005). There are some exceptions including left-handers (Dassonville et al., 1997; Kawashima et al., 1997; Kim et al., 1993; Singh et al., 1998; Solodkin et al., 2001; Verstynen et al., 2005). Yet, the focus of the latter studies was primarily restricted to asymmetries in primary, pre and supplementary motor regions and occasionally the cerebellum, whereas in our study, activation in the whole brain was considered. At least for simple manual movements, left- and right-handers seem to show comparable asymmetrical patterns of activation (Solodkin et al., 2001).

A second concern when comparing functional brain activation is matching performance levels of both hands. For both left- and right-handers, the preferred hand outperforms the non-preferred in many, but not all tasks (for example see Lavrysen et al., 2003). This is for the most part due to the unequal amount of practice that both hands have experienced during the course of life. Therefore, both hands should be trained towards comparable performance levels, such that differences in underlying activation more likely reflect functional specialization at the brain level instead of skill or practice differences.

Therefore, the goal of the present study was to evaluate behavioral and neural differences in eye–hand coordination when using either the right or the left hand. The present experiment extends previous work of Lavrysen et al. (2008) in right-handed participants by combining the data of right-handers with a newly tested group of left-handed participants, using exactly the same paradigm. Qualitative analyses of movement kinematics in combination with brain imaging techniques (fMRI) were used to examine the mechanisms underlying manual asymmetries. Both groups were trained beforehand to ensure that the level of performance of unimanual cyclical hand movements was equal for both sides. We hypothesized that, if left-handers would show a reversed pattern of neural activation compared to right-handers, this would indicate that the effects are related to hand preference. If, on the contrary, the effects at the neural level would be similar for both handedness groups, this would support the hemispheric specialization hypothesis.

Materials and methods

Participants

The right-handed group was the same as in Lavrysen et al. (2008). Twelve young healthy right (7 males and 5 females) and twelve left-handed volunteers (6 females and 6 males) were included in the study (age range 18–28 years). The right-handers had an average score on the Edinburgh Handenedness Inventory of 94.8±5.5 and the left-handers of −82.5±8.5 (with a value of +100 representing extreme right hand preference and −100 extreme left hand preference; Oldfield, 1971). Participants had no neurological or psychiatric disease, had normal or corrected-to-normal vision and hearing capabilities. None of them were taking psycho- or vasoactive medication. The experiment was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki including the latest amendments. Because of technical difficulties in eye data recording during the scan session, the behavioral (eye and hand) data of two left-handed participants were excluded from the analysis. Yet, their performance evaluated in the preceding practice session was comparable to other participants, so that no meaningful differences were to be expected between the obtained results and the omitted behavioral data.

Experimental design

The apparatus, task and procedure were identical to Lavrysen et al. (2008). The participants made 40° wrist flexion–extension movements lying with their forearms supported by cushions. Non-ferromagnetic forearm orthoses were attached to both arms. Wrist angular position was registered with high-precision shaft encoders with an accuracy of 0.09° at a sampling frequency of 200 Hz. An Applied Sciences Laboratory head-mounted eye tracker (ASL 5000 model 501 for practice sessions and ASL Model 504 LRO in the scanner environment) recorded two-dimensional point of gaze (PG) coordinates. The 504 LRO eye tracker has a system accuracy of 0.5° and an angle resolution of 0.25° visual angle. The visual range covers 50° horizontally and 40° vertically and the sampling frequency was 200 Hz. Direct vision of the limb was prevented, but angular flexion and extension was represented by a cursor moving left (left hand extension and right hand flexion) and right (left hand flexion and right hand extension) on a 17” computer screen across a distance of 20 cm. Both in the training and scanner environment, this screen was seen via a mirror. The distance between screen and eyes was about 50 cm, thus, the distance between the target squares corresponded to ±20° visual angle (Fig. 1).

Fig. 1. The visual presentation screen (top) showed the position of the target and fixation points and (only in practice conditions) the position of the cursor. The participant saw the screen through a mirror attached to the scanner wall.
The task consisted of making 40° wrist flexion–extension movements with the right or the left hand in coordination with saccades towards two target squares at a 20° visual angle distance (Right Coordination–Left Coordination). Apart from eye–hand coordinated movements, participants also performed trials moving the effectors in isolation (Eyes Alone, Right Hand, Left Hand). All conditions were paced at 2 Hz by an auditory metronome applied through the hospital headphones. Both the extension and flexion reversal points were paced, so that participants produced one complete (flexion–extension) cycle every second. In the Rest conditions, they were instructed to look at a central fixation point on the screen.

To keep visual information identical in the different conditions, both the target and the fixation squares were visible during each condition. In the experimental trials, the participants did not receive any visual feedback related to their hand movements on the screen. In addition, looking at their moving hand directly was not possible.

To become familiarized with the task and the environment participants took part in a one-hour training session in a dummy scanner on a separate day prior to the actual fMRI session. They were trained to obtain equal temporal and spatial accuracy with both the right and the left hand. This enabled us to attribute any behavioral and/or neural differences to functional specialization of the hand/hemisphere systems. During the first part of the practice session, feedback of angular position was provided by the presentation of a 10 mm diameter round cursor that reflected their hand position and had to be aligned with the left and right target alternatively. This cursor moved horizontally in synchrony with the flexion–extension movements of the wrist. Later on during practice and in the subsequent fMRI session, the experimental conditions were performed without visual feedback of the ongoing hand movements.

During the two-hour scanning session, the participants lay supine inside the scanner with their upper arms next to their bodies and their forearms supported by a cushion so that they could make unrestricted hand movements. A bite-bar was used to minimize head motion. After a short initial practice session with feedback of the cursor the participants completed five test sequences, each consisting of 21 trials lasting 14 s. During one sequence, each movement condition was presented three times, and the rest condition was presented six times. Here is an example of a series that was repeated three times per sequence: Eyes Alone, Right hand, Left Hand, Rest, Right Coordination, Left Coordination, Rest. Except for Rest trials that were delivered at fixed positions, all movement conditions were presented in a random sequence to prevent any order effects. In between trials, there was a fixed interval of two seconds, during which the instructions for the next condition were presented on the screen. Neither auditory instructions nor feedback of performance were given during the course of a sequence. To ensure initial accuracy, each sequence was preceded by a practice sequence of co-ordinated eye and hand movements with feedback of the hand position, consisting of two 14 s trials for each hand.

The MR images were acquired in a 3-T Intera MR scanner (Philips, Best, Netherlands), using an 8 channel receive only SENSE head coil. For functional time series, each consisting of 145 whole brain gradient-echo (GE) echo-planar scans (EPI), the data were acquired every 2.6 s (TR/TE = 2600/30 ms, field of view = 220 × 220 mm, acquisition matrix = 80 × 80, slice thickness = 3.0 mm, interslice gap = 0.3 mm, 42 transversal slices, SENSE factor = 2). Each scanning session ended with the acquisition of a 3D SENSE high resolution T1-weighted image (TR/TE = 9.68/4.6 ms, TI = 1100 ms, field of view = 250 × 250 mm, acquisition matrix = 256 × 256, slice thickness = 1.2 mm, 182 slices, SENSE factor = 2) for anatomical detail.

Behavioral data analysis

Hand movements

In line with previous work (Lavrysen et al., 2006, 2007, 2008), the hand data were filtered using a 1st order low-pass Butterworth filter with a cut-off frequency of 20 Hz. The average movement time of the hand (MTh) and average amplitude (AMPTh) between reversal points were calculated as the temporal and spatial accuracy measures of hand performance. A reversal point was defined as the point where maximal flexion or extension amplitude was reached, or, in other words, the movement was reversed. Mean time to peak velocity as a percentage of MTh (%TTPV) was used to evaluate the amount of time used after peak velocity for making movement corrections (Elliott et al., 1999).

Eye movements and eye–hand coordination

As the movements occurred in the horizontal plane, only the horizontal gaze coordinates were taken into consideration. In line with previous work (Lavrysen et al., 2006, 2008), a 1st order Butterworth low-pass filter with a cut-off frequency of 30 Hz was applied on the horizontal eye data. The methods used to analyze the eye movements were similar to the ones described previously (Helsen et al., 1998a; Lavrysen et al., 2008). A fixation was defined as a stable gaze position (standard deviation of PG less than 1°) which was maintained for at least 100 ms. The amplitude and movement time of the primary saccade were calculated respectively as the displacement and time between start and completion of the primary saccade. The start and the completion of the primary saccade were expressed relatively to the movement time of the corresponding hand movement.

Statistical analysis

Each movement condition was presented three times in each of the five sequences of the fMRI session. The first and last movements of each 14 s trial were disregarded for the analyses. The remaining movements were averaged over those fifteen trials to yield one global estimate per subject for each variable for each condition. Eye and hand data of 22 participants were used in the analyses, because behavioral data of two left-handers could not be included due to technical problems during scanning. All results are presented as means ± standard deviations. The dependent variables for hand movements and eye–hand coordination were analyzed using paired t-tests. Statistical significance (α) was set at p < 0.01.

fMRI image analysis

The data preprocessing and analysis for the left-handers in this study was done in accordance with the analysis of the right-handers in Lavrysen et al. (2008). Data were analyzed using SPM5 (Wellcome Department of Cognitive Neurology, London, UK), implemented in Matlab 7.2 (The Mathworks Inc.). For each subject, all echo-planar imaging (EPI) volumes were realigned to the first volume of the first time series and a mean image was created of the realigned volumes. The mean image was smoothed with a Gaussian kernel of 10 mm full width at half maximum (FWHM). Additionally, the anatomical image was co-registered with this smoothed mean image. The structural image was spatially normalized to a reference system (Talairach and Tournoux, 1988), using a symmetric brain template. This symmetric brain template was created by averaging a representative brain (Montreal Neurological Institute, MNI) with its mirror image. This normalization was performed using affine and nonlinear transformations, mapping the anatomical scan to the template. The normalized image was sampled to a voxel size of 2 × 2 × 2 mm and smoothed with a Gaussian kernel of 10 mm FWHM. All statistical analyses were done in the context of the General Linear Model (Friston et al., 1995). First, a general linear model was defined for each subject, and with each single condition modelled by a delayed boxcar function convolved with the haemodynamic response function. An appropriate high-pass filter (cut-off frequency = 256 s) was applied to remove low frequency drifts. Additionally, six movement parameters derived from realignment were added as covariates of no interest to correct for confounding effects induced by head movement.

There are indications of volumetric differences across sensorimotor areas between dominant and non-dominant hemispheres as well as between right- and left-handers (Amunts et al., 2000; Foundas et al., 2008).
Therefore, a symmetrical template has been frequently used for normalization of the images (see for example Callaert et al., 2011 and Caeyenberghs et al., 2009). Moreover, this procedure permits the normalized data of one side (e.g. left-hand movements) to be flipped horizontally in order to allow a direct comparison of activation in symmetrical brain regions. This allows to compare functional similarities or differences of certain structures independent of hand preference or hand used.

For each subject, the movement conditions were contrasted with the rest condition to obtain the first level contrasts (Left Hand vs. Rest, Right hand vs. Rest, Eyes vs. Rest, Left Coordination vs. Rest and Right Coordination vs. rest). To evaluate differences between right and left coordination (Left Coordination vs. Rest > Right Coordination vs. Rest and Right Coordination vs. Rest > Left Coordination vs. Rest) for left- and right-handers, these four contrasts were entered into a mixed effects second-level analysis with group (left versus right-handers) as between and hand (left versus right hand) as within factors. Within this design, all pairwise comparisons involving left and right hand movements of left- and right-handers were inspected. Left hand activation was compared between left- and right-handers (LH Left Coordination vs. Rest > RH Left Coordination vs. Rest; RH Left Coordination vs. Rest > LH Left Coordination vs. Rest). The same was done for the right hand (LH Right Coordination vs. Rest > RH Right Coordination vs. Rest; RH Right Coordination vs. Rest > LH Right Coordination vs. Rest) and also for preferred (LH Left Coordination vs. Rest > RH Right Coordination vs. Rest; RH Right Coordination vs. Rest > LH Right Coordination vs. Rest) and non-preferred hands (LH Right Coordination vs. Rest > RH Left Coordination vs. Rest; RH Left Coordination vs. Rest > LH Right Coordination vs. Rest). Furthermore, we compared the preferred hand of both handedness groups with the non-preferred hand and vice versa ((LH Left Coordination vs. Rest + RH Right Coordination vs. Rest) > (LH Right Coordination vs. Rest + RH Left Coordination vs. Rest) and (LH Right Coordination vs. Rest + RH Left Coordination vs. Rest) > (LH Left Coordination vs. Rest + RH Right Coordination vs. Rest)). In a separate analysis, left and right hands were pooled across both hand preference groups and comparisons were made for left versus right hand movements ((LH Coordination vs. Rest + RH Left Coordination vs. Rest) > (LH Right Coordination vs. Rest + RH Right Coordination vs. Rest)) and right versus left hand movements ((LH Right Coordination vs. Rest + RH Right Coordination vs. Rest) > (LH Left Coordination vs. Rest + RH Left Coordination vs. Rest)). Unless reported otherwise, voxels were considered to be significantly activated when a p < 0.05 was reached after correction for multiple comparisons by using the false discovery rate (FDR) procedure (T = 4.00). The minimum cluster size was set to 30 voxels. All results are reported in MNI coordinates.

Results

Below, the focus is on presenting data of left-handers only and the comparison of left- and right-handers’ performance. For detailed behavioral data of the right-handers, we refer to Lavrysen et al. (2008).

Behavioral data

Hand movements

Left-handers showed no statistically significant effects for mean amplitude (44° ± 5) and movement time (498 ms ± 2). This indicates that participants’ temporal and spatial accuracy did not differ between left and right hand movement conditions. Interestingly, similar to right-handers, hand peak velocity was reached earlier when moving with the left than the right hand (right hand: 60.7% ± 6.4; left hand: 57.3% ± 6.2; paired t-test: p < 0.05).

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**Fig. 2.** Group statistical parametric maps (SPMs) for the contrast of left (blue) versus right-sided movements (red) resulting from the first level analyses of hand alone (top panel) and eye–hand coordination (bottom panel) of left-handers (left; n = 12) and right-handers (right; n = 12). The activations (FDR, p < 0.05; T = 4) are overlaid on a rendered image of a representative normalized brain. The left side of the images correspond to the left side of the brain. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Eye movements and eye-hand coordination

Primary saccades of left-handers were on average 37.5° ± 1.7 in amplitude and lasted 71 ms ± 13. There was no difference between left and right coordination conditions. The saccades were initiated at 34.4° ± 12.5 and arrived near the target at 48.7° ± 13.1 of hand movement time. Again, this pattern was independent of the hand used.

Comparing performance of left- and right-handers

T-tests were performed to compare spatial (amplitude) and temporal (movement time) performance between left- and right-handers. The performance of left-handers was not significantly different (p<0.05) from right-handers tested under the same circumstances (Lavrysen et al., 2008). Similar to right-handers, the left-handed participants exhibited comparable performance levels for both hands as intended. Importantly, the comparable spatio-temporal performance between left- and right-hand movements will allow us to interpret potential brain activation differences in the absence of behavioral confounds.

Interestingly, similar to right-handers, peak velocity was reached earlier when using the left than the right hand, independent of hand preference. On the other hand, the subtle differences found in eye-hand coordination in right-handers were not repeated in left-handers, i.e., the primary saccades were neither initiated nor completed earlier when using the left as compared to the right hand.

fMRI data

In the results below, we will firstly show the unflipped data projected on a standard brain for Hand vs. Rest and Coordination vs. Rest conditions for the right and left hand movement conditions. Subsequently, the activation maps for the left execution modes were left-right flipped (mirrored), in the same way for left- and right-handed participants. This horizontal flipping procedure allowed us to compare contra- and ipsilateral activation for both hands directly. As such, activation projected on the right part of the brain corresponds to the hemisphere ipsilateral to the movement and activation on the left part refers to the contralateral hemisphere.

Coordinated versus isolated eye and hand movements

Fig. 2 shows the unflipped data projected on a standard brain for Hand vs. Rest and Coordination vs. Rest conditions for the right and left hand movements for right- and left-handers. Activation for right-hand movements is shown in red and for left-hand movements in blue. An analysis was performed evaluating the difference between eye-hand coordination versus independent control of eyes and hand (Fig. 3). The contrasts represent the supplementary activation associated with eye-hand coordination vs. independent eye and hand control (conjunction between left and right side). In right-handers (see Lavrysen et al., 2008), this analysis yielded peaks in the ipsilateral anterior cerebellum and contralateral central sulcus. Similarly, in left-handers, cerebellar activation was found extending to the occipital cortex, but also contralateral central sulcus and thalamus (see Fig. 3A).

Statistical comparison of the degree of symmetry of the activation in left-handers was done through paired t-tests on the flipped data (see right panel of Fig. 3). Although for this analysis no voxels survived the threshold for statistical significance at FDR level, the results found at a lower threshold (uncorrected for multiple comparisons, p<0.001, T=4, cluster size>30 voxels) were similar to the hand alone condition.1 Left vs. Right Coordination vs. Independent control yielded a locus with peak activation in the contralateral superior temporal gyrus at coordinates [-40, -28, 4] (see Fig. 3B) and Right vs. Left Coordination vs. Independent control yielded an activation cluster in the cuneus [0, -78, 8] and two near the contralateral lingual gyrus (peak coordinates [18, -70, 0] and [20, -52, -2]; see Fig. 3C). Right-handers (Lavrysen et al., 2008) had more activation when using the left hand in frontal regions, central sulcus, post-central gyrus and cerebellum. Comparably, left-handers showed a trend of less additional activation for eye-hand coordination versus independent control that was confirmed in the hand alone condition.

Asymmetries in goal-directed eye–hand movements in left-handers only

The next step was to evaluate the activation differences between using the left or the right hand in goal-directed combined eye and hand movements. Again, if these differences would be the same in left- as in right-handers, the asymmetries would probably not be attributable to hand preference effects but rather to functional hemispheric specialization. Firstly, the contralateral and ipsilateral activation for left-handers using the left versus right hand was evaluated using pairwise comparisons (t-tests, uncorrected for multiple comparisons), in the same manner as the previously reported analysis in right-handers (see Figs. 7A and B in Lavrysen et al., 2008). Contrasting left (flipped) versus right eye-hand coordination (Left Coordination vs. Rest>Right Coordination vs. Rest) yielded activation in two frontal regions: the contralateral precentral gyrus and the insula (see Table 1 and Fig. 4). The first locus corresponds to the dorsolateral premotor cortex and the second to the insula, often activated in metronome-paced tasks. Contrasting the right versus left (flipped) movement conditions (Right Coordination vs. Rest>Left Coordination vs. Rest) yielded

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1 As remarked by an anonymous reviewer, the t-tests comparing Left and Right Coordination versus independent conditions were not significant at the FDR level. Following his suggestions, t-tests were performed comparing left and right in the hand alone conditions. The analysis for left vs right yielded significant activation in superior temporal gyrus, visual cortex and insula. The opposite analysis (right>left) did not yield significant results. Thus, although the analysis for coordination versus independent conditions failed to reach the FDR threshold in the coordination versus independent conditions, this trend was affirmed by the hand alone data. More detailed results of this analysis can be obtained through the authors.
specific parietal activation, in particular an area covering the ipsilateral postcentral and intraparietal sulci.

**Asymmetries in goal-directed eye–hand movements in left- and right-handers**

As shown in the kinematics and the imaging data of left-handers only, there was little evidence that the asymmetry effects differed substantially between left and right-handers. Moreover, the two groups showed quite comparable results in terms of asymmetric control of both hands. Additional control analyses confirmed that there were no significant differences between all other pairwise comparisons involving left and right hand movements nor between preferred and non-preferred hands of left- and right-handers. Therefore, eye–hand coordination conditions of left- and right-handers were pooled in order to investigate hand effects independent of handedness. Before evaluating statistical differences between left and right-sided movements in left- and right-handers, a conjunction analysis was performed on the four conditions (left flipped and right coordination for left- and right-handers) to evaluate the overall activation pattern for eye–hand coordinated movements. The activated loci were predominantly located in sensory and motor regions, including cerebellum, motor, premotor and supplementary motor areas, thalamus and occipital and parietal cortices (see Table 2).

Firstly, the comparison of right versus left hand movements for both hand preference groups pooled failed to reach significance (FDR, p < 0.05). However, the contrast left versus right hand pooled across both hand preference groups did yield specific loci of activation (see Fig. 5 and Table 3). There was more activation in the contralateral precentral sulcus, superior precentral gyrus, middle frontal gyrus, insula and the ipsilateral caudate nucleus when the left than when the right hand moved. The precentral activations correspond functionally to ventral (PMv) and dorsal premotor cortex (PMd) and the middle frontal activation to dorsolateral prefrontal cortex (DLPFC). As is obvious from the contrast estimates (left panel of Fig. 5), the activation was higher in both left- and right-handers when using the left hand than the right hand. This is true for all loci, except for the middle frontal gyrus (bottom) where the left-right effect is only present for right-handers.

**Discussion**

The aim of this study was to examine the neural correlates that underlie coordinated goal-directed eye and hand movements with regard to manual asymmetries. Participants made 40° wrist flexion–extension movements without visual feedback in an MR scanner. If the left-handers’ activation pattern (fMRI) would be opposite to that of the right-handers, the activation was assumed to be due to differences between the hands as a result of lifelong practice. Conversely, if the underlying brain activation would be similar for left- and right-handers, the observed effects would provide evidence for functional hemispheric specialization that is independent of hand preference.

**Behavioral performance**

In this study, we tried to maximize hemispheric specialization by selecting extremely lateralized left- and right-handers and by verifying that performance of both hands was behaviorally equivalent. We ensured that participants reached similar movement times and amplitudes when using either the right or the left hand by providing them with sufficient training before the scan session and by using a

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### Table 1

Regions which are significantly more activated during eye–hand coordinated aiming with the right than with the left hand, and vice versa, resulting from the group analysis of left-handers only (n = 12).

<table>
<thead>
<tr>
<th>Hemisphere area</th>
<th>MNI coordinates</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>LEH &gt; REH</em></td>
<td>Precentral gyrus</td>
<td>−48</td>
<td>2</td>
<td>22</td>
<td>4.68</td>
</tr>
<tr>
<td></td>
<td>Insula</td>
<td>−34</td>
<td>−24</td>
<td>18</td>
<td>4.50</td>
</tr>
<tr>
<td><em>REH &gt; LEH</em></td>
<td>Postcentral sulcus</td>
<td>44</td>
<td>−38</td>
<td>60</td>
<td>4.68</td>
</tr>
<tr>
<td></td>
<td>Intraparietal sulcus</td>
<td>28</td>
<td>−40</td>
<td>50</td>
<td>4.47</td>
</tr>
</tbody>
</table>

Uncorrected, Extent Threshold = 4, cluster size > 30 voxels. Z scores correspond to voxels of peak activity in locations provided by stereotactic coordinates (MNI template). The activations are described as contra- or ipsilateral to the hand movement.

### Table 2

Regions which are significantly more activated during right and left goal-directed eye and hand movements, resulting from the conjunction analysis of left- and right-handers (n = 24).

<table>
<thead>
<tr>
<th>Hemisphere area</th>
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<th>x</th>
<th>y</th>
<th>Z</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Cerebellum</em></td>
<td>Vermis VI</td>
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<td>−14</td>
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<tr>
<td></td>
<td>Vermis VI</td>
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<td>6.67</td>
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<td></td>
<td>Vermis VII (cruz II)</td>
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<td>−30</td>
<td>6.54</td>
</tr>
<tr>
<td></td>
<td>Vermis VIII</td>
<td>0</td>
<td>−64</td>
<td>−42</td>
<td>5.31</td>
</tr>
<tr>
<td><em>Ipsi</em></td>
<td>Hemisphere IV-V (VI)</td>
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<td>−56</td>
<td>−16</td>
<td>6.19</td>
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<tr>
<td></td>
<td>Hemisphere VI (cruz I)</td>
<td>−30</td>
<td>−58</td>
<td>−32</td>
<td>4.35</td>
</tr>
<tr>
<td></td>
<td>Hemisphere VIII</td>
<td>22</td>
<td>−62</td>
<td>−50</td>
<td>4.04</td>
</tr>
<tr>
<td></td>
<td>Hemisphere VIII</td>
<td>18</td>
<td>−64</td>
<td>−50</td>
<td>4.09</td>
</tr>
<tr>
<td><em>Frontal cortex</em></td>
<td>Central sulcus</td>
<td>−26</td>
<td>−26</td>
<td>70</td>
<td>4.64</td>
</tr>
<tr>
<td></td>
<td>Precentral gyrus</td>
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<td>−20</td>
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<td></td>
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<tr>
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<td>−26</td>
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<td></td>
<td>Superior frontal gyrus</td>
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<td><em>Parietal cortex</em></td>
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FDR. 05 Extent Threshold = 4, cluster size > 30 voxels. Z scores correspond to voxels of peak activity in locations provided by stereotactic coordinates (MNI template). The activations are described as contra- or ipsilateral to the hand movement.
Fig. 5. Group statistical parametric maps (SPMs) for the contrast of left (flipped) versus right-sided movements resulting from the group analyses of left-handers and right-handers (n = 24). The activations (FDR, p < 0.05; T = 4) are overlaid on a representative normalized brain. The left side of the images correspond to the contralateral side of the brain. From top to bottom in the figure: contralateral dorsal premotor (PMd), ventral premotor (PMv), insula, dorsolateral prefrontal (DLPFC), and ipsilateral caudate nucleus. Contrast estimates are plotted for each of these regions (effect size and error bars in %).
metronome. As established with right-handers (see Starkes et al., 2002 for a review), the left-handers also showed a right coupling between eye and hand movements, with the eyes arriving at the target in advance of the hand movement. The hand left the target first, typical for this type of cyclical movements.

Interestingly, the left-handers’ right hand reached peak velocity later than the left hand (cfr right-handers in Lavrysen et al., 2007, 2008; Mieschke et al., 2001; Roy et al., 1994). Most likely, this is compatible with the concept that the right hand/left hemisphere is more efficient (faster) in utilizing response-produced feedback (Elliott et al., 1999), even in the absence of visual information (see also Buekers and Helsen, 2006). In contrast to right-handers, left-handers in the present study did neither alter their saccade initiation nor completion according to the hand being used. Perhaps the non-preferred left hand of right-handers is in need of augmented planning and monitoring, in particular because it also holds a priori a disadvantage in visuomotor processing speed. On the other hand, the extensive use of the left-handers’ preferred hand has brought performance up to the level of the more competent right body side (see Lavrysen et al., 2003 for an example of performance leveling of initiation time after a left-hand advantage). With both left- and right-handers showing the same asymmetries in behavioral performance, the imaging data should be considered to better understand the underlying mechanisms.

Network for eye–hand coordination

For the imaging data, the conjunction analysis combining all conditions revealed a typical network involved in the planning and execution of goal-directed movements (Battaglia-Mayer et al., 2006; Lavrysen et al., 2008; Winston et al., 1997). The cortical activation was mainly unilateral both in left- and right-handers, thus enabling the comparison of functional specialization differences between both hemispheres. This predominantly lateralized activation pattern is seemingly in contrast with previous studies where left-handers showed reduced lateralization (Dassonville et al., 1997; Kim et al., 1993; Willems and Hagoort, 2009). Though, it should be noted that the complexity of finger sequencing in previous work may have caused substantial ipsilateral involvement of motor regions (Verstynen et al., 2005; Winston et al., 1997). As we used a simpler task, this task complexity factor reflecting effector-independent hemispheric dominance did not confound our present results.

Comparing coordinated versus independent eye and hand movements in left-handers revealed activation in the cerebellum, thalamus and around the central sulcus. The activation in the thalamus corresponds with the ventrolateral nucleus, which is a connection structure between the cerebellum and motor cortex. Expectedly, these regions are the same as found in right-handers (Lavrysen et al., 2008), reflecting enhanced sensory processing and coordination when making combined compared to isolated eye and hand movements.

Left-handers also show asymmetrical activation

As the main focus of this work was the asymmetrical functional organization, the key analyses involved comparisons between left- and right-sided movements. The first analyses in left-handers only compared the left versus the right hand for coordinated vs. independent eye–hand movements (Fig. 3). Left eye–hand coordination vs independent movements resulted in a trend towards more activation in the superior temporal gyrus, whereas Right Coordination vs. independent control induced more activation in visual areas. Although not significant (FDR 0.05) for the coordinated task, the results for right vs. left were similar to right-handers (Lavrysen et al., 2008) and were consistent with the hand alone data. However, Left Coordination elicited less surplus activation. Again, the practice advantage of the preferred hand might play a role here.

The second asymmetry analysis involving left-handers was done on the eye–hand coordination vs. rest data. Right-hand movements more strongly engaged the ipsilateral postcentral and intraparietal sulci. These anatomical regions are part of a distributed motor network that is typically involved in visual processing and visuomotor coordination. More specifically, the superior parietal region contributes to the integration of somatosensory and visual information to monitor limb position in egocentric space (Wenderoth et al., 2006) and in directing eye movements, reaching and visual attention (Culham et al., 2006). This suggests that left-handers required higher sensorimotor processing demands when using the non-preferred hand. Surprisingly, the left-handers’ (dominant) left hand movements were accompanied by more activation in the contralateral precentral gyrus (PMv) and insula. The PMv activation may reflect increased sensory monitoring while activation at the insular cortex might reflect timekeeper operations (Karabanov et al., 2009; Rao et al., 1997) and attention control typically observed in metronome-paced tasks (Heuninckx et al., 2005). So despite the fact that they were moving with the preferred hand, additional activation was found in the contralateral hemisphere, suggesting a subordinate role of the left hand/right hemisphere in eye–hand coordination.

In our previous study (Lavrysen et al., 2008), the apparent disparity of the two hemispheres in right-handers may have resulted from the eyes arriving later at the target when using the left hand, allowing longer and more intense visual processing in the deceleration phase. In the present study, left-handers ended their saccade when the hand had travelled about 50% of its time, without hand differences. Moreover, the observed loci did not correspond to functional asymmetries purely due to the saccadic control (Petit et al., 2009). This reinforces the idea that the observed neural effects are related to subtle differences in more general perceptuomotor processing abilities between both hemispheres rather than oculomotor control independent of hand preference.

Asymmetries in brain activation independent of hand preference

Finally, the data of left- and right-handers were combined in a full factorial analysis to study asymmetries independent of hand preference. First of all, the comparison between preferred and non-preferred hands did not yield significant effects. This confirms that the observed differences were not related to lifelong practice advantages, at least not for a simple repetitive eye–hand coordination task. Also, there was no additional activation when contrasting right- versus left-sided movements (Right > Left Coordination). Again, this plausibly points toward the ease of the right hand/left brain system in performing the visuomotor task in comparison to the left hand/right brain. The inverted comparison (left more than right independent of hand preference) did reveal distinct loci of activation.

When using the left hand, there was more activation in the basal ganglia (more specifically in the head of the caudate nucleus) and near the junction of the precentral and superior frontal sulci (FFC, Gerardin et al., 2003). As the caudate receives projections from the
Conclusions

Above presented activation asymmetry provides support for more independent of hand preference and surpass the lifelong practice advantage. The brain/right hand system in fast motor processing appears to be independent of dominant hand preference. This research equipment and the search Council for their support of this research project (OT/00/40). The imaging results revealed more elaborate perceptuomotor processing. More importantly, differences emerged when using the left compared with the right hand and/or the need for inhibition of the dominant side is greater for right- than for left-handers (see Fig. 5). In any case, the above presented activation asymmetry provides support for more intense planning and monitoring of left-hand movements by the right hemisphere independent of hand preference.

References


