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Research Report

Hand preference influences neural correlates of action observationRoel M. Willems^{a,*}, Peter Hagoort^{a,b}^aDonders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands^bMax Planck Institute for Psycholinguistics, Wundtlaan 1, 6525 XD Nijmegen, The Netherlands

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ABSTRACT

It has been argued that we map observed actions onto our own motor system. Here we added to this issue by investigating whether hand preference influences the neural correlates of action observation of simple, essentially meaningless hand actions. Such an influence would argue for an intricate neural coupling between action production and action observation, which goes beyond effects of motor repertoire or explicit motor training, as has been suggested before. Indeed, parts of the human motor system exhibited a close coupling between action production and action observation. Ventral premotor and inferior and superior parietal cortices showed differential activation for left- and right-handers that was similar during action production as well as during action observation. This suggests that mapping observed actions onto the observer's own motor system is a core feature of action observation — at least for actions that do not have a clear goal or meaning. Basic differences in the way we act upon the world are not only reflected in neural correlates of action production, but can also influence the brain basis of action observation.

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1. Introduction

Most individuals have a strong preference to use either the left or the right hand as dominant hand when performing common activities. This distinguishing feature among individuals is at least partially genetically determined, settles early in development and is observed across cultures (see e.g. Annett, 2002; McManus, 2002). Hand preference has been found to differentially influence the cortical motor production system of left- and right-handers (e.g. Kim et al., 1993; Kloppel et al., 2007). Here we investigated whether analogously, hand preference influences neural correlates of action observation.

Research shows that action production and action observation are closely linked at the neural level, most notably in

the form of mirror neurons in monkey area F5 in ventral premotor cortex and area PF in inferior parietal cortex (see Rizzolatti et al., 2001; Rizzolatti and Craighero, 2004 for review). Also in humans it was shown that the ventral part of the premotor cortex and the inferior part of the parietal cortex become active during action observation (for review see Rizzolatti et al., 2001; Rizzolatti and Craighero, 2004; Binkofski and Buccino, 2006; Iacoboni and Dapretto, 2006).

Compelling evidence for a close link between action production and action observation would be if differences between individuals in terms of motor production lead to different neural correlates during action observation. That is, neural correlates of action observation may be modulated by the motor production 'specifics' of the observer. There is some recent evidence from comparing motor experts to

* Corresponding author. Fax: +31 24 3610989.

E-mail address: roel.willems@donders.ru.nl (R.M. Willems).

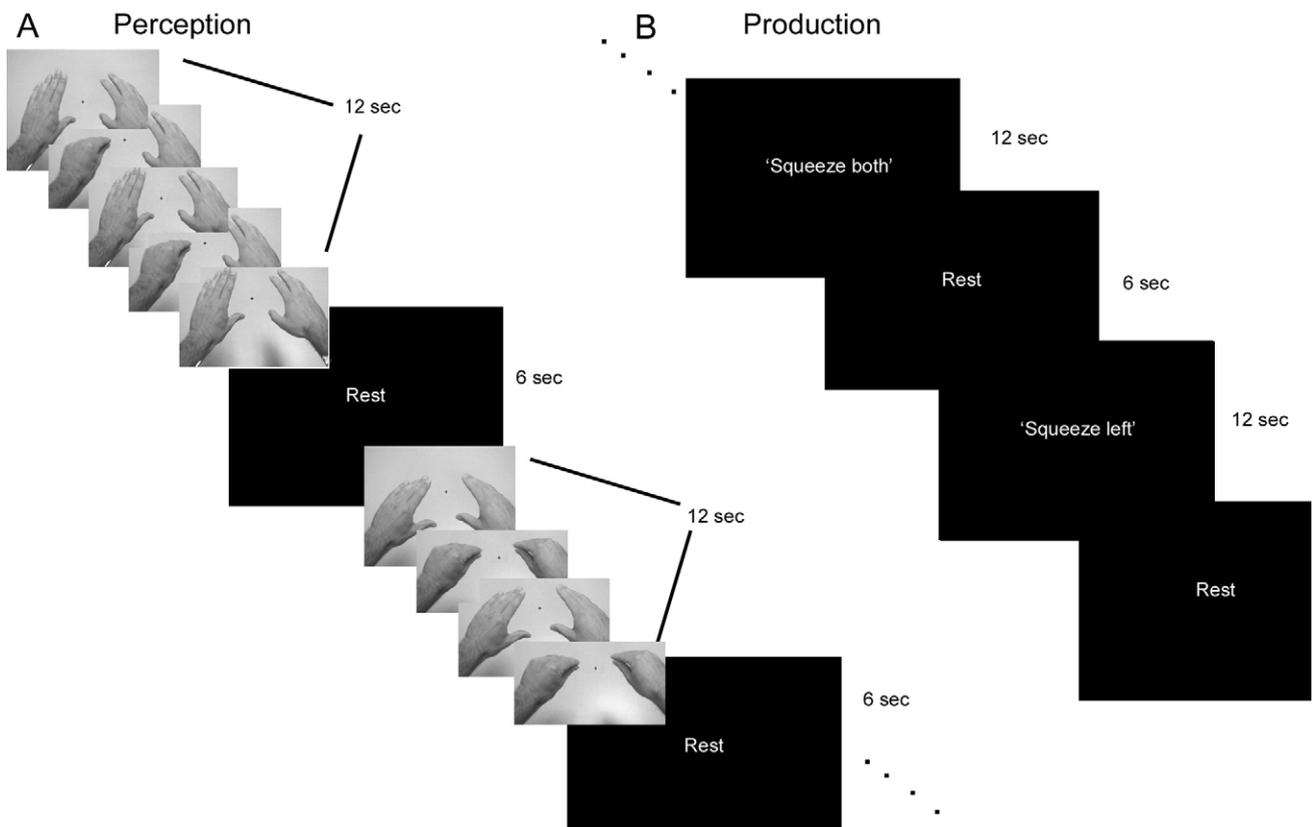


Fig. 1 – The experimental design. (A) Participants first observed movie clips intermingled with rest blocks. In the movie clips, the left, the right, or both hands could perform an action. Both hands were however always visible. For example, in the first condition depicted in the figure, only the left hand performed an action, whereas the right hand remained still. In the second example block, both hands performed an action. Note that the original movies were presented in color. **(B)** Second, during the production blocks participants were informed by a written instruction to execute the actions that they had seen in the perception blocks.

non-experts which suggests that this is indeed the case. Neural networks activated in response to observation of dance movements were for instance different for expert as

compared to non-expert dancers (Calvo-Merino et al., 2005; see also Calvo-Merino et al., 2006; Cross et al., 2006; Reithler et al., 2007).

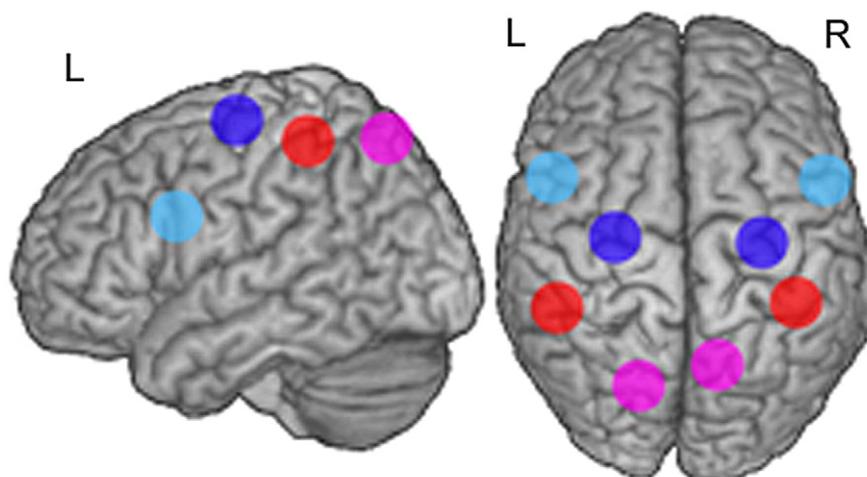


Fig. 2 – Locations of the regions of interest in dorsal (dark blue) and ventral (light blue) premotor cortex and in inferior (red) and superior (pink) parietal cortex. Regions of interest were defined on the basis of morphological and functional data (dorsal premotor cortex, [x y z] [–26 –14 62; 30 –17 64] (Amiez et al., 2006), cytoarchitectonics (ventral premotor cortex, [–50 9 24; 54 8 23] (Amunts et al., 1999)), and previous functional findings of an influence of motor expertise on inferior ((Calvo-Merino et al., 2006) [–48 –42 54; 42 –39 57]) and superior ((Reithler et al., 2007), [–17 –71 53; 13 –63 54]) parietal cortex. All regions were spheres with an 8 mm radius and all coordinates are in MNI space.

The theoretical basis for this line of research is that action understanding is neurally implemented through motor simulation¹. That is, we understand another person's action by implicitly simulating that action with our own motor system (Jeannerod, 2001; Rizzolatti et al., 2001; Rizzolatti and Craighero, 2004; Goldman, 2006; Iacoboni and Dapretto, 2006). The rationale of the 'experts' studies cited above is that if action understanding indeed evokes motor simulation, the specific way in which our motor system is shaped, for instance through training, should lead to activation of the motor system during action observation in a different way than in individuals who did not have such motor training.

Here we aim to extend these findings by asking whether hand preference influences the observation of simple hand movements. We used a more implicit type of 'motor expertise', namely being left- or right-handed, to test whether observed actions are mapped onto the observer's motor system in a subject-specific manner.

Using functional Magnetic Resonance Imaging (fMRI), we compared activation in parts of the motor system in left- and right-handed individuals when they performed or observed simple finger extensions and contractions (Fig. 1). If handedness has an effect upon action observation we expect that areas that show distinctive activation patterns between the two groups during action production, will show a similar pattern during observation of the same actions. This would mean that a long-term feature of motor production has an effect upon action observation and that effects of motor production on action observation go beyond motor repertoire or motor expertise. Contractions and extensions of the fingers are actions clearly within the motor repertoire of all participants. Nor did left- or right-handers have a greater expertise in performing the simple hand movements. That is, although left-handers have more 'expertise' in using the left hand, it is not the case that the participant groups were specifically trained on the movements that they observed, as was the case in previous studies (Calvo-Merino et al., 2005, 2006; Cross et al., 2006; Reithler et al., 2007).

A recent fMRI study with a comparable design as ours indicates that left- and right-handers differ in the degree of lateralization and involvement of the mirror neuron system during action production and action observation (Rocca et al., 2008). During execution, left-handers showed a more bilateral pattern of activation in areas of the motor system including

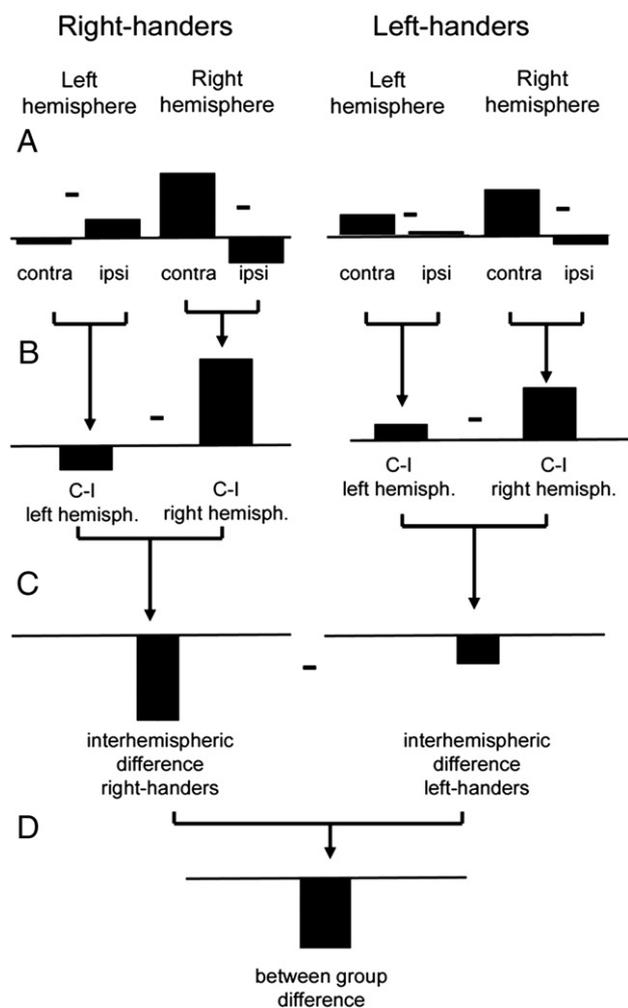


Fig. 3 – Illustration of region of interest analysis steps. This figure serves as an illustration; a full representation of the data is given in Figs. 4–6. The figure graphically represents the analysis steps taken to test the between-group difference on one of the two interhemispheric difference scores. For this example, the difference score computed was contralateral minus ipsilateral hand production and the data are taken from the ROIs in the inferior parietal cortex. A minus sign (-) indicates that the data from two bars were subtracted to form the next level of analysis. In (A) we see activation levels in left and right inferior parietal cortex for right- and left-handed participants in reaction to production of actions with the contralateral hand or with the ipsilateral hand (x-axis). In (B) we see the difference score contralateral hand minus ipsilateral hand (C-I) for each hemisphere and group separately. Previous literature has shown that left- and right-handers differ in terms of lateralization of this difference score during action production. This is clearly visible in (C) which represents the left hemisphere minus right hemisphere difference for both groups separately. In right-handers the interhemispheric difference is bigger as compared to left-handers. In panel D we see the between group difference. Statistical analysis showed this difference to be significant (see text and Fig. 6C, right panel).

¹ We use the term 'simulation' as proposed by Goldman (2006): "Generic simulation (initial): Process P is a simulation of another process P'. P duplicates, replicates, or resembles P' in some significant respects (significant relative to the purpose of the task)." (p. 36). Hence, simulation implies that similar effects are observed during action production as during action observation. This is also in line with the proposal by Jeannerod (2001): "The simulation theory to be developed in this paper postulates that covert actions are in fact actions, except for the fact that they are not executed. The theory therefore predicts a similarity, in neural terms, between the state where an action is simulated and the state of execution of that action." (Jeannerod, 2001, p. 103). See other literature for a computationally explicit definition of simulation processes (Oztop and Arbib, 2002; Oztop et al., 2006; Bonaiuto et al., 2007).

inferior frontal gyrus. During observation, left-handers showed an increased involvement of superior temporal sulcus. These activation differences were interpreted as due to an increased involvement of imitative processes during execution and observation in left-handers as compared to right-handers (Rocca et al., 2008). Importantly, the differences between the two groups were not the same during execution and observation. Here we use a more fine-grained analysis strategy than standard whole brain analysis to investigate whether neural differences between left- and right-handers are the same during action production as during action observation.

The rationale of our analysis was as follows: in several regions of the cortical motor system we computed two lateralization difference scores which have been previously shown to distinguish left- and right-handers in terms of action production (Kim et al. 1993; Kloppel et al., 2007, see below). We then used these difference scores to assess whether there were similar differences between the groups in terms of action production as well as in terms of action observation. These differences scores go unnoticed in standard whole brain analysis, since they depend upon lateralization differences between the groups. Therefore our analysis is potentially more sensitive than whole brain analysis for finding the same differences between the groups during action production and action observation.

We defined four regions of interest in the motor system. That is, in human neuroimaging studies, besides ventral premotor cortex, also a more dorsal part of the premotor cortex is found activated during action observation (e.g. Buccino et al., 2001; Calvo-Merino et al. 2005; Calvo-Merino et al., 2006; Cross et al., 2006). In the parietal lobe, besides the often observed activation of inferior parts of the parietal lobe, also a more superior part has been found to be implicated in motor learning and motor simulation (Reithler et al., 2007). The activation of these areas in response to action observation has been found to be influenced by effects of motor expertise (Calvo-Merino et al., 2005, 2006; Cross et al., 2006; Reithler et al., 2007). Neither area is described as part of the mirror motor system in the monkey, however (Rizzolatti and Craighero, 2004; Rizzolatti et al., 2001), and their role in the human action observation system is unclear. Therefore, we investigated the 'classical' motor areas with mirror-like properties, ventral premotor and anterior inferior parietal cortex, as well as responses in dorsal premotor and superior parietal cortex (Fig. 2).

2. Results

2.1. Regions of interest analysis

The rationale of our analysis was as follows: in several regions of interest we computed two difference scores which have been previously shown to distinguish left- and right-handers in terms of action production. First, we assessed whether we could replicate these previous findings. Second, we assessed whether differences between the groups in terms of action production, were also present during observation of these actions. The analysis steps are illustrated in Fig. 3 (see Materials and Methods for a full description).

The first difference score is bimanual minus unimanual contralateral hand production and is based upon the finding that left- and right-handers differ on this difference score during action production (Kloppel et al., 2007). Kloppel et al. found that right-handers showed a stronger activation to bimanual button presses as compared to unimanual contralateral button presses. This difference was stronger in right sensorimotor cortex as compared to left sensorimotor cortex. On the contrary, left-handers showed no differential activation levels in both hemispheres. Therefore, we chose to take the difference between left- and right-hemisphere in terms of difference between bimanual minus unimanual contralateral hand production as our first dependent measure to distinguish between left- and right-handers. We subsequently investigated whether a similar difference would be present during action observation.

The second difference score is contralateral minus ipsilateral hand production. Again, the choice for this measure is based upon earlier findings showing lateralization differences between left- and right-handers during finger movements (Kim et al. 1993). Kim et al. observed interhemispheric differences for contralateral and ipsilateral hand production in right-handers, but not in left-handers. We chose to take the difference between left- and right-hemispheres in terms of difference between contralateral minus ipsilateral hand production as our second dependent measure to distinguish between left- and right-handers. Again, we subsequently tested whether the same difference was present during perception.

We graphically present the results of the ROI analysis in three figures which represent the same data, but presented in a different manner. Fig. 4 shows the mean parameter estimates (relative to implicit baseline) for every condition in every region of interest. Although instructive, these estimates do not clearly show the interhemispheric differences known to distinguish between left- and right-handed participants. For this we computed two difference scores, which are graphically presented in Fig. 5. The figure depicts the difference scores for every region of interest in every hemisphere. Previous studies indicate that left- and right-handers differ in the amount of interhemispheric differences between these difference score (Kim et al., 1993; Kloppel et al., 2007). This can be inferred from the figure, but is illustrated more clearly in Fig. 6. Here we see the difference between the left and the right hemispheric ROIs with respect to the two difference scores. A between-group difference is indicated with an asterisk. Figs. 4 and 5 are included for those interested in the specific direction of effects in all conditions. For illustration of the main purpose of this paper (potential overlap between motor production preference and neural correlates of action production and perception) the reader is referred to Fig. 6.

2.2. Bimanual minus unimanual contralateral difference score

An omnibus repeated measures analysis of variance (ANOVA) was employed on this difference score, with factors Group (left-handed, right-handed), ROI (dorsal premotor, ventral

premotor, inferior parietal, superior parietal) and Modality (perception, production).

As expected, the omnibus ANOVA revealed a main effect of Group ($F(1,30)=12.22$, $MSe=0.112$, $p=0.001$). Moreover, there was a main effect of ROI ($F(3,90)=2.81$, $MSe=0.019$, $p=0.044$) and a ROI \times Group interaction ($F(3,90)=3.02$, $MSe=0.019$, $p=0.034$) (Table 1A), indicating that the interhemispheric difference scores led to differences between the groups in some ROIs, but not in others. To assess the difference between ROIs in more detail, the data were tested in each ROI separately (left column of Table 2) in an ANOVA with factors Modality (perception, production) and Group (left-handed, right-handed).

There was a marginally significant main effect of Modality in dorsal premotor cortex ($F(1,30)=3.26$, $MSe=0.015$, $p=0.081$), but no main effect of Group ($F(1,30)=2.34$, $MSe=0.024$, $p=0.137$), or a Group \times Modality interaction ($F(1,30)=2.21$, $MSe=0.015$, $p=0.148$). This indicates that production and perception yielded different types of effects in this region. Indeed, planned comparisons showed that there was a larger degree of lateralization in right-handers compared to left-handers during production ($t(30)=1.99$, $p=0.054$). No difference was observed during perception ($t(30)<1$) (Fig. 6A, left panel; Table 2).

In ventral premotor cortex, there was a main effect of Group ($F(1,30)=13.85$, $MSe=0.040$, $p=0.001$), but no main effect of Modality ($F<1$) or Group \times Modality interaction ($F<1$), indicating that left- and right-handers differed on this difference score, but in a similar way for perception and production. Indeed, planned comparisons showed that the difference between groups was similar for production ($t(30)=2.41$, $p=0.022$) and for perception ($t(30)=3.35$, $p=0.002$) (Fig. 6B, left panel; Table 2).

Also in inferior parietal cortex, there was a main effect of Group ($F(1,30)=6.98$, $MSe=0.074$, $p=0.013$), but no main effect of Modality ($F<1$) or Modality \times Group interaction ($F<1$). Again, this means that the groups differ in their activation pattern in this region, but not in a way that was specific for production or perception. Planned comparisons showed that the difference between groups during production was not statistically reliable, however ($t(30)=1.38$, $p=0.175$). However, in perception, the difference between the groups was significant ($t(30)=2.61$, $p=0.014$) (Fig. 6C, left panel; Table 2). In this region, in this comparison, the groups could thus only be distinguished in terms of perception, but not in terms of production.

The pattern of responses in superior parietal cortex was qualitatively similar to that in inferior parietal cortex. There was a main effect of Group ($F(1,30)=13.99$, $MSe=0.029$, $p=0.001$) and no main effect of Modality ($F<1$) or Modality \times Group interaction ($F<1$). Planned comparisons showed the groups, only to differ along this dimension during perception, but not during production (production: $t(30)=1.72$, $p=0.096$; perception: $t(30)=3.33$, $p=0.002$) (Fig. 6D, left panel; Table 2).

To summarize the results from this first difference score, we point out that just like previous literature, we also found a difference between left- and right-handers with respect to interhemispheric differences when comparing bimanual to unimanual contralateral hand movements (Kloppel et al., 2007). Importantly, a similar difference was observed in several regions of the motor system during action observation.

2.3. Contralateral minus ipsilateral difference score

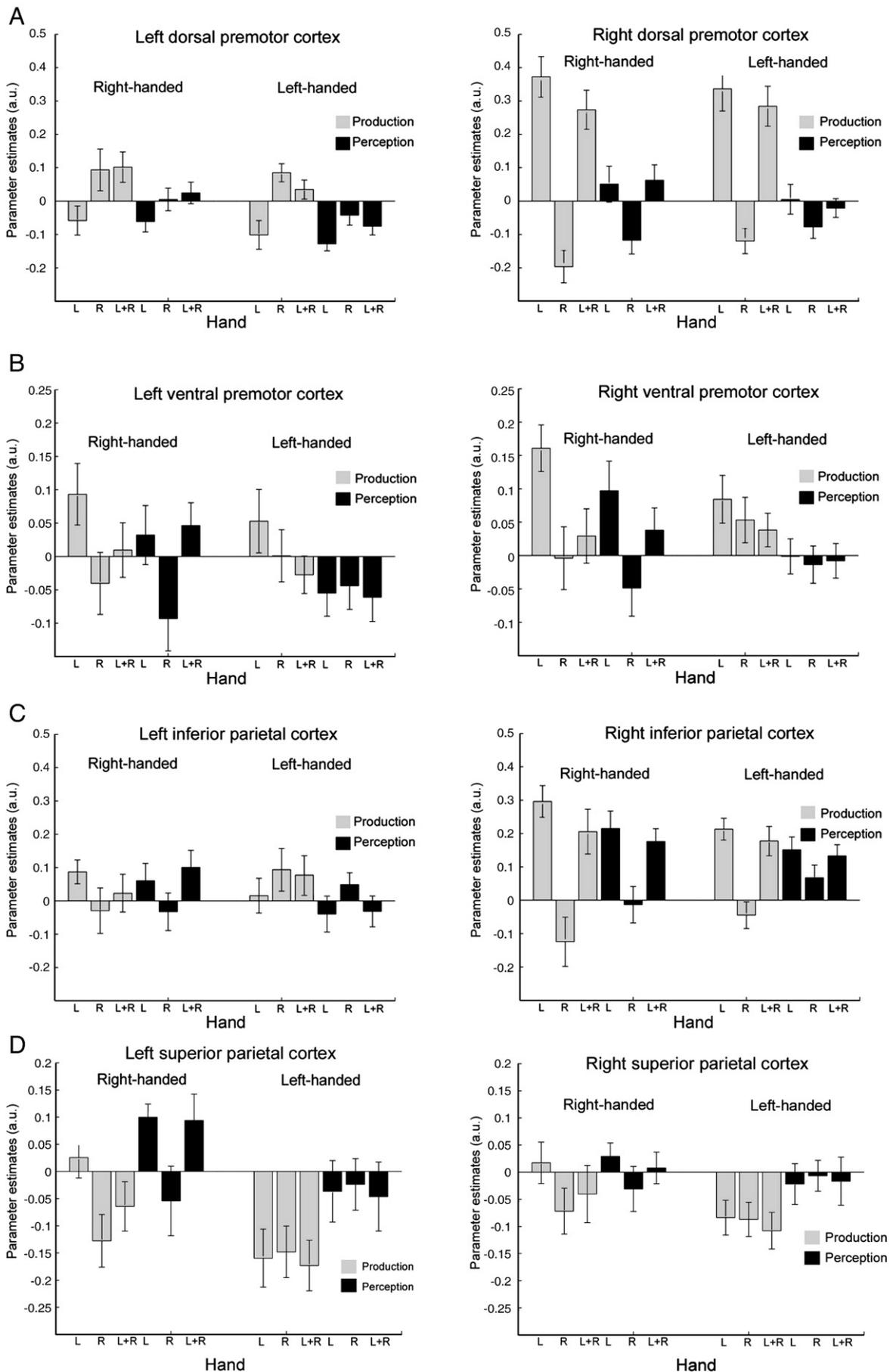
Again, first an omnibus ANOVA with factors Group (left-handed, right-handed), ROI (dorsal premotor, ventral premotor, inferior parietal, superior parietal) and Modality (perception, production) was employed.

The omnibus ANOVA revealed main effects of Group ($F(1,30)=8.56$, $MSe=0.427$, $p=0.006$) and ROI ($F(3,90)=5.11$, $MSe=0.051$, $p=0.003$), as well as a Modality \times ROI interaction ($F(3,90)=7.04$, $MSe=0.044$, $p=0.001$) and a marginally significant ROI \times Group interaction ($F(3,90)=2.42$, $MSe=0.051$, $p=0.071$) (Table 1B). These findings indicate that left- and right-handers differ in terms of this difference score. Moreover, different ROIs exhibit different effects and the similarity between production and perception is different between ROIs. To assess this overlap between perception and production in the different ROIs in more detail, the data were tested in each ROI separately (right column of Table 2) in an ANOVA with factors Modality (perception, production) and Group (left-handed, right-handed).

There was a main effect of Modality in dorsal premotor cortex ($F(1,30)=16.81$, $MSe=0.083$, $p<0.001$), but no main effect of Group ($F(1,30)=1.95$, $MSe=0.130$, $p=0.17$) or Modality \times Group interaction ($F<1$). This indicates that perception and production yielded different effects in this region, but that this difference score in this region did not distinguish between left- and right-handers. Indeed, planned comparisons showed that although the difference between the hemispheres appears to be bigger in right-handed participants as compared to left-handed participants in dorsal premotor cortex, it was not reliably so ($t(30)=-1.26$, $p=0.219$). No differences were observed during perception ($t(30)<1$) (Fig. 6A, right panel; Table 2).

However, in ventral premotor cortex, again, there was a main effect of Group ($F(1,30)=8.29$, $MSe=0.113$, $p=0.007$) and no main effect of Modality ($F<1$) or a Modality \times Group interaction ($F<1$). This suggests that the groups can be distinguished in terms of this interhemispheric difference score in a similar manner for production and perception. Planned comparisons indeed showed that the difference between right-handed and left-handed participants, which was marginally present in production ($t(30)=-1.79$, $p=0.082$),

Fig. 4 – Mean parameter estimates in regions of interest. Bars represent mean parameter estimates (relative to implicit baseline) for all conditions in both groups. Note that no obvious differences between left- and right-handers can be inferred from these raw parameter estimates. They are included for illustration purposes. In grey are production conditions, in black are perception conditions. On the x-axis are the conditions: left hand (L), right hand (R) or both hands (L+R). The difference scores that do distinguish between the groups are graphically represented in Figs. 5 and 6. Error bars indicate standard error (s.e.m.). Parameter estimates represent the beta weights (scaled to grand mean) in arbitrary units (a.u.).



was also present during perception ($t(30)=-2.60$, $p=0.014$) (Fig. 6B, right panel; Table 2).

In inferior parietal cortex there was a main effect of Group ($F(1,30)=7.57$, $MSe=0.247$, $p=0.010$) as well as Modality ($F(1,30)=4.34$, $MSe=0.147$, $p=0.046$), but no Group \times Modality interaction ($F<1$). In other words, the groups differ from each other in this region and production and perception lead to different effects. However the lack of an interaction suggests that the difference between groups is the same for perception and production. Indeed, planned comparisons show that the stronger lateralization in the right hemisphere in right-handers as compared to left-handers was present both during production as well as during perception (production: $t(30)=-2.17$, $p=0.038$; perception: $t(30)=-2.19$, $p=0.036$) (Fig. 6C, right panel; Table 2).

Finally, in superior parietal cortex there was a main effect of Group ($F(1,30)=10.65$, $MSe=0.091$, $p=0.003$) and no main effect of Modality ($F<1$) or Modality \times Group interaction ($F<1$). This shows that the groups differ, but in a similar way in production and in perception. Indeed, planned comparisons show that the difference that (marginally) distinguished the groups during production ($t(30)=-1.92$, $p=0.064$) was also present during perception ($t(30)=-2.12$, $p=0.043$) (Fig. 6D, right panel; Table 2).

As for this second difference score, we partially replicate the previous finding of Kim et al. (1993) who showed a decreased lateralization in right-handers when comparing contra- minus ipsilateral finger movements. We replicate that left- and right-handers differ in this respect. However, in our data the contra minus ipsilateral difference score was sometimes negative, which was not observed in that previous study. Most important for the present paper, several areas in the cortical motor system exhibit a similar pattern of responses during action observation, arguing for a production-perception overlap.

To summarize, in premotor cortex, both dorsal and ventral premotor cortices show differential patterns of activation between left- and right-handed participants in terms of action production (although for dorsal premotor cortex this was only the case in one of the difference scores). However, importantly, it is only ventral premotor cortex which exhibits the same pattern of activation during perception. Put differently, ventral premotor cortex exhibits a close coupling between action production and action perception in the sense that the same difference which distinguishes left- and right-handers during action production is also observed during action perception (Fig. 6B; Table 2).

Inferior and superior parietal cortices show a similar pattern of responses. Both areas distinguish between left- and right-handed participants in terms of production as well as in terms of perception in one comparison (contralateral-ipsilateral hand). In the other comparison (bimanual-unimanual contralateral hand), activation in these areas was different between the groups only during perception, but not during action production. In other words, these areas exhibit a strong coupling between action production and action perception in one of the dependent measures that were used. In the other dependent measure, groups differed only in terms of perception (Fig. 6C and D; Table 2).

2.4. Whole brain analysis

To see whether there were other regions than the ROIs distinguishing between left- and right-handers, whole brain analysis was performed. A model with factors Group (left-handed, right-handed), Modality (perception, production) and Hands (left, right, both) was tested. We briefly describe the results below; they are visualized in Supplementary Figures 1–4 as well as in Supplementary Tables 1–3.

The main effect of Modality evoked wide-spread activations in the visual system (including primary visual cortex and the inferior temporal area previously described as extrastriate body area (EBA) (Peelen et al., 2006)), bilateral precentral gyrus and supplementary motor areas (SMA) and the cerebellum bilaterally (Supplementary Table 1). As expected the motor related areas responded much more strongly to the Production conditions, whereas the visual system responded strongly to the Perception conditions (Supplementary Fig. S1).

The main effect of Hands led to activations in a network of motor related areas: precentral gyrus and central sulcus, bilateral SMA, bilateral cerebellum, as well as in the thalamus, putamen, insula and primary visual cortex bilaterally (Supplementary Table 1). As can be seen from the parameter estimates in supplementary Fig. S2, the direction of activation was strongest to the contralateral hand action that was observed/produced, except for the cerebellum which showed strongest activation to ipsilateral hand action observation/production as has been reported previously (Aziz-Zadeh et al., 2006).

Areas differentially activated by Perception/Production of left, right or both hands (interaction between Modality \times Hands) revealed a network of areas in precentral gyrus and central sulcus, bilateral cerebellum, right SMA, right insula, bilateral primary visual cortex and right thalamus and right putamen (Supplementary Table 1).

No areas were activated to the main effect of Group or to any of the other interactions².

For the sake of completeness, we also performed several within-group comparisons, testing for differences between left- and right-hand production or perception in each group separately (e.g. Right-handers Production left>Production right). In both groups in response to action production we observed the classical pattern of motor cortex activation with stronger activation in the contralateral primary motor cortex and in ipsilateral cerebellum (Supplementary Fig. S3A, Supplementary Table 2). During perception, contralateral precentral sulcus activations were observed for right-handers, but not for left-handers (Supplementary Fig. S3B, Supplementary Table 2). The latter group instead exhibited lateralization differences in visual areas. It should be noted that at a lower statistical threshold, left-handers also showed differential lateralization of contralateral precentral sulcus during action observation.

Moreover, conjunction analyses testing for overlapping regions sensitive to production/perception of left- and right-hand actions were performed. For instance, one comparison was Perception Right>Left \cap Production Right>Left in Right-handers, looking at how differences during perception were similar as during production within each group separately.

² Also no areas were found to be activated when statistical threshold was set using False Discovery Rate (FDR) $q<0.05$.

Briefly, we found such production–perception overlap in contralateral precentral/central sulci in all comparisons except in precentral sulcus (left>right comparison) in left-handers (Supplementary Fig. S4, Supplementary Table 3). However, informal inspection at a lower statistical threshold showed such overlap to be present in this comparison as well.

3. Discussion

Our study shows that neural differences related to preferred handedness during action production are also present during observation of the same actions in several parts of the cortical motor system. This is strong evidence for an intricate neural coupling between action production and action observation. One mechanism to explain this is that the observer implicitly simulates the observed action by mapping it onto his/her own motor system (Iacoboni and Dapretto, 2006; Jeannerod, 2001; Rizzolatti and Craighero, 2004; Rizzolatti et al., 2001). This implies that differences between individuals in motor production should be reflected in differential neural activation during action production as well as during action observation. Here we provide direct evidence for such a coupling, testing for overlap between production and perception within the same study (see Turella et al., 2007). An important advance of our results is that we show that an individual's basic motor production properties are also reflected in the neural correlates of action observation.

Such effects of motor production expertise on neural correlates of action observation have been found in expert versus non-expert dancers (Calvo-Merino et al., 2005, 2006; Cross et al., 2006). Moreover, a recent study found an effect of motor training on subsequent observation of learned motor trajectories (Reithler et al., 2007). These studies suggested that action observation is crucially influenced by the motor repertoire and expertise of the observer. Here we show that motor simulation does not necessarily depend upon the motor repertoire or expertise of the observer. That is, the actions in this study were clearly within the motor repertoire of all participants. Similarly, neither left- nor right-handers had a greater expertise in performing the simple hand movements. That is, although left-handers use their left hand more often than right-handers, it is not the case that the participant groups were specifically trained on the observed movements, as was the case in previous studies (Calvo-Merino et al., 2005, 2006; Cross et al., 2006; Reithler et al., 2007). Still, a relative preference for one hand during production influences the neural correlates of action observation.

In premotor cortex, it is only ventral and not dorsal premotor cortex which shows a close coupling between action production and perception. Dorsal premotor did show differential activations in terms of action production but was not differentially influenced by handedness of the observer during action observation. Therefore, we argue that the dorsal part of the premotor cortex may be activated in response to action observation (e.g. Buccino et al., 2001; Calvo-Merino et al., 2005, 2006), but it does not exhibit a close coupling between motor production and observation since it is not shaped by the motor production specifics of the observer. The pattern of response in dorsal premotor cortex during production as well as during perception is in line with previous findings showing increased

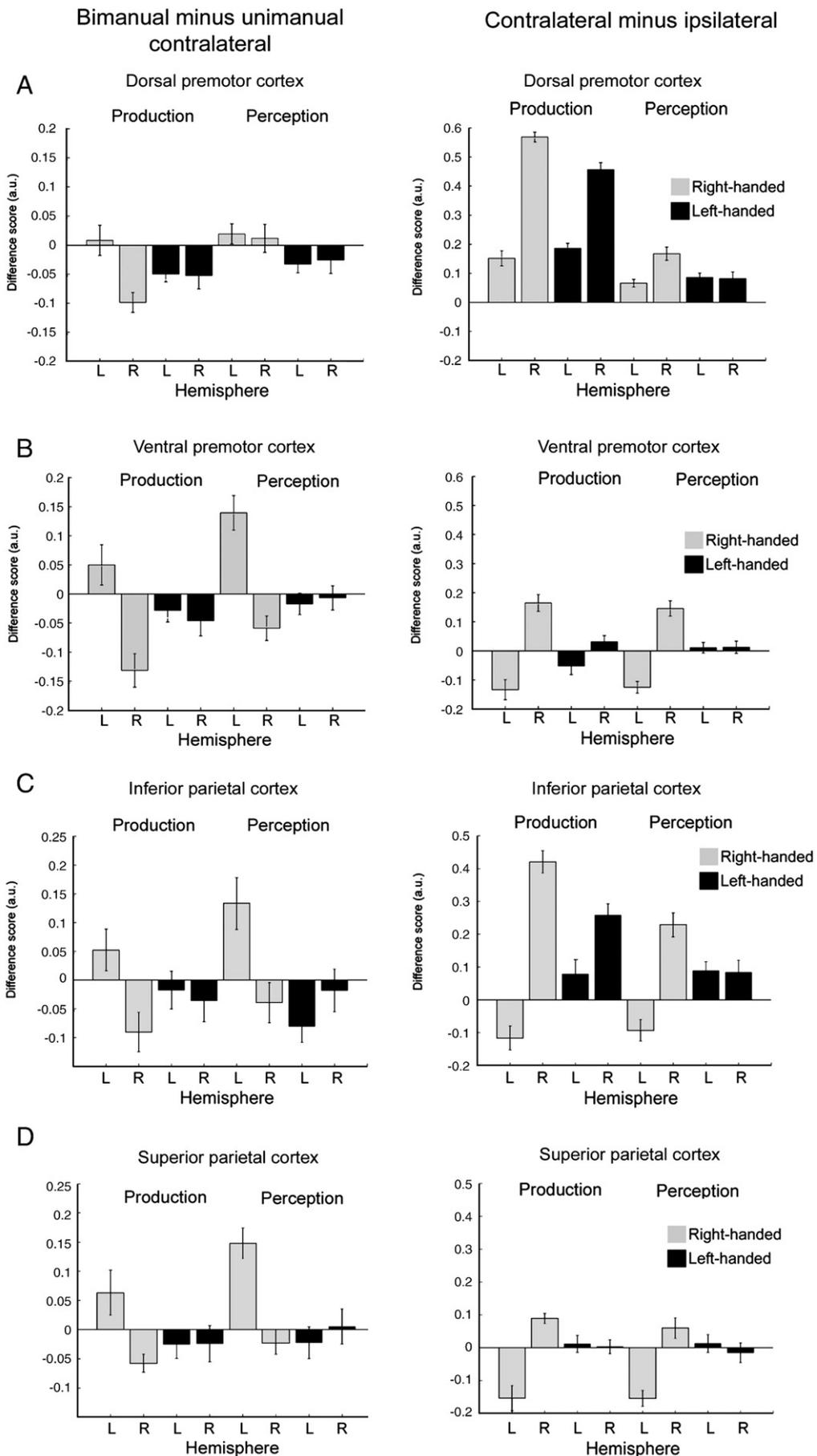
contralateral motor cortex excitability to observation of hand actions (Aziz-Zadeh et al., 2002).

In parietal cortex, both inferior as well as superior parietal cortex showed an influence of handedness during both action production and perception in one of the difference scores only. In the other difference score, a similar difference as in ventral premotor cortex was found during perception, but not during production. Inferior parietal cortex has been implicated in action observation in a large variety of studies (for review see Iacoboni and Dapretto, 2006; Rizzolatti and Craighero, 2004; Rizzolatti et al., 2001). Moreover, it has been found to be modulated by the motor repertoire of the observer (Calvo-Merino et al., 2005, 2006; Cross et al., 2006). We extend previous findings by the finding that also a more superior part of the parietal cortex shows an effect of motor production upon motor observation. This was suggested by a recent study, in which superior parietal cortex was part of the motor network activated during motor learning as well as during subsequent observation of a learned trajectory (Reithler et al., 2007). Therefore, it seems that superior parietal cortex is also part of the set of areas that exhibit motor simulation properties.

A recent study with a similar design as ours reports a more bilateral activation in inferior frontal gyrus in left-handers during action production, and more reliance on superior temporal sulcus in left-handers during action observation (Rocca et al., 2008). In the present paper we did not find a main effect of Group or a Group \times Modality interaction in the whole brain analysis, which is at odds with this previous report. We can only speculate as to why our results and the results of Rocca et al. are different in this respect. The sample size in the Rocca et al. paper was rather small and not balanced between groups ($n=8$ and $n=11$ for left- and right-handers respectively), but this cannot easily explain the difference. It should be noted that other studies have also not found strong differences in a whole brain analysis for action production between left- and right-handers. Kloppel et al. (2007) only report different activation in one area in a whole brain analysis and Solodkin and colleagues only employed region-of-interest analysis (Solodkin et al., 2001; see also Dassonville et al., 1997). It seems that perhaps whole brain analysis is not the most appropriate manner for detecting changes in terms of action production in left- and right-handers.

Our data suggest that a more fine-grained assessment of inter-hemispheric differences in specific ROIs is a more appropriate way of determining how left- and right-handers differ when producing or observing hand actions. For the action observation results, an intriguing but highly speculative suggestion for the difference between our study and the Rocca et al. paper, is that our stimuli were presented from a 'first-person' perspective, whereas the stimuli in Rocca et al. were presented in 'third-person' perspective. Differences in neural activation during action observation have been reported depending upon the perspective of the observer and the congruency between the observer's posture and the observed action (Maeda et al., 2002; Hamilton et al., 2004; Fourkas et al., 2006). Future research is needed to test this suggestion.

So far we have not touched upon the issue as to why the cortical motor systems of left- and right-handers may differ



in the way that they do. Handedness arises from a not fully understood interaction between genetic and environmental factors (see e.g. Annett, 1973; Coren and Halpern, 1991; Annett, 2002; McManus, 2002; McManus and Hartigan, 2007). It has been suggested that the fact that left-handers live in a world primarily inhabited by right-handers leads to the motor cortex differences observed. For instance Kloppel (2007; p. 279) speculate that there is no difference between bimanual and unimanual contralateral hand movement production in left-handers (whereas there is such difference in right-handers), because 'left-handers may be more used to a bimanual mode of motor control'. Rocca et al. (2008) speculate that there is more involvement of areas of the mirror neuron system in left-handers because more imitative processes are involved in action execution and observation in left-handers as compared to right-handers. Whereas such explanations seem plausible, we want to point out that data of the type presented here cannot decide between such issues as influence of environmental or genetic factors with regard to handedness. We refrain from further speculation accordingly.

We do not claim that motor production preference *always* has an influence on the neural correlates of action observation. Recent findings indicate that the action observation system is sensitive to the context an action occurs in and may code the *meaning* or *goal* of the action rather than the exact way in which the action is performed (Rijntjes et al., 1999; Bekkering et al., 2000; Gergely et al., 2002; Gazzola et al., 2007; Jonas et al., 2007; Newman-Norlund et al., 2007; Willems and Hagoort 2007; Willems et al., 2007; de Lange et al., 2008). We postulate that in the observation of actions to which it is not easy to ascribe a clear meaning or goal (as in the present study), the cortical motor system does simulate the specific basic motor properties of the observed action. This may relate to the 'broadly congruent' versus 'strictly congruent' distinction made in neurons in monkey area F5 (Gallese et al., 1996). In strictly congruent neurons the coupling between action production and observation is very specific, e.g. a neuron might fire both during execution and observation of a precision grip, but not during execution and observation of a power grip. On the contrary, broadly congruent neurons do not require that the action that they fire to in production is exactly the same during observation (Gallese et al., 1996; Rizzolatti and Craighero 2004).

4. Conclusion

The present study indicates that for simple hand actions there is a strong influence of observer's hand preference in several parts of the cortical motor system. This suggests that observed actions are mapped onto the observer's motor repertoire and

that this is an important mechanism of action observation. Basic differences in the way we act upon the world are not only reflected in neural correlates of action production, but also influence the brain basis of action observation.

5. Experimental procedures

5.1. Participants

Thirty-two healthy individuals with no known neurological impairment and normal or corrected-to-normal vision took part in the study. Handedness was assessed by means of a translated and adapted version of the Edinburgh Handedness Inventory (Oldfield, 1971). Half of the participants was left-handed ($n=16$, 9 female, mean age=25.5; mean handedness score -88.3 , range -33 to -100 ; median -100 ; modus -100), the other half was right-handed (Oldfield, 1971) ($n=16$, 10 female, mean age=21.6; mean handedness score 81.6 , range 33 to 100 ; median 85 ; modus 100). The absolute laterality quotients did not differ between the groups ($t(30)=-0.99$; $p=0.33$). None of the participants reported to have had the preference to primarily use the non-dominant hand during development or to being forced to use their non-preferred hand as dominant hand (e.g. in school). Participants were paid for participation and signed informed consent in accordance with the declaration of Helsinki.

5.2. Stimuli

The actions were repeated contractions ('squeeze'), or extensions ('stretch') of all fingers. In the perception blocks, movie clips were shown in which one of these hand actions was produced at a steady pace (17 contractions/extensions in 12 s) with both hands visible on the screen in all conditions. The left hand, the right hand, or both hands performed an action. That is, in the unimanual conditions the hand that was not moving was visible, but remained still (Fig. 1A). In the production blocks, a written instruction was given on the screen for which action to perform, e.g. 'squeeze left' or 'stretch both' (Fig. 1B).

5.3. Experimental set-up

Stimuli were presented in experimental blocks of 12 s intermingled with rest blocks (with the word 'rest' presented on the screen) of 6 s (Fig. 1). Each experimental block contained one condition and an experimental block was always followed by a rest block. First, 12 perception blocks were presented, followed by 12 production blocks. Blocks were presented in pseudo-randomized order with the constraint that no condition was presented two times in a row.

Fig. 5 – Difference scores in regions of interest. The left column represents the bimanual minus unimanual contralateral hand difference score; the right column represents the contra- minus ipsilateral hand difference score for right-handers (grey) and for left-handers (black). Each panel shows the difference score during production (left) and perception (right), for each hemisphere separately (x-axis). The similarity of activation patterns during production and perception is clearly visible in ventral premotor and inferior and superior parietal cortices (B–D), but not in dorsal premotor cortex (A). Error bars indicate standard error (s.e.m.). The difference scores are differences in beta weights (scaled to grand mean) in arbitrary units (a.u.).

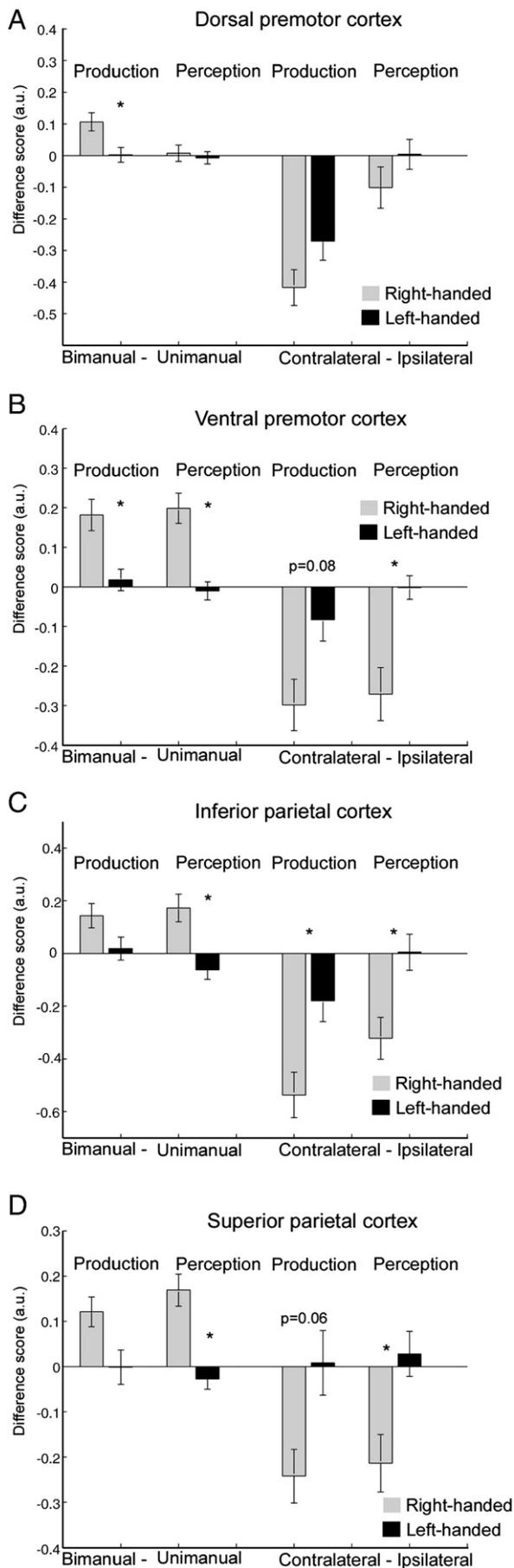


Table 1 – Results of omnibus ANOVA.

Effect	F	MSe	p
A) Bimanual minus unimanual difference score			
Modality	F(1,30) < 1	0.101	ns
Modality × Group	F(3,90) < 1	0.101	ns
ROI	F(3,90) = 2.81	0.019	0.044
ROI × Group	F(3,90) = 3.02	0.019	0.034
Modality × ROI	F(3,90) = 1.03	0.012	0.381
Modality × ROI × Group	F(3,90) = 2.49	0.012	0.065
Group	F(1,30) = 12.22	0.112	0.001
B) Contralateral minus ipsilateral difference score			
Effect	F	MSe	p
Modality	F(1,30) = 3.67	0.359	0.065
Modality × Group	F(3,90) < 1	0.359	ns
ROI	F(3,90) = 5.11	0.051	0.003
ROI × Group	F(3,90) = 2.42	0.051	0.071
Modality × ROI	F(3,90) = 7.04	0.044	0.001
Modality × ROI × Group	F(3,90) < 1	0.044	ns
Group	F(1,30) = 8.56	0.427	0.006

Two difference scores were computed for every region and every hemisphere separately: (A) Bimanual hand production/perception minus contralateral unimanual hand production/perception and (B) Contralateral hand production/perception minus ipsilateral hand production/perception. A model was tested with within-subject factors Modality (perception/production) and Region of Interest (dPM/vPM/IPL/SPL) and between-subject factor Group (left-handed/right-handed). Subsequent follow-up ANOVAs in specific regions of interest are reported in Table 2. dPM=dorsal premotor cortex; vPM=ventral premotor cortex; IPL=inferior parietal cortex; SPL=superior parietal cortex. For coordinates and selection of regions of interest see Experimental procedures section. Huynh-Feldt correction for violation of sphericity assumption (Huynh and Feldt, 1976) was applied when appropriate, but original degrees of freedom are reported. Statistically significant effects ($p < 0.05$) are indicated in bold.

After the perception blocks and before the start of the production blocks a written instruction was presented on the screen in which participants were told that they would have to produce the actions they saw before. It was indicated that the actions were named 'squeeze' and 'stretch'. This means that participants were not explicitly trained on these simple

Fig. 6 – Group differences in lateralization of the difference scores. The bars represent the interhemispheric difference (left hemisphere minus right hemisphere) of the two difference scores for each handedness group (see Fig. 3C). This is the mean of the data that went into the region of interest analysis. The bimanual minus unimanual contralateral difference score is depicted in the left panels, the contralateral minus ipsilateral difference score is depicted in the right panels. An asterisk indicates a statistically significant between-group difference at the $p < 0.05$ level (see Table 2). Between-group differences are present during production as well as perception in ventral (B), but not dorsal premotor cortex (A). In inferior (C) and superior parietal (D) regions of interest between-group differences are present during perception in both comparisons, but only during production as well as perception in the contra-ipsilateral hand comparison (right). Error bars indicate standard error (s.e.m.).

Table 2 – Results in regions of interest.

	Bimanual minus unimanual contralateral diff. score				Contralateral minus ipsilateral diff. score			
	Factor	F	MSe	p	Factor	F	MSe	p
dPM	Modality	F(1,30)=3.26	0.015	0.081	Modality	F(1,30)=16.81	0.083	<0.001
	Group	F(1,30)=2.34	0.024	0.137	Group	F(1,30)=1.95	0.130	0.173
	Cond × Group	F(1,30)=2.21	0.015	0.148				
<i>Planned comparisons (right-handed versus left-handed)</i>								
Production		t(30)=1.99		0.054	Production	t(30)=-1.26		0.219
Perception		t(30)<1		ns	Perception	t(30)<1		ns
vPM	Modality	F(1,30)<1	0.028	ns	Modality	F(1,30)<1	0.088	ns
	Group	F(1,30)=13.85	0.040	0.001	Group	F(1,30)=8.29	0.113	0.007
<i>Planned comparisons (right-handed versus left-handed)</i>								
Production		t(30)=2.41		0.022	Production	t(30)=-1.79		0.082
Perception		t(30)=3.35		0.002	Perception	t(30)=-2.60		0.014
Inf par	Modality	F(1,30)<1	0.055	ns	Modality	F(1,30)=4.34	0.147	0.046
	Group	F(1,30)=6.98	0.074	0.013	Group	F(1,30)=7.57	0.247	0.010
<i>Planned comparisons (right-handed versus left-handed)</i>								
Production		t(30)=1.38		0.175	Production	t(30)=-2.17		0.038
Perception		t(30)=2.61		0.014	Perception	t(30)=-2.19		0.036
Sup Par	Modality	F(1,30)<1	0.040	ns	Modality	F(1,30)<1	0.151	ns
	Group	F(1,30)=13.99	0.029	0.001	Group	F(1,30)=10.65	0.091	0.003
<i>Planned comparisons (right-handed versus left-handed)</i>								
Production		t(30)=1.72		0.096	Production	t(30)=-1.92		0.064
Perception		t(30)=3.33		0.002	Perception	t(30)=-2.12		0.043

Given the results of the omnibus ANOVAs (Table 1), subsequent ANOVAs were performed in each region of interest separately. A model was tested with within-subject factor Modality (perception, production) and between-subject factor Group (left-handed, right-handed). The Group × Modality interaction is only reported if $F > 1$. Huynh–Feldt correction for violation of sphericity assumption (Huynh and Feldt, 1976) was applied when appropriate, but original degrees of freedom are reported. Planned comparisons assessed the difference between right- and left-handers in production and perception separately. Results of the bimanual minus unimanual contralateral difference score are reported in the left column; results of the contralateral minus ipsilateral difference score are reported in the right column. dPM=dorsal premotor cortex; vPM=ventral premotor cortex; IPL=inferior parietal cortex; SPL=superior parietal cortex.

movements before the start of the experiment, but that they saw the hand actions in the perception blocks and could use this as a reference as to how to produce the actions themselves in the production blocks.

Every condition (left squeeze, right squeeze, both squeeze, left stretch, right stretch, both stretch) was replicated two times in both the perception and the production blocks. The stimuli in the perception block were projected from outside of the scanner room onto a mirror mounted onto the head coil. The movies in the perception blocks subtended 20 (width) by 16 (height) cm at a viewing distance of 80 cm ($14 \times 11^\circ$ visual angle). Because they were lying in supine position on the scanner bed and because the mirror was above the participant's eyes, participants were unable to see their own hand movements during the production blocks. Participants were instructed to keep their arms lying at rest and to only move their hands. This was done to minimize head movements as well as to additionally ensure that the hands would not be visible to the participant. Participants were instructed to fixate a fixation cross in the middle of the screen during all conditions. Performance of the participants was monitored visually from outside of the scanner room. All participants performed the task correctly.

5.4. Data acquisition and analysis

MR scanning was performed on a Siemens Magnetom scanner with 3 T magnetic field strength. Echo planar images were acquired using the following parameters: time to repetition (TR) 2130 ms, time to echo (TE) 30 ms, flip angle 80° , 32 transversal 3 mm slices (gap 17%), field of view 224 mm, $3.5 \times 3.5 \times 3$ mm voxel size. Approximately 225 volumes per participant were collected in one run. Data analysis was done using SPM5 (<http://www.fil.ion.ucl.ac.uk/spm/>). Preprocessing was done by discarding the first three volumes, motion correction by means of rigid body transformation along six rotations and translations, slice timing correction of all slices to the onset of the first slice, normalization of images to an EPI template in MNI space and spatial smoothing with a kernel of 8 mm FWHM. It was made sure that head motion estimates did not exceed 2 mm and 2° in any rotation or translation. 'Squeeze' and 'stretch' blocks were collapsed during data analysis leading to six conditions (perception/production × left/right/both) consisting of 4 blocks each. First level single subject statistics were computed in the context of the general linear model with the six conditions convolved with a canonical two gamma haemodynamic response function as

regressors of interest. Regressors were modeled for the duration of each block, that is, in a blocked design fashion. The estimates derived from the motion correction algorithm were included in the model as regressors of no interest.

5.5. Regions of interest analyses

As described in the introduction, we defined regions of interest (ROIs) in several parts of the cortical motor system: dorsal premotor cortex, ventral premotor cortex, inferior parietal cortex (the anterior part of the intraparietal sulcus) and superior parietal cortex (Fig. 2). Dorsal premotor cortex was defined on the basis of a study combining functional and morphological information (Amiez et al., 2006) (MNI coordinates: left: $-26 -14 62$; right: $30 -17 64$). Ventral premotor cortex was defined on the basis of the centre coordinates of a cytoarchitectonic map of Brodmann Area (BA) 44 (Amunts et al., 1999; Eickhoff et al., 2005) (MNI coordinates: left: $-50 9 24$; right: $54 8 23$)³. Inferior parietal cortex was defined on the basis of Calvo-Merino et al. (2006) who found effects of observer's motor repertoire in this region (MNI coordinates: left: $-48 -42 54$; right: $42 -39 57$). Superior parietal cortex was defined on the basis of a study that observed effects of motor training on subsequent perception in this region (Reithler et al., 2007) (MNI coordinates: left: $-17 -71 53$; right: $13 -63 54$)⁴. All regions of interest were spheres with an 8 mm radius. Beta weights from the voxels in the ROIs were weighted with a Gaussian sphere to give most weight to the centre coordinates. Subsequently, the mean of all voxels in each ROI was computed and used in further analysis.

For every subject, the difference between the difference scores of the left- and right-hemispheric ROIs was taken as dependent variable. The analysis steps are graphically represented in Fig. 3. For each ROI, and for production and perception conditions separately, the two difference scores described above were computed. Left- and right-handers are known to differ in the degree of lateralization of these difference scores during action production. Therefore, we computed the difference between the difference scores of the left- and right-hemispheric ROI as a measure on which the two groups were expected to differ (Figs. 3C and D). Put differently, for every subject, the following four measures were computed: (a) difference score 1 Production, left ROI – difference score 1 Production, right ROI; (b) difference score 1 Perception, left ROI – difference score 1 Perception, right ROI; (c) difference score 2 Production, left ROI – difference score 2 Production, right ROI; (d) difference score 2 Perception, left ROI – difference score 2 Perception, right ROI.

Subsequently, statistical analysis involved repeated measures analysis of variance (ANOVA) on the two interhemispheric difference scores separately with within-subject factors Modality (perception, production) and ROI (dorsal

premotor, ventral premotor, inferior parietal, superior parietal) and between-subject factor Group (left-handed, right-handed). The data that went into this analysis are the differences graphically illustrated in Fig. 3C (but for every participant separately).

To test the spatial specificity of differences between left- and right-handers, in the case of a main effect of ROI or a Group \times ROI interaction, subsequent follow-up ANOVAs were performed on the data of each ROI separately. This involved a 2×2 model with between-subject factor Group (left-handed, right-handed) and within-subject factor Modality (perception, production). We expect a main effect of Group if the difference score indeed distinguishes between left- and right-handers in that particular ROI. If such a difference between groups during production is also present during perception, we expect no main effect of Modality and no Modality \times Group interaction. In the case of a main effect of Group or Modality, planned comparisons were conducted to test for group effects for production and perception separately. That is, in these planned comparisons it was specifically tested whether left- and right-handers differ from each other a) in terms of production and b) in terms of perception. This entailed testing for between-group differences of the difference scores during production and perception separately by means of two-sided two-sample *t*-tests (*df*: $n-2=30$). So, if a region exhibits a close coupling between production and perception this will be indicated by two significant differences between the groups in the planned comparisons: one for production and one for perception. For instance, in the contralateral–ipsilateral hand production comparison, the between group difference in this planned comparison was given by $t(30) = (((\text{Contralateral} - \text{Ipsilateral production left hemisphere, right-handers}) - (\text{C} - \text{I prod right hemisphere, right-handers})) - ((\text{C} - \text{I prod left hemisphere, left-handers}) - (\text{C} - \text{I prod right hemisphere, left-handers}))) / \text{standard error}$.

In short, we used two interhemispheric difference scores which have been previously shown to distinguish left- and right-handers in terms of action production and tested whether similar differences between the groups can be observed during action observation in various regions which have been shown to exhibit mirror-like properties.

5.6. Whole brain analysis

Although the focus of our analysis was on the regions of interest (see above), for general interest a whole brain analysis was performed. Single subject contrast maps were taken to a second level random effects group analysis with a model with within-subjects factor Modality (perception, production) and Hands (left, right, both) and between subjects factor Group (left-handed, right-handed). All results are family-wise error corrected for multiple comparisons using the theory of Gaussian random fields (Friston et al., 1996; Worsley et al., 1996).

For the sake of completeness, we also tested for within-group differences comparing left > right and right > left hand action perception/production in each group differently. Since this is a more exploratory analysis, multiple comparison correction was implemented by combining a $p < 0.001$ voxel-

³ Defining ventral premotor cortex based upon a morphological analysis of inferior precentral sulcus (Germann et al., 2005) led to qualitatively the same results.

⁴ The original findings were in Talairach coordinates (Talairach and Tournoux 1988) (*x y z*; $-17 -66 52$; $13 -59 53$), which were converted into anatomical MNI coordinates by means of the transform as suggested by M. Brett (see <http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml>).

level threshold with a cluster extent threshold to arrive at $p < 0.05$ corrected (Friston et al., 1996). Conjunction analyses (Nichols et al., 2005) were performed within each group separately by testing for overlapping regions to perception left > right differences and production left > right differences and vice versa. For results see [Supplementary materials](#).

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.brainres.2009.02.057](https://doi.org/10.1016/j.brainres.2009.02.057).

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