



Research report

Praxis and language are linked: Evidence from co-lateralization in individuals with atypical language dominance

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ARTICLE INFO

Article history:

Received 19 September 2011

Reviewed 24 October 2011

Revised 28 October 2011

Accepted 1 November 2011

Action editor Roberto Cubelli

Published online 19 November 2011

Keywords:

Evolution

fMRI

Praxis

Language

Lateralization

ABSTRACT

We determined the neural correlates of word generation and tool use pantomiming in healthy subjects with typical ($n = 10$) or atypical ($n = 10$) language dominance to investigate similarities in response pattern and hemispheric specialization between language and praxis. All typical language dominant volunteers also revealed left hemisphere changes during tool use pantomiming in prefrontal, premotor, and posterior parietal regions. All atypical language dominant participants displayed right hemisphere engagement for tool use. Co-lateralization of the language and praxis networks was observed on group and individual level, regardless of the participant's handedness. Activation maps of the word generation and tool use pantomiming contrasts displayed overlap in five cortical regions: supplementary motor area, dorsal and ventral premotor cortex, dorsolateral prefrontal cortex, and posterior parietal cortex. Individual lateralization indices were calculated for each region and revealed significant positive group correlations between .51 and .95 with every other region within the paradigms. Positive cross-task correlations ranged between .72 (supplementary motor complex) and .97 (dorsal premotor cortex) and illustrate that the strength of hemispheric specialization of one task significantly predicts the side and degree of lateralization of the other task, suggesting a functional and topographic link between language and praxis. These findings support models that link gestures and speech to explain the evolution of human language. We argue that the existence of a common and co-lateralized network underlying the production of complex learned movement, whether it be speech or tool use, may represent the evolutionary remnant of a neural system out of which proto-sign and proto-speech co-evolved.

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doi:10.1016/j.cortex.2011.11.003

1. Introduction

In the human brain, hemispheric specialization is a common finding, with some cognitive functions like language and arithmetic preferentially activating the left hemisphere, and others like face processing and spatial attention displaying right hemispheric dominance (Toga and Thompson, 2003). Most humans show this ‘standard’ asymmetric organization, although a minority of individuals reverse or negate the usual hemispheric specialization with no apparent behavioral consequences (Knecht et al., 2001). Functional asymmetries are believed to rely on phylogenic and ontogenic mechanisms, and co-lateralization in direction or degree of distinct cognitive functions might constitute evolutionary traces on how these mental abilities evolved (Pinel and Dehaene, 2010). Here, we investigate the co-lateralization of praxis and speech as both functions are associated with learned movement and have been hypothesized to share a common evolutionary origin (Arbib, 2005; Corballis, 1999; Hewes, 1973).

Strong left hemispheric asymmetry for language at the population level is a robust finding in neuropsychology and cognitive neuroscience (Josse and Tzourio-Mazoyer, 2004; Toga and Thompson, 2003). In normal individuals, language lateralization has been determined by a variety of behavioral and physiological measurements using a wide range of linguistic tasks. Solid findings have been obtained with word generation paradigms while participants undergo functional magnetic resonance imaging (fMRI), and this method was successfully validated against the more invasive intracarotid amytal procedures used with patients (Deblaere et al., 2004; Sabbah et al., 2003). Praxis refers to the ability to perform learned gestures, that is, to generate, coordinate, and execute an acquired intentional motor program. Dysfunction of learned movement is known as apraxia, a neurological disorder frequently seen following left brain damage. In behavioral neurology and clinical neuropsychology, the pantomime of tool use is considered to be a sensitive test for apraxia (Bartolo et al., 2008; Goldenberg et al., 2003). Tool pantomimes mimic an instrumental grasp and movement with an imaginary object, and have been frequently applied in neuroimaging studies to investigate the neural correlates of praxis skills (Lewis, 2006). Without exception, these imaging studies revealed a left hemispheric dominance of the activated regions of right-handed volunteers in line with lesion studies in apraxic patients (Buxbaum et al., 2005; Goldenberg et al., 2007; Haaland et al., 2000).

It has been claimed that the lateralization of praxis is rooted in symbolic representations that also underlie language and are preferentially organized in the left hemisphere (Duffy and Duffy, 1981; Geschwind and Damasio, 1985; Geschwind, 1975). If this relation is obligatory, then individuals with right hemispheric language dominance (RLD) should also reveal a right hemispheric lateralization upon the activation of purposeful action scripts. Clinical data that challenge this association is extremely scarce. Although patients with apraxia often also present aphasia, this comorbidity is not absolute as both dysfunctions may be caused by lesions in different locations within the same hemisphere and are

commonly described independently (Heilman et al., 1973, 1986; Margolin, 1980; Rapsak et al., 1995; Selnes et al., 1991; Sirigu et al., 1995). Interestingly, a few cases have also been described of comorbidity of aphasia and apraxia in ‘crossed’ form, that is patients showing aphasia and apraxia following unilateral right hemispheric damage (Poeck and Kerschensteiner, 1971; Poeck and Lehmkuhl, 1980; Raymer et al., 1999). Other clinical indications of congruent praxis and language skills stem from the presurgical intracarotid amobarbital procedure performed on epilepsy patients. This procedure revealed that in patients with atypically represented language the ability to pantomime tool use actions appeared closely associated with language dominance, although this might be due to cerebral reorganization as a result of the chronic lateralized brain disease (Meador et al., 1999). Recently, Króliczak et al. reported coinciding atypical inferior parietal lateralization during gesture planning of familiar transitive and intransitive movements in healthy left-handers with atypical (right hemispheric or bilateral) language dominance assessed by a verbal fluency task in Broca’s area using fMRI (Kroliczak et al., 2011). Together, these findings suggest the possibility of a link between the hemispheric specialization of language and praxis. To investigate this relation in more detail, we will compare the neural response changes of 10 healthy volunteers showing RLD against a matched group of left hemispheric language dominant (LLD) participants during tool use pantomimes, and evaluate whether language and gesture production elicit modulation of activity in shared regions of an underlying neural network.

2. Methods

2.1. Participants

Ten healthy volunteers (eight women and two men, age range: 19–23 years, mean age: 21.4) were recruited via a study on atypical language dominance of the Department of Experimental Psychology of Ghent University (Van der haegen et al., 2011). These participants showed RLD during a word generation paradigm (described below) while undergoing fMRI. They agreed to take part in the praxis study. Eight participants were left-handed as determined by the Edinburgh handedness inventory (EHI) (Oldfield, 1971), one was right-handed and one was ambidexter. Their neural response patterns during tool pantomiming and word generation were compared with those of 10 volunteers with confirmed LLD. RLD and LLD participants were matched for gender, age, and side and degree of handedness (Table 1). As a result, no significant group differences were found for age and handedness. A significant group difference was found for lateralization index of word generation task activation (LI_{WGEN}) ($t[18] = 9.44$, $p < .001$), but when absolute values were chosen (removal of the sign), the degree of hemispheric dominance (regardless of its side) showed no significant between-group difference. None of the participants had a history of neurological or psychiatric disease. The study was approved by the local ethics committee and all volunteers gave written informed consent.

Table 1 – Individual data on the age, gender, and handedness matched groups with typical and atypical language lateralization.

RLD					LLD				
ID	Gender	Age	LI _{EHI} ^a	LI _{WGEN} ^b	ID	Gender	Age	LI _{EHI} ^a	LI _{WGEN} ^b
#1	F	23	-.90	.74	#11	F	21	-.90	-1.00
#2	F	22	-.90	.43	#12	F	21	-.90	-1.00
#3	F	20	.00	.21	#13	F	20	.00	-.82
#4	F	19	-.83	.99	#14	F	21	-1.00	-.15
#5	F	19	-.83	.60	#15	F	20	-1.00	-.59
#6	F	23	1.00	.79	#16	F	26	1.00	-.95
#7	F	23	-1.00	.99	#17	F	25	-1.00	-.31
#8	F	22	-1.00	.48	#18	F	21	-1.00	-1.00
#9	M	23	-1.00	.98	#19	M	27	-1.00	-.12
#10	M	20	-.92	.55	#20	M	22	-.92	-.61
Mean [standard deviation (SD)]		21.4 (1.7)	-.64 (.65)	.68 (.27)			22.4 (2.6)	-.67 (.66)	-.65 (.36)

a LI_{EHI}: [(R - L)/(R + L)].
b LI_{WGEN}: over the inferior frontal cortex, [(R - L)/(R + L)].

2.2. Word generation paradigm

Stimuli. This task is an adapted Dutch version of a paradigm used before to ascertain language dominance in volunteers with typical and atypical language lateralization (Cai et al., 2010). Ten letters served as stimuli (b, d, k, l, m, n, p, r, s or t). Target letter selection was based on a pretest with native Flemish–Dutch speakers. This allowed the exclusion of letters for which only a few words could be generated. Stimuli were displayed in white on a black background.

Task. The task consisted of 10 cycles. Each cycle included one word generation task (duration 15 sec), one control task (15 sec), and two 15 sec rest periods between the tasks. A cycle started with a generation task during which a letter was displayed at the center of the screen and participants were requested to silently generate as many words as possible that started with that letter. The generation task was followed by a rest period during which a short line was displayed on the screen and participants were requested to relax. In the subsequent control task, the letter sequence “BABA” was displayed on the screen and participants were instructed to mentally repeat baba, which is pronounceable but meaningless in Flemish–Dutch. The control task was followed by another rest period. This four-block cycle was repeated 10 times with different letters in random order. The task took 10 min to complete.

2.3. Tool pantomime paradigm

Stimuli. This tool pantomime paradigm has been used before to investigate praxis lateralization in right- and left-handed volunteers (Vingerhoets et al. in press). Every stimulus of this paradigm presents two objects, one on the right and one on the left, and three lines, one below each object and one between the objects. The objects are presented in color, two of the lines are always black, and one is always red. In the tool conditions the depicted objects are familiar tools selected from a validated collection (Vingerhoets, 2008). In 20 slides, the line under the right tool object is red and these slides were mirrored over the vertical axis to obtain 20 similar slides in

which the line under the left object is red. In 20 further slides, the line between the two tool objects is red. In the control conditions, designed to control for object-related movements in general (that is, movement unrelated to tools), the objects are eggs. Eggs are familiar objects that are easy to manipulate, but are not associated with tool-like gestures. In the control slide one of the eggs is aligned vertically. Six slides are constructed for each control condition and the required responses toward eggs were marked in the same way as above. Some examples of the stimuli are depicted in Fig. 1 and a list of the familiar tools used in the unimanual and bimanual conditions can be found in the Appendix.

Task. Participants were instructed that the position of the red line indicated the type of movement to be performed. If the red line was *under one* of the objects, an unimanual response on the same side, using left or right hand, was expected, and if the line *between* the objects was marked red, then a bimanual movement had to be performed. During unimanual pantomimes, the non-active hand had to remain still on the scanner table alongside the body. Bimanual pantomimes consisted of actions typically involving both hands (e.g., sharpening a pencil, threading a needle). In such trials the position of the objects dictated how the bimanual movement had to be performed. The object on the left (e.g., the sharpener) had to be pantomimed with the left hand, the object on the right (e.g., the pencil) with the right hand. We felt it necessary to switch hands in bimanual conditions as well, because in most bimanual tasks one hand is clearly dominant over the other, and left and right handers typically perform these tasks differently. In the unimanual control conditions the volunteers were instructed to pantomime a rotating movement with the wrist while holding the egg with the fingers. In the bimanual control conditions they were asked to pantomime holding one egg in a central position, while rotating the other egg around it. In these bimanual conditions the vertically depicted egg indicated the side (hand) with which the dominant movement had to be made. Together, these instructions give rise to eight different conditions: (1) unimanual right tool pantomime, (2) unimanual left tool pantomime, (3) bimanual right dominant tool pantomime, (4) bimanual left dominant tool pantomime, (5)

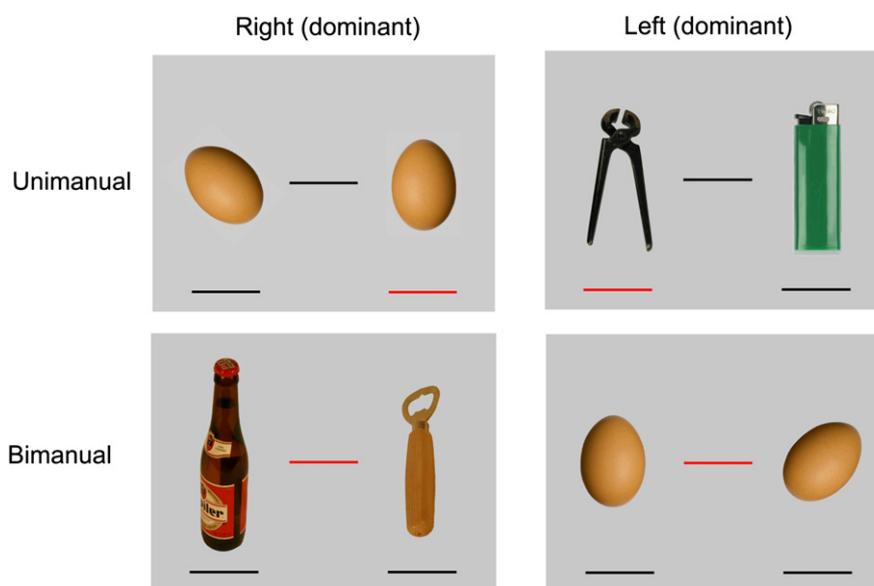


Fig. 1 – Some examples of tool and control stimuli. The red line indicates whether the pantomime is bimanual (between objects) or unimanual (under one object). The position of the object determines the side of execution (or execution dominance in bimanual trials) (left object/left hand, right object/right hand). In bimanual control trials, the side of the vertically aligned egg determines the hand that makes the dominant movement.

unimanual right control pantomime, (6) unimanual left control pantomime, (7) bimanual right dominant control pantomime, and (8) bimanual left control pantomime. By probing learned unimanual and bimanual gestures and having them performed with the dominant and the non-dominant hands, we can make abstraction of the participant's hand preference and effector bias on praxis skills by using a conjunction analysis comparing each tool condition with its respective control condition: $(\text{UniRightTool} > \text{UniRightControl}) \cap (\text{BiRightTool} > \text{BiRightControl}) \cap (\text{UniLeftTool} > \text{UniLeftControl}) \cap (\text{BiLeftTool} > \text{BiLeftControl})$ (Vingerhoets et al. in press). Participants were presented with several examples of the stimuli until they correctly understood all instructions. The paradigm was arranged as a conventional block design with eight conditions. Each condition consisted of eight blocks. A block lasted 21 sec and consisted of six stimuli of the same type each presented for 3500 msec. The total experiment thus took 22.4 min. Blocks were ordered semi randomly to avoid consecutive presentation of two blocks with the same type of stimuli. Stimuli were randomly distributed over their conditions' blocks. The performance of the participants was monitored by one of the co-authors by observing the pantomimes of the volunteer inside the magnet. All participants were able to perform the required pantomimes during their fMRI session.

2.4. Procedure

Prior to scanning, the volunteers completed a pre-scan MRI-safety questionnaire and the EHI. In the post-scan session, participants completed a post-scan MRI-safety questionnaire, and were debriefed. In each participant, the word generation protocol was scanned on a different day than the pantomime paradigm. Pre- and post-scan safety procedures and participant position were identical for both paradigms.

The volunteers were positioned head first and supine in the magnet. Their left and right arms were positioned comfortably alongside the body on the scanner table. Participants were reminded of the fact that MR-imaging is very sensitive to movement and were instructed to restrict head movements and to lie as still as possible to prevent motion artifacts. Their heads were gently fixed in place with foam cushions. In the pantomiming paradigm, a nylon ribbon was tightened over the chest and arms at the elbows, thus limiting movements of the upper arms. We asked the volunteers to perform the pantomimes rather calmly, using only their underarms, wrists and hands. Stimulus presentation was controlled by a commercially available experiment generator (Presentation, Neurobehavioral Systems Inc., Albany, CA, USA) digitally synchronized with the MRI-scanner. The stimuli were back projected on a screen at the back of the magnet bore and viewed via a mirror attached to the head coil.

2.5. Scanning procedure

Scanning was performed at 3.0 T on a Siemens Trio MRI scanner (Siemens Medical Systems, Erlangen, Germany) equipped with echo planar imaging (EPI) capabilities using an eight-channel phased-array head coil for radio frequency transmission and signal reception. After automatic shimming of the magnetic field on each participant, a three-dimensional (3D) high-resolution T1 anatomical image of the whole brain in the sagittal plane was acquired for coregistration with the functional images (3D MPRAGE, 176 slices, slice thickness = .9, in-plane resolution = $.9 \times .9$ mm, repetition time (TR) = 2530 msec, echo time (TE) = 2.58). Next, 545 functional EPI images in the axial plane were acquired for the tool pantomime paradigm, and 240 for the word generation paradigm. They had the following parameters: TR = 2.5 sec, TE = 33 msec; flip

angle = 90°, 33 slices, slice thickness = 2.5 mm, slice gap = 1.25 mm, field of view = 192 mm and matrix = 64 × 64, resulting in a resolution of 3 × 3 × 2.5 mm.

2.6. Image analysis

Data analysis was performed using Brain Voyager QX for preprocessing and statistical inference (Goebel et al., 2006). Functional data of each paradigm were subjected to a standard sequence of preprocessing steps comprising slice scan time correction by means of sinc interpolation, 3D motion correction by spatial alignment to the first volume also by means of sinc interpolation, and temporal filtering using linear trend removal and high pass filtering for low-frequency

drifts of three or fewer cycles. Spatial smoothing with a Gaussian filter (full width at half maximum = 4 mm) was applied for the volume-based analysis. The anatomical data for each subject were resampled to 1-mm resolution, and transformed into Talairach standard space using sinc interpolation. The functional data for each subject were coregistered with the subject's 3D anatomical dataset and transformed into Talairach space.

For each subject's paradigm, a protocol file representing the onset and duration of each block for the different conditions were derived. Factorial design matrices were defined automatically from the created protocols. The blood-oxygen-level dependent response in each condition was modeled by convolving these neural functions with a canonical

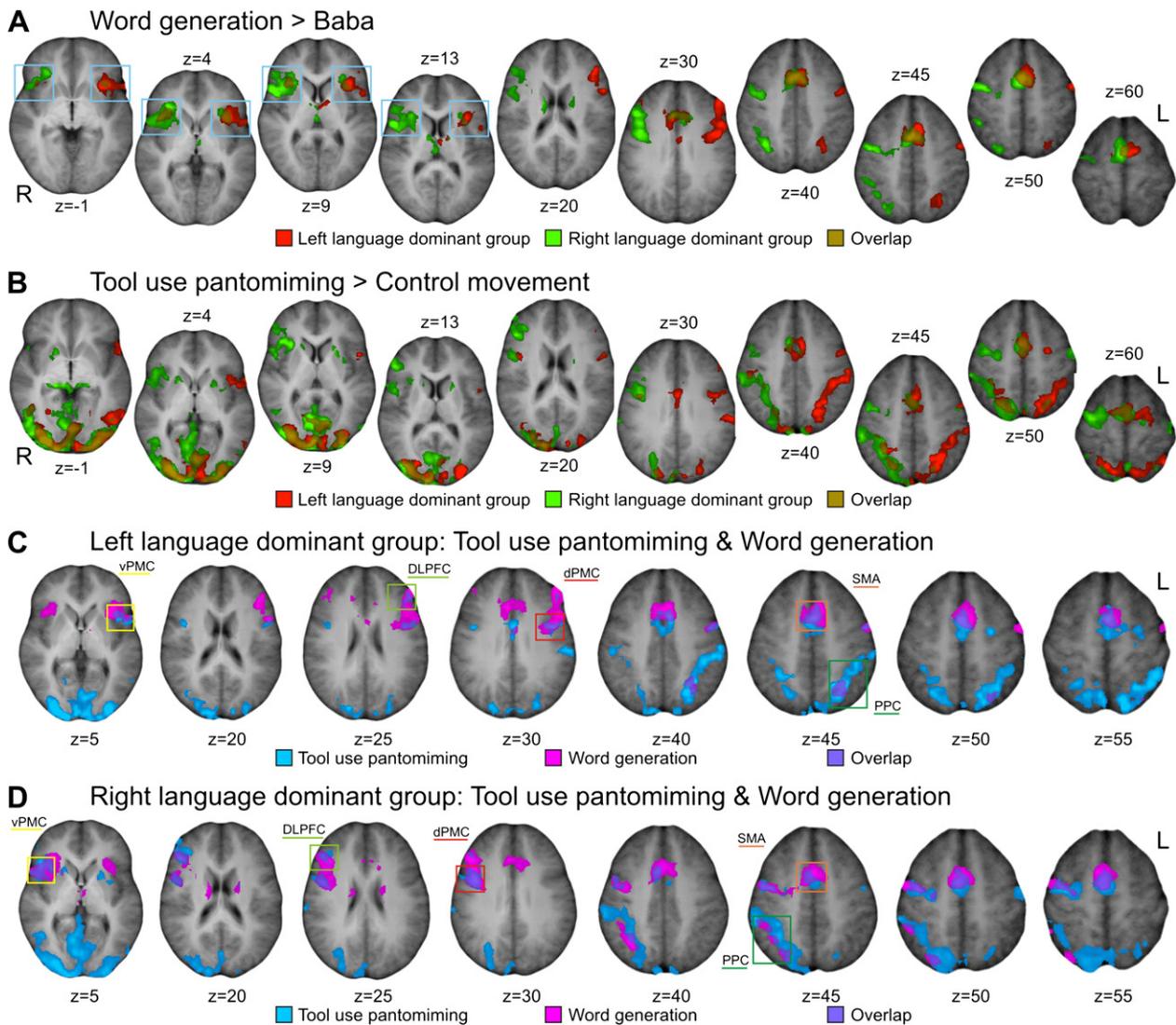


Fig. 2 – A. Main contrast for word generation versus baba-repetition in typical (red) and atypical (green) language dominant subjects. Brown color depicts regions of overlap. Blue box marks the lateral inferior frontal ROI on which LI_{WGEN} was calculated. B. Main contrast for tool use pantomiming versus control movements in typical (red) and atypical (green) language dominant subjects. Brown color depicts regions of overlap. C. Overlay of the tool use pantomiming (blue) and word generation (pink) contrasts for the typical language dominant group. Purple color depicts regions of overlap, and can be found in vPMC (yellow box), DLPFC (light green box), dPMC (red box), SMA (orange box), and PPC (dark green box). D. Overlay of the tool use pantomiming (blue) and word generation (pink) contrasts for the atypical language dominant group. Purple color depicts regions of overlap, and can be found in vPMC (yellow box), DLPFC (light green box), dPMC (red box), SMA (orange box), and PPC (dark green box). All activation maps at alpha (FDR) < .05.

hemodynamic response function (γ) to form covariates in a General Linear Model (GLM). After the GLM had been fitted, group (random effects procedure) t -maps were generated to evaluate the effects of tool pantomiming and word generation under different conditions. In all analyses we applied a threshold of $p < .05$ corrected for multiple comparisons using False Rate Discovery (FDR) correction (Genovese et al., 2002).

2.7. Lateralization indices

We calculated the lateralization index (LI) of the activated voxels in the lateral inferior frontal region for the contrast word generation against baba-repetition (LI_{WGEN}). A functional region of interest (ROI) was determined based on this contrast for the entire group ($N = 20$). At alpha (FDR) $< .05$, the ROI encompassed the cerebral matter of Brodmann areas 44 and 45 between Talairach coordinates $x = 56$ and 21 (right hemisphere)/ -21 and -56 (left hemisphere), $y = 37$ and 4 , and $z = 19$ and -7 (Mai et al., 2008; Talairach and Tournoux, 1988) (boxed areas in Fig. 2A). This symmetrical ROI encompassed 29,822 voxels. To take inter-individual variability into account, the statistical threshold was individually adapted to expose the 10% most active voxels of the total ROI-volume for each participant. Then we counted the number of active voxels in the right and left hemisphere and calculated the LI with the formula $[(R - L)/(R + L)]$, resulting in values that range between $+1$ (complete right hemispheric lateralization) and -1 (complete left hemispheric lateralization).

The response patterns of word generation and tool pantomiming exhibited overlap in five symmetrically distributed cortical regions depicted in Fig. 2C and D: dorsolateral prefrontal cortex (DLPFC), ventral premotor cortex [vPMC; we prefer this function-neutral term over Broca's region (Binkofski and Buccino, 2006)], dorsal premotor cortex (dPMC), supplementary motor area (SMA), and posterior parietal cortex (PPC). Symmetrical regions of interest were created encompassing the maximal overlap for each group and hemisphere. Statistical

threshold was again individually adjusted to reveal the 10% most active voxels in the combined left and right hemisphere over each region, and the number of the above threshold voxels in each hemisphere were used to compute the LIs. Differences in the relative strength of lateralization were calculated on the absolute LI-values (removal of the sign) by means of a repeated measures analysis of variance with ROI (PPC, vPMC, DLPFC, dPMC, and SMA) and Task (word generation, tool pantomiming) as within subject factors and Group (RLD, LLD) as between subject factors. To evaluate the side of lateralization, we correlated the LIs for each region and task using Pearson correlation coefficients in a two-tailed test of significance.

3. Results

Word generation. The generation of words elicited response changes in the middle and inferior frontal gyrus in particular in Broca's region and extending anterior to the DLPFC and posterior to the precentral gyrus. Activation was also found in the medial frontal cortex extending to the cingulate gyrus, in the thalamus, posterior parietal lobule, and ventral and lateral temporal cortex. In the inferior frontal and medial frontal gyri, the modulation of activity appeared bilateral, although a clear lateralization could be observed with the RLD-group showing a right hemispheric bias, and the LLD-group showing a left hemispheric dominance (Fig. 2A). In the dorsolateral prefrontal, dorsal premotor, and precentral gyri, and in the inferior parietal lobule, the remaining increase at alpha (FDR) $< .05$ appeared completely lateralized to the left (LLD) or right (RLD) hemisphere. LLD and RLD-group coordinates of the cortical activation peaks are listed in Table 2.

Tool pantomiming. Significant signal change during tool pantomiming is observed in the medial frontal cortex, middle and inferior frontal gyri, dorsal precentral gyrus, precuneus and inferior parietal lobule extending to the postcentral gyrus,

Table 2 – Word generation paradigm. Coordinates of peak activity in the left hemisphere for the LLD-group and in the right hemisphere for the RLD-group, alpha (FDR) $< .05$.

Brain region	BA	Talairach coordinates Left			t_{max}	Talairach coordinates Right			t_{max}
		X	Y	Z		X	Y	Z	
WGEN > baba									
Frontal clusters									
Medial frontal gyrus	32/6	-1	7	47	13.76	1	7	47	13.57
Cingulate gyrus	32	-5	15	36	10.76	4	16	36	11.69
Insula	45/44	-34	17	3	10.90	35	18	6	9.11
Middle frontal gyrus	46/9	-44	31	27	5.35	38	28	24	7.19
Middle frontal gyrus	6	-24	43	-1	3.59	22	41	0	3.84
Inferior frontal gyrus	44	-43	5	28	4.19	43	4	30	6.80
Precentral gyrus	6	-23	-11	51	4.26	26	-14	51	6.82
Precentral gyrus	6	-50	-4	48	3.25	48	-4	49	4.52
Parietal clusters									
Precuneus	7	-24	-62	47	3.36	20	-63	-47	4.76
Inferior parietal lobule	40	-45	-41	44	4.33	39	-39	42	4.23
Inferior parietal lobule	39	-30	-57	32	3.75				
Superior parietal lobule	7					32	-59	60	3.90
Temporal clusters									
Fusiform gyrus	37	-49	-55	-12	4.41	41	-61	-9	5.25
Mid/sup temporal gyrus	21/22	-52	-29	1	3.86	49	-30	3	5.37

Table 3 – Tool pantomiming paradigm. Coordinates of peak activity in the left hemisphere for the LLD-group and in the right hemisphere for the RLD-group, alpha (FDR) < .05.

Brain region	BA	Talairach coordinates Left			t_{\max}	Talairach coordinates Right			t_{\max}
		X	Y	Z		X	Y	Z	
Tool pantomiming > control movements									
<i>Frontal clusters</i>									
Medial frontal gyrus	6	–4	–1	49	9.66	1	–1	50	10.29
Insula	45	–40	16	4	4.90	45	10	5	8.37
Middle frontal gyrus	9	–40	35	36	4.70	34	39	31	4.02
Inferior frontal gyrus	44	–53	2	32	5.27	39	1	30	9.49
Inferior frontal gyrus	45/46	–50	41	13	3.87	41	31	17	7.96
Precentral gyrus	6	–19	–11	64	7.86	22	–11	58	7.88
<i>Parietal clusters</i>									
Postcentral gyrus	1, 2, 3	–49	–29	37	6.29	48	–26	40	8.16
Precuneus	7	–23	–64	50	7.35	20	–64	–51	9.64
Inferior parietal lobule	40	–41	–34	42	6.32	32	–37	41	7.55
Inferior parietal lobule	40	–33	–45	43	5.20	31	–47	45	9.09
<i>Temporal and occipital clusters</i>									
Inferior occipital gyrus	18	–31	–91	–6	13.10	27	–90	–6	18.78
Fusiform gyrus	37	–30	–58	–15	15.75	25	–47	–14	16.59
Cuneus	18	–4	–95	7	8.15	5	–95	9	13.80
Lingual gyrus	18	–2	–77	2	10.39				

ventral temporal, and several visual occipital regions. With exception of the occipital and medial frontal regions, and to a lesser degree the posterior parietal regions, most areas showed a clear lateralization with the LLD-group presenting a left hemispheric bias and the RLD-group presenting a rightward specialization (Fig. 2B). LLD and RLD-group coordinates of the cortical activation peaks are listed in Table 3. Co-lateralization of language dominance and hemispheric specialization for learned movements can also be observed on the individual level as illustrated in Fig. 3.

Lateralization indices. We projected the word generation pattern over the tool pantomiming pattern for the left (Fig. 2C) and the right (Fig. 2D) language dominant groups to reveal regions that are commonly activated during both tasks. Five cortical regions exhibited overlap in both groups: (vPMC, center of mass (com): $x = \pm 47$, $y = 12$, $z = 5$, caudal BA 44/45), (dPMC, com: $x = \pm 42$, $y = 3$, $z = 31$, rostral BA 44/caudal BA 6), (DLPFC, com: $x = \pm 44$, $y = 30$, $z = 25$, BA 9/46), (PPC, com: $x = \pm 30$, $y = -55$, $z = 44$, BA 40/7, intraparietal sulcus), and the (SMA, com: $x = \pm 2$, $y = 5$, $z = 47$, BA 6). Only the SMA displayed bilateral engagement in both groups, all other regions unveiled strictly lateralized overlap at alpha (FDR) < .05. We determined the individual's LIs over these five ROIs for each task based on the 10% most active voxels. Fig. 4 summarizes these data and displays the strength of the association between regions in each task. The mean group LIs for each region are presented inside the ellipses (LLD on the left/RLD on the right). In both paradigms, the dPMC exposes the strongest lateralization, especially during word generation, whereas the lowest values are obtained in the PPC for word generation and in the SMA for tool pantomiming. These results were corroborated by a repeated measures analysis of variance on the absolute LIs, showing a main effect of ROI (Hotelling's $T[4,15] = 9.1$, $p = .001$), a main effect of Task (Hotelling's $T[1,18] = 5.8$, $p < .05$), and a ROI by Task interaction effect (Hotelling's $T[4,15] = 8.2$, $p = .001$). Fig. 4 only displays the

significant correlations, but we observe that the lateralization of each of these five regions is significantly and positively associated with every other region. With two exceptions (SMA–PPC and SMA–vPMC, both during tool pantomiming, both at $p < .05$), all correlations are significant at the $p < .01$ level. During word generation, the lateralization of the (highly asymmetric) dPMC response is most associated with the LIs of two other lateral frontal regions DLPFC and vPMC, and this is also the case during tool pantomiming. In the latter task, we observe a relative decrease in co-lateralization between the three lateral frontal regions and the SMA, but also a relative increased association between the lateral frontal sites and the PPC. All five regions also reveal significant cross-task lateralization correlations (illustrated in gray), with a marked co-lateralization of the dPMC in both paradigms.

Individual patterns. In most volunteers, all five regions co-lateralized to the same hemisphere within a task. There were some exceptions to this rule. During word generation two volunteers showed dissimilar dominance in PPC (#11 and #19), one in vPMC (#14), and two in SMA (#4 and #8). In tool use pantomiming one participant exposed incongruous dominance in PPC (#12), one in vPMC (#17), one in DLPFC (#3), one in dPMC (#3), four in SMA (#3, #4, #8, and #18). With the exception of #19 ($LI_{PPC} = .92$), the divergent LIs are small and center around $\pm .20$. Only one participant (#12) revealed a cross-task discrepancy showing a robust left inferior frontal lateralization during word generation, and a slightly right lateralized engagement in PPC during tool use pantomiming ($LI_{PPC} = .15$).

4. Discussion

4.1. Functional implications of co-lateralization

We found that normal individuals displaying a LLD invariably show a left hemispheric asymmetry for praxis as well. The

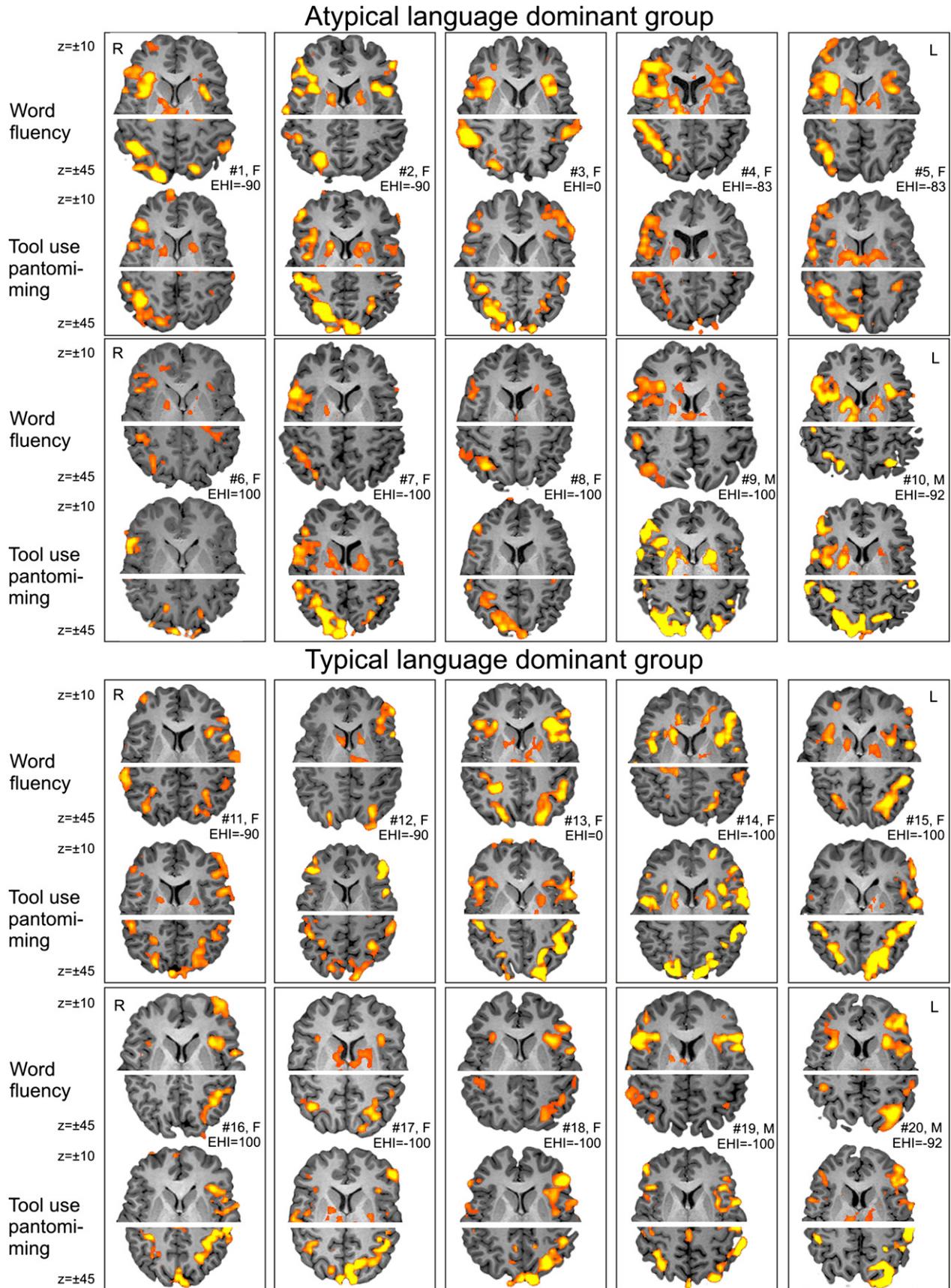


Fig. 3 – Individual response patterns around $z = 10$ and $z = 45$ (Talairach coordinates) during the word fluency and tool use pantomiming tasks. Notice the similarity in activated regions and the degree of lateralization evoked by both tasks that can be appreciated on an individual level.

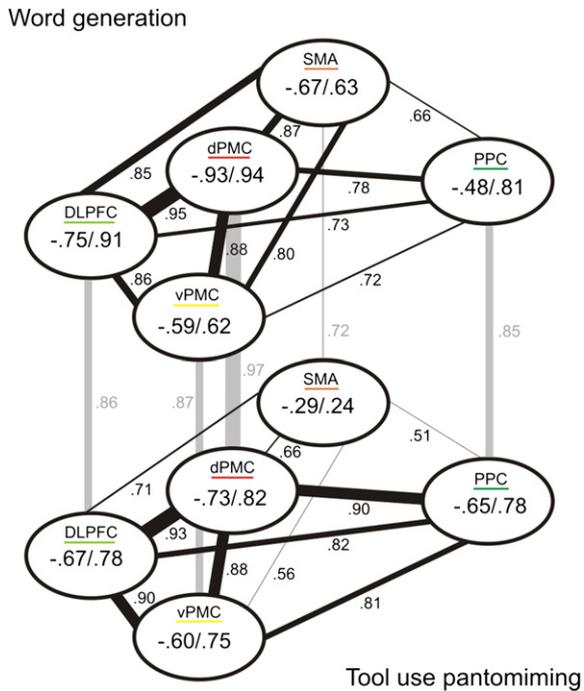


Fig. 4 – Illustration of the strength of co-lateralization within and between paradigms. Word generation and tool use pantomiming contrasts demonstrate overlap in five cortical regions (see Fig. 1C and D). The LI of each region of overlap is listed inside the ellipses (typical/atypical language dominance group) for the two paradigms. Black connecting lines illustrate significant correlations between the LIs of a region with every other region within each paradigm. Gray connecting lines represent significant lateralization correlations in the five regions between paradigms. Higher correlations are represented by thicker lines for better visualization.

argument of co-lateralization between language and praxis is strengthened by demonstrating that participants with RLD (atypical) reveal a right hemispheric asymmetry for praxis, and that this association can be observed at the level of the individual. Given the limited number of cases, it remains unclear whether this link is obligatory or only highly correlated. One of the sinistrals reported by Kroliczak et al. (2011) revealed a right posterior parietal LI during familiar gesture planning and a left ventral premotor LI during verbal fluency (similar to #12 in the present study), suggesting that there may exist exceptions in the relative contributions of different regions of the praxis and language network.

LIs of the five cortical regions that show overlap exhibit strong within-task correlations suggesting functional connectivity that appears to be modulated by the task at hand (e.g., there is a stronger involvement of the SMA within the network during word generation vs an increased engagement of the PPC in tool use pantomiming). Regional LIs also show substantial cross-task correlation again indicating a possible functional relationship within this network that transcends the particular tasks and contributes to the cognitive process in a more general manner. Neural overlap of different types of

learned gestures within the left hemisphere has been reported before, for example in inferior frontal and posterior temporal regions during symbolic gestures and spoken language (Xu et al., 2009), and in posterior parietal and dorsal premotor areas during tool pantomimes and symbolic gestures (Kroliczak and Frey, 2009). The results of the present study suggest a common network underlying the recollection of learned movements, whether they be articulated words or gestures associated with the use of tools. Both types of learned movements not only share symbolic meaning, they also require precise and articulated movements of specialized body parts. They must be presented in a correct temporal order and obey a hierarchical structure in order to make sense. Finally, their common product is ‘movement’ which necessitates coordinated interplay between cortical and subcortical nodes of the motor modality system. So maybe, these five regions constitute a model- or rule-based movement generator, subserving the production of complex movement sequences that need to adhere to (learned) structural features in order to make sense and convey meaning. Recent neuroimaging studies explored the possible role of some of these regions, and in addition often report interactions with other parts of the identified network. The SMA-complex is implicated in internally guided sensorimotor actions and the precise timing of motor acts underlying the execution of learned movement sequences, including those of speech (Bohland and Guenther, 2006; Debaere et al., 2003; Kennerley et al., 2004; Tanji, 2001). The dPMC has also been associated with the timing and sequencing of motor commands (Bortolotto and Cunnington, 2010), and recently conjoint activation of the left SMA-complex and the left dPMC was uncovered during a task that required the prediction of transiently occluded actions, suggesting that these regions play a role in the simulation of action (Stadler et al., 2011). The remarkably high co-lateralization between dPMC and DLPFC of the present study is very akin to its interaction during a sequence recognition task that suggested a role of segmenting (attentional selection) for the DLPFC and binding/sequencing for the ipsilateral dPMC (Abe et al., 2007). Task overlap in the vPMC is maximal around $x = \pm 47$, $y = 12$, $z = 5$, which is the opercular part of the inferior frontal gyrus, a classically defined part of Broca’s area (Keller et al., 2009). Broca’s area, in particular BA 44, has been proposed to be involved in encoding hierarchical structures in language, action, and music (Fadiga et al., 2009), and recent work demonstrated its role in the selection and nesting of action segments, integrated in hierarchical behavior plans, similar to a syntactic structure (Fazio et al., 2009; Koechlin and Jubault, 2006). Finally, PPC activity is a common finding in research on motor cognition, but is hardly ever mentioned in studies on word generation (Culham and Valyear, 2006; Fogassi and Luppino, 2005). Nevertheless, the same paradigm that revealed hierarchical encoding in vPMC (Koechlin and Jubault, 2006), demonstrated left intraparietal sulcus (IPS) (BA 40) involvement (in right handers) in representing and processing the abstract serial (but not hierarchical) structure of ongoing sequences of both motor acts and cognitive tasks (Jubault et al., 2007). It remains to be determined whether the IPS guides and keeps track of sequential progression in speech production, although some indications have been reported

(Bitan et al., 2005; Majerus et al., 2006). The present study does not validate any of the claims regarding the specific function of the parts of this neural network, but this short overview demonstrates that regions previously associated with predominant motor, language, or spatial functions increasingly appear to underlie supramodal cognitive functions that are able to organize learned actions in a coordinated and goal-directed fashion. The current study does suggest that the circuit underlying the organization of learned movement is lateralized in the human brain, and that there is a significant co-lateralization of the networks involved in language and praxis.

4.2. Evolutionary implications of co-lateralization

The neural wiring of language and learned gestures may also pertain to the current debate on the evolution of language in the human species. Although most scholars agree that modern language must have evolved from a proto-language – a hypothetical stage of language evolution interposed between modern language and ancestral system(s) of thought and communication, there is considerable disagreement on the nature of this proto-language with arguments favoring lexical, gestural, or even musical origins (Fitch, 2010). The gestural hypothesis assumes a manual/visual communication mode that served as a precursor toward our current vocal language system and that traces of this gestural proto-language can still be observed in contemporary conversation (Arbib, 2005; Corballis, 2002; Hewes, 1973). Two lines of neuroscientific data have been interpreted in favor of gestural origin: hemispheric lateralization and the discovery of mirror neurons.

The observation that hand preference and language show a left hemispheric preference in most humans has been taken as evidence for a relation between the two (Kimura, 1993; Kimura and Archibal, 1974). In addition, neuropsychological findings and neuroimaging studies indicate that praxis appears to be left lateralized in most humans too (Buxbaum et al., 2005; Goldenberg et al., 2007; Johnson-Frey et al., 2005; Vingerhoets et al., 2009). However, there are also arguments against the hypothesis that language dominance and handedness are connected. Over the last decades, evidence has been accumulating that hemispheric specialization for communication and vocalization are not uniquely human, but can be found in many species including birds, mammals and reptiles (Bisazza et al., 1998; Vallortigara et al., 1999). As these species did not evolve language and have less clear foot preferences, these findings make a putative link between language and handedness less likely. Moreover, handedness studies revealed that most left-handers also show LLD (Knecht et al., 2000, 2001), and recent neuroimaging data provided evidence that most left-handers reveal the usual left hemispheric lateralization for praxis skills (Vingerhoets et al. *in press*). These data suggest that there is no causal relation between manual preference and language or praxis. Although the hemispheric lateralization argument may have lost its power in the light of these findings, we argue that the data of the present study add a new flavor to the discussion if one considers language/praxis asymmetry rather than handedness/language or handedness/praxis asymmetry, and is prepared to interpret the asymmetry not in terms of language

or praxis, but in terms of a network involved in the adequate production of complex learned movements that an individual brain develops to steer speech and praxis and appears to prefer an asymmetric cerebral organization. The finding that every individual showed asymmetry for praxis and language in the same direction is a powerful argument for a functional and topographic link between the two, and supports models that link gestures and speech in an effort to explain the evolution of language.

This brings us to the second neuroscientific argument of a gestural origin of language, namely the discovery of mirror neurons in the macaque monkey (Rizzolatti et al., 1996), and the subsequent model on language evolution that was developed from it (Arbib, 2005; Rizzolatti and Arbib, 1998). Arbib proposed a seven-stage evolutionary model that is based on the development of imitation, proto-sign, and proto-speech through collateralization of gestural control circuits invading neighboring speech control regions (Arbib, 2005). Rather than positing a joint emergence of speech and sign by a network supporting control of learned movement, Arbib states that “the brain came to support *proto-speech* through the *invasion* of the vocal apparatus by collaterals from the *proto-sign* system” (Arbib’s emphasis). In other words the former evolved from the latter, and it is “open to debate whether the machinery supporting language overlaps the machinery for praxis or rather exploits an evolved variant” (Arbib, 2006). Arbib underlines his case for a segregation of both systems by pointing out the clinical dissociations between limb apraxia, speech apraxia, and aphasia (Arbib, 2006). At the same time, Arbib argues that the “mechanisms...supporting proto-sign and proto-speech thereafter evolved in an expanding spiral” (Arbib, 2006), suggesting a longstanding and gradual transition (Fitch, 2010). Although our study focused on the overlapping activation patterns between word generation and tool pantomiming, Fig. 1C and D clearly show that the overlap is only partial, and that damage to non-overlapping parts might hamper language but not praxis or vice versa, in agreement with the clinical observations of double dissociation mentioned in the introduction and elsewhere (Arbib, 2006). Lesions of the overlapping parts would also explain the frequent co-occurrence of language and praxis disorders. The question remains whether the overlapping fMRI responses reflect response changes of the same or different neural populations, which could have implications for the way we view the temporal relation between proto-sign and proto-speech. Suppose that the overlapping regions of word generation and tool pantomiming activate a common neural population, that is, neurons that activate irrespective of the task, and that this would even be the case in several nodes of the network. This could be seen as an argument for positing the existence of a common network underlying the production of complex learned movement out of which proto-sign and proto-speech co-evolved, each recruiting adjacent regions for specific control, but stemming from a core network underlying complex motor programming. Such a system would allow shared motor representations of body/limbs and face/mouth/sound enacting the outside world (objects, actions) through imitation and simulation and gradually develop in more symbolic representations. If on the other hand, conjoint word generation and tool pantomiming regions appear to activate (at least partly) separate neural populations

that are interleaved on a spatial scale below the resolution of fMRI, then this would offer a strong case for Arbib's "evolved variant" hypothesis, in which the shift toward functional segregation would be expected to surpass that of functional integration. Future studies, using high-resolution fMRI may help to dissociate these responses, whereas further research on co-lateralization of functions with conventional fMRI could contribute to our understanding of shared hubs in the neural networks underlying lateralized cognitive functions.

Acknowledgment

This study was supported by grant number G.0555.11 of the Fund for Scientific Research – Flanders.

Appendix

Tools used in the *unimanual* conditions: clothes pin, coffee spoon, comb, computer mouse, cup, eraser, filling-knife, fountain pen, garden shears, hair brush, house key, ice-cream scoop, office stamp, paintbrush (painting), paintbrush (wall), pincers, salt shaker, sponge, wire brush, wire cutters.

Tools used in the *bimanual* conditions: badminton racket and shuttle, ballpoint pen and measuring rule, beer bottle and bottle opener, can and can opener, cork screw and wine bottle, dustpan and brush, fountain pen and notebook, hammer and chisel, knife and fork, lemon and lemon squeezer, nut and nut cracker, oyster and oyster knife, paper and scissors, pencil and pencil sharpener, saw and miter box, screw and screwdriver, tennis racket and ball, thread and needle, tooth paste and tooth brush, whisk and bowl.

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