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Activation of Broca's area during the production of spoken and signed language: a combined cytoarchitectonic mapping and PET analysis

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Abstract

Broca's area in the inferior frontal gyrus consists of two cytoarchitectonically defined regions—Brodmann areas (BA) 44 and 45. Combining probabilistic maps of these two areas with functional neuroimaging data obtained using PET, it is shown that BA45, not BA44, is activated by both speech and signing during the production of language narratives in bilingual subjects fluent from early childhood in both American Sign Language (ASL) and English when the generation of complex movements and sounds is taken into account. It is BA44, not BA45, that is activated by the generation of complex articulatory movements of oral/laryngeal or limb musculature. The same patterns of activation are found for oral language production in a group of English speaking monolingual subjects. These findings implicate BA45 as the part of Broca's area that is fundamental to the modality-independent aspects of language generation.

Keywords: Neuroimaging; American Sign Language; Brain; Human; Brodmann areas

1. Introduction

The name Broca's area has been applied to the posterior portion of the left inferior frontal gyrus containing the pars triangularis and the pars opercularis (Broca, 1861; Tomaiuolo et al., 1999). The cytoarchitectonic areas (Brodmann, 1909) said to comprise this region are Brodmann areas (BA) 44 and 45 (Uylings et al., 1999). Damage in the vicinity of this structure often results in a Broca's aphasia: an impairment of language characterized by non-fluent, agrammatical verbal output with relatively preserved language comprehension (Benson & Geschwind, 1985). Nonetheless, there is much controversy concerning the relationship between Broca's area and language-related function. Lesions restricted to Broca's area do not always lead to a Broca's aphasia (Dronkers, Shapiro, Redfern, & Knight, 1992; Mohr et al., 1978), and conversely, patients with a Broca's aphasia do not always have a lesion in Broca's area (Dronkers & Ludy, 1998; Dronkers et al., 1992). Although numerous functional neuroimaging studies have reported activation of Broca's area by language tasks (Caplan, Alpert, Waters, & Olivieri, 2000; Dapretto & Bookheimer, 1999; Just, Carpenter, Keller, Eddy, & Thulborn, 1996; Rumsey et al., 1997; Salmelin, Schnitzler, Schmitz, & Freund, 2000; Zatorre, Evans, Meyer, & Gjedde, 1992), a number of investigators have shown that this area also can be activated by non-language tasks (Binkofski et al., 2000; Iacoboni et al., 1999). Even the boundaries of Broca's area are ill-defined; a cytoarchitectonic study of BA44 and BA45 by Amunts et al. (1999) in 10 human brains found that the cytoarchitectonic boundaries of these areas did not have a fixed relationship to sulcal landmarks, and that there was much intersubject variability amongst the 10 brains.

Because BA44 is just anterior to the mouth area of the motor strip, it had been widely conjectured that the location of Broca's area reflects the involvement of this cortex with the motor articulatory aspects of speaking (Goodglass, 1993) (however, see Corina et al., 1999 for evidence counter to this view). However, several studies of fluent speakers of sign language have shown that Broca's area seems to play a crucial role in language production, even though the production in signers relies primarily on the use of arms and hands (Braun, Guillemin, Hosey, & Varga, 2001; Hickok, Bellugi, & Klima, 1998; McGuire et al., 1997; Petitto et al., 2000).

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This paper examines the role that the two cytoarchitectonic subdivisions of Broca's region play in language production in hearing subjects fluent in both American Sign Language (ASL) and English. By examining languages whose modes of comprehension-production are dramatically different (i.e. auditory-oral for spoken languages such as English, visual-gestural for ASL), any conclusions we draw should pertain to the most general aspects of language production.

Probabilistic maps of the two Brodmann areas constituting Broca's area were obtained by Amunts et al. (1999). These maps were derived by histological analysis that determined the locations and spatial extents of BA44 and BA45 in the left and right hemispheres in serial coronal sections of 10 individual brains, as mentioned above, after which the cytoarchitectonic data were transposed to a common space so as to form a probabilistic atlas, where voxel value indicates the percentage of brains having that location as BA44 or BA45. We combined these maps with functional brain activation data obtained by positron emission tomography (PET) (Braun et al., 2001), thus allowing us to determine the probability that BA44 or BA45 was activated during language production tasks relative to motor control tasks. Most neuroimaging studies of language employ relatively simple tasks in which specific linguistic elements can be isolated and individually studied. We chose to have our subjects "tell a story" while they were being scanned, thus allowing us to examine language production in connected discourse as it is used in everyday life. In this way, the interpretation of any differences in the activation of BA44 and BA45 will not depend upon any single linguistic element.

2. Materials and methods

2.1. Positron emission tomography

2.1.1. Subjects

The PET data used in this study were obtained from two groups of subjects: (1) Bilinguals—11 healthy volunteers (six males and five females, age range: 28–56 years) who were the adult children of deaf parents and were fluent in both English and ASL (Braun et al., 2001); these subjects were exposed to both English and ASL as native languages from birth, and continued to use both languages daily at the time of the study; (2) Monolinguals—20 healthy volunteers (12 males and 8 females, age range: 23–50 years) who were native speakers of English and had no knowledge of ASL (Braun et al., 1997). All subjects were right handed, and were free of medical or neuropsychiatric disorders. These studies were conducted under a protocol approved by the NIDCD-NINDS IRB (NIH 92-DC-0178). Written informed consent was obtained according to the declaration of Helsinki. Subjects were compensated for participating. Details about subjects and procedures, and portions of the PET data, can be found in Braun et al. (2001, 1997).

2.1.2. Tasks

In the studies of Braun et al. (1997, 2001), a number of experimental conditions were employed, of which five are considered here: (1) REST—each subject lay quietly in the scanner with his/her eyes patched (eyes remained covered for all conditions); (2) SPEECH—each subject was told to recount spontaneously a remembered incident from his life (e.g. some event that occurred during a vacation) using vocal speech with normal speech rate, intonation and rhythm; (3) ASL—same as (2), except the subject was instructed to use ASL rather than spoken English to produce a spontaneous narrative using normal production rate, extent of signing space, and rhythm; (4) ORAL_CTRL—each subject produced self-generated laryngeal and oral articulatory movements and associated sounds devoid of linguistic content employing all of the muscle groups activated during speech; (5) LIMB_CTRL—subjects made self-generated bilateral, non-symmetrical, non-routinized movements of the hands and arms, along with simple movements of the upper and lower face, similar in rate and range as those used during signing, but lacking linguistic content.

The bilingual subjects were scanned during all five conditions; the monolingual subjects were scanned during REST, SPEECH, and ORAL_CTRL. The sequence of tasks was randomized across subjects; the stories that the bilingual subjects recounted for one language (English or ASL) were continuations of those produced for the other language. Subjects underwent training in all tasks before PET scanning.

2.1.3. PET scanning and data analysis

Details of the scanning protocol were presented in Braun et al. (1997, 2001). In brief, data were acquired on a Scanditronix PC2048-15B tomograph (Uppsala, Sweden): 15 contiguous slices with a resolution of 6.5 mm FWHM in all directions. A transmission scan was used to correct for attenuation. For each scan 30 mCi of H_2O^{15} was injected intravenously. Regional brain radioactivity concentration was used as an index of regional cerebral blood flow (rCBF) (Fox, Mintun, Raichle, & Herscovitch, 1984).

Data obtained from PET were analyzed using SPM (Wellcome Department of Cognitive Neurology, London, UK, http://www.fil.ion.ucl.ac.uk/spm/). Preprocessing steps included image registration, spatial smoothing (15 mm × 15 mm × 9 mm), and spatial normalization into the stereotactic space of the Talairach & Tournoux atlas (1988). In this paper we are only interested in activations in the region of the inferior frontal gyrus and so we limited our statistical analysis solely to this area. We performed a series of pairwise SPM contrasts and retained all voxels with a Z exceeding 2.33 (which corresponds to $P < 0.01$, one-tailed, uncorrected). Use of this threshold for our analysis is conservative because it protects against claims about differences in activation for ASL and SPEECH in BA44 and BA45.

2.2. Cytoarchitectonic data analysis

2.2.1. Cytoarchitectonic analysis and probabilistic mapping

The cytoarchitectonic analysis was presented in detail in Amunts et al. (1999). Briefly, cytoarchitectonic mapping of BA44 and BA45 of 10 individual brains (five males, five females) was accomplished using an observer-independent method (Schleicher, Amunts, Geyer, Morosan, & Zilles, 1998) that evaluates the gray level index representing volume fraction of cell bodies along vertical trajectories from the cortical surface to the white matter. Statistically significant changes in the laminar distribution of the gray level index are used to detect transitions between cytoarchitectonic areas.

A high resolution MR of each of the 10 individual brains was transformed (Schormann & Zilles, 1998) into the standardized space of the European Computerized Human Brain Database (ECHBD) (Roland & Zilles, 1996), which uses the coordinates of Talairach space. The probabilistic value for a particular Brodmann area for each voxel in this space was computed as the percentage of the 10 subjects having their cytoarchitectonic data for that Brodmann area mapped to that voxel. For our purposes, we divided each of the two Brodmann regions (BA44 and BA45) into a core area consisting of voxels that were found in the majority of postmortem brains (five or more for BA45; four or more for BA44, since there was no voxel common to more than eight brains) and a peripheral area consisting of voxels which were found in a minority of the postmortem brains (images of the cytoarchitectonic data can be found at http://www.fz-juelich.de/ime/ProbabilityMaps_eng.html).

2.2.2. Combining PET and cytoarchitectonic data

The PET data were resliced so that their voxel size matched the volumes containing the cytoarchitectonic data (1 mm × 1 mm × 1 mm). The PET data were then mapped onto the cytoarchitectonic volumes. Differences between the various templates used for standardized space are small in the region around Broca's area [e.g. see (Brett, Christoff, Cusack, & Lancaster, 2001) (http://www.mrc-cbu.cam.ac.uk/imaging/mnispace.html) for a comparison of the brain template of the Montreal Neurological Institute (MNI) and the Talairach atlas; Indefrey et al. (2001) discuss the MNI template as compared to the ECHBD template].

Our findings will be illustrated in Figs. 1 and 2, where the following convention is employed. The cytoarchitectonic data are shown in blue; dark blue corresponds to core voxels and light blue to peripheral voxels. Voxels that were significantly activated in one task condition relative to another are

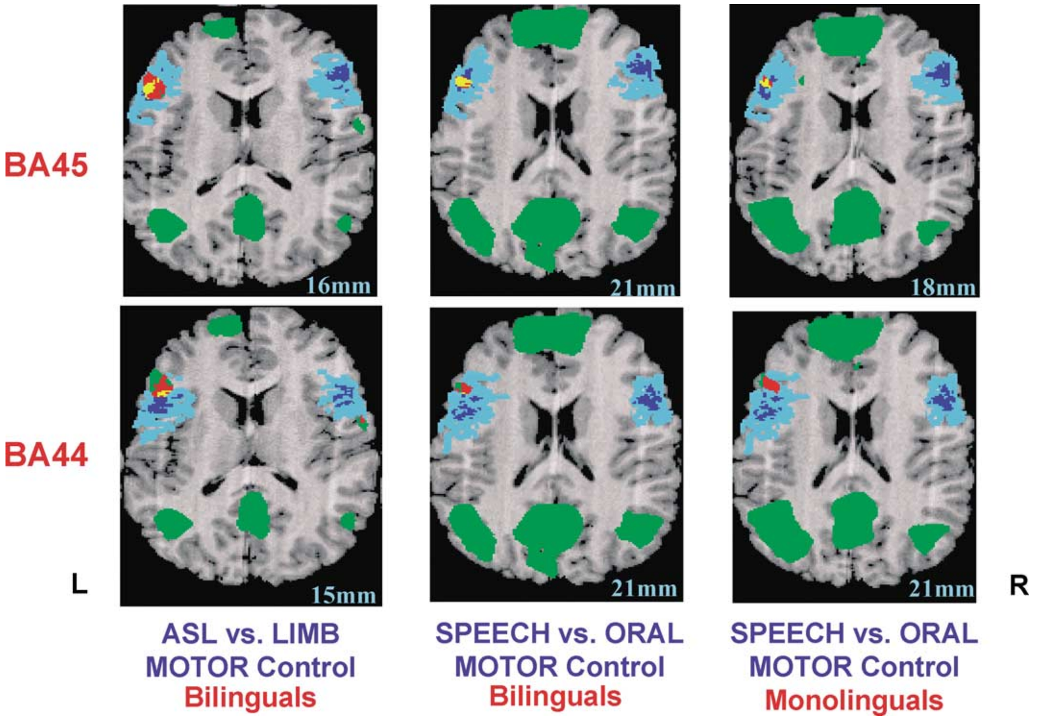

Fig. 1. Activations of BA45 (top row) and BA44 (bottom row) during production of language narratives compared to a motor control task. Shown are representative horizontal slices (left side of each image corresponds to the left side of the brain; the level in mm superior to the AC-PC plane (z-coordinate of Talairach & Tournoux, 1988) is indicated on each slice). Images displayed in the two columns on the left are from the bilingual (English and ASL) subjects, and those in the column on the right are from the monolingual English speakers. Voxels in dark blue correspond to core parts of the specific Brodmann area, those in light blue to peripheral voxels. Voxels significantly more active in one condition compared to a second ($Z > 2.33$) are shown in green. Voxels in the peripheral part of a Brodmann area that had a significant PET activation are displayed in red, and core voxels that were significantly activated are shown in yellow.

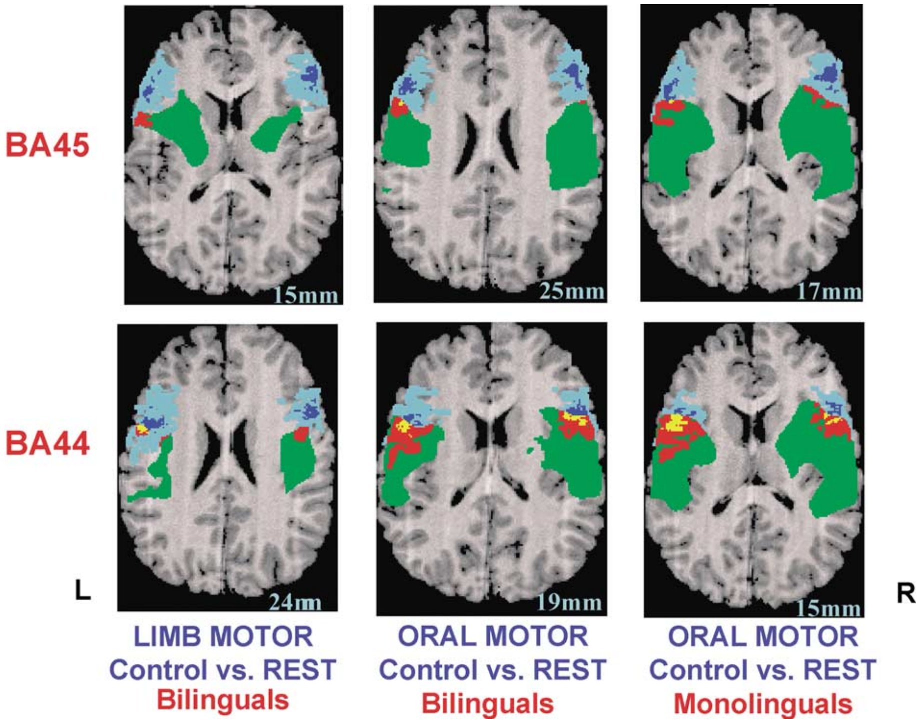

Fig. 2. Activation of BA45 (top) and BA44 (bottom) comparing each motor control task to a resting condition. See caption to Fig. 1 for the conventions used.

shown in green. PET activations in core voxels are shown in yellow and in peripheral voxels in red.

The number and percentage of core voxels that were activated by the various contrasts of interest in each hemisphere were computed.

3. Results

Our results are presented in Tables 1 and 2. Shown are the Talairach *z* (dorsal–ventral with respect to the anterior–posterior (AC–PC) commissure plane)-coordinates for the slices in which core BA45 (Table 1) and core BA44 (Table 2) were activated in each hemisphere in the various contrasts. Also shown are the number and percentage of core voxels activated for the two cytoarchitectonically defined regions. Results are presented separately for the bilingual and monolingual groups.

For BA45 we found consistent core activation in the left hemisphere when language production, whether produced verbally or using ASL, was compared to the appropriate motor control task, as illustrated in Fig. 1 (images

Table 1
Number and percentage of activated core BA45 voxels

Task comparisons	Left hemisphere		Right hemisphere	
	Core slices activated	Total no. of activated core voxels (percentage of total) (total no. of core voxels = 1053)	Core slices activated	Total no. of activated core voxels (percentage of total) (total no. of core voxels = 1493)
Bilinguals				
SPEECH–ORAL_CTRL	15–24 mm	186 (18%)	None	0 (0%)
ASL–LIMB_CTRL	7–21 mm	346 (33%)	None	0 (0%)
ASL–SPEECH	None	0 (0%)	None	0 (0%)
SPEECH–ASL	None	0 (0%)	None	0 (0%)
ORAL_CTRL–REST	24–26 mm	21 (2.0%)	None	0 (0%)
LIMB_CTRL–REST	None	0 (0%)	None	0 (0%)
Monolinguals				
SPEECH–ORAL_CTRL	14–30 mm	392 (37%)	None	0 (0%)
ORAL_CTRL–REST	16–18, 24 mm	16 (1.5%)	None	0 (0%)

Table 2
Number and percentage of activated core BA44 voxels

Task comparisons	Left hemisphere		Right hemisphere	
	Core slices activated	Total no. of activated core voxels (percentage of total) (total no. of core voxels = 2193)	Core slices activated	Total no. of activated core voxels (percentage of total) (total no. of core voxels = 1405)
Bilinguals				
SPEECH–ORAL_CTRL	32–36 mm	16 (0.7%)	None	0 (0%)
ASL–LIMB_CTRL	7–21 mm	134 (6%)	None	0 (0%)
ASL–SPEECH	None	0 (0%)	None	0 (0%)
SPEECH–ASL	None	0 (0%)	None	0 (0%)
ORAL_CTRL–REST	6–36 mm	1068 (49%)	9–30 mm	587 (42%)
LIMB_CTRL–REST	12–29 mm	314 (14%)	17–19 mm	7 (0.5%)
Monolinguals				
SPEECH–ORAL_CTRL	26 mm	6 (0.3%)	None	0 (0%)
ORAL_CTRL–REST	6–36 mm	1402 (64%)	9–28 mm	380 (27%)

showing the results for all brain slices for each contrast can be found at http://www.nidcd.nih.gov/research/scientists/horwitzb_supp.asp). This was the case for both the bilingual subjects and for the monolingual subjects. Not a single BA45 core voxel in the right hemisphere was activated in these contrasts. Although ASL, compared to its motor control task, appeared to activate almost twice the number of core voxels as did SPEECH compared to its motor control task in the bilingual subjects, when the two language production tasks (ASL and SPEECH) were compared directly to each other, no core voxels in BA45 were significantly more active for one language relative to the other in either hemisphere.

The findings in BA44 are considerably different than those in BA45. Essentially, very few voxels were activated in either hemisphere when SPEECH was contrasted to its motor control task in both the bilingual and monolingual subjects (see Table 2 and Fig. 1). There was a small amount of left BA44 activation for ASL compared to its control task, but, as a percentage of the total number of core voxels, it was only one-third that seen for BA45 (an examination of the images presented in the supplementary material indicates that the PET voxels that extend into the core part of BA44 for the ASL-control task contrast arise from the posterior part of the PET activation centered on BA45). As was the case for BA45, not a single right hemisphere BA44 core voxel was activated in either group by either language production task. When the two language production tasks (ASL and SPEECH) were compared directly to each other in the bilingual group, no core voxels in BA44 were significantly more active in either hemisphere for one language versus the other.

The reason for the lack of significant BA44 activation is clear if we contrast each of the motor control tasks against REST (see Tables 1 and 2). Although few BA45 core voxels show significant activation, there is extensive core BA44 activation in the left hemisphere in both bilingual and monolingual subjects. This is especially the case for the oral motor control task, for which there is also an extensive activation in core BA44 in the right hemisphere. Fig. 2 illustrates these findings.

4. Discussion

In this study, we combined probabilistic cytoarchitectonic maps of Brodmann areas 44 and 45, the major constituents of Broca's area, with PET activation data obtained during language production from subjects who were bilingual for both spoken English and American Sign Language. We divided each cytoarchitectonic area into core and peripheral portions, with the core parts consisting of those voxels occurring in the majority of the mapped brains. We found consistent activation of the core part of BA45 for both ASL and SPEECH in the left hemisphere. There were no significant differences in any core or peripheral voxels contrasting ASL and SPEECH directly, suggesting that the same parts of BA45 are used for both sign and speech. There was very little, if any, BA45 core activation during the motor control tasks, when compared to rest. Comparable results were found for a group of monolingual speakers. For BA44 in the left hemisphere, very little core activation was found for SPEECH in the bilingual and monolingual groups, but there was a small amount of core BA44 activation for ASL. However, there was extensive activation of the core BA44 when comparing both motor control tasks to rest. These results provide important information about the role of these two cytoarchitectonic subdivisions in language production.

The advantages of using a probabilistic atlas to better define the spatial location of PET or fMRI activations has been commented on by a number of researchers (Binkofski et al., 2000; Indefrey et al., 2001; Morosan et al., 2001; Roland & Zilles, 1998). It has been argued that cytoarchitectonics represents a better structural correlate for defining brain functional fields than does gyral/sulcal location, even though cytoarchitectonics itself is a limited measure and likely to be supplemented when more information about the regional distribution of numerous neurochemical markers (e.g. receptors) becomes available (for reviews, see Roland & Zilles, 1998 and Zilles et al., 2002). However, at present cytoarchitectonic designations can only be obtained in autopsied tissue. The probabilistic brain atlas approach, therefore, represents a workable compromise for assigning cytoarchitectonic designations to brain locations in subjects undergoing functional brain imaging studies.

We have two key results. First, we found extensive involvement of BA45 and little or no involvement of BA44 for language production when one "subtracts out" non-linguistically meaningful motor and auditory production. Consistent with this result, we found extensive activation in BA44, and hardly any in BA45, for the motor control tasks compared to rest. The second key result is that these patterns of activation were the same for both SPEECH and ASL in the bilingual subjects. Moreover, the activation patterns observed in the monolingual subjects were similar to those in the bilingual subjects for both the speech production task and for the oral motor control task.

There have been extensive discussions in the literature concerning the fractionation of the left inferior frontal gyrus into functionally distinct subregions. For example, Fiez (1997), Poldrack et al. (1999) and Bokde et al. (2001) have provided evidence indicating that for single words the dorsal/posterior part of this gyrus is involved with phonological processing, whereas the ventral/anterior portion is engaged by semantic processing. Likewise, it has been suggested that a part of Broca's area, the pars opercularis (which traditionally is associated with BA44) is implicated in processing syntactic information, whereas the lower portion of the left inferior frontal gyrus, the pars orbitalis (usually assigned to BA47), is selectively involved in processing the semantic aspects of a sentence (Dapretto & Bookheimer, 1999). Indeed, many authors have suggested that Broca's area is activated by syntactic processing (see Caplan, 2001 for a review), although the critical location(s) remain uncertain.

The finding that it is BA45, and not BA44, that is extensively activated by our narrative production tasks, after controlling for generation of the movements and sounds associated with language production, is a clear demonstration that there is a functional fractionation of the left inferior frontal gyrus. Specifically, our results reveal that this functional fractionation seems to respect the cytoarchitectonic subdivisions associated with Broca's area. The consistent activation of left BA45 during both speech production and ASL production in the bilingual subjects, and by speech production in the monolingual subjects, strongly indicates that BA45 in the left hemisphere plays a fundamental role in language production, possibly processing the more modality-independent features of language (e.g. syntax). Indeed, neither the oral nor the limb motor control tasks generated much activation of the core voxels of BA45. Our data cannot rule out a significant role for BA45 in semantic processing, although the evidence cited above (e.g. Bokde, Tagamets, Friedman, & Horwitz, 2001; Dapretto & Bookheimer, 1999) points to a greater involvement of the more ventral and anterior portions of the inferior frontal gyrus. Future studies using finer-grained linguistic tasks (and control tasks) will be necessary to ascertain exactly which processes activate BA45, and which do not, and whether these linguistic processes are the mediated by BA45 for both sign and speech.

In contrast to BA45, we found that the more posterior portion of the inferior frontal gyrus, BA44, was not activated by the language production tasks to any great extent in the monolingual subjects, nor was it greatly activated in the bilingual subjects for either speech or sign production. Rather, almost all of the activation in core BA44 could be accounted for by the complex, non-linguistic, laryngeal and limb motor and sound production components associated with speech and sign production. That tasks lacking linguistic components can activate BA44 has been shown by Binkofski et al. (2000); they found, using the probabilistic cytoarchitectonics for Broca's area, that BA44 was activated by a motion imagery task. The posterior part of Broca's area (thought to include BA44) has been activated during object manipulation tasks (Binkofski et al., 1999) and imitation (Iacoboni et al., 1999). The presumed homologous area in macaque monkey (F5) contains so-called 'mirror' neurons—neurons whose activity increases when the monkey either performs a specific action, or observes the performance of that action (Gallese, Fadiga, Fogassi, & Rizzolatti, 1996). Rizzolatti and Arbib (1998) have proposed that such neurons constitute an important part of the neural substrate on which human language evolved.

Another functional brain imaging study that has employed the probabilistic cytoarchitectonics of Broca's area, that of Indefrey et al. (2001), examined speech generation and found some activation in BA44 when comparing sentence generation versus single word generation, although the most prominent effect involved an area caudal to BA44, most likely in the Rolandic part of BA6. Comparison with our findings is difficult because both of the tasks compared by Indefrey et al. contained linguistic features. We emphasize that we are not claiming that BA44 plays no role in language production. Rather, our results suggest that comparable amounts of neural resources in BA44, as indexed by rCBF, are used for both language and complex motor production. It may be that it is differences in the interregional functional connectivity of this region that determines how these resources are used (Horwitz & Braun, in press; Horwitz, Jeffries, & Braun, 2000). It is also possible that if we had used a simpler motor control task, then we would have been able to demonstrate activation of BA44.

The narrative production tasks we used in this study correspond to language production in its fullest, most ecologically valid, form (Braun et al., 1997, 2001; Mazoyer et al., 1993). As such, they include the classical subdivisions of language—phonology, syntax, and semantics—as well as higher-order linguistic elements such as pragmatics. The advantages and disadvantages of utilizing such tasks have been addressed in detail (Braun et al., 1997, 2001; Mazoyer et al., 1993). Some discussion of the disadvantages was given in the two previous paragraphs. One key advantage, as stressed by Braun et al. (2001), is that tasks designed to investigate a specific linguistic component are obviously artificial and could very well engender a specific strategy not utilized during natural language functioning, which in turn, could affect the observed patterns of activation.

The fact that the pattern of activation in the core parts of BA44 and BA45 in the bilinguals was statistically the same for both speech and sign speaks to the neural organization of language, at least when acquired early in life[1]. It has been demonstrated by several groups that subjects who learn a second language early in life appear to utilize the same neural resources in the left frontal lobe for both (Kim, Relkin, Lee, & Hirsch, 1997; Klein, Milner, Zatorre, Meyer, & Evans, 1995; Perani et al., 1998), even for languages such as spoken English and ASL, which employ totally different mechanisms for sensory input and motor output (Braun et al., 2001; Neville et al., 1998). Also, Petitto et al. (2000) demonstrated that profoundly deaf signers use similar left hemisphere neural resources for language processing as do normal speakers. What could not be determined from these studies was whether these results extended to the level of defined cytoarchitecture in the inferior frontal gyrus. Our findings suggest that even at the level of cytoarchitectonic subdivisions, languages as diverse as spoken English and ASL when learned early in life engage the same neural resources in Broca's region, specifically BA45.

As more researchers employ probabilistic brain atlas data in conjunction with functional neuroimaging, a number of technical issues need to be addressed in order to develop an efficient and reliable method for combining the two data sets. First, use of the probabilistic atlas with functional imaging depends on having both the cytoarchitectonic and the functional imaging data mapped into the same standard brain space. Each subject's data, whether cytoarchitectonic or functional, is put into this common space by using some algorithm to transform the subject's brain (which could be represented by an MRI, or by images of the functional data) so as to match a template brain as closely as possible. Even though the coordinate system of the space of the template brains corresponds to the Talairach & Tournoux atlas (1988), there are several template brains that have been used as the targets of the spatial mapping algorithms (e.g. the brain in the Talairach atlas, the MNI brain template and the ECHBD template). As was mentioned in Section 2, each differs from the others, although the differences are most pronounced in the superior and inferior axial planes (Brett et al., 2001). Each template has particular advantages and disadvantages (e.g. the MNI template corresponds to the average of a large number of individual MRI scans, but does not have the detailed anatomical definition of the ECHBD template, which was obtained from scanning a single subject using high resolution MRI). A second complication is that there are also multiple algorithms for spatially normalizing an individual brain to match the template brain (e.g. Ashburner & Friston, 1999; Schormann & Zilles, 1998), and these different methods will not necessarily result in identical mappings. As more probabilistic cytoarchitectonic maps are produced, and more researchers want to label the locations of their activations in terms of cytoarchitectonic fields, it will probably become necessary for the major statistical analysis packages in current use (e.g. SPM, AFNI) to adopt a unified convention as to which target brain (or brains) to employ, and which spatial normalization algorithm(s) to use. A thorough discussion of many of these issues can be found in Brett, Johnsrude, and Owen (2002).

A final issue concerns spatial smoothing of functional brain imaging data. The use of probabilistic cytoarchitectonic atlases with functional neuroimaging data places two conflicting demands on how much spatial smoothing is applied to the PET or fMRI data. On the one hand, it would seem that one should reduce (or even eliminate) the smoothing that is generally employed (15 mm × 15 mm × 9 mm for the PET data we used; a typical value for fMRI data is 6 mm in all three dimensions), to prevent the convolving together of activations from different cytoarchitectonic fields. Conversely, the scanning devices themselves have intrinsic spatial resolutions that are much greater than the cytoarchitectonic data. Furthermore, the statistical analyses used to determine the significant activations of the PET/fMRI data require a certain amount of smoothing so that the assumptions of Gaussian random field theory are met (Worsley et al., 1996). Determining the correct amount of smoothing to employ that meets these opposing requirements, and that is sensitive to the exact nature of the study (e.g. whether the analysis is investigating a group of subjects, or looking at individuals), will necessitate further investigation.

In conclusion, using probabilistic cytoarchitectonic maps of BA44 and BA45 (Broca's area) and PET data, we have shown that it is essentially BA45, not BA44, that is engaged during the production of language narratives in bilingual subjects fluent from early childhood in both English and ASL when the generation of complex movements and sounds are accounted for. It is BA44 that is activated by the generation of complex movements in both modalities, not BA45. Finally, the same patterns were obtained in a group of English speaking monolingual subjects during speech production. These findings thus implicate BA45 as the part of Broca's area that represents the conceptual-language

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[1] The situation in late bilinguals—those who learned a second language after early childhood—is complicated by a number of issues, including the age at which the second language was acquired, and the degree of proficiency (Perani et al., 1998). As far as frontal cortex is concerned, there is some disagreement as to whether or not late bilinguals utilize the same areas for both the first and second language (e.g. different areas, Kim, Relkin, Lee, & Hirsch, 1997; same areas, Klein, Milner, Zattore, Meyer, & Evans, 1995). In one study involving sign language, Newman et al. (2002) showed that both ASL native signers and signers who had learned ASL post-puberty activated the left inferior frontal gyrus to the same extent during the processing of ASL sentences; no significant activations were reported in the corresponding part of the right hemisphere.

interface that is fundamental to the modality-independent aspects of language generation.

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