Perisylvian Language Networks of the Human Brain

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Early anatomically based models of language consisted of an arcuate tract connecting Broca's speech and Wernicke's comprehension centers; a lesion of the tract resulted in conduction aphasia. However, the heterogeneous clinical presentations of conduction aphasia suggest a greater complexity of perisylvian anatomical connections than allowed for in the classical anatomical model. This article re-explores perisylvian language connectivity using in vivo diffusion tensor magnetic resonance imaging tractography. Diffusion tensor magnetic resonance imaging data from 11 right-handed healthy male subjects were averaged, and the arcuate fasciculus of the left hemisphere reconstructed from this data using an interactive dissection technique. Beyond the classical arcuate pathway connecting Broca's and Wernicke's areas directly, we show a previously undescribed, indirect pathway passing through inferior parietal cortex. The indirect pathway runs parallel and lateral to the classical arcuate fasciculus and is composed of an anterior segment connecting Broca's territory with the inferior parietal lobe and a posterior segment connecting the inferior parietal lobe to Wernicke's territory. This model of two parallel pathways helps explain the diverse clinical presentations of conduction aphasia. The anatomical findings are also relevant to the evolution of language, provide a framework for Lichtheim's symptom-based neurological model of aphasia, and constrain, anatomically, contemporary connectionist accounts of language.

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After Paul Broca's report[1] of a patient with disordered speech production and a lesion of the left posterior inferior frontal gyrus, Carl Wernicke[2] described a posterior temporal area devoted to auditory word processing. Wernicke postulated the existence of a direct connection between the two areas, and that a lesion of this theoretical pathway would cause an aphasia characterized by normal language comprehension and fluent conversational speech but the inability to repeat what had just been heard. In fact, a prominent pathway connecting posterior frontal and superior temporal lobes had already been described by Burdach and was later confirmed by Dejerine who referred to the pathway as Burdach's arcuate fasciculus.[3] Clinical evidence for Wernicke's theoretical "conduction" aphasia has accumulated over many years.[4] However, such descriptions fall short of supporting Wernicke's model. The trouble is that many of the cases have lesions involving both the arcuate fasciculus and its overlying cortex. In some patients, the lesion extends directly into Wernicke's or Broca's areas, whereas in others it extends to the inferior parietal lobe, a region now recognized as having an important linguistic function in its own right.[5] Wernicke's conduction aphasia thus could be equally well explained by cortical deficits as by a true disconnection of Wernicke's and Broca's areas.

The advent of structural imaging allowed this issue to be addressed in aphasic patients without recourse to postmortem dissection. Such studies confirmed that Wernicke's conduction aphasia could occur with lesions restricted to white matter tracts[6,7]; however, it also became clear that Wernicke's original anatomical formulation was incomplete. Wernicke's model predicted that lesions at any point along the course of the arcuate fasciculus should result in an identical aphasia. Yet, clinically, this is known not to be the case with conduction aphasias forming a heterogeneous group ranging from "Broca-like" to "Wernicke-like" deficits.[6,8] Clearly, Wernicke's model requires revision. What has been missing is a detailed description of the arcuate fasciculus that takes into account developments in linguistic anatomy since Burdach's and Dejerine's original arcuate dissections.

In 1985, the modification of a conventional magnetic resonance imaging (MRI) sequence permitted quantification of the diffusion characteristics of water molecules in vivo.[9] Within cerebral white matter, water molecules diffuse more freely along myelinated tracts

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than across them[10]; such directional dependence of diffusivity is termed *anisotropy*. By combining anisotropy data with the directional dependence of the hindrance of water diffusion, it is possible to obtain estimates of fiber orientation.[11] This has led to diffusion tensor "tractography"[12–16] in which the three-dimensional pathways of white matter tracts are reconstructed by sequentially piecing together discrete and shortly spaced estimates of fiber orientation to form continuous trajectories. Although the fiber tracts dissected are virtual and require further anatomical validation, the technique has been successfully used to study human brain thalamic connections,[17] occipitotemporal connections,[18] and other white matter tracts,[12,19,20] and therefore appears to be a powerful technique with which to re-examine the anatomy of the arcuate fasciculus and the connectivity of perisylvian language areas.

Subjects and Methods

Subjects and Data Acquisition

Eleven subjects (mean age, 33.3 ± 4.7 years) were recruited. All gave written informed consent, and the study was approved by the Institute of Psychiatry research ethics committee. Because sex[21] and handedness influence language laterality, the study contained only right-handed male subjects. Data were acquired on a GE Signa 1.5 Tesla LX MRI system (General Electric, Milwaukee, WI) with 40mT/m gradients, using an acquisition sequence fully optimized for diffusion tensor magnetic resonance imaging (DT-MRI) of white matter, providing isotropic resolution (2.5 × 2.5 × 2.5 mm) and coverage of the whole head. The acquisition was gated to the cardiac cycle using a peripheral gating device placed on the subjects' forefingers. Full details of the acquisition sequence are provided in Jones and colleagues.[22] After correction for the image distortions introduced by the application of the diffusion-encoding gradients, the diffusion tensor was determined in each voxel following the method of Basser and colleagues.[11] After diagonalization of the diffusion tensor, the fractional anisotropy,[23] a scalar measure that reflects the degree to which the diffusivity depends on the orientation in which it is measured, was computed in each voxel.

Spatial Normalization and Averaging of Diffusion Tensor Magnetic Resonance Imaging Data Sets

The DT-MRI data sets were spatially normalized to the anatomical reference space defined by the MNI EPI template supplied as part of the of the functional imaging analysis software package SPM99 (Statistical Parametric Mapping; Wellcome Department of Cognitive Neurology, London, UK; www.fil.ion.ucl.ac.uk/spm/spm99.html). Spatial normalization of tensor volumes is more complicated than that for scalar volumes (eg, T1-weighted intensity maps), because the orientations of the tensor must be correctly preserved.[24] Once normalized, a mean of 10 diffusion tensors in each voxel was computed to produce a mean diffusion tensor volume data set. Full details of the spatial normalization procedure and generation of an average DT-MRI volume have been provided previously.[25]

Tractography: Definition of the Regions of Interest and Three-Dimensional Visualization

A virtual dissection of the arcuate fasciculus of the left hemisphere was performed using approaches with one and two regions of interest (ROIs), as described in Catani and colleagues.[19] Guided by color fiber orientation maps,[26] an ROI was defined on the fractional anisotropy map computed from the average DT-MRI volume to encompass the horizontal fibers lateral to the corona radiata and medial to the cortex extending from Talairach $z = 22$ to $z = 28$ (Fig 1). All fibers passing through this ROI (a one-ROI approach) were reconstructed in three dimensions and visualized using illuminated streamtubes.[19] The fractional anisotropy volumes were resliced in axial, coronal, and sagittal planes and displayed in conjunction with tractography results to allow approximate neuroanatomical location of the tract reconstructions. A two-ROI approach was used to perform further detailed dissection of the arcuate fasciculus, allowing us to separate different sets of fibers within the arcuate bundle. Here, two spatially separated regions are defined in the fractional anisotropy volume, and all fibers passing through both are visualized, as described earlier. The approach does not constrain tracts to start and end within the defined regions, only to pass through them. The delineation of regions used in two-ROI dissections was guided by the results of the one-ROI dissection (see later).

Results

Figure 2 shows the reconstructed arcuate tract defined using a one-ROI approach. The tract originated in the cortex of the posterior part of the ventrolateral frontal lobe, passing backward to the inferior parietal lobe where it arched around the lateral fissure to terminate in the posterior part of the superior and middle temporal gyrus (the terms *origin* and *termination* are arbitrary because tractography is blind to fiber direction). The ventral portion of the frontoparietal tract segment ran dorsal to the external capsule and to the insular cortex (see Fig 2). These reconstructions correspond exactly to the descriptions of the arcuate fasciculus made by Burdach and Dejerine. An unexpected feature was that, although in its medial portion the arcuate fasciculus appeared homogenous along its entire length, at its most lateral aspect, its fibers projected to three distinct cortical regions (see Fig 2). The presence of a parietal projection is inconsistent with Wernicke's model, and this result prompted us to perform further virtual dissections to explore the anatomy of the arcuate fasciculus in more detail. Using a two-ROI approach based on the three distinct regions identified in Figure 2, we identified three types of connections: (1) a long segment corresponding to the classical arcuate fasciculus connecting frontal and temporal lobes located medially (red fibers in Fig 3); (2) a posterior lateral segment connecting temporal and parietal lobes (yellow fibers in Fig 3); and (3) an anterior lateral segment connecting frontal and parietal lobes (green fibers in Fig 3).

To confirm that this pattern of tractography-defined

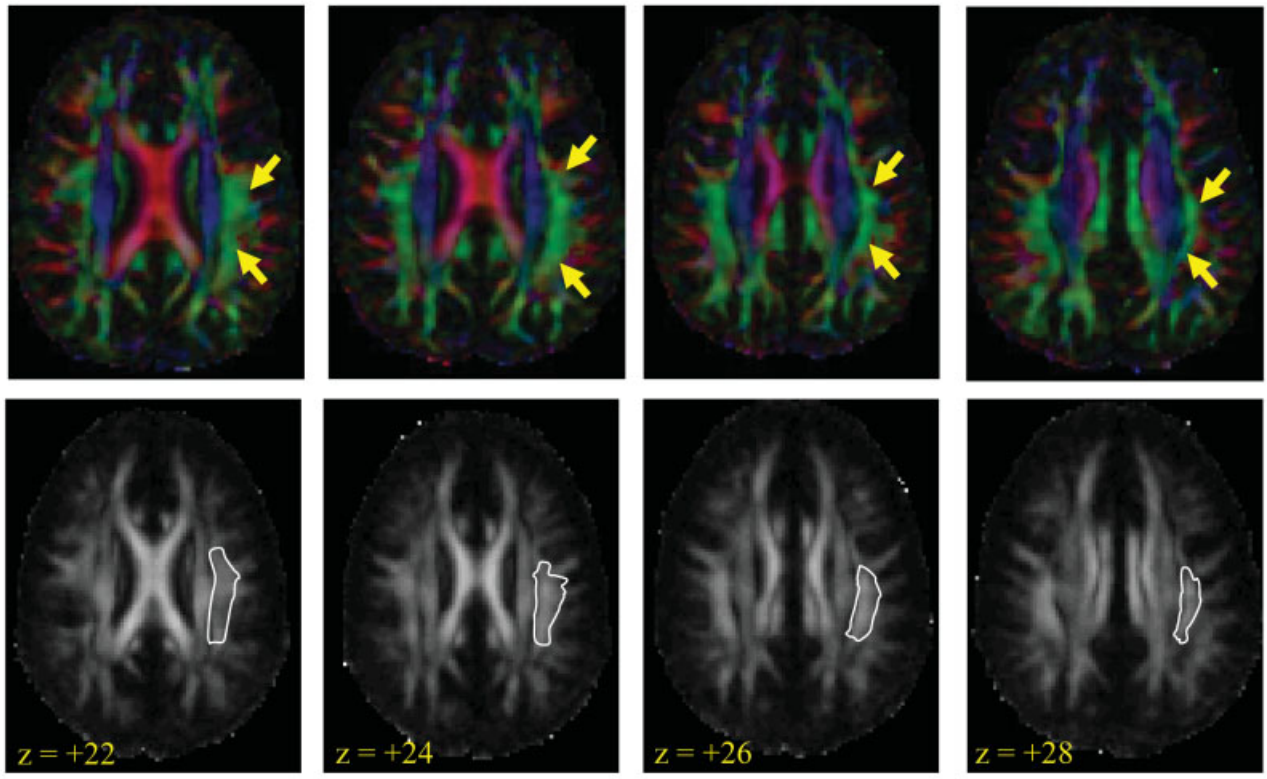

Fig 1. Delineation of the region of interest around the arcuate fasciculus. The top row shows axial color fiber orientation maps from a single subject (Talairach z *= 22–28). Fibers that are predominantly oriented lateral-to-lateral are shown in red, anterior-posteriorly or vice versa in green, and superior-inferiorly or vice versa in blue. Green fibers lateral to the vertical corona radiata belong to the arcuate fasciculus (yellow* arrows *indicate the anterior and posterior extent of the arcuate fibers). Guided by the color fiber orientation map, a region of interest (encircled in white) was defined around the fibers in the average fractional anisotropy image.*

connectivity was not an artifact of averaging (ie, the results in Figs 2 and 3 were obtained from the average brain DT-MRI data set), we examined six individual brains chosen at random from the group for evidence of the same perisylvian network. Figure 4 shows the tractography results for the six subjects. The three distinct segments of the arcuate fasciculus are present in all, although individual variations are also evident. For

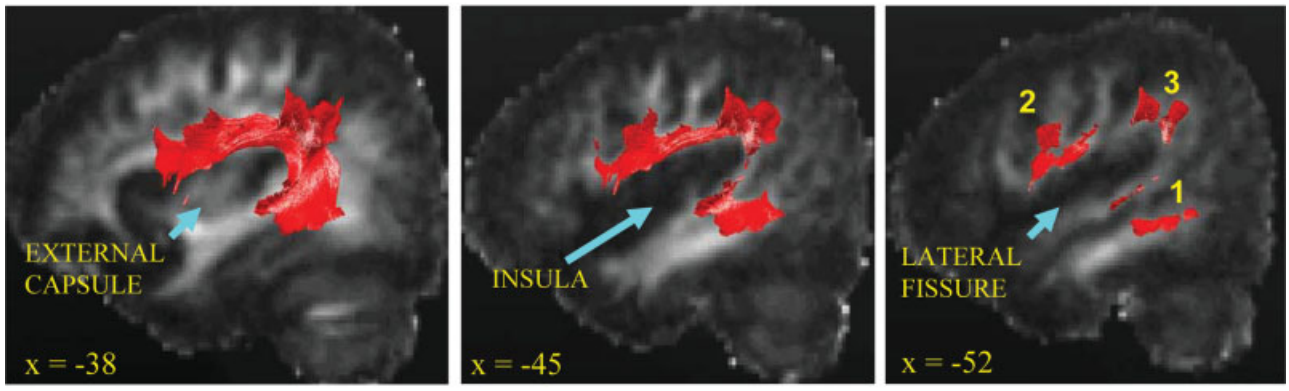

Fig 2. Tractography reconstruction of the arcuate fasciculus using the one-region of interest approach. Sagittal sections (Talairach x *= −38 to −52) of the arcuate fasciculus (red) in the average brain superimposed on the fractional anisotropy image. Note the color coding used in tractography images differs from that used for the color fiber orientation maps. The reconstruction has a close correspondence to classical postmortem anatomical descriptions of the arcuate bundle that originates in the posterior part of the ventrolateral frontal lobe, arches around the external capsule medially (left panel) and insula cortex laterally (middle panel), and ends in the temporal lobe. The lateralmost section (Talairach* x *= −52) shows three cortical termination territories (numbered 1–3).*

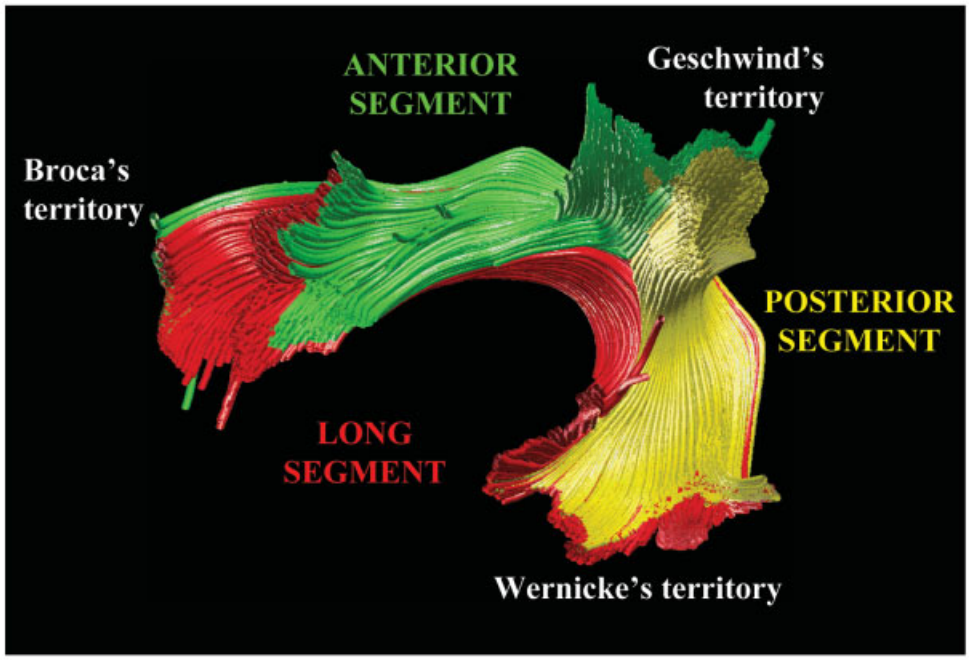

Fig 3. Tractography reconstruction of the arcuate fasciculus using the two-region of interest approach. Broca's and Wernicke' territories are connected through direct and indirect pathways in the average brain. The direct pathway (long segment shown in red) runs medially and corresponds to classical descriptions of the arcuate fasciculus. The indirect pathway runs laterally and is composed of an anterior segment (green) connecting the inferior parietal cortex (Geschwind's territory) and Broca's territory and a posterior segment (yellow) connecting Geschwind's and Wernicke's territories. Note the color coding in this figure differs from that used in Figures 1 and 2.

example, in Subject 1, the anterior segment (see Fig 4, green) is more prominent than the posterior segment (see Fig 4, yellow), whereas the opposite is true in Subject 6. The temporal lobe terminations also vary across subjects. For example, the long posterior segment terminations extend further along the temporal lobe in Subjects 3, 5, and 6 than in Subjects 1, 2, and 4.

Discussion

DT-MRI tractography helped visualize putative pathways in vivo between perisylvian language areas of the left hemisphere. The results point to two parallel pathways connecting temporal and frontal regions: a direct pathway (long segment) corresponding to the pathway anticipated by Wernicke, and a novel, indirect pathway connecting temporal with parietal (posterior segment) and parietal with frontal regions (anterior segment). Although the indirect pathway requires further anatomical validation, several independent lines of evidence support its existence. First, classical anatomists had noted the presence of cortico-cortical fibers lateral to the arcuate fasciculus[3]; however, unaware of the linguistic functions of the parietal lobe, they had no reason to consider the fibers as part of a perisylvian language network. Second, intraoperative electrocorticography studies investigating perisylvian language networks in humans have shown bidirectional connectivity from Broca's area to both superior temporal and inferior parietal regions.[27] Of further relevance to the indirect pathway, an unexplained delay was found in the response evoked in superior temporal cortex by stimulation of Broca's area and vice versa.[27] The delay is consistent with the presence of an extra synapse in the pathway, and although the authors suggest a possible Broca–subcortical–Wernicke pathway to account for the results, they are equally explicabley by our indirect Broca–parietal–Wernicke pathway. Third, path analysis of functional MRI activity during linguistic processing points to a functional connection between Broca's area and parietal cortex unaccounted for by the classical arcuate model.[28] In the next section, we propose functions for the two parallel pathways based on previous studies of aphasic patients, place the anatomical model in an evolutionary context, and discuss its implication for neurological models of language.

The Function of Direct and Indirect Perisylvian Pathways

Our study suggests a greater complexity of connectivity between frontal and temporal language regions than previously supposed, allowing for a variety of distinct disconnection syndromes not predicted by the classical arcuate model. McCarthy and Warrington[29] reported

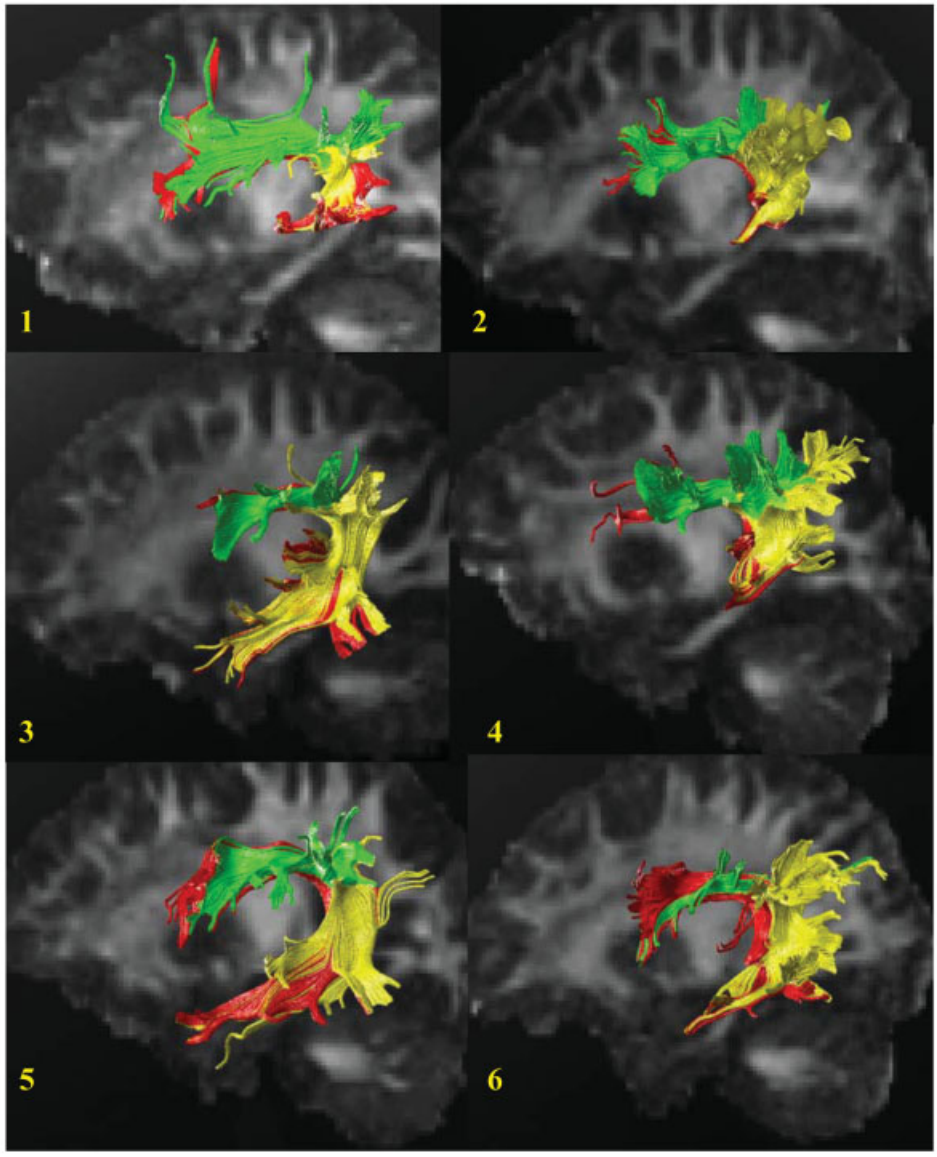

Fig 4. Tractography reconstructions of the direct and indirect pathways in six individual subjects superimposed on sagittal fractional anisotropy data. The three segments are color coded using the conventions of Figure 3. Both direct and indirect pathways are present in each subject, but an intersubject variance is evident.

three aphasic patients, two of which had a complementary deficit to the third. The two patients had a temporoparietal lesion that resulted in an impaired performance in repetition tasks but relatively preserved spontaneous speech and comprehension (classical conduction aphasia). In contrast, the third patient had a superficial parietal lesion resulting in impaired spontaneous speech but relatively intact repetition (transcortical motor aphasia). The patients with a deep lesion were facilitated in repetition tasks that required active semantic processing, whereas the patient with a superficial lesion was impaired. The opposite dissociation was observed in tasks that required passive repetition. The patients with a deep lesion were impaired, whereas the patient with a superficial lesion was facilitated. The authors proposed a two-route model of speech production: a direct pathway between Wernicke's and Broca's areas acting in fast, automatic word repetition, and an indirect pathway where a stage of verbal comprehension and semantic/phonological transcoding intervened between verbal input and articulatory output. Our tractography findings appear to provide an anatomical substrate for the findings of McCarthy and Warrington.[29] The deep intracerebral lesions in the first two patients would have affected predominantly the direct long segment pathway (the classical arcuate fasciculus) that lies medial to the indirect pathway. In contrast, the superficial cortical lesion of the third patient

would have affected predominantly the indirect pathway or its parietal cortical relay station.

Our revised arcuate anatomy also suggests the possibility of two further aphasic disconnection syndromes: one based on an isolated lesion of the anterior segment, and the other based on an isolated lesion of the posterior segment. We would speculate that, for the McCarthy and Warrington model,[29] semantic/phonological transcoding would be affected in both syndromes but in different ways. A lesion of the anterior segment would be expected to alter connectivity between Broca's area and the parietal region, resulting in a failure to vocalize semantic content. In contrast, a lesion of the posterior segment would be expected to alter connectivity between Wernicke's area and the parietal region, resulting in a failure of auditory semantic comprehension. These two theoretical syndromes bear some resemblance to the subtypes of aphasia first described by Lichtheim,[30] which have later been referred to as transcortical motor and sensory aphasia.[31] In the former, spontaneous speech is reduced, but comprehension and repetition are intact. In the latter, comprehension is reduced, but fluency and repetition are spared. The location of the lesion in transcortical sensory aphasia is entirely consistent with damage to the posterior segment between the posterior temporal and parietal lobes.[31,32] Transcortical motor aphasia is associated with widespread frontal lesions, some of which are likely to have affected the anterior segment.[33]

In summary, the combined evidence from patients with aphasic disconnection syndromes, and our interpretation of such evidence in light of the parallel pathway model, suggests the following functions for indirect and direct pathways: the indirect pathway appears to relate to semantically based language functions (such as auditory comprehension and vocalization of semantic content), whereas the direct pathway relates to phonologically based language functions (such as automatic repetition). This is not to say that these functions are restricted to perisylvian areas, but merely that within the parallel pathways we describe, the two functions are anatomically dissociable. Exactly how other functions such as verbal working memory, syntax, reading, and writing relate to the parallel pathways, or how the pathways themselves connect to other extrasylvian language areas, remains unclear.

Broca-like and Wernicke-like Conduction Aphasia

The direct and indirect pathways model provides a novel explanation for the clinical observation that conduction aphasias fall into two distinct groups: the Broca-like syndrome in which the deficit in repetition is accompanied by a relative impairment in fluency and the Wernicke-like syndrome in which the deficit in repetition is accompanied by a relative impairment in comprehension.[6,8] One explanation for this dichotomy is that more anterior lesions encroach on Broca's area, whereas more posterior lesions encroach on Wernicke's area; the two resulting aphasias being a mixture of cortical deficits (Broca's or Wernicke's) and subcortical conduction deficits. However, cases of Broca-like or Wernicke-like conduction aphasias have been described in patients with pure subcortical lesions,[6] an observation that suggests this explanation is incorrect. We suggest that Broca-like and Wernicke-like conduction aphasias result from lesions involving direct and indirect pathways at different points along their course. A lesion located anteriorly and involving the long and anterior segments would lead to Broca-like conduction aphasia, whereas a lesion located posteriorly involving the long and posterior segments would lead to a Wernicke-like conduction aphasia. Our explanation is consistent with clinical evidence that Broca-like conduction aphasias occur with subcortical frontal lesions, whereas Wernicke-like conduction aphasias occur with subcortical temporoparietal lesions.[6]

From Language Centers to Language Territories

The distribution of arcuate fiber terminations found by tractography extends beyond the classical limits of Broca's areas (Brodmann Area, BA44 and 45)[34] to include part of the middle frontal gyrus and inferior precentral gyrus. This wider distribution is consistent with several lines of evidence that Broca's area (in the restricted sense used earlier) is surrounded by cortical regions with specializations for higher level aspects of language.[27,34,35] We refer to this extended region as Broca's *territory*. Interestingly, the tractography evidence appears to suggest that long segment direct fibers project to anterior Broca's territory, whereas the anterior segment of the indirect pathway projects more posteriorly (see Fig 3). This anatomical segregation of arcuate fibers suggests a rostrocaudal segregation of function within Broca's territory, a segregation that echoes the findings of functional imaging studies.[36,37]

Although Wernicke's original description was of a temporal lobe language area, the term Wernicke's area subsequently has been used to include inferior parietal areas, as well as posterior temporal areas,[38] a region that encompasses BA22, 37, 39, and 40.[34] Our tractography results suggest that the posterior temporal and inferior parietal regions of Wernicke's area are extensively connected but distinct, an observation that agrees with functional anatomical studies of Wernicke's area that have argued that the term should be reserved for the posterior temporal region.[39] As is the case for Broca's territory, the distribution of tractography-defined fibers in the posterior temporal region is wider than the classical model, suggesting a segregation of function and an extended Wernicke's territory (including the posterior part of both the superior and middle temporal gyrus) rather than a localized center. This view is supported by func-

tional imaging and neuroanatomical studies suggesting a segregation of language functions in the posterior temporal lobe.[37,40]

Our tractography results highlight the importance of the inferior parietal cortex as a separate primary language area with dense connections to classical language areas through the previously undescribed indirect pathway. The region corresponds to BA39 and 40, and although its importance as a linguistic area has been recognized for some time, recent neuroimaging studies have highlighted its importance for semantic processing.[41] Norman Geschwind[5] emphasized the importance of the region in ideational speech, suggesting that, through cortico-cortical interactions, the convergence of multimodality sensory inputs in the inferior parietal lobe allowed the development of semantic content. The development of this area and its perisylvian connections is thought to have coincided with the emergence of language in humans[5,34] (see later). In recognition of Geschwind's contribution, we refer to this region as *Geschwind's territory.*

Comparative Anatomy and Phylogeny of Perisylvian Language Networks

Perisylvian connections in the monkey brain have been studied extensively using fiber tracing techniques; however, their significance with respect to language remains controversial because the homologies between cortical areas in monkeys and humans are unclear.[42,43] Initial studies concluded that there was no equivalent of the arcuate fasciculus in the monkey, with fibers originating in the posterior superior temporal gyrus (the putative homologue of Wernicke's area) projecting to a region of frontal cortex, dorsal and anterior to the putative homologue of Broca's area (in proximity to the inferior extent of the arcuate sulcus).[44] However, later work using more sensitive techniques showed a specific pattern of connectivity between both the inferior parietal cortex and the putative Wernicke homologue with the Broca homologue and areas surrounding it.[45,46] A recent review[42] concludes that in the macaque, a rudiment of the arcuate fasciculus may exist; however, both its origin and termination sites appear to be more diverse than in the human brain, and prominent connections are found between the inferior partial lobule and Broca's homologue, for which "there is no information of such corresponding connections in the human brain." Our tractography results perfectly bridge these apparent discrepancies between monkey and human anatomy. First, our fiber tracts extend beyond the classical language areas to form the territories described earlier, corresponding to the diversity of origin and termination sites found in the macaque. Second, our finding of an anterior segment connecting Geschwind's and Broca's territories mirrors the prominent inferior parietal to frontal fiber pathway described in the monkey. Finally, the tractography-defined cortical distribution of fibers within Broca's territory bears a striking resemblance to that described in the monkey. In the monkey, a rostrocaudal separation of projections to inferior frontal cortex is found; that is, the more rostral regions receive projections from the Wernicke homologue and the more caudal regions receive projections from the inferior parietal lobe.[45] This mirrors our finding that long segment fibers (from Wernicke's) connect to anterior portions of Broca's territory, whereas anterior segment fibers (from Geschwind's) connect to the posterior portions of Broca's territory.

One theory of the evolution of language from monkey to human is that it involves a change in the strengths of perisylvian connections. Aboitiz and Garcia[34] argue that two evolutionary tendencies are involved. First, posterior superior temporal and inferior parietal regions became increasingly connected, linking the auditory system and a pre-existing parietal–premotor loop involved in the generation of complex vocalizations. Second, the development of connections between posterior superior temporal and inferior frontal regions links auditory information to orofacial premotor regions. We would argue that these two tendencies correspond to the evolution of posterior and long segments, respectively, the anterior segment being, phylogenetically, the oldest component of the perisylvian network. An alternative theory argues that human language evolved from the mirror neuron system in the monkey through a sequence of stages involving grasp imitation, protosigns, and protospeech.[42] Although the theory does not invoke the strengthening of connections, the mirror neuron system includes inferior frontal, inferior parietal, and superior temporal regions overlapping those in our model.

Methodological Issues

We should stress the difference between measuring anatomical connections directly and inferring white matter trajectories with DT-MRI tractography. The former would require the ability to identify the cell bodies that give rise to the axons of interest, then to identify the neurons with which the axonal terminals synapse, in addition to the trajectory of the axons from one site to the other. Obtaining this information in the human brain in vivo noninvasively is, of course, currently impossible. The intrinsic resolution of our DT-MRI data was $2.5 \times 2.5 \times 2.5$ mm. With such resolution, one cannot hope to resolve individual axons, neurons, and synapses. Therefore, we have to rely on proxy techniques to infer information about white matter pathways. DT-MRI tractography takes the bulk-averaged tissue properties in each voxel and, by fitting a model to the data, infers the dominant fiber orientation within each voxel. These discrete estimates of fiber orientation are pieced together to provide estimates of the

trajectory of the fasciculus of interest. Each estimate of fiber orientation is subject to noise contamination,[47] which can lead to accumulated errors and low repeatability (precision) in tract reconstructions (although our use of the two-ROI approach serves to minimize the effect of this confound). Furthermore, inadequacies in the model (eg, incomplete modeling of the diffusion process at intersections/crossing of fibers[48]) can also contribute to errors in tract reconstruction. Therefore, one should perhaps always refer to the trajectories elucidated by DT-MRI tractography as "tractography-defined" pathways, and, clearly, any results obtained through tractography should be investigated using "gold standard" techniques such as postmortem dissection. However, even within these confounds, the tractography-defined direct pathways presented in this article correspond exactly to previously published postmortem descriptions, and the indirect pathway is largely consistent across the six subjects examined individually. Furthermore, electrocorticographic and functional MRI path analysis studies provide independent evidence for a functional connection between Geschwind's and Broca's territories, as would be predicted by the tractography-defined parallel pathway model.[27,28] Tractography is also unable to determine the exact cortical origin and termination of fibers, therefore we can only infer the territories of projection.[18,25] It should be noted that in this article we only studied the connections of perisylvian cortex and that other brain regions are likely to connect to the network (eg, the insula). Also, our network is limited to long associative fiber connections and does not include superficial U-shaped fibers or thalamic connections, which may also play a role in language.[38] Finally, our study is restricted to the left hemisphere of right-handed male subjects. Whether the pattern of connectivity identified in this article varies with hemisphere, sex, or handedness are questions for future study.

From Associationist to Connectionist Models of Language

In 1885, Lichtheim[30] proposed an extension to the existing Broca–arcuate–Wernicke model, based on the careful observation of aphasic symptoms he encountered clinically. He hypothesized an additional pathway between Wernicke's and Broca's areas through a theoretical third center thought to be related to semantic processing, which he referred to as the concept center. Although the existence of a concept center and its connections remained theoretical through lack of anatomical evidence, Lichtheim's model proved a useful clinical classificatory tool, widely adopted by clinicians for the bedside assessment of aphasia. Our tractography findings provide anatomical support for Lichtheim's original scheme. In fact, the direct and indirect pathway model suggested by our tractography dissections closely matches the theoretical wiring diagram outlined in Lichtheim's 1885 article. This is not to say that Lichtheim's model is entirely consistent with contemporary views. Lichtheim conceived language in associationist terms of *centers* and *pathways,* the general assumption being that visual and auditory linguistic information was processed in localized cortical regions with the serial passage of information between such regions through white matter tracts. However, such associationist models have been criticized on several grounds.[49] An alternative "connectionist" account has been proposed in which linguistic functions are conceived as resulting from parallel distributed processing performed by distributed groups of connected neurons rather than individual centers.[50,51] Although tractography evidence alone cannot distinguish between these alternative models, some aspects of our results are more supportive of the connectionist account. First, our finding of extended language territories argues against the associationist concept of localized centers. Second, the fiber bundles identified appear unnecessarily large for the simple serial transfer of signals from one region to another. Instead, their size suggests that subsets of fibers connect different linguistic subregions in parallel. The picture that emerges is of multiple parallel connections among subspecialized cortical regions of Broca's, Wernicke's, and Geschwind's territories consistent with Mesulam's large-scale neural network model of language.[52]

Conclusions

We have shown that the perisylvian language areas of the left hemisphere are connected by two parallel pathways. The findings may provide an explanation for the observation that lesions disconnecting Broca's and Wernicke's areas cause different clinical aphasia syndromes depending on their location. Although the pathways shown by our tractography method are closely related to those hypothesized by Lichtheim, they go beyond his model in their support of a connectionist account of linguistic function with processing distributed between brain territories rather than localized within specific centers. Tractography appears to be a valuable technique both in helping to understand normal and aphasic language function and in providing anatomical constraints for connectionist accounts of language.

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