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Contemporary model of language organization: an overview for neurosurgeons

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Classic models of language organization posited that separate motor and sensory language foci existed in the inferior frontal gyrus (Broca's area) and superior temporal gyrus (Wernicke's area), respectively, and that connections between these sites (arcuate fasciculus) allowed for auditory-motor interaction. These theories have predominated for more than a century, but advances in neuroimaging and stimulation mapping have provided a more detailed description of the functional neuroanatomy of language. New insights have shaped modern network-based models of speech processing composed of parallel and interconnected streams involving both cortical and subcortical areas. Recent models emphasize processing in "dorsal" and "ventral" pathways, mediating phonological and semantic processing, respectively. Phonological processing occurs along a dorsal pathway, from the posterosuperior temporal to the inferior frontal cortices. On the other hand, semantic information is carried in a ventral pathway that runs from the temporal pole to the basal occipitotemporal cortex, with anterior connections. Functional MRI has poor positive predictive value in determining critical language sites and should only be used as an adjunct for preoperative planning. Cortical and subcortical mapping should be used to define functional resection boundaries in eloquent areas and remains the clinical gold standard. In tracing the historical advancements in our understanding of speech processing, the authors hope to not only provide practicing neurosurgeons with additional information that will aid in surgical planning and prevent postoperative morbidity, but also underscore the fact that neurosurgeons are in a unique position to further advance our understanding of the anatomy and functional organization of language.

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The pursuit of defining how the human brain processes language is one of the greatest challenges in neuroscience. Pierre Broca and Karl Wernicke made fundamental contributions at a time when the practice of localization by phrenology was pervasive. Their careful studies were some of the first to define functional localization in the brain by studying patients with defined brain injuries and lesions. Over time, their names have become synonymous with two key brain areas for language function: the inferior frontal gyrus and superior posterior temporal area, respectively.

The brain regions that bear their names are now universal in every medical student's education. However, the dichotomy of language production based in the frontal lobe and language comprehension based in the temporal lobe is a commonly oversimplified interpretation of their work. For example, injuries to Wernicke's area result in abnormal speech production in addition to deficits in comprehension. Frontal lesions can also result in higher-order comprehension deficits. Thus, the language network is more complicated and integrated than commonly appreciated. In the last 15 years, an exponential increase in the number of studies on the neurobiology of language has improved our understanding of potential mechanisms, but many fundamental questions remain unresolved.

Our goal in this overview is to provide an update to neurosurgeons by comparing classic with more recent models of language organization. It is not meant to be an exhaustive review of language research, which is beyond our intended scope, but rather to introduce contemporary theories and briefly review selected neurosurgical experience with stimulation-based language mapping. This will

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ABBREVIATIONS DTI = diffusion tensor imaging; fMRI = functional MRI; IFOF = inferior fronto-occipital fasciculus; MTG = middle temporal gyrus; PVWM = periventricular white matter; SLF = superior longitudinal fasciculus; SMA = supplementary motor area; STG = superior temporal gyrus; STS = superior temporal sulcus.

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enable the practicing neurosurgeon to better understand how language may be affected when operating within different brain regions.

Classic Models

Early theories of language organization revolved around the assignment of cortical activity based on lesion studies. Even before Broca's landmark 1861 paper appeared in *Bulletin de la Société Anatomique*, Jean-Baptiste Bouillaud followed a series of patients with frontal lobe abnormalities in either hemisphere. Because these patients demonstrated long-term clinically evident speech loss, he made the claim that speech arrest occurred exclusively from frontal lobe lesions.[103] It was in this setting that Broca made his significant contributions. He described this speech loss as follows: "What is lost…is not the memory of the words nor the action of the nerves and of muscles of phonation and articulation. It is a particular faculty…to articulate language; for without it, no articulation is possible."[5]

Initially, Broca held that speech loss could arise from lesions to either hemisphere, as was described previously. Over time, however, he grew to believe that articulate language was organized in a specific dominant hemisphere, while speech comprehension was carried out bilaterally. Broca described numerous patients who had lost the ability to speak for many years, including the famous Leborgne and Lelong, who each developed right-sided paralysis later in their course of illness. Most of these patients had lesions to the pars opercularis and pars triangularis in the left inferior frontal gyrus or in adjacent peri-sylvian parietal structures.[5] Still, Broca acknowledged that hemispheric dominance and handedness were probably related—that left-handed individuals were as such due to an organic preference for the right hemisphere of the brain—so that some individuals could have right hemispheric articulate speech organization. In fact, he argued that articulate speech is organized similarly irrespective of hemispheric dominance.[5] Finally, Broca described the case of a 47-year-old epileptic woman with intact speech whose autopsy revealed congenital atrophy of the peri-sylvian structures of the left hemisphere, suggesting that neural plasticity and reorganization could cause right hemisphere dominance. These theories were later supported when Hughlings Jackson described a left-handed man with aphasia that was caused by a right-hemisphere lesion[16] and in other acquired lesional case studies and confirmed with the advent of intracarotid amobarbital injection.[91,108]

Soon after Broca made his groundbreaking observations, Karl Wernicke, influenced by his mentor Theodor Meynert, described lesions in the posterior superior temporal lobe that caused paraphasic errors with impaired naming, repetition, and comprehension, but with fluent speech.[111] He dubbed this region "the area of word images," and went a step further in postulating that this region was connected to the anterior peri-sylvian region described by Broca. In doing so, Wernicke implicitly acknowledged the presence of two discrete language sites: an area anterior to the Rolandic cortex involved in motor processing and an area posterior to the Rolandic cortex serving sensory functions[1,90] (Fig. 1). Wernicke believed that lesions to these commissural fibers deep to the insula led to repetition errors with intact fluency and comprehension, a syndrome he termed "conduction aphasia." While numerous individuals challenged Wernicke's theory, Norman Geschwind reaffirmed the "disconnection hypothesis" by proposing that lesions to the arcuate fasciculus—the white matter tract connecting the posterior portion of the superior temporal lobe to the inferior frontal lobe—caused conduction aphasias.[41] This revived the connectionist theories of language, which posit that most behavioral phenomena of language arise from the emergent processes of interconnected networks.

Based on these anatomical findings, the Wernicke-Geschwind language model proposed that upon hearing a word as a child, a sensory word image was created; simultaneously, a motor word image would emerge as a result of the cortico-cortical connections between the two primary language areas (Fig. 1). These sensory and motor word images, however, were not equivalent to the associated concepts. Instead, the sensory (acoustic) word image was located purely in the auditory cortex, and the meaning behind the word (the concept) existed in various, diffuse cortical connections emanating from the language centers. Thus, the Wernicke-Geschwind model proposed that spontaneous speech production involved "awakening" of the concept, which then sequentially activated the sensory and motor word images. In this way, the acoustic image was deemed necessary for the selection of the proper motor word image.

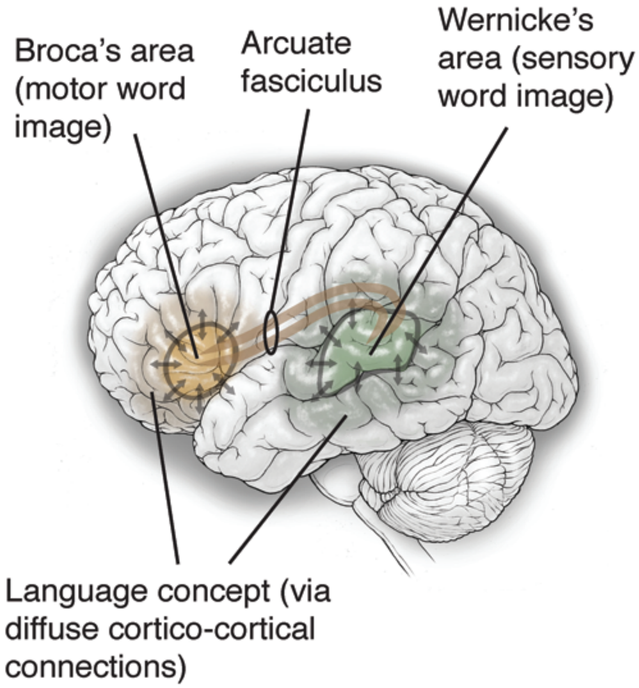

FIG. 1. Classical model of language organization in the left hemisphere of the brain. Broca's area *(gold)* is located in the inferior frontal lobe and Wernicke's area *(green)* in the posterior superior temporal lobe, connected by the arcuate fasciculus. Language concepts *(shaded)* surround each canonical language area. *Arrows* represent diffuse cortico-cortical connections between Broca's/Wernicke's area and the widely dispersed language concepts. Copyright Edward F. Chang. Published with permission.

Unfortunately, the classic model of language organization falls short in a few areas, as has been described previously.[90] First, the Wernicke-Geschwind model fails to take into account inherent linguistic complexities, including the computational differences between phonological (sound), lexical (word), and semantic (meaning) processing.[90] Second, many reports now describe the fact that these classically described aphasias (Broca's, Wernicke's, and conduction aphasias) do not exclusively occur from lesions to their anatomically prescribed regions.[1,10,26,48,72,104] Specifically, Dronkers and colleagues in 2007 used modern MRI to characterize the brains of Leborgne and Lelong.[25] Besides damage to the canonical Broca's area, they revealed significant lesions to the inferior parietal lobe and insula as well as subcortical structures, including the basal ganglia and various white matter tracts. Thus, the full extent of long-term articulatory language loss described by Broca likely involved these additional lesions. This underscores the importance of noncortical structures, which previously were not believed to be involved in language representation.

Two such subcortical structures are the thalamus and basal ganglia, although their exact functions in language processing remain unclear. Various models exist for their role, but a shared theme is that certain thalamic nuclei relay sensory inputs to cortical structures, whereas others are involved in cortico-thalamo-cortical pathways. Patients with compromised perfusion to the dominant thalamic hemisphere often display a transcortical aphasia-like syndrome similar to that observed in isolated supplementary motor area (SMA) lesions, with initiation deficits, mutism, dysnomia, and paraphasias, but intact repetition.[54,55] These studies, however, cannot differentiate between various thalamic nuclei due to overlapping vascular territories.

On the other hand, in patients undergoing thalamotomy for movement disorders, stimulation of the posterior ventrolateral and pulvinar nuclei caused anomia with mostly omission errors but intact speech,[80,81] while stimulation of the anterior ventrolateral nucleus led to repetition errors in which the same incorrect response was repeated for each stimulus.[78] Further studies showed that the anterior and mid-ventrolateral regions are involved in short-term recall and encoding of verbal memory.[81,82] These results occurred nearly exclusively in the dominant, left thalamic hemisphere. The basal ganglia likely play a complementary role, although the precise nature of the interaction remains controversial. Multiple theories exist regarding the role of the basal ganglia, including coordinating the timing cues for release of the language plan into speech,[11,19,68] simplifying the language plan itself by inhibiting redundant lexical information,[110] and applying grammatical rules to language.[106] Thus, even though it is clear that these subcortical gray matter structures play a role in speech production, further research is needed to explicitly characterize their involvement.

Modern Theories

Dual Stream Model of Language

Two recent models of cortical language organization have been proposed, both of which feature "dual streams" of information processing.[51,92] These models were heavily influenced by a widely accepted theory of dual stream neural processing in the vision system.[45] As visual information exits the occipital lobe, it follows either a ventral or dorsal stream. The ventral stream of vision, or "what" pathway, traverses the temporal lobe to support object recognition, whereas the dorsal stream of vision, or "how" pathway, terminates in the parietal lobe to process spatial location in the viewer's reference frame to help coordinate movement.

In the dual stream model of language, a similar scheme exists for information flow but originates from auditory processing. Speech sounds are initially processed by spectro-temporal and phonological analyses in the posterior superior temporal gyrus (STG) and the superior temporal sulcus (STS), the major components of the traditional Wernicke's area (Fig. 2). The ventral stream flows through to the anterior and middle temporal lobe, and is involved in speech recognition and the representation of lexical concepts. In addition to engaging in spatial processing, the dorsal stream is believed to carry out sensorimotor integration by mapping phonological information onto articulatory motor representations. Two separate auditory-motor

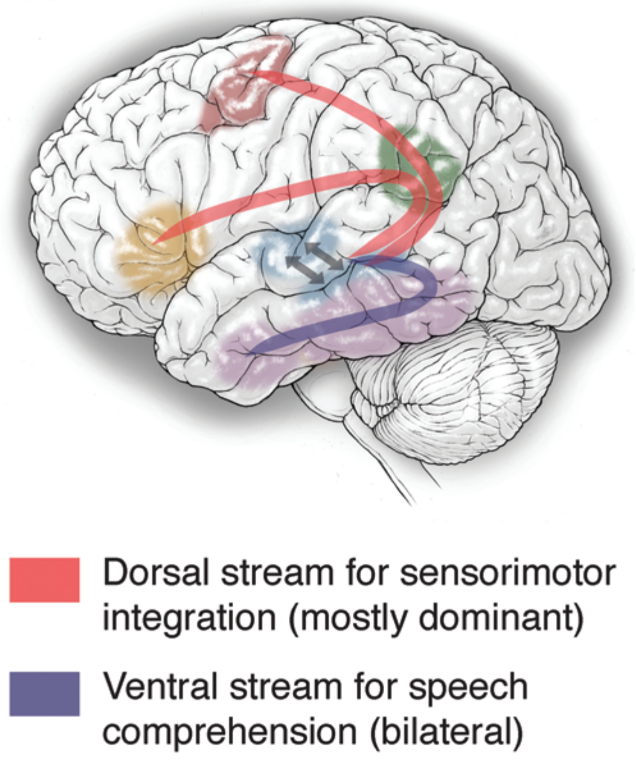

FIG. 2. Dual stream model of language. Regions shaded *blue* represent initial cortical processing of language in the STG and STS, engaging in spectro-temporal and phonological analysis, respectively. The ventral stream *(dark blue)* flows through to the anterior and middle temporal lobe *(shaded purple)*, and is involved in speech recognition and the representation of lexical concepts. The dorsal stream *(orange)* is believed to carry out sensorimotor integration by mapping phonological information onto articulatory motor representations. The premotor cortex *(shaded red)*, inferior frontal gyrus *(shaded gold)*, and the parietotemporal boundary region *(shaded green)* are involved in dorsal stream processing. Copyright Edward F. Chang. Published with permission.

interactions are believed to be engaged in dorsal stream processing: one that involves individual speech segments and is used to acquire and maintain basic articulatory phonetic skills, and a second involving sequences of speech segments that enable the learning of new vocabulary. This dorsal pathway, involving the posterior frontal lobe and the sylvian parietotemporal region, is likely left dominant based on lesion data involving the left dorsal STG and the temporoparietal junction.[20]

While the key features of these recent models are similar, there are also some important differences. For example, the Hickok-Poeppel model argues that speech perception is bilaterally processed, citing evidence from chronic lesion, acute stroke, Wada, and split-brain studies, whereas the Rauschecker-Scott model posits that speech is processed only in the dominant language hemisphere.[50,92] Functional imaging studies have shown that listening to speech activates bilateral dorsal STG and STS, suggesting that distinct recognition pathways exist in each hemisphere,[50] although the nondominant hemisphere appears to be selective for longer-term integration compared with the dominant hemisphere.[9] In addition, both lesion and functional neuroimaging studies have shown that the nondominant hemisphere is crucial to the processing of prosodic features such as emotional tone, which are important facets of everyday communication.[12,40,52,83,84] There are also differences in the localization of intermediate nodes in the dorsal stream: the Hickok-Poeppel model posits an area called sylvian parietotemporal region in the vicinity of the planum temporale/parietal operculum, whereas the Rauschecker-Scott model localizes this function to a more medial position in the inferior parietal lobe. The Hickok-Poeppel model argues that the sylvian parietotemporal region is important for auditory sensorimotor integration, but the Rauschecker-Scott model adds that auditory spatial information is also processed here.

The dual stream model of language processing has nonetheless had a dramatic influence on contemporary thinking about localization, and many language studies are now interpreted in this framework. It should be pointed out, however, that these general concepts were originally conceived by Wernicke in 1874. At that time, he already proposed that sensory representations of speech in the posterior temporal lobe interfaced with two distinct systems, a broadly distributed conceptual system for comprehension and the motor system to help support the production of speech. Therefore, the major contribution from recent models has been the refinement of anatomical localization, specification of language subprocesses, and most importantly, confirmation using best available evidence from the past half decade with modern imaging and careful lesion-deficit studies.

Intraoperative Cortical Mapping

Wilder Penfield published the first report of a large series of patients who underwent awake craniotomy with speech mapping at the Montreal Neurological Institute. It is unequivocal that the ability to perform resective operations in the so-called "forbidden territory" of language cortex was enabled and greatly advanced by Penfield. During awake craniotomy, patients undergo local anesthesia to facilitate the awake portion of the surgery, and general anesthesia for the exposure and closure.[85,86] Electrical stimulation (either bipolar or monopolar) is usually applied at 50–60 Hz, often manually with a handheld probe. Electrocorticography is often used to monitor for epileptic afterdischarges. When a positive effect is produced, a small ticket bearing a number or letter is placed on the brain surface intraoperatively. The routine language battery used by Penfield included counting, naming, and occasionally reading and writing tasks. As a testament to his ingenuity, the technique of speech mapping has been largely unchanged over time except for minor modifications in this above described technique, and can also be performed extraoperatively with implanted electrode arrays.[59,60]

Penfield described several forms of speech interference from electrical stimulation, including total speech arrest (anarthria), hesitation, slurring, distortion, repetition, and confusion (jumping from "six" to "twenty" and then back to "nine").[86] During the picture-naming task, he described other more complex effects such as the inability to name with retained ability to speak and the perseveration of words that were presented previously. In general, the locations of sites corresponding to these effects were found throughout the peri-sylvian region in the dominant left hemisphere (Fig. 3A).

Speech arrest sites were mostly found in the pars opercularis or precentral gyrus, but could also be found throughout the frontal operculum as well as the temporoparietal region. Penfield also described speech arrest sites in the nondominant right hemisphere at the pars opercularis, but without any sites located outside of this region. He reasoned that speech arrest occurring in the pars opercularis and along the ventral precentral gyrus was related to motor aspects of speech production. In contrast, he categorized the other types of errors, such as the inability to name with the retained ability to speak, as "aphasic" types of responses. These induced errors were largely localized to the posterior inferior frontal gyrus and the posterior temporal and inferior parietal regions of the dominant hemisphere. This distribution has been verified in subsequent large series from Ojemann and colleagues, and then Berger and coworkers in patients with tumors (Fig. 3B and C), and is similarly organized in patients with right-hemisphere language dominance.[16,24,32]

The collective findings from these stimulation studies have given rise to a more nuanced view of language organization compared with the various theories previously described. While the overall distribution of naming sites in peri-sylvian regions is largely consistent, there are some important distinctions. First, in a given individual, the location of essential language sites can be extremely variable and nearly impossible to predict preoperatively. Large patient series have contributed a new probabilistic perspective to localization. Because of the variability across patients, mapping is virtually always required for safely navigating language areas. Lesions or pathology—especially slow-growing low-grade gliomas—can induce cortical reorganization and plasticity with redistribution of eloquent areas into the tumor itself, adjacent parenchyma, or even in the contralateral hemisphere.[6,56,57,70] This

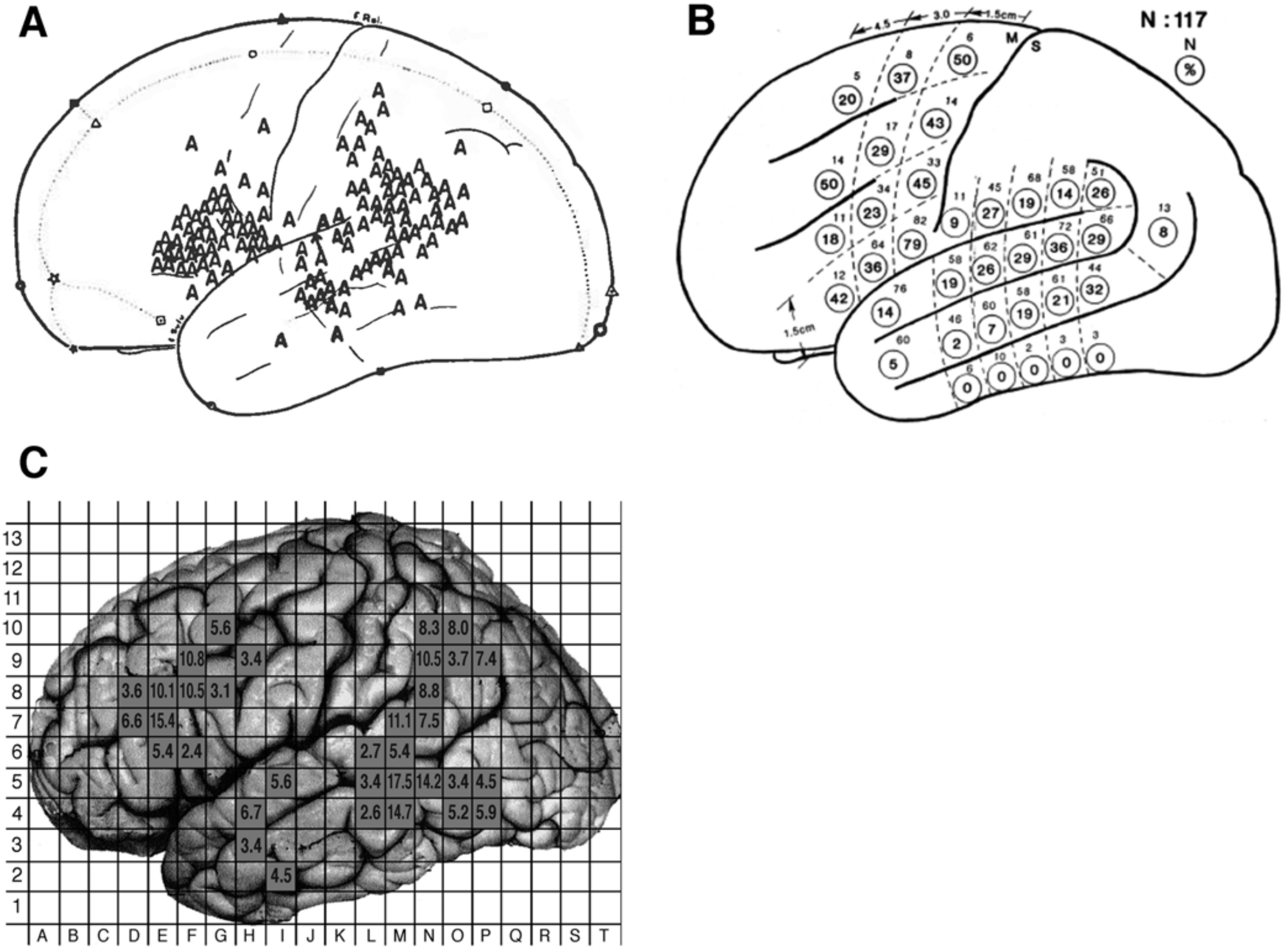

FIG. 3. Comparison of large patient series of cortical language mapping. **A:** Dysphasic and aphasic responses occur with stimulation of pars opercularis, the precentral gyrus, or the temporoparietal region, as presented in Penfield and Roberts (1959).[86] Sites leading to such responses are represented by the letter "A." Penfield, Wilder; *Speech and Brain Mechanisms.* © 1959 Princeton University Press, 1987 renewed PUP. Reprinted by permission of Princeton University Press. **B:** Stimulation sites leading to naming errors are highly variable between patients. One hundred seventeen patients were described in the study. The upper, noncircled number in each cortical zone (demarcated by *dashed lines*) represents the number of patients in whom stimulation occurred in the particular zone. Each circled number represents the proportion of those patients with significant language disturbance upon stimulation. "M" and "S" represent the precentral and postcentral gyrus, respectively. From the patient series of Ojemann et al., 1989.[77] **C:** Naming sites are distributed across frontal, temporal, and parietal regions. Of all stimulation sites, only a limited proportion cause language disturbance. Even within regions that cause anomia, positive stimulation sites may be adjacent to negative ones. Each shaded grid square represents a stimulation site. Inside each square is the percentage of stimulations that produced anomia. Adapted from Sanai N, Mirzadeh Z, Berger MS: Functional outcome after language mapping for glioma resection. *N Engl J Med 358:*18–27. Copyright © 2008 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

makes operative localization even more variable, requiring the use of functional boundaries for resection.

Second, essential cortical sites are usually found in a spatially confined (approximately 1 cm^2) cortical area and often are directly adjacent to sites that do not have any apparent effect from stimulation.[77,86] This mapping often conflicts with the far broader distribution of neural activation during similar tasks observed with functional imaging such as functional MRI (fMRI). An important distinction here is that the spatially discrete cortical sites identified during stimulation are essential for function, whereas most imaging captures areas that are involved but may not be critical. The likelihood of long-term postoperative language deficit appears to be correlated with the distance between the resection margin and essential cortical site, but not necessarily related to all fMRI activation areas. Resections have generally been tolerated up to 1 cm from these essential language sites without inducing permanent morbidity, although recent reports suggest that equivalent rates of permanent deficits occur when resections are performed without leaving a margin from positive stimulation sites.[43,46] It is important to note, however, that this "no-margin" technique does have higher rates of transient postoperative deficits.

Third, naming interruption is also found in the temporal and parietal areas, which challenges the traditional dichotomy of frontal lobe language production and temporal lobe language reception. Therefore, production and perceptual aspects of language are more fully integrated than commonly appreciated. Picture naming is the most common task used in language mapping. This seems appropriate given that dysnomia and word-finding difficulties are the most common language deficits after surgery or injury. Picture naming is a cognitive behavior with many subprocesses, which include (but are not limited to) visual object recognition, memory recall, semantic processing, lexical retrieval, phonological encoding, and articulatory planning and execution. Early models described a serial organization of these naming subprocesses; however, a new framework proposed by Hughes Duffau and colleagues argues that the phonological and semantic subprocesses occur in parallel, with dorsal and ventral streams, in a manner similar to that described by the Hickok-Poeppel model (see Duffau et al., 2014 for an excellent review).[34,61]

Although the most common effect of cortical stimulation during naming is no response,[18] when less frequent but specific errors are elicited, they can help further differentiate some selective linguistic subprocesses. For example, visual paraphasias have been reproducibly elicited during stimulation of the basal occipitotemporal cortex.[66] Semantic errors are often widespread and can be found in the posterior middle temporal gyrus (MTG) and anterior supramarginal gyrus as well as the inferior frontal gyrus.[3,18] Phonological paraphasias, neologisms, and circumlocutions are found in the STS. Errors in phonological processing can be observed in the posterior STG.[18]

Variations of the naming task have also elucidated other aspects of language organization. For example, auditory naming tasks have demonstrated a more anterior temporal localization compared with those found for picture naming.[47] Different localization has also been observed for noun versus verb naming, though the exact locations varied in individual subjects.[17] Specific functions can also be determined when essential sites identified with picture naming are compared with other tasks such as counting and reading. For example, posterior STG stimulation can cause speech arrest for all of these tasks, suggesting its potential role in the final pathway for temporal lobe speech planning before motor commands are executed in the frontal lobe. On the other hand, stimulation of the posterior inferior and central middle temporal gyri has been found to be selective for picture naming, suggesting a visual object representation input lexicon. Reading could be interrupted in the posterior MTG and inferior parietal lobule.[101] In contrast to the relatively variable localization for naming, sites for auditory discrimination using syllables and phonetic stimuli have been highly conserved in the posterior STG and MTG.[8,71]

Cortical stimulation in bilingual patients has demonstrated both distinct and shared sites supporting both languages.[62,109] Therefore, it is necessary to map both languages as part of operative planning. Traditionally, large craniotomies were required to fully evaluate all potential language areas. As surgeons have gained more experience with speech mapping, however, smaller craniotomies have been used, as negative mapping along the cortical surface can rule out potential language involvement during tumor resection.[96]

Although fMRI is unable to determine essential language sites, it is still a widely used tool for preoperative planning. Such studies are effective at language lateralization but depend both on the task used and the baseline to which neural activity during those tasks is compared.[7,95] Language expression tasks typically include verb generation, picture naming, and silent (covert) speech production, whereas comprehension tasks include passive listening as well as semantic speech or tone decision tasks, which involve working memory and general executive functions.[7] One particular task, the semantic decision/tone decision contrast developed by Binder and colleagues (2008), is predictive of postoperative verbal memory deficits and is highly concordant with Wada language testing in left hemisphere dominant individuals.[7,53] Furthermore, inclusion of fMRI in preoperative assessments has been shown to alter neurosurgical decision making[87] and is useful in determining the regions of interest that are used during white matter tractography.

Unfortunately, while tremendous advances have been made with fMRI, the results from those studies are unable to localize specific language areas that are confirmed with cortical stimulation mapping. A number of studies comparing fMRI signals to intraoperative electrostimulation in the vicinity of tumors have shown variable positive predictive values from 29% to 52%[93,94,102] and demonstrated that silent speech mapping with fMRI fails to activate articulatory regions outside of the inferior frontal gyrus.[89] Additionally, as mentioned previously, fMRI detects all areas that are involved in a given function, but not necessarily critical or essential regions. Therefore, while preoperative fMRI can serve as an adjunct, it cannot yet replace intraoperative stimulation mapping.

Subcortical Fiber Mapping

Subcortical mapping has become an important strategy aimed at identifying functional white matter pathways. Diffusion tensor imaging (DTI) utilizes anisotropic diffusion of water molecules along fiber tracts obtained from MRI to reconstruct white matter bundles (see Gierhan 2013 for review).[14,42] Duffau and others have made major contributions over the past decade by characterizing how subcortical fiber pathways can be mapped during electrical stimulation. Information about these individual pathways produces a more complete picture regarding the functional network underlying language processing. A brief review of the subcortical pathways believed to be involved in language organization follows and can be visualized in Fig. 4.

The arcuate fasciculus and superior longitudinal fasciculus (SLF) are the major fiber tracts involved in the dorsal stream of language processing. The SLF is composed of 4 major subcomponents: SLF I, II, and III join the frontal and parietal cortices, while the SLF-tp subcomponent joins the temporal and parietal lobes. SLF I is not significantly involved in language processing and so will not be discussed hereafter. SLF II connects the dorsal premotor and prefrontal cortices to the angular gyrus[39,88,100] whereas the operculo-opercular pathway known as the SLF III

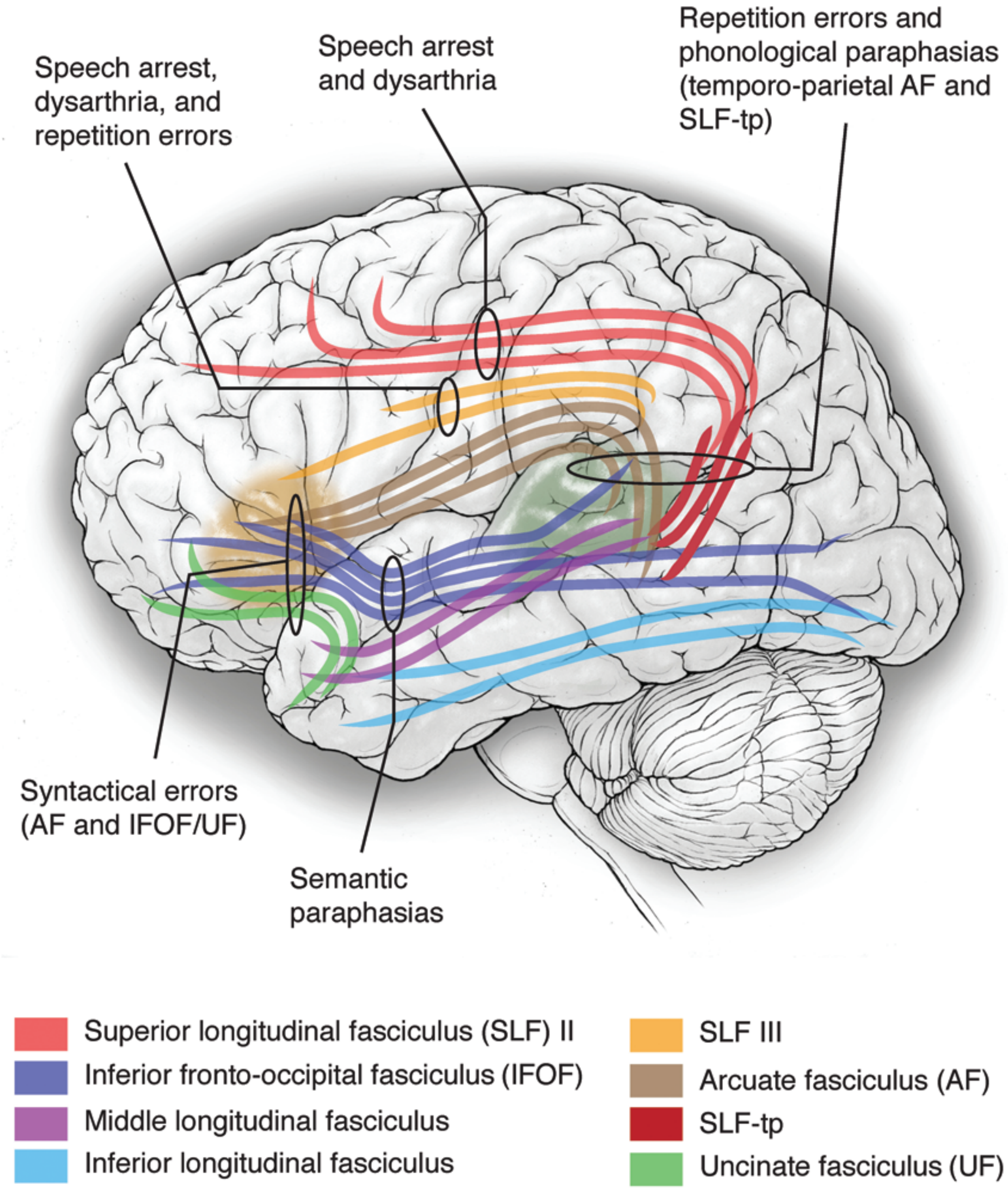

FIG. 4. Subcortical anatomy of language. Schematic illustration of various subcortical tracts involved in language processing. Individual white matter tracts are color coded (see legend). Stimulation and lesions to individual tracts lead to characteristic language deficits, represented by callouts from each tract. The subcallosal fasciculus is not shown. See text for more details. Copyright Edward F. Chang. Published with permission.

joins the ventral prefrontal areas to the supramarginal gyrus.[15,27,39,63–65] Stimulation of these white matter tracts causes dysarthria and other impairments in articulatory processing.[38,39,58,63,65] The SLF-tp runs in a posterior direction from the inferior parietal lobe to the posterior temporal lobe. Although there remains some controversy as to whether it is a component of either the ventral-running middle or inferior longitudinal fascicles,[36,39,63] lesion studies have shown that the region is involved in phonological processing, suggesting that it composes a portion of the dorsal processing stream previously described.[15,28,39,44,99] Stimulation of both SLF III and SLF-tp have also been shown to lead to repetition errors, which is consistent with their known roles in articulatory and phonological processing, respectively.[37,98]

The arcuate fasciculus connects fronto-opercular cortical sites with the posterior temporal cortex. While it continues to be taught as a long-range white matter tract connecting canonical Broca's and Wernicke's areas, the arcuate fasciculus has been shown to have more diverse terminations. The frontal terminations include the pars opercularis of the inferior frontal gyrus and the ventral premotor cortex.[15,36,38,63,99] The major temporal termination is in the posterior STG and MTG, although postmortem cortex-sparing dissection techniques and DTI suggest that the arcuate fasciculus may also extend caudally to the inferior temporal gyrus.[69,105]

Lesions to this subcortical pathway have long been believed to cause conduction aphasias, although stimulation of cortical areas can also lead to the phonemic paraphasias and anomia characteristic of conduction aphasias.[1,28,64,65] Subcortical mapping studies have confirmed that the arcuate fasciculus can be accurately and reliably identified intraoperatively and that stimulation of that bundle leads to phonological errors.[28,58,64,65] Syntactical errors have also been ascribed to the arcuate fasciculus based on DTI tractography[35,38] and subcortical stimulation studies.[107]

Some question exists regarding the nomenclature of the temporoparietal tract involved in phonological processing and repetition. While Catani and colleagues (2005) referred to this tract as an indirect pathway of the arcuate fasciculus,[15] others specify that the arcuate fasciculus connects Broca's area to Wernicke's area, which is consistent with its historically ascribed connectivity, as described by Wernicke and Geschwind.[39] In addition, many prior studies describe phonemic paraphasias as resulting from stimulation of pathways deep to the lateral portion of the SLF.[28,58,64,65] Irrespective of its name, however, it is clear that a temporoparietal white matter tract exists, whose function is to participate in phonological processing in the dorsal stream. Further studies combining DTI and subcortical stimulation are needed to determine precisely which tract is involved in phonological processing.

The ventral stream is composed of a few fiber tracts that take part in semantic and syntactic processing. The inferior fronto-occipital fasciculus (IFOF) is an anterior-posterior white matter bundle that connects the inferior frontal cortex and dorsolateral prefrontal cortex to the posterior temporal and occipital lobes. After passing through the anterior floor of the external capsule, the IFOF courses medially in the temporal lobe and sends radiations to the middle and inferior temporal gyri as well as the occipital lobe.[97] Stimulation of this bundle deep to the STS and extending anteriorly, as well as the overlying cortex in the temporal and frontal cortices, elicited numerous semantic paraphasias, whereas stimulation of other adjacent structures, including the middle longitudinal fascicle (connecting anterior and posterior temporal regions) and the inferior longitudinal fasciculus (connecting the temporal pole to the occipital lobe), does not.[2,22,30,31,58,64,65,67] The uncinate fasciculus, which connects the anterior temporal lobe to inferior frontal areas, may also play a role in semantic function, although conflicting data exist regarding the effect of uncinate fasciculus resection on language. One study showed that surgical removal leads to an impairment of "famous face naming,"[82] while another has shown that stimulation and partial resection do not lead to any lasting deficits.[31] This discrepancy may be due to plasticity of the pathways as a result of slowly growing tumors or the different neuropsychological testing methods used. Another major study limitation is possible resection of the IFOF leading to confounding results; thus, additional studies with postoperative tractography may help answer these questions.

Ventral pathways have also been implicated in syntactic processing of language (see above for discussion of dorsal tracts involved). Fiber tractography studies have shown that ventral white matter pathways connecting the inferior frontal cortex to the posterior MTG and anterior STG are involved in the ability to learn simple grammatical rules in which subsequent words are based on local transition probabilities.[35,38] It remains unclear whether this ventral pathway is the IFOF or the uncinate fasciculus, however. Some debate exists regarding the precise roles of the ventral and dorsal pathways in syntactical organization, so further research into the possibility of redundant information in these pathways is needed. Overall, the role of these tracts in ventral stream semantic and syntactic connectivity further confirms the dual stream model of language organization.

The language function of the subcallosal fasciculus (not shown in Fig. 4), which passes between the caudate and the cingulate gyrus or SMA, was first described by Naeser et al. (1989) in a study of patients with strokes located in the medial subcallosal fasciculus.[73] They found that stroke patients who completely lost the ability to speak or developed stereotypic language were more likely to have combined extensive lesions in the subcallosal fasciculus and middle third of the periventricular white matter (PVWM) than were patients who developed nonfluent Broca's aphasias; however, lesions in a single subcortical pathway (either the subcallosal fasciculus or PVWM) were not associated with specific language disturbances.[73] Subcortical mapping studies have also implicated these sites: patients with precentral gliomas developed a transcortical motor aphasia during intraoperative stimulation of the medial subcallosal fasciculus, and stimulation of the PVWM adjacent to the body of the lateral ventricle caused dysarthria or anarthria, leading to its description as the "final common pathway" involved in speech production.[27–29] The findings described by stimulation of the subcallosal fasciculus mirror the constellation of impairments noted in patients undergoing resection of tumors located in dominant SMA, known as the SMA syndrome. From a language perspective, the hallmark of SMA syndrome is a transient deficit in speech initiation with intact repetition, which usually resolves over the course of months to years. With this in mind, it is important to note that resection of tumors in the SMA is safe as speech does return to normal within 1 year, as long as functional mapping is used to determine the posterior and lateral resection boundaries; in particular, resection of the subcallosal fasciculus and the middle third of the PVWM should be avoided.[28,56,57]

Of note, a subcortical pathway connecting the superior, middle, and inferior frontal gyri, named the "frontal aslant tract," has also been recently described.[13,105] A system of fibers connects these 3 cortical regions and then projects inferiorly to the striatum in a manner similar to that previously attributed to the subcallosal fasciculus. It is likely that the frontal aslant tract subsumes the subcallosal fasciculus, although the language function of the frontal lobe cortico-cortical connections remains unknown.

Subcortical mapping has been supplemented with advances in noninvasive, preoperative imaging-based tractography. A comparison of two series of patients revealed improvement in postoperative neurological status in patients who received functional stimulation mapping,[33] and combining DTI with direct stimulation decreases both operative duration and the number of clinical seizures.[4] Like fMRI, however, DTI has some significant limitations. Whereas DTI can reconstruct fibers that have been displaced by tumors, it cannot easily reconstruct tracts that have been invaded by tumor and are still functional.[58] The correlation between preoperative DTI and intraoperative subcortical stimulation is variable, with some studies showing that positive stimulation mapping is correlated with DTI in 80% of stimulations[58,102] and others demonstrating that sensitivity depends partly on the tract being visualized, with high sensitivity for SLF (approximately 98%) but lower for the IFOF and uncinate fasciculus (89% each).[4] In addition, implementation of DTI tractography in neuronavigation can be erratic due to shifting of white matter tracts during surgery, which is why a 5-mm safety margin has been suggested when approaching these fibers.[23,74–76] To minimize brain shift, landmarks should be checked regularly, and the resection should begin near the site of expected subcortical tracts. Given that the reliability of these noninvasive strategies is still questionable, subcortical stimulation appears to be the more useful method of preserving language function and should continue to be used even when DTI has been performed preoperatively. In particular, low-grade gliomas tend to infiltrate tracts and even have tracts embedded within, whereas high-grade gliomas tend to displace white matter tracts or leave them unchanged,[2,4] so it is crucial that direct subcortical stimulation at least be combined with DTI for resection of low-grade gliomas.

Considerations for Surgery in Eloquent Areas

Our analysis of the literature has highlighted 3 major considerations that neurosurgeons should take into account prior to embarking on surgery in eloquent areas. First, functional neuroimaging cannot differentiate between essential and compensable regions of the brain. Thus, while fMRI can be useful in determining hemispheric speech dominance, it should not be used to determine functional localization. In addition, while DTI is useful in determining subcortical anatomy preoperatively, it does not provide any functional detail and therefore should not be used in isolation.

Second, and as a corollary to the first consideration, surgeons should use cortical and subcortical mapping in all circumstances when operating within peri-sylvian regions or near subcortical systems known to be involved in language processing. This provides functional information that should ultimately inform the boundaries of resection. In fact, functional mapping is the gold standard and has been shown to both significantly reduce late-stage postoperative neurological deficits and increase the proportion of gross-total resections.[22] As described earlier, recent "no-margin" techniques demonstrate rates of permanent speech deficit that are equivalent to those for "1-cm–margin" techniques but improve the extent of tumor resection.[43] Patients should still be informed, however, that there is a high rate of transient postoperative deficit using this technique and that intensive speech rehabilitation is necessary for optimal recovery.

Finally, even with the complexities of language as we know it, surgery to remove lesions can still be performed safely if the previously mentioned methods are used. Part of this safety comes from the knowledge that the brain possesses an innate ability to redistribute some of its functions both ipsilateral and contralateral to the site of the lesion. Having a full understanding of the cortical and subcortical anatomy of language, as well as some insight into the mechanisms of neural plasticity, will provide the neurosurgeon with an arsenal of tools to improve each patient's overall quality of life.

Conclusions

The integration of cortical and subcortical stimulation has allowed neurosurgical language mapping to converge with modern thinking about language as an emergent property of a dynamic, plastic, and highly interconnected system. This concept has been called "hodotopy," derived from the Greek terms "hodos" (path) and "topos" (place), and is a novel paradigm proposing that CNS networks have substantial subcortical connections that allow for reorganization over time.[21,27,34] The use of functional stimulation mapping increases the safety and extent of resection in tumor and epilepsy surgeries.

The goal of our review was to compare classic and modern models of language organization, especially as they pertain to neurosurgery in the current decade. There has been much progress since Penfield's seminal work, and the field has advanced tremendously to facilitate effective resective surgeries with reduced morbidity. Neurosurgery also has much to offer with regard to the basic mechanisms of language, and new technologies spearheaded by surgeons will be vital components of future scientific discovery in the detailed microcircuitry of these brain regions. In addition, prior to operating on eloquent areas, neurosurgeons should consider a number of factors highlighting the use of both cortical and subcortical mapping as the gold standard for reducing postoperative deficits and maximizing the extent of resection. We hope that this review will be of use as brain mapping methods continue to become more widespread in neurosurgical practice.

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Author Contributions

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