Seminars in
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Imaging of Cortical and White Matter Language Processing

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Although investigations into the functional and anatomical organization of language within the human brain began centuries ago, it is recent advanced imaging techniques including functional magnetic resonance imaging and diffusion tensor imaging that have helped propel our understanding forward at an unprecedented rate. Important cortical brain regions and white matter tracts in language processing subsystems including semantic, phonological, and orthographic functions have been identified. An understanding of functional and dysfunctional language anatomy is critical for practicing radiologists. This knowledge can be applied to routine neuroimaging examinations as well as to more advanced examinations such as presurgical brain mapping.
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Introduction

The functional and anatomical relationships for language in the human brain have been widely studied using anatomical dissections, lesion localization studies, intraoperative stimulations, high-resolution imaging, and now functional imaging techniques including functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), and magnetoencephalography. Unlike more elementary brain functional systems such as vision and sensorimotor, both of which have very similar anatomico-functional organization between human and nonhuman species, understanding the complex and uniquely human language system has been more elusive. From the beginning, models of language organization in the human brain have been proposed, accommodating data from the various methods of investigation. These language models are continuously modified as findings from cutting-edge research methods are added to our conceptualization. Although there is no doubt that our conceptualization of human language is incomplete and is subject to more modifications, it is important as radiologists to understand where we are. Radiologic practice is now more than ever integrated with the clinical neurosciences through instant access to the electronic health record. Being able to use anatomical, functional, and radiologic expertise in addition to clinical symptomatology and other nonimaging diagnostic parameters enables radiologists to provide accurate imaging interpretations and optimally influence patient management in scenarios ranging from routine stroke imaging to advanced applications such as presurgical brain mapping. The following is a discussion of important language cortical brain regions and white matter tracts in the context of functional language processing.

Functional Neuroanatomy of Language Processing

The scientific study of aphasia began in the early 19th century with Paul Broca's description of a patient who lost the ability to express but not comprehend speech following damage to the posterior portion of the inferior frontal lobe. Shortly after Broca's discovery, Carl Wernicke described a different form of aphasia in which language comprehension was disrupted but not speech expression following damage to the posterior superior temporal gyrus (STG). Based on these clinical-anatomical observations, Wernicke proposed the first brain behavioral model in which language was localized to two main regions: (1) an area in the left inferior frontal lobe (now known as Broca's area) that contains the motor memories responsible for speech production and (2) an area in the left posterior temporal lobe (now known as Wernicke's area) that contains

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the auditory images of words responsible for speech perception. These two regions communicate with each other through a bundle of fibers later identified as the arcuate fasciculus (AF). This model was the first to associate specific language deficits with discrete anatomical regions.

Although the basic principles and predictions of Wernicke's classical localization model still hold true, mainly that the inferior frontal lobe plays an important role in speech production and the posterior temporal region is important for speech comprehension, the advent of modern structural and functional imaging has expanded our knowledge of the neuroanatomical underpinnings and functional components of language processing. It is now accepted that language involves a number of conceptually distinct but interacting linguistic subsystems located in a widely distributed network, including several regions outside the classic language areas. What follows is a brief review of the organization and neuroanatomy of language processing.

Orthographic Processing

Orthography refers to information concerning written letter combinations and is important for reading and writing. Clinical and functional neuroimaging studies have identified an area in the left ventral occipitotemporal cortex, now referred to as the visual word form area (VWFA), as a putative region for orthographic processing (Fig. 1, area colored in light blue). This area is reliably activated during reading, and the focus of this activation is often within a few millimeters across studies and across languages. It has also been shown that neurons in this region become tuned to processing orthographic content, as this region shows greater activation in literate than in illiterate individuals.[1] This region activates more strongly to words or wordlike nonwords than to consonant strings or false font characters,[2-5] and the activation in this area is not modulated by letter case or other basic visual characteristics of the stimuli.[6,7] It has also been demonstrated that activation in the VWFA is specific to written stimuli when compared with spoken stimuli, independent of the stimuli's semantic content.[7] These findings have led to the belief that the VWFA extracts an abstract representation of the letter identity. Additionally, in an fMRI study by Binder et al,[8] the VWFA demonstrated a unique graded response to the orthographic regularity or letter sequence probability of meaningless letter strings. The more the letter strings approximated English orthography, the greater the activation. This response was specific to the VWFA. Lesion studies further support the role of this region in orthographic processing. Damage to the VWFA results in a pure alexia, a condition where language functions are normal (including speaking and comprehension), and patients can often identify single letters without much difficulty but reading letter strings is extremely slow and effortful and limited to a letter-by-letter reading strategy.

Phonological Processing

Phonology refers to the articulatory and perceptual characteristics of speech sounds and is important for speech perception and the selection of speech sounds during production of spoken speech. There is evidence from lesion and functional imaging studies suggesting the existence of separable input and output phonological pathways. Listening to speech sounds (eg, syllables, words, pseudowords, and reversed speech) when compared with silence activates large areas in the STG

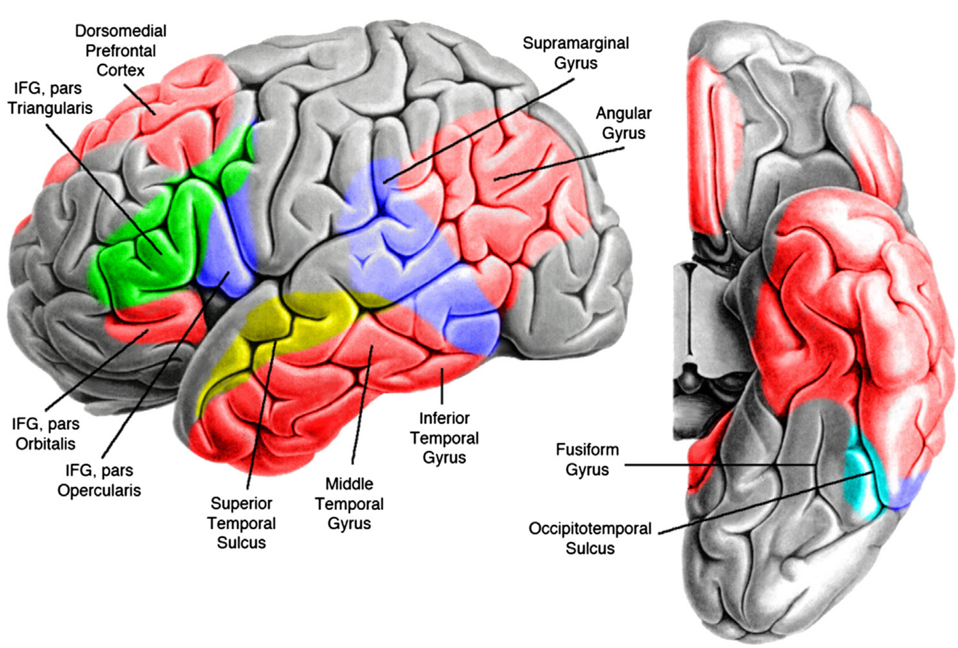

Figure 1 Yellow = phoneme and auditory word form perception areas, red = semantic storage and retrieval systems, blue = phonological access and phonological output systems, light blue = visual word form perception area, green = general verbal retrieval, selection, and working memory functions. (Reproduced with permission from Binder JR: *Functional Neuroradiology: Principles and Clinical Applications*, 2011.) (Color version of figure is available online.)