SPECIAL COMMUNICATION

Neurobiology of Language Recovery After Stroke: Lessons From Neuroimaging Studies

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Language is organized in large-scale, predominantly left-lateralized, temporo-parieto-frontal networks in the human brain. After focal brain damage (eg, ischemic stroke), this network organization enables the brain to adaptively reorganize language functions in order to compensate lesion effects. Here, we summarize how structural and functional neuroimaging methods contribute to the current understanding of loss and recovery of language functions after stroke. This includes voxelwise lesion-behavior mapping, functional imaging for mapping reorganizational mechanisms from acute to chronic stroke, as well as imaging based outcome prediction. The review is complemented by an introductory section on language organization in the healthy brain.

Key Words: Aphasia; Magnetic resonance imaging; Rehabilitation; Stroke.

THIS REVIEW SUMMARIZES how structural and functional neuroimaging methods contribute to the current understanding of loss and recovery of language functions after stroke. For a detailed review on the basic principles of functional magnetic resonance imaging (fMRI), we refer the reader to Smits et al[1] in this issue. We first discuss imaging studies on language networks in the healthy brain and introduce the dual-stream model for language organization. The second part deals with lesion studies using voxelwise lesion-behavior mapping (VLBM). We then review the current literature on functional imaging of spontaneous reorganization mechanisms in acute and chronic stroke. This is complemented by imaging based prediction of language outcome. Finally, we provide an overview of neuroimaging studies dealing with treatment-induced plasticity.

IMAGING LANGUAGE NETWORKS IN THE HEALTHY BRAIN

A profound understanding of language organization in the healthy human brain is mandatory for the interpretation of activation changes due to reorganizational mechanisms in patients with brain damage. While early models of language organization were solely based on behavioral deficits in patients with brain lesions (eg, Broca[2] and Wernicke[3], see Shalom and Poeppel [4] for a review), a new decade of studies on language organization in the human brain has started with the advent of modern functional imaging techniques such as positron-emission tomography (PET), fMRI, electroencephalography, and magnetoencephalography in the late 20th century. In contrast to the lesion-deficit approach, functional neuroimaging studies are not limited to the assumption that cognitive processes or operations are confined to discrete anatomical regions but allow for the investigation of functional specialization which emerges from the interaction between different areas. These studies now focus on the direct correlation between mental operations and indices of brain activity, and thus provide the perfect complement to lesion studies in that the neural systems sufficient for one task compared with another can be identified.

Based on an analogy to the dual-stream model of visual processing,[5] Hickok and Poeppel[6-8] introduced a functional-anatomic model of auditory language processing that distinguishes 2 neuroanatomically segregated routes. A ventral stream, projecting from the core auditory cortices to various temporal lobe regions, is involved in auditory recognition and processes speech signals for language comprehension. The ventral stream thus maps sound onto meaning (ie, lexical-semantic processing). A dorsal stream, projecting from the auditory cortices to temporo-parietal and frontal lobe articulatory networks, is the interface between auditory and motor processing and maps sound onto articulatory-based representations (ie, phonologic processing). A task that consecutively activates the dorsal stream is the verbal repetition of heard speech, during which access to a motor-based representation is necessary.

The framework posits that early cortical stages of language perception involve auditory fields in the bilateral superior temporal gyri.[9] This cortical processing system then diverges into the ventral and dorsal stream. The ventral stream projects ventro-laterally toward posterior and anterior parts of the middle temporal gyrus and serves lexical-semantic processing[9,10] (see[11] for a review). The dorsal stream projects dorso-posteriorly, involving a region in the posterior Sylvian fissure at the parieto-temporal boundary (area Sylvian-parietal-temporal),

List of Abbreviations

DWI	diffusion-weighted imaging
fMRI	functional magnetic resonance imaging
IFG	inferior frontal gyrus
LRS	language recovery score
MRI	magnetic resonance imaging
PET	positron-emission tomography
PLORAS	predicting language outcome and recovery after stroke
PWI	perfusion-weighted MRI
SVM	support vector machine
tDCS	transcranial direct current stimulation
TMS	transcranial magnetic stimulation
VLBM	voxelwise lesion-behavior mapping

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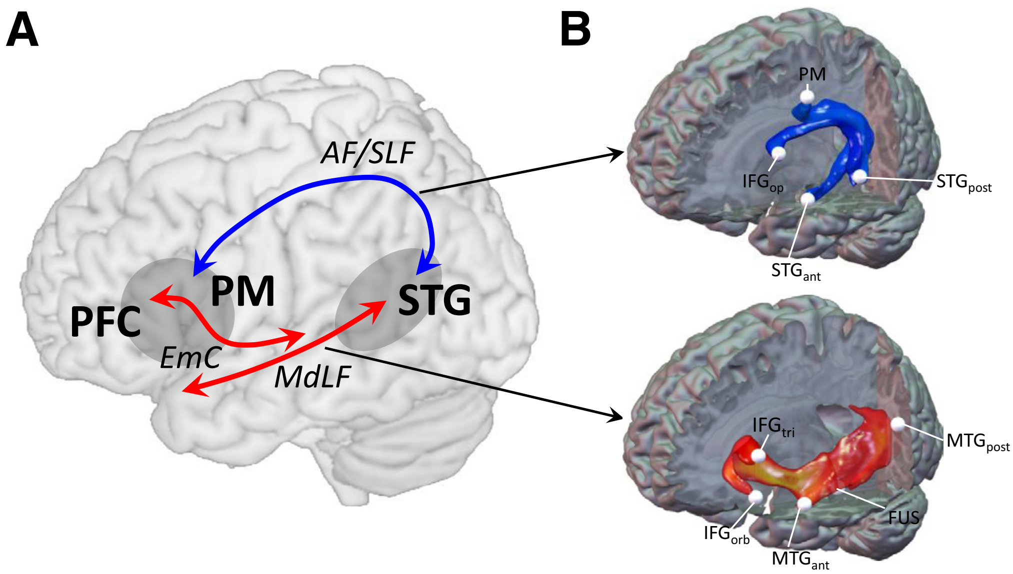

Fig 1. The 2 pathways of auditory language processing. (A) Schematic diagram of the ventral and dorsal streams projecting to the prefrontal and premotor cortices. Regions in gray show Broca's area in the frontal gyrus (left) and Wernicke's area in the temporal gyrus (right). (B) Results from diffusion tensor imaging-based tractography show 2 distinct pathways connecting posterior brain regions with anterior areas via the fasciculus arcuatus/longitudinalis superior (ie, the dorsal pathway) and the fasciculus longitudinalis medialis/capsula extrema (ie, the ventral pathway). Abbreviations: AF/SLF, fasciculus arcuatus/longitudinalis superior; EmC, capsula extrema; FUS, fusiform gyrus; IFG$_{orb}$, pars orbitalis; IFG$_{op}$, pars opercularis of the IFG; IFG$_{tri}$, pars triangularis of the IFG; MdLF, fasciculus longitudinalis medialis; MTG$_{ant}$, anterior middle temporal gyrus; MTG$_{post}$, posterior middle temporal gyrus; PFC, prefrontal cortex; PM, premotor cortex; STG, superior temporal gyrus; STG$_{ant}$, anterior superior temporal gyrus; STG$_{post}$, posterior superior temporal gyrus. Modified from Saur et al.[14] Reprinted with permission. © 2009 National Academy of Sciences, USA.

and ultimately projects to premotor areas in the frontal cortex, including the posterior aspect of Broca's area (ie, pars opercularis of the inferior frontal gyrus [IFG]). Area Sylvian-parietal-temporal is involved in translating acoustic speech signals into articulatory representations in the frontal lobe,[12] which is essential for intact language production as well as for speech development (see[13] for a review). Under normative circumstances, both pathways interact. While the dorsal stream is proposed to be left-hemisphere dominant, the ventral stream is more bilaterally distributed.

In a recent multimodal imaging study, Saur et al[14] used combined fMRI and diffusion tensor imaging-based tractography in healthy subjects to identify the most probable anatomical pathways connecting brain regions preferentially associated with auditory comprehension and repetition, respectively. The authors demonstrated that temporo-frontal interactions are subserved by 2 distinct fiber bundles (fig 1). The repetition of heard pseudowords (ie, meaningless nonwords) is subserved by a dorsal stream connecting the superior temporal lobe and premotor areas in the frontal lobe (including pars opercularis in the IFG) via the arcuate and superior longitudinal fascicle. In contrast, higher-level language comprehension (ie, listening to normative sentences compared with meaningless pseudosentences) is mediated by a ventral pathway connecting the middle temporal lobe and the ventrolateral prefrontal cortex via the extreme capsule. The functional relevance of these anatomical pathways is now widely discussed.[15-19] In sum, these results question the classical view of the temporal lobe (ie, Wernicke's area) being solely connected with frontal regions (ie, Broca's area) via the arcuate fascicle.[20] Rather, these results point toward an organization of language in distinct ventral and dorsal large-scale networks. Further, this implies various routes of compensation after focal brain damage.

VOXEL-BASED LESION STUDIES OF LANGUAGE

Since the days of Broca and Wernicke in the second half of the 19th century, research aims at defining functional-anatomic models of language organization in the human brain. While the modularity assumption (ie, discrete anatomical modules deal with different cognitive functions) of the classical lesion-deficit approach has frequently been criticized (eg,[21,22] for reviews), the recent advent of new techniques offers a complementary approach to the use of imaging studies in healthy volunteers. With modern voxelwise lesion studies, the researcher aims at identifying whether differences in lesion frequency between patients showing a particular disorder and those who do not, might be due to chance or are reliable predictors of behavior.[22] For example, VLBM is a technique to determine whether a specific region is critically contributing to a given task by analyzing the statistical relationship between lesion data and behavioral measures[22-24] (fig 2). In contrast to classical lesion-deficit studies, VLBM is not restricted to specified regions of interest but allows for additional areas to emerge in the exploration of networks that support a given behavior.[23] In VLBM, lesions are manually identified for each patient by marking the damaged region with special software (see[24] for an overview of different techniques) and statistical maps are generated at the group level afterward to reveal patterns of damage associated with the behavioral deficit. Importantly, statistical analyses of the relationship between tissue damage and observed behavior are carried out on a voxel-by-voxel basis by using continuous information both at the behavioral level (ie, avoiding arbitrary cutoffs) and the neuroanatomical level (ie, including patients independent of their lesion location).

An increasing number of studies have used VLBM to identify the critical contribution of different brain areas to specific