Uncovering the Neuroanatomy of Core Language Systems Using Lesion-Symptom Mapping

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Abstract
Recent studies have integrated noninvasive brain-imaging methods and advanced analysis techniques to study associations between the location of brain damage and cognitive deficits. By applying data-driven analysis methods to large sets of data on language deficits after stroke (aphasia), these studies have identified the cognitive systems that support language processing—phonology, semantics, fluency, and executive functioning—and their neural basis. Phonological processing is supported by dual pathways around the Sylvian fissure, a ventral speech-recognition component and a dorsal speech-production component; fluent sentence-level speech production relies on a more anterior frontal component, and the semantic system relies on a hub in the anterior temporal lobe and frontotemporal white-matter tracts. The executive function system was less consistently localized, possibly because of the kinds of brain damage tested in these studies. This review synthesizes the results of these studies, showing how they converge with contemporary models of primary systems that support perception, action, and conceptual knowledge across domains, and highlights some divergent findings and directions for future research.

Keywords
language, speech, aphasia, neuroimaging, neuropsychology

For more than 150 years, associations between the location of brain damage and cognitive deficits have shed light on the brain systems that are critical for human cognition and behavior. Contemporary advances in noninvasive neuroimaging methods and sophisticated analysis techniques have made it possible to apply this classic lesion method on a much finer anatomical scale. Recent research on the neural basis of language using large data sets from individuals with language deficits after stroke (aphasia) has provided new insights into the functional neuroanatomy of the human language system by identifying the cognitive subsystems that support language processing and the neural basis of those subsystems.

The modern version of the lesion method is called lesion-symptom mapping (Bates et al., 2003; Rorden & Karnath, 2004) and uses brain scans (MRI or computed tomography) to localize brain damage (lesions) for each individual in a group of participants with varying degrees of deficit. For each small patch of the brain (a voxel; typically a 1-mm × 1-mm × 1-mm or 3-mm × 3-mm × 3-mm cube), a lesion-symptom mapping analysis tests whether people with damage in that patch have a more severe deficit than people who do not have damage in that patch (because their brain damage is in a different location). Lesion-symptom mapping has been used to examine a wide variety of different cognitive or behavioral symptoms on the basis of one of three broad approaches. The clinical approach compares participants with different clinical diagnoses, for example, Broca’s aphasia versus Wernicke’s aphasia. The theoretical approach compares performance on a test or measure that is relevant to a particular theory or hypothesis. For example, a theory about the processing steps involved in word production might identify speech sound errors, such as saying “giraffe” instead of “giraffe,” as a key symptom to use for lesion-symptom mapping. The newest approach defines symptoms in a
data-driven way—researchers start with many different measures of cognitive performance and use a statistical method that combines highly correlated measures to identify a few scores that capture most of the variability across all of the measures and likely reflect the underlying cognitive systems. The long-term goal is for these three approaches to converge: to develop cognitive theories that explain the observed data-driven syndrome clusters in ways that are clinically relevant.

Recent studies from four independent research groups using the data-driven approach have identified four cognitive systems of language processing and their associated brain regions: phonology, semantics, fluency, and executive functions. Figure 1 illustrates how different language tasks relate to these four identified systems. Language tasks rarely rely on a single system—even seemingly simple language tasks, such as naming common objects, repeating words, or matching words to pictures, draw on multiple systems. These systems are complementary and interactive, working together to perform everyday language tasks. A key unique contribution of the data-driven approach is that performance on multiple tasks is combined in order to overcome the limitations of any single task, thus triangulating the dissociable underlying cognitive systems. For example, phonological-discrimination, repetition, and picture-naming tasks each draw on phonology as well as other systems, but data-driven methods provide a composite score that reflects the common latent phonology factor that underlies performance in all of those tasks and removes the contribution of other systems. The substantial convergence across different laboratories, each using a somewhat different battery of tests and testing different groups of individuals with aphasia, reveals that this organization of language processing is quite robust.

**Phonology**

The first and most thoroughly described system is phonology: the speech sounds that make up words. Phonological processing is the intermediate step between higher-level language processes, such as sentence- and word-level processing, and lower-level auditory perception and articulation of language. Phonological deficits include difficulty judging whether two syllables are the
same or different, difficulty judging whether two words rhyme or not, and difficulty repeating a word or nonword. Several of the reports also differentiated between articulation-production of speech sounds and recognition of speech sounds. This distinction requires using measures that are specific to deficits in phonological production or perception rather than measures that reflect both (e.g., repetition requires both correct perception and production; see Table S1 at https://osf.io/6gnvb/).

Deficits in the phonological-production subsystem are associated with damage in a dorsal pathway primarily involving inferior parietal and frontal regions (Fig. 2a, darker green). Deficits in the phonological-recognition subsystem are associated with damage in a ventral pathway extending from the posterior to anterior superior temporal lobe (Fig. 2a, lighter green). This dual-stream architecture of the phonological system broadly aligns with the contemporary view of the computational neuroanatomy of speech processing (Hickok & Poeppel, 2007). These two subsystems interact and work together: The goal of speech production is particular speech sounds, so the speech-perception system plays an important role in setting speech-production targets and monitoring articulation (Hickok, 2012). When speech perception and production were not dissociated, a general phonological factor was identified and associated with damage along the superior temporal sulcus, including Heschl’s gyrus and planum temporale. This region, where the two phonological subsystems come into contact, may be critical for the auditory-motor transformations involved in setting auditory targets and monitoring speech programs.

**Semantics**

The second system is **semantics**: conceptual knowledge about objects and the meanings of words. Semantic knowledge about an object includes what that object looks and sounds like, how it acts and how we act on or with it, the emotions it evokes in us, and so forth. This knowledge is distributed across modality-specific perceptual, motor, and emotional systems and integrated in convergence zones or hubs (Barsalou, Simmons, Barbey, & Wilson, 2003; Meyer & Damasio, 2009; Rogers et al., 2004). Semantic deficits are most often exhibited in comprehension tasks such as matching words or sentences to pictures or judging whether two words are synonyms, but they can also affect nonverbal tasks such as matching related pictures (e.g., whether a pyramid goes with a palm tree or a pine tree).

Deficits in the semantic system are associated with anterior temporal lobe damage (Fig. 2a, yellow), including the temporal pole and the midanterior portions of the middle and superior temporal gyri. For comprehension tasks, this is the continuation of the ventral stream:
The progression from posterior to anterior temporal regions corresponds to the progression from recognizing speech sounds and syllables to recognizing words and comprehending what those words mean (see also DeWitt & Rauschecker, 2012). This progression aligns with extensive evidence that the anterior temporal lobe is a critical hub for integrating semantic knowledge that is distributed across modality-specific systems (Binder & Desai, 2011; Lambon Ralph, Jefferies, Patterson, & Rogers, 2017; Patterson, Nestor, & Rogers, 2007).

Poststroke semantic deficits are also associated with damage to white-matter pathways, particularly the inferior fronto-occipital fasciculus and the uncinate fasciculus (Fig. 2b), which appear to be critical for effective functioning of the distributed semantic system. Damage to white-matter bottlenecks—regions where multiple tracts come together—is particularly disruptive (Griffis, Nenert, Allendorfer, & Szafarski, 2017; Mirman, Chen, et al., 2015; Mirman, Zhang, Wang, Coslett, & Schwartz, 2015). This is, presumably, because these bottlenecks are locations where even a small amount of damage can disrupt multiple tracts, producing broad semantic network dysfunction (for a computational approach see L. Chen, Lambon Ralph, & Rogers, 2017).

**Fluency**

The third system, which was identified in a subset of the studies, is fluency: the ability to produce connected speech rapidly and smoothly. This requires rapid coordination of multiple processes (e.g., Nozari & Farooqi-Shah, 2017; Wilson et al., 2010), including articulatory-phonological planning and execution, which corresponds to the phonological production system discussed above, and retrieving words to fit the semantic and syntactic constraints, which corresponds to the semantic system discussed above (see also Q. Chen, Middleton, & Mirman, 2018). The data-driven studies identified a distinct fluency system that corresponds to planning and structuring sentences, including syntax and working or short-term memory. People with deficits in this sentence-level planning and structuring system tend to produce shorter utterances, slower speech (fewer words per minute), and less grammatically complex sentences (e.g., fewer embedded clauses). They also tend to make more syntactic omissions, such as omitting closed class words (determiners, prepositions, etc.) or producing incomplete sentences. However, sentence-comprehension deficits are not strongly associated with this system, suggesting that it is more closely related to sentence-level planning and execution rather than general syntactic processing (see also Linebarger, Schwartz, & Saffran, 1983; Thothathiri, Kimberg, & Schwartz, 2012).

Fluency deficits are associated with damage in the insula and inferior frontal and precentral areas (Fig. 2a, red). This is anterior to the region associated with phonological production deficits and may reflect a higher level of speech-production planning and coordination, that is, sentence- or utterance-level planning rather than word- or syllable-level planning or articulation of individual speech sounds. Related research also suggests that fluency deficits are associated with middle frontal gyrus damage and frontal white-matter damage (Basilakos et al., 2014; Catani et al., 2013; Fridriksson, Guo, Fillmore, Holland, & Rorden, 2013; Rogalski et al., 2011; Wilson et al., 2010), including the anterior segment of the arcuate fasciculus (Fig. 2b, red) and the frontal aslant tract, which connects superior and inferior portions of the frontal lobe. The frontoparietal speech-production system is neuroanatomically similar to the frontoparietal system for the production of skilled tool-use actions (e.g., Brandi, Wohlschlager, Sorg, & Hermsdorfer, 2014; Johnson-Frey, 2004). Anterior-to-posterior progression within the speech-production planning system aligns with general theories about the hierarchical organization of frontal planning systems (Botvinick, 2008) in which more anterior regions are responsible for higher-level planning and maintenance of tasks and goals (e.g., making a cup of coffee, or producing a full sentence or narrative) and more posterior regions are responsible for lower-level planning of individual actions involved in accomplishing those tasks or goals (e.g., scooping coffee grounds into the coffee maker or sugar into the cup, or saying a single word).

**Executive Functions**

The final factor, which was identified in a subset of the studies, is executive functioning: cognitive abilities, such as planning, reasoning, cognitive flexibility, cognitive control, and selective attention (e.g., Jurado & Rosselli, 2007), that are not specific to language but are important for language processing. Lacey, Skipper-Kallal, Xing, Fama, and Turkeltaub (2017) reported that executive function deficits were associated with damage in middle frontal gyrus (dorsolateral prefrontal cortex) and posterior frontal white matter, but the other studies did not converge on a consistent lesion correlate. This may be because (a) some of the regions that are critical to executive functions are outside the territory of the middle cerebral artery, so they are unlikely to be damaged by strokes that affect language processing, and (b) the executive function system is distributed across both hemispheres of the brain, so damage within the left hemisphere may not be sufficiently strongly associated with executive function deficits. Thus, executive functions may be impaired in poststroke aphasia, but
the relationship between executive functions and language remains unclear (see also Fedorenko, 2014).

Conclusions and Future Directions

Two systems form the core of spoken language: phonology and semantics. The phonological system has two subcomponents organized in dual pathways around the Sylvian fissure, a dorsal-stream production component and a ventral-stream recognition component, which is consistent with contemporary dual-stream models of speech recognition and production (Hickok, 2012; Hickok & Poeppel, 2007). The semantic system is broadly distributed and relies on a hub in the anterior temporal lobe and frontotemporal white-matter tracts, which is consistent with the current theories and neurocomputational models of semantic cognition (Lambon Ralph et al., 2017). Fluent speech-production deficits are primarily associated with frontal damage, anterior to the regions where damage is associated with single-word phonological-production deficits. This suggests that language production may rely on the same computational and neural systems that support other kinds of hierarchical, sequential action planning and execution (Botvinick, 2008; Hickok, 2012; see also Weiss et al., 2016). A key overarching theme is that language processing is situated in the context of primary systems that support perception, action, and conceptual knowledge across domains.

Two psycholinguistic constructs have not emerged in these data-driven lesion-symptom mapping studies. One is the lexicon—a mental inventory of words. It may be that the lexicon is an emergent property of interactions between phonological and semantic systems rather than a discrete system. The other is syntax—knowledge of a language’s grammatical rules. Although often associated with nonfluent aphasia, fluency (rapid and smooth production of connected speech) is neither necessary nor sufficient for syntax. In fact, substantial syntax knowledge is preserved in so-called agrammatism (e.g., Lemberger et al., 1983), and syntax deficits in aphasia may be a result of a more general reduction in cognitive resources (e.g., Caplan, Michaud, & Hufford, 2013).

The clinical relevance of data-driven lesion-symptom mapping studies has yet to be established, although there is potential for improved diagnosis, stronger integration with neural systems, and clearer guidance for treatment selection. Ideally, a new data-driven classification system would make contact with the outcome that is of utmost importance for people with aphasia and for their clinicians—functional communication—but it is not yet clear how these systems relate to the ability to communicate in real-world settings. In addition, data-driven methods are necessarily limited by the data that are driving them. Pragmatic aspects of language and communication were not assessed in any of these studies, and fluency, written language, and executive functions were only minimally assessed, and not in all of the studies.

Finally, lesion-symptom mapping methods are continuing to develop and evolve. A new generation of multivariate methods captures the contributions of multiple brain regions more effectively (Pustina, Avants, Faseyitan, Medaglia, & Coslett, 2018; Zhang, Kimberg, Coslett, Schwartz, & Wang, 2014). Updating the classic lesion method, contemporary lesion-symptom mapping leverages advanced neuroimaging, statistical, and machine-learning techniques to identify brain regions that are critical for specific cognitive functions. Data-driven lesion-symptom mapping has recently revealed the core systems that support language function and their neural basis and informed theoretical accounts of language in ways that are clinically meaningful.

Recommended Reading


Action Editor

Randall W. Engle served as action editor for this article.

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Note
1. The four research groups were based in Philadelphia, Pennsylvania (Mirman, Chen et al., 2015; Mirman, Zhang et al., 2015); Columbia and Charleston, South Carolina (Fridriksson et al., 2016, 2018); Washington, DC (Lacey et al., 2017); and Manchester, England (Butler, Lambon Ralph, & Woollams, 2014; Halai, Woollams, & Lambon Ralph, 2017).

References


