Association for Psychological Science

Current Directions in Psychological Science
2018, Vol. 27(6) 455–461

DOI: 10.1177/0963721418787486
www.psychologicalscience.org/CDPS
SAGE

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

Daniel Mirman and Melissa Thye
Department of Psychology, University of Alabama at Birmingham

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 "girappe" instead of "giraffe," as a key symptom to use for lesion-symptom mapping. The newest approach defines symptoms in a

Corresponding Author:
Daniel Mirman, University of Alabama at Birmingham, Department of Psychology, CH 415, 1300 University Boulevard, Birmingham, AL 35294
E-mail: dan@danmirman.org

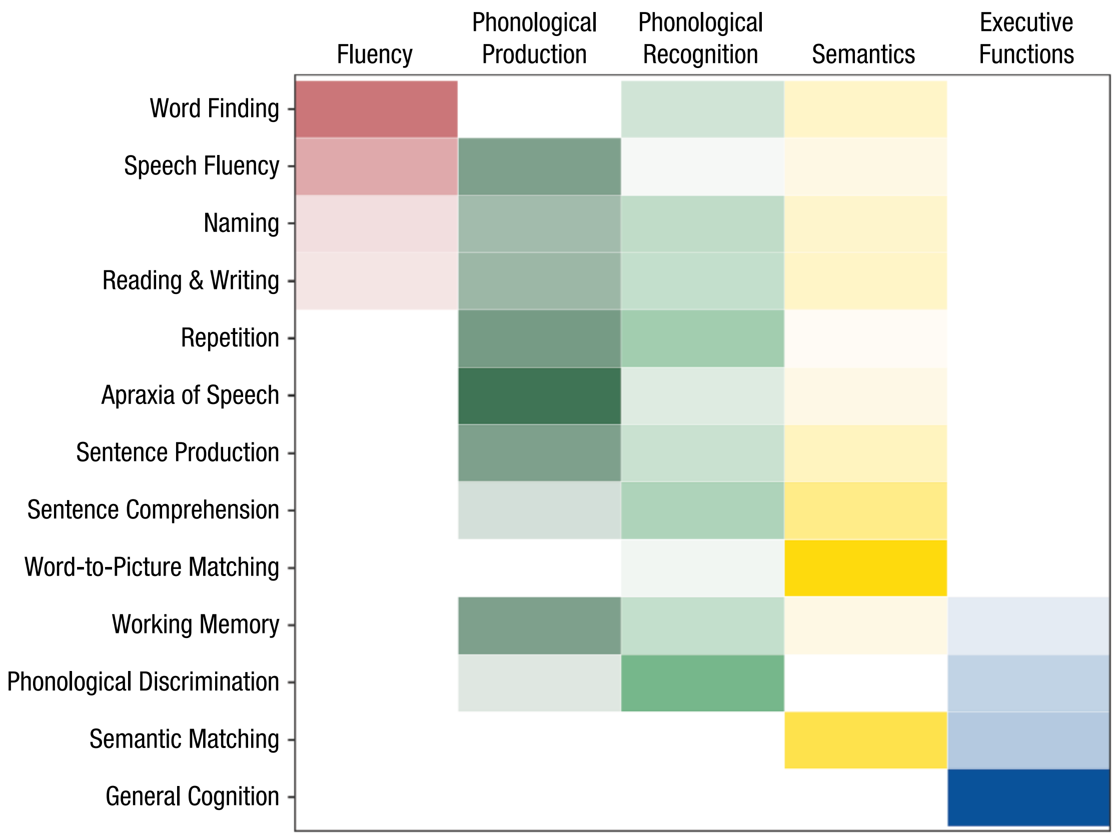

Fig. 1. Schematic depiction of the extent to which various language tasks and deficits (rows) rely on four language systems (columns): fluency, phonology (separated here into phonological production and phonological recognition), semantics, and executive functions. Saturation of the cells shows the approximate strength of the relationship between these systems and language tasks or deficits. Detailed results, including specific tests and factor loadings, are provided in Table S1 at https://osf.io/6gnvb/.

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[1] 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

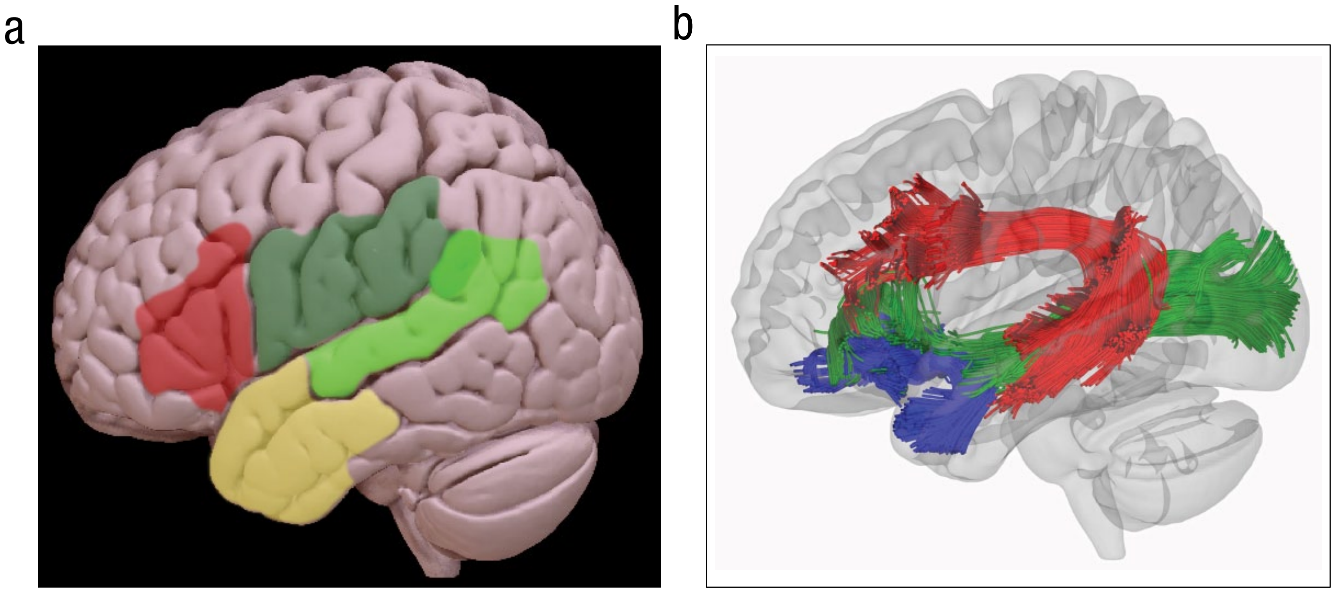

Fig. 2. Brain regions critical for language processing. The neuroanatomy of core language systems (a) is shown on the lateral surface of the left hemisphere: semantics (yellow), fluency (red), and phonology (green; lighter green shows the phonological recognition system, whereas darker green shows the phonological production system; the two systems overlap in the posterior portions of the Sylvian fissure and the superior temporal gyrus). White-matter tracts particularly important for language processing are shown in (b): arcuate fasciculus (red), inferior fronto-occipital fasciculus (green), and uncinate fasciculus (blue). A more detailed description of the brain regions involved in each system, including peak voxel coordinates, is provided in Table S2 at https://osf.io/6gnvb/.

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, & Szaflarski, 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 & Faroqi-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., Linebarger 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

Dronkers, N. F., Ivaonova, M. V., & Baldo, J. V. (2017). What do language disorders reveal about brain-language relationships? From classic models to network approaches. *Journal of the International Neuropsychological Society*, *23*, 741–754. A review of how language disorders have elucidated the neural basis of language.

Hickok, G., & Small, S. L. (Eds.). (2016). *Neurobiology of language*. San Diego, CA: Academic Press. An encyclopedic collection of short chapters covering the neurobiology of language.

Karnath, H.-O., Sperber, C., & Rorden, C. (2018). Mapping human brain lesions and their functional consequences. *NeuroImage*, *165*, 180–189. doi:10.1016/j.neuroimage.2017.10.028. A somewhat more technical overview of lesion-symptom mapping.

Mesulam, M.-M., Rogalski, E. J., Wieneke, C., Hurley, R. S., Geula, C., Bigio, E. H., . . . Weintraub, S. (2014). Primary progressive aphasia and the evolving neurology of the language network. *Nature Reviews Neurology*, *10*, 554–569. doi:10.1038/nrneurol.2014.159. A review of progressive language deficits that result from neurodegenerative diseases (primary progressive aphasia), which offers a different perspective on the neuroanatomy of language.

Wilson, S. M. (2017). Lesion-symptom mapping in the study of spoken language understanding. *Language, Cognition and Neuroscience*, *32*, 891–899. doi:10.1080/23273798.2016.1248984. An accessible overview of the lesion-symptom mapping method.

Action Editor

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

ORCID iDs

Daniel Mirman https://orcid.org/0000-0001-5472-0220
Melissa Thye https://orcid.org/0000-0002-6383-6361

Acknowledgments

A preliminary version of this summary was presented at the 2016 American Speech-Language-Hearing Association Convention (Philadelphia, Pennsylvania). We thank Peter Turkeltaub, Ajay Halai, and Matthew Lambon Ralph for providing the statistical maps of their results, which allowed us to more accurately describe their findings.

Declaration of Conflicting Interests

The author(s) declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

Funding

Preparation of this article was supported by the University of Alabama at Birmingham.

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

Barsalou, L. W., Simmons, W. K., Barbey, A. K., & Wilson, C. D. (2003). Grounding conceptual knowledge in modality-specific systems. *Trends in Cognitive Sciences*, *7*, 84–91.

Basilakos, A., Fillmore, P. T., Rorden, C., Guo, D., Bonilha, L., & Fridriksson, J. (2014). Regional white matter damage predicts speech fluency in chronic post-stroke aphasia. *Frontiers in Human Neuroscience*, *8*, Article 845. doi:10.3389/fnhum.2014.00845

Bates, E., Wilson, S. M., Saygin, A. P., Dick, F., Sereno, M. I., Knight, R. T., & Dronkers, N. F. (2003). Voxel-based lesion-symptom mapping. *Nature Neuroscience*, *6*, 448–450. doi:10.1038/nn1050

Binder, J. R., & Desai, R. H. (2011). The neurobiology of semantic memory. *Trends in Cognitive Sciences*, *15*, 527–536. doi:10.1016/j.tics.2011.10.001

Botvinick, M. M. (2008). Hierarchical models of behavior and prefrontal function. *Trends in Cognitive Sciences*, *12*, 201–208. doi:10.1016/j.tics.2008.02.009

Brandi, M.-L., Wohlschlager, A., Sorg, C., & Hermsdorfer, J. (2014). The neural correlates of planning and executing actual tool use. *The Journal of Neuroscience*, *34*, 13183–13194. doi:10.1523/JNEUROSCI.0597-14.2014

Butler, R. A., Lambon Ralph, M. A., & Woollams, A. M. (2014). Capturing multidimensionality in stroke aphasia: Mapping principal behavioral component to neural structures. *Brain*, *137*, 3248–3266.

Caplan, D., Michaud, J., & Hufford, R. (2013). Dissociations and associations of performance in syntactic comprehension in aphasia and their implications for the nature of aphasic deficits. *Brain & Language*, *127*, 21–33. doi:10.1016/j.bandl.2013.07.007

Catani, M., Mesulam, M. M., Jakobsen, E., Malik, F., Martersteck, A., Wieneke, C., . . . Rogalski, E. J. (2013). A novel frontal pathway underlies verbal fluency in primary progressive aphasia. *Brain*, *136*, 2619–2628. doi:10.1093/brain/awt163

Chen, L., Lambon Ralph, M. A., & Rogers, T. T. (2017). A unified model of human semantic knowledge and its disorders. *Nature Human Behaviour*, *1*, Article 0039. doi:10.1038/s41562-016-0039

Chen, Q., Middleton, E., & Mirman, D. (2018). Words fail: Lesion-symptom mapping of errors of omission in post-stroke aphasia. *Journal of Neuropsychology*. Advance online publication. doi:10.1111/jnp.12148

DeWitt, I., & Rauschecker, J. P. (2012). Phoneme and word recognition in the auditory ventral stream. *Proceedings of the National Academy of Sciences*, *USA*, *109*, E505–E514. doi:10.1073/pnas.1113427109

Fedorenko, E. (2014). The role of domain-general cognitive control in language comprehension. *Frontiers in Psychology*, *5*, Article 335. doi:10.3389/fpsyg.2014.00335

Fridriksson, J., den Ouden, D.-B., Hillis, A. E., Hickok, G., Rorden, C., Basilakos, A., . . . Bonilha, L. (2018). Anatomy of aphasia revisited. *Brain*. Advance online publication. doi:10.1093/brain/awx363

Fridriksson, J., Guo, D., Fillmore, P. T., Holland, A., & Rorden, C. (2013). Damage to the anterior arcuate fasciculus predicts non-fluent speech production in aphasia. *Brain*, *136*, 3451–3460. doi:10.1093/brain/awt267

Fridriksson, J., Yourganov, G., Bonilha, L., Basilakos, A., Den Ouden, D.-B., & Rorden, C. (2016). Revealing the dual streams of speech processing. *Proceedings of the National Academy of Sciences, USA*, *113*, 15108–15113. doi:10.1073/pnas.1614038114

Griffis, J. C., Nenert, R., Allendorfer, J. B., & Szaflarski, J. P. (2017). Damage to white matter bottlenecks contributes to language impairments after left hemispheric stroke. *NeuroImage: Clinical*, *14*, 552–565. doi:10.1016/j.nicl.2017.02.019

Halai, A. D., Woollams, A. M., & Lambon Ralph, M. A. (2017). Using principal component analysis to capture individual differences within a unified neuropsychological model of chronic post-stroke aphasia: Revealing the unique neural correlates of speech fluency, phonology and semantics. *Cortex*, *86*, 275–289. doi:10.1016/j.cortex.2016.04.016

Hickok, G. S. (2012). Computational neuroanatomy of speech production. *Nature Reviews Neuroscience*, *13*, 135–145. doi:10.1038/nrn3158

Hickok, G. S., & Poeppel, D. (2007). The cortical organization of speech processing. *Nature Reviews Neuroscience*, *8*, 393–402.

Johnson-Frey, S. H. (2004). The neural bases of complex tool use in humans. *Trends in Cognitive Sciences*, *8*, 71–78. doi:10.1016/j.tics.2003.12.002

Jurado, M. B., & Rosselli, M. (2007). The elusive nature of executive functions: A review of our current understanding. *Neuropsychology Review*, *17*, 213–233. doi:10.1007/s11065-007-9040-z

Lacey, E. H., Skipper-Kallal, L. M., Xing, S., Fama, M. E., & Turkeltaub, P. E. (2017). Mapping common aphasia assessments to underlying cognitive processes and their neural substrates. *Neurorehabilitation & Neural Repair*, *31*, 442–450. doi:10.1177/1545968316688797

Lambon Ralph, M. A., Jefferies, E., Patterson, K., & Rogers, T. T. (2017). The neural and computational bases of semantic cognition. *Nature Reviews Neuroscience*, *18*, 42–55. doi:10.1038/nrn.2016.150

Linebarger, M. C., Schwartz, M. F., & Saffran, E. M. (1983). Sensitivity to grammatical structure in so-called agrammatic aphasics. *Cognition*, *13*, 361–392. doi:10.1016/0010-0277(83)90015-X

Meyer, K., & Damasio, A. (2009). Convergence and divergence in a neural architecture for recognition and memory. *Trends in Neurosciences*, *32*, 376–382. doi:10.1016/j.tins.2009.04.002

Mirman, D., Chen, Q., Zhang, Y., Wang, Z., Faseyitan, O. K., Coslett, H. B., & Schwartz, M. F. (2015). Neural organization of spoken language revealed by lesion-symptom mapping. *Nature Communications*, *6*, Article 6762. doi:10.1038/ncomms7762

Mirman, D., Zhang, Y., Wang, Z., Coslett, H. B., & Schwartz, M. F. (2015). The ins and outs of meaning: Behavioral and neuroanatomical dissociation of semantically-driven word retrieval and multimodal semantic recognition in aphasia. *Neuropsychologia*, *76*, 208–219. doi:10.1016/j.neuropsychologia.2015.02.014

Nozari, N., & Faroqi-Shah, Y. (2017). Investigating the origin of nonfluency in aphasia: A path modeling approach to neuropsychology. *Cortex*, *95*, 119–135. doi:10.1016/j.cortex.2017.08.003

Patterson, K. E., Nestor, P. J., & Rogers, T. T. (2007). Where do you know what you know? The representation of semantic knowledge in the human brain. *Nature Reviews Neuroscience*, *8*, 976–987. doi:10.1038/nrn2277

Pustina, D., Avants, B. B., Faseyitan, O. K., Medaglia, J., & Coslett, H. B. (2018). Improved accuracy of lesion to symptom mapping with multivariate sparse canonical correlations. *Neuropsychologia*, *115*, 154–166. doi:10.1016/j.neuropsychologia.2017.08.027

Rogalski, E. J., Cobia, D., Harrison, T. M., Wieneke, C., Thompson, C. K., Weintraub, S., & Mesulam, M.-M. (2011). Anatomy of language impairments in primary progressive aphasia. *The Journal of Neuroscience*, *31*, 3344–3350. doi:10.1523/JNEUROSCI.5544-10.2011

Rogers, T. T., Lambon Ralph, M. A., Garrard, P., Bozeat, S., McClelland, J. L., Hodges, J. R., & Patterson, K. E. (2004). Structure and deterioration of semantic memory: A neuropsychological and computational investigation. *Psychological Review*, *111*, 205–235.

Rorden, C., & Karnath, H.-O. (2004). Using human brain lesions to infer function: A relic from a past era in the fMRI age? *Nature Reviews Neuroscience*, *5*, 813–819.

Thothathiri, M., Kimberg, D. Y., & Schwartz, M. F. (2012). The neural basis of reversible sentence comprehension: Evidence from voxel-based lesion symptom mapping in aphasia. *Journal of Cognitive Neuroscience*, *24*, 212–222. doi:10.1162/jocn_a_00118

Weiss, P. H., Ubben, S. D., Kaesberg, S., Kalbe, E., Kessler, J., Liebig, T., & Fink, G. R. (2016). Where language meets meaningful action: A combined behavior and lesion analysis of aphasia and apraxia. *Brain Structure & Function*, *221*, 563–576. doi:10.1007/s00429-014-0925-3

Wilson, S. M., Henry, M. L., Besbris, M., Ogar, J. M., Dronkers, N. F., Jarrold, W., . . . Gorno-Tempini, M. L. (2010). Connected speech production in three variants of primary progressive aphasia. *Brain*, *133*, 2069–2088. doi:10.1093/brain/awq129

Zhang, Y., Kimberg, D. Y., Coslett, H. B., Schwartz, M. F., & Wang, Z. (2014). Multivariate lesion-symptom mapping using support vector regression. *Human Brain Mapping*, *35*, 5861–5876. doi:10.1002/hbm.22590