Aphasia : Progress in the last quarter of a century

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ABSTRACT In the last 25 years, characterization of aphasia has shifted from descriptions of the language tasks that are impaired by brain damage to identification of the disrupted cognitive processes underlying language. At the same time advances in technology, including functional imaging, electrophysiologic studies, perfusion imaging, diffusion tensor imaging, and transcranial magnetic stimulation, have led to new insights regarding the relationships between language and the brain. These insights, together with computational models of language processes, converge on the view that a given language task relies on a complex set of cognitive processes and representations carried out by an intricate network of neural regions working together. Recovery from aphasia depends on restoration of tissue function or reorganization of the cognitive/neural network underlying language, which can be facilitated by a number of diverse interventions. The original research by the author reported in this article was supported by NIH R01 DC05375. **NEUROLOGY 2007;69:200–213**

In the nineteenth century, Dax,[1] Broca,[2] Wernicke,[3] and their contemporaries made a number of important discoveries about the locations of brain lesions that cause disruption of language (aphasia) by studying the brains of individuals who had been aphasic. The most reliable finding was that damage to the left hemisphere was discovered in patients who had had language impairment. Another novel and important observation was that damage to more anterior parts of the brain, particularly the left posterior inferior frontal cortex, was usually found in patients whose spoken output was limited or poorly articulated,[4] while damage to more posterior regions in the temporal lobe was found in patients whose spoken output was well articulated but meaningless.[3]

Although localization of functions in the brain lost favor in the early 20th century, these early observations provided some of the groundwork for Norman Geschwind's[5] seminal writings on aphasia classification and associated sites of lesions, briefly reviewed in this article. Geschwind's students and colleagues in Boston developed a well known clinical test, the Boston Diagnostic Aphasia Examination (BDAE[6]) to assist clinicians in identifying patients with each type of aphasia. Although the earliest descriptions of aphasia may have confounded impairments of speech (the motor processes involved in production of verbal language) and language (the abstract symbols or representations and syntactic processes that underlie verbal and written communication), Geschwind and his followers used the term to describe disorders of language. When CT scans became available, other investigators confirmed that the various types of aphasia identified by Geschwind and classified with the BDAE are generally associated with lesions in relatively distinct areas of the brain[7,8] (but see contradictory evidence[9]).

However, in the 1980s three developments revolutionized our thinking about aphasia. First, PET and later functional MRI (fMRI) and magnetoencephalography showed that areas in both hemispheres of the brain are activated specifically during language tasks, although the left hemisphere reliably shows more activation in the majority of neurologically normal adults.[10-13] Furthermore, these functional imaging studies have revealed not only coordinated activations in the previously described language centers, but also activation of more distant

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areas of cortex, such as inferior and anterior temporal cortex[14] and in the basal ganglia and thalamus.[15] Secondly, there was mounting appreciation for the complexity of the most basic language tasks, such as naming a picture or understanding a word. Linguists, psychologists, neuroscientists, and mathematicians began to dissect out the cognitive processes and representations that are computationally necessary to accomplish such seemingly simple tasks. Advances in technology, such as parallel processing, allowed development of computational models that simulated tasks of reading, naming, or word recognition.[16,17] The complexity of the tasks seemed to fit well with the complexity of the network of neural regions that are engaged during the tasks as revealed by functional imaging. Third, the recognition that focal neurodegenerative disease could cause primary progressive aphasia[18] allowed exploration of patterns of language deficits that are caused by atrophy of regions of the brain that are not typically damaged by stroke. For example, progressive atrophy of left more than right anterior and inferior temporal cortex (which are rarely affected by stroke) is associated with progressive dissolution of modality-independent semantics, or meanings of words and objects in a syndrome known as semantic dementia.[19,20]

Furthermore, new technologies that permit the investigator to cause (or image) temporary dysfunction of focal regions of brain have allowed direct tests of hypotheses about structure/function relationships derived from functional imaging. To illustrate, functional imaging studies reliably show activation in midfusiform gyrus during reading tasks,[21] indicating that this area is consistently engaged in reading. Other studies show reliable activation in the left midfusiform gyrus during naming and other lexical tasks.[22] To test the hypothesis that this area is necessary for a particular component of reading and/or naming, one might cause temporary dysfunction of the left midfusiform gyrus by inhibiting this region with cortical stimulation in patients undergoing surgery during awake craniotomy[23] or through implanted subdural grids.[23,24] If this area is essential for some component of the reading or naming tasks, these functions should be disrupted during the inhibitory stimulation. In fact, cortical stimulation of nearby posterior basal temporal cortex disrupted reading of kanji (which represent meanings, not sounds) and picture naming, which both require conversion of semantic to phonologic representations, but did not affect comprehension of spoken words, reading of kana (which represent sounds of words), copying, or tool use.[25] Alternatively, one might observe whether transient hypoperfusion in this area (seen on perfusion MRI or PET) in cerebral ischemia disrupts reading or naming. In fact, hypoperfusion or infarct of this area is strongly associated with impaired oral reading and naming in acute stroke.[26] Another way to test if an area is essential for a particular task is to use inhibitory repetitive transcortical magnetic stimulation (rTMS) in normal subjects during that task.[27] More detailed examples of these methods of exploring brain/language relationships are described later, after first reviewing recent insights regarding the aphasias described by Geschwind.[5]

"CLASSIC APHASIA CATEGORIZATION": VASCULAR SYNDROMES Broca's aphasia is characterized by nonfluent spontaneous speech and sentence repetition with relatively spared comprehension. "Nonfluency" often includes reduced phrase length, impaired melody and articulatory agility, diminished words per minute, or agrammatic sentence production. Because the concept is multidimensional, it is often difficult to judge. A patient might have poor melody and/or disrupted articulation, but produce complete, grammatic sentences or have fluently articulated agrammatic speech. Fluency in each of these dimensions is also a continuum rather than a dichotomy. Furthermore, many patients have predominantly nonfluent speech along all or most dimensions, but have islands of fluent production, particularly of "overlearned" or social phrases, such as, "You know what I mean." For these reasons, many patients cannot be reliably classified.[6,28] Nevertheless, poor fluency in each of these dimensions tends to co-occur, so that some patients have pervasively nonfluent speech, that is reliably perceived as such. These individuals tend to have good comprehension of conversations, single words, and grammatically simple sentences, but have trouble

understanding sentences with grammatically complex or "non-canonical" sentence structure, such as passive voice sentences and sentences with object relative clauses (e.g., "The girl that the boy kissed ran away"[29]) and those requiring maintenance and processing of word order or comparisons of word meanings (e.g., "Is a horse larger than a dog?"[30]). Such sentences are generally understood in conversation because the context limits the possible interpretations. Broca's aphasia is often associated with impaired spelling of familiar words, as well as difficulty using letter-sound associations (phonics) to read or spell unfamiliar words.

Whether the various language deficits observed in Broca's aphasia can be accounted for by a single underlying deficit has been a matter of energetic debate. One proposal was that the agrammatic speech and impaired comprehension of grammatically complex sentences could be explained by an underlying syntactic processing deficit.[31] However, this hypothesis was undermined by the reports of patients with agrammatic speech without difficulty understanding grammatically complex sentences.[32] Reduced lexical activation[33] or impairment in maintaining and processing the sequence of linguistic elements might account for many of the frequently observed deficits, including those in reading, spelling, and repetition,[30] but like all "unifying" impairments would have difficulty explaining cases that show selective impairment of just one of the tasks. Furthermore, individuals with Broca's aphasia often have difficulty naming verbs relative to nouns[34,35] or producing particular verb forms, in addition to comprehension of grammatically complex structures and other deficits described above. This array of deficits may be difficult to explain by proposing a single underlying impairment. The various dissociations between frequently impaired language functions have led some authors to argue that Broca's aphasia is not a theoretically coherent syndrome with a single underlying impairment.[36] Nevertheless, it may well be a vascular syndrome—impairment of a collection of speech and language functions that depend on nearby brain regions all supplied by the superior division of the left middle cerebral artery (MCA). This hypothesis would explain the frequent association between agrammatic speech, impaired articulation, verb production, and asyntactic comprehension in the same way as the frequent association between agrammatic speech and right hemiplegia—they are both caused by damage or dysfunctional tissue in posterior frontal cortex, but are not caused by a single underlying functional deficit.

Consistent with the concept of a vascular syndrome, Broca's aphasia is generally associated with damage or dysfunction in posterior, inferior frontal gyrus, which includes Broca's area (Brodmann area 44 and 45). However, when damage is isolated to Broca's area, or part of Broca's area, then the only deficit may be impaired motor planning and programming of motor speech ("apraxia of speech"), which frequently is observed in Broca's aphasia but can occur in isolation.[37] The entire syndrome of Broca's aphasia may require damage or neural compromise of a larger area surrounding Broca's area supplied by the superior division of the left MCA. The motor deficit of apraxia of speech that is usually associated with the language deficits in Broca's aphasia can account for several aspects of impaired fluency, including disrupted articulatory agility and prosody.

There is one caveat in attempting to relate language syndromes to particular areas of the brain, whether one identifies areas by Brodmann areas, gyri, or groups of voxels on scans registered to a particular atlas, spatial coordinates, or an "idealized" brain image. There is a great deal of individual variability in the boundaries of the cytoarchitectural fields identified by Brodmann, as well as in the pattern of sulci and gyri and general shape of individual brains.[38,39] Therefore, "localization" of functions can only be approximate.

It is also important to note that dysfunctional neural tissue surrounding an infarct can also contribute to the observed deficits. Thus, patients with hypoperfusion but no infarct in and around Broca's area often have the typical vascular syndrome described above.[30,40] Deficits have been attributed to hypoperfusion, rather than the small, usually deeper, infarcts in the same patients, because restoring blood flow to the hypoperfused regions resulted in immediate recovery of language functions.[30,41-44]

Wernicke's aphasia is characterized by fluent but relatively meaningless spontaneous speech and repetition and relatively poor comprehension of words, sentences, and conversation. Spoken language may be limited to jargon comprised of either real words or neologisms (nonwords such as "klimorata") or a combination of the two. In contrast to those with Broca's aphasia, the individual with Wernicke's aphasia is typically unaware of the errors. The appropriate melody or intonation may give the impression that the person is speaking another language. Particularly in the acute stage, there is often a profound impairment of comprehension, such that the patient may listen to others and respond fluidly with language-like, meaningless utterances for hours, with no apparent inkling that he or she has neither understood anything others have said

nor said anything that could be understood by others. Often the person will intermittently include a coherent "social" phrase, such as, "yes, that's right." Written output is typically similar to spoken output—written words with little or no content, often including nonword letter strings. Reading comprehension is typically no better than spoken comprehension. Repetition is generally similar to spontaneous speech—fluent jargon. These deficits have been attributed to impaired inhibition of lexical activation, so that the person cannot select the appropriate word, sound, or meaning from competing linguistic units that are also activated.[33] Although such an underlying impairment would account for many of the observed language deficits, it could not easily account for cases with relatively preserved or relatively impaired categories of words, such as animals or tools,[45] or impaired nouns relative to verbs.[35] This collection of deficits is usually caused by neural dysfunction in regions supplied by the inferior division of the left MCA, including Wernicke's area (most of Brodmann area 22, in the posterior, superior temporal gyrus). This hypothesis can account for occasional dissociations between the typical deficits or anomalous lesion sites in patients with Wernicke's aphasia by the fact that there is individual variability in the cerebral vasculature and the areas supplied by particular arteries.

Global aphasia refers to the combination of deficits described in Broca's and Wernicke's aphasia. Typically, the person has severely impaired comprehension of single words, sentences, and conversation, and very limited, if any, spoken output. Spontaneous speech, naming, and repetition may be limited to a single perseverative word (e.g., no, no, no) or nonword utterance. Reading and writing are also profoundly impaired. In most cases, both Broca's area and Wernicke's area are damaged[46] or functionally compromised.[40]

The transcortical aphasias refer to language syndromes similar to those described above, but with relatively normal sentence repetition. Transcortical motor (TCM) aphasia has many of the characteristics of Broca's aphasia, except that repetition is fluent and grammatic. This vascular syndrome is caused by lesions just anterior or superior to (surrounding) Broca's area,[47] often caused by occlusion of the anterior cerebral artery (ACA)[48,49] or "watershed" areas between the ACA and the MCA. This observation may account for the overlap in syndromes, consistent with Mohr's proposal that damage to Broca's area alone causes a motor speech deficit, while damage to the surrounding areas causes the other symptoms of Broca's aphasia. In TCM, motor speech is spared, as evidenced by spared repetition, while other functions typically affected in Broca's aphasia are impaired. Likewise, transcortical sensory (TCS) aphasia is similar to Wernicke's aphasia, except that repetition is accurate. It is caused by lesions involving areas surrounding Wernicke's area, in the watershed territories between the MCA and posterior cerebral artery (PCA) or the PCA territory.[50] Finally, mixed transcortical aphasia (MTA) is comparable to global aphasia, except that sentence repetition is spared. These individuals appear to be echolalic and have lesions surrounding Broca's and Wernicke's area, but sparing language cortex itself.[51] Because of this localization, the syndrome is sometimes known as "isolation of the speech area," as it appears to disconnect speech and language from broadly distributed meanings of words.

Conduction aphasia is characterized by relatively fluent, accurate spontaneous speech with phonemic paraphasias (well articulated responses that are phonetically similar to the target word) sometimes produced in a series of increasingly closer approximations of the target (e.g., "splant, plant, plants, pants" for pants—termed "conduit d'approche") and disproportionately impaired repetition. Geschwind[5] hypothesized that the repetition deficit was caused by a lesion in the arcuate fasciculus, a white matter tract that runs between Broca's and Wernicke's areas. This hypothesis has been challenged on the basis that patients with conduction aphasia more often have lesions in the supramarginal gyrus or deep parietal white matter,[52] and on the basis that lesions of the arcuate fasciculus do not reliably cause conduction aphasia.[53] For these reasons, the author believes that lesions in the arcuate fasciculus have no causative role in the clinical syndrome of conduction aphasia.

Pure alexia (alexia with agraphia) refers to impaired reading in the presence of spared writing and relatively spared recognition of words spelled aloud. This syndrome often results from a combination of two lesions, both caused by occlusion or stenosis of the left posterior cerebral artery. A lesion in the left occipital cortex results in right homonymous hemianopsia, such that all visual information is initially processed in the right occipital cortex. A second lesion in the splenium of the corpus callosum prevents visual information in the right hemisphere from being transferred to the left hemisphere language cortex. Therefore, the person cannot read printed words but can recognize words spelled aloud (because the latter can initially be processed in the left hemisphere of the same patients[54-58]). In one case the patient had a left occipital infarct and

Table 1 Vascular aphasic syndromes

	Broca	Wernicke	Conduction	TCM	TCS	MTA and global	Anomic	Optic
Fluency*	Poor	Good	Fair–good	Poor	Good	Poor	Good	Good
Content	Good	Poor	Good	Good	Poor	Poor	Good	Good
Comprehension	Intact words and simple sentences	Poor	Intact words and simple sentences	Intact words and simple sentences	Poor	Poor	Good	Good
Repetition	Poor, nonfluent	Poor, fluent jargon	Poor	Good	Good	MTA good; global poor	Good	Good
Naming	Worse for verbs	Worse for nouns	Fair–good	Fair–good	Poor	Poor	Worse for nouns	Poor with visual stimuli
Spelling	Poor	Poor	May be spared	May be spared	Poor	Poor	May be spared	Good
Reading	Poor	Poor	May be spared	May be spared	Poor	Poor	May be spared	Poor
Associated signs	Right arm weakness; apraxia of speech	Superior visual field cut	Poor working memory	Abulia	Right field cut	Right hemiplegia		Right hemianopia

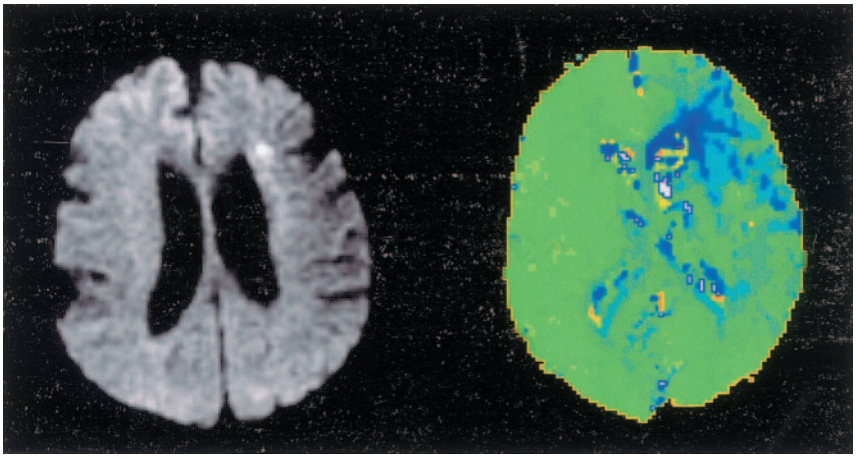
*Fluency includes grammaticality, prosody, melody, articulatory agility, and rate of speech, which can be differentially affected.
TCM = transcortical motor; TCS = transcortical sensory; MTA = mixed transcortical aphasia.

hypoperfusion of the splenium; his reading recovered when the splenium was reperfused.[59] Consistent with this hypothesis of a "disconnection" between right occipital cortex and left hemisphere language areas as an account of pure alexia, many pure alexic patients also are unable to name visual stimuli, although they can name the same items from tactile exploration or in response to a verbal description. This pattern of performance, known as optic aphasia,[60,61] can also result from the combination of left occipital and splenium lesions, and can be seen as a disconnection between visual processing in the right hemisphere and language output in the left hemisphere.[58,59]

Patients with optic aphasia can often produce gestures for visual objects that they cannot name, indicating that they can access at least some meaning. However, tests of picture association demonstrate that they cannot reliably distinguish between semantically related pictures.[58] Their errors in naming and word/picture matching likewise show access to some meaning, but not sufficient meaning to select between semantically related items. That is, they often produce semantic paraphasias, names that are related in meaning to the target (e.g., mitten named as "sock"). Interestingly, given sufficient time, they often slowly hone in on the precise meaning. For example, in an attempt to name a shoe, a patient said, "I tie them . . . wear them . . . not for the hand but for the foot." In contrast, the same patient was able to immediately name a shoe from tactile exploration. This pattern of errors seems to reflect slow, bit by bit access to semantic information from vision, perhaps due to slow transmission of visual information to the left hemisphere language cortex, caused by disrupted white matter connections in the splenium. Similarly, patients with pure alexia can often read very slowly, letter-by-letter, perhaps for the same reason. The naming error pattern observed in optic aphasia was simulated by Plaut and Shallice[62] with a parallel distributed processing model of naming, by causing disrupted interactions between visual input and semantics. Pure alexia and optic aphasia are not strictly aphasic syndromes, since the representations and processes that constitute language are intact, but there is impaired access to them. However, they have been discussed here, because they have relatively reliable associated lesions and because they often are mistaken for aphasia. However, there is inadequate space to discuss other related vascular syndromes, such as alexia with agraphia, pure agraphia,[63] and pure word deafness.[64]

In summary, the classic aphasia classifications are vascular syndromes consisting of frequently associated deficits that reflect damage or dysfunction of regions of neural tissue (essential for particular language functions) supplied by a particular artery. For example, occlusion or critical stenosis of the superior division of the left MCA causes tissue dysfunction in left posterior inferior frontal cortex and insula, which apparently includes areas necessary for grammatic sentence production, planning and programming of speech articulation, and other functions that are impaired in Broca's aphasia. The same branch supplies the lateral motor strip, accounting for the frequent association between Bro-

Figure 1 Imaging in a patient with Broca's aphasia



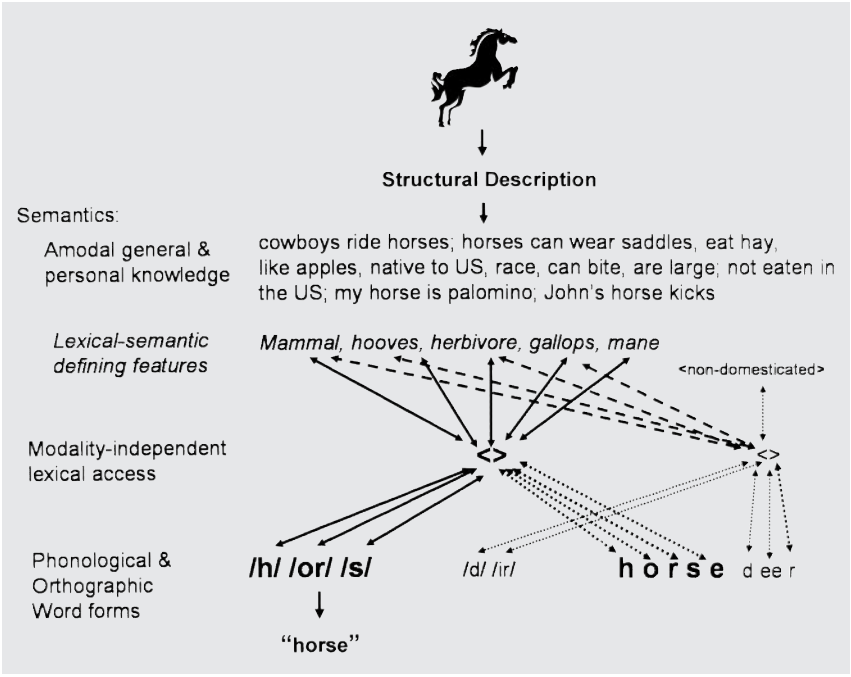
Diffusion-weighted image (left) and perfusion-weighted image (right) in a patient with Broca's aphasia associated with a tiny diffusion abnormality, but much larger perfusion abnormality involving Broca's area.

ca's aphasia and right arm weakness. These vascular syndromes are summarized in table 1.

The vascular syndromes are clinically useful, in that they allow strong predictions about what parts of the brain are ischemic. Although recent structural imaging, particularly diffusion-weighted imaging (DWI), is highly sensitive to dense ischemia or infarct, it does not reveal all areas that are dysfunctional due to hypoperfusion. Dynamic contrast (bolus-tracking) perfusion-weighted imaging (PWI) or CT perfusion scans can be used to reveal areas of poor blood flow that that often better account for the patient's clinical deficits.[43,44,65] However, perfusion imaging is not always obtainable, for example when a patient has no vascular access for contrast injection. The clinical syndrome and severity of deficits can predict the site and volume of perfusion abnormality, and can be used with the DWI to identify patients with a large diffusion–clinical mismatch who might benefit from aggressive treatment to restore blood flow.[66] For example, the patient whose scans are shown in figure 1 had a classic Broca's aphasia, but just tiny areas of infarct on DWI a few hours after onset of symptoms. The clinical syndrome indicated there was likely to be a perfusion abnormality that included posterior inferior frontal cortex. In this case, the perfusion abnormality was confirmed with PWI. However, even if it had it not been confirmed, this patient would be considered someone who needs urgent treatment to reperfuse the cortex and prevent infarct in the critical language cortex. Each of the classic aphasia types has been observed with hypoperfusion of the areas typically associated with the syndrome in a study of patients with small subcortical stroke, and patients with similar subcortical strokes who did not have hypoperfusion of the cortex did not have aphasia.[40] The aphasia syndromes have also been useful for predicting recovery[67] and for selecting patients for particular language therapies.[68]

APHASIA CHARACTERIZED BY DISRUPTION OF SPECIFIC COGNITIVE PROCESSES UNDERLYING LANGUAGE TASKS Although the classic aphasia syndromes have been useful clinically, they have been less useful for developing theories of how language is represented and processed. Most recent theories of sentence comprehension, sentence production, naming, reading, and so on, assume that these tasks require a number of distinct cognitive representations and processes that might rely on different brain regions. The proposal that each underlying component can be individually disrupted by brain damage can account for the various patterns of performance on language tasks that have been described. Not only are language tasks decomposable into discrete representations and processes, but many of the cognitive representations might be composites of features distributed across regions of the brain. For example, the semantic representation of "horse" might include features of how it moves, represented in areas of the brain critical for motion recognition (middle temporal visual area—area MT—and middle superior temporal area—area MST),[69,70] features specifying what it eats in another area, and features of how it is used by humans in another area of the brain.[71] Activation of all of the features simultaneously in different areas of cortex might constitute a "semantic representation" (the meaning, for example, what makes a horse a horse). Such distributed semantic representations might account for patients with category-specific language deficits. For example, damage to area MT/MST, disrupting activation of features of movement, might affect access to the meaning of animals and modes of transportation, but not buildings. In fact, patients with selective deficits in naming and comprehending the names of animals, as well as patients with selective preservation of animals (and to a lesser extent, transportation), have been described.[45,70] Many cases of selective impairments involving "living things" or "biologic kinds" relative to artifacts, or the opposite, have been reported.[72-76] Several computational models of semantics have simulated category-specific semantic deficits by disrupting access to a particular type of feature.[77] Others have accounted for selective impairments involving living things by assuming that living things have strongly correlated features (e.g., the presence of eyes, ears, and limbs are highly correlated) or that their distinctive features are selectively lost because they are weakly correlated to other features.[78] Others have proposed that category-specific deficits have an evolutionary basis, such that certain

Figure 2 Cognitive processes and representations underlying picture naming



A schematic representation of the cognitive processes and representations underlying picture naming

areas of the brain became devoted to processing particular categories (e.g., animals, which were both enemies and food[79]). Still others have proposed that names of tools and action verbs are represented in areas critical for producing associated limb motions (e.g., posterior frontal cortex[70]) or that manipulable items activate frontoparietal regions subserving hand motion representations.[80] Although controversies remain, the category-specific language deficits have provided essential data for developing models of particular language functions.

This new approach to conceptualizing aphasia will be illustrated by considering one language task that is most frequently impaired by left hemisphere damage (and frequently tested at the bedside)—picture naming. Impaired naming may be the residual deficit after partial recovery from almost any aphasia type, and thus may result from damage to a variety of brain regions. These observations can be explained by assuming that picture naming requires a number of different cognitive representations and processes that each depend on distinct, but perhaps overlapping, brain regions. Damage to any one of these areas might disrupt picture naming, but perhaps in different ways. It would not be possible to review all of the many theories and simulations of cognitive processes underlying picture naming.[62,81-85] However, it is widely agreed that naming a picture of a horse would require, at the least, processes for abstracting from the visual stimulus the features that allow recognition of the item as something familiar (access to the structural description in figure 2); access to the meaning of horse (the semantic representation); access to the learned pronunciation of horse (the phonologic representation); and motor planning/programming of the muscles of the lips, tongue, palate, vocal folds, and muscles of respiration required to articulate the word. Many investigators also include a modality-independent level of lexical (word) access (e.g., a "lemma" level, which specifies the syntactic role of the word, but not the meaning or phonology[84,85]). A schematic representation of these cognitive processes underlying naming is shown in figure 2. Although this depiction suggests serial processing from one level to the next, there is evidence that these sorts of cognitive representations may be activated in parallel or in cascade, and there are likely to be feedback as well as feedforward interactions, at least between some levels of processing.[86]

Evidence for proposing each of these components of the naming process comes from patterns of impaired performance after brain damage or degenerative disease. Evidence that naming requires access to a structural description for visual recognition comes from patients with apperceptive visual agnosia, who cannot distinguish drawings of real items from unreal items (e.g., a dog with antlers) or name visual stimuli, but can name the same items in response to a verbal description. Patients with optic aphasia, described earlier, can distinguish real from unreal objects but are impaired in activating a complete semantic representation from the structural description. They can, however, access full semantics from tactile exploration or verbal description. Optic aphasia can be accounted for by assuming partially impaired access to semantics from an intact structural description.

In contrast, patients with semantic dementia cannot fully access semantics, particularly of less familiar items, from any modality. They often use objects inappropriately (e.g., try to eat soup with a knife) and cannot identify associations between pictures. Evidence for proposing a distinction between the complete semantic representation and a subset of "defining" or "identification" features is found in the contrasting patterns of performance by patients with semantic dementia and patients who fail to understand words (e.g., point to a picture of a knife when asked to point to spoon) but do not use objects inappropriately. The latter pattern, which is common after stroke, indicates that access to some general knowledge (e.g., about how to use an object) and personal knowledge (e.g., which brush is my brush) is intact, but there is inadequate semantic information to identify which related items are linked to a particular name. A person with this sort

of lexical semantic deficit might call a horse a cow or a deer, and might point to a picture of a cow or deer when asked to point to a horse, but would not try to saddle a cow or deer. This distinction between semantic errors after stroke vs the semantic errors in patients with semantic dementia has been eloquently described by Jeffries and Lambon Ralph,[87] although their characterization of the cause of semantic errors after stroke is somewhat different.

Evidence for proposing a level of modality-independent lexical access is that damage to such a level of processing would account for the common deficit of "anomia," in which the individual can retrieve neither the phonologic representation (learned pronunciation) nor the orthographic representation (learned spelling) of a particular item, despite intact semantics. Such a deficit is experienced as the tip of the tongue phenomenon. Patients with anomia have full access to the meaning and may retrieve semantically related names or phonologically related names, but are aware that such names are not what they are searching for. They know the grammatic word class, and sometimes partial phonologic information (e.g., the first letter or the approximate length of the word).

Separate modality-specific representations of the name must also be postulated to explain performance of patients who are able to retrieve the phonologic representation to say the name but not the orthographic representation to spell the name, or the opposite pattern, despite the absence of motor output deficits.[88-93] Sometimes these deficits are specific to a particular grammatic category. For example, one reported patient was selectively unable to orally name or read aloud verbs but could write the same verbs and could orally name or read aloud (and write) nouns, while another patient had the opposite pattern with respect to output modality—she was selectively unable to retrieve the written name of verbs, but could retrieve the oral names of verbs and oral and written names of nouns.[89] Yet another patient was selectively impaired in oral naming of nouns relative to verbs using the same stimuli.[93] Although such patients sometimes produce semantically related words in the affected output modality, they do not have deficits in accessing meanings (semantics) or linking meanings to words (lexical-semantic deficits), as demonstrated by their accurate naming in the other modality and by excellent word comprehension.

Finally, evidence for proposing a distinct system for motor planning and programming of speech articulation comes from patients who have no dysarthria (i.e., no impairment in the rate, range, strength, or timing of movements of the lips, tongue, jaw, palate, respiratory muscles, or vocal folds), but nevertheless make numerous and variable errors in articulation of words, particularly longer words. Such a deficit, sometimes called apraxia of speech, results in disruption of prosody as well as distortions, transpositions, omissions, additions, and substitutions of phonemes. The patient is quite aware of the errors and tries to correct them, but often shows articulatory struggle and frustration. Although apraxia of speech is a motor speech disorder rather than a true language disorder, it frequently co-occurs with aphasia. In isolation, it is rare and usually transient.

The pattern of errors across tasks, as well as error types, provide indications regarding the component of naming that is impaired in a particular aphasic patient, as illustrated in table 2.

It is important to note that while selective deficits in particular cognitive processes underlying a task such as naming have been very informative for developing theories, such discrete deficits are relatively uncommon. The majority of aphasic individuals have impairments involving more than one cognitive process.

NEURAL CORRELATES OF THE COGNITIVE PROCESSES UNDERLYING NAMING Functional imaging studies of naming show widespread activation of perisylvian language cortex, including Broca's area and Wernicke's area, as well as more inferior and anterior temporal and occipital cortex during picture naming.[11,14] Some studies have reported more localized areas of activation associated with particular components of naming.[95] Such results are consistent with the hypothesis that complex neural networks, as well as complex cognitive systems, are recruited for apparently simple language tasks such as picture naming.[11,14,94-96] Various language tasks, including naming and word comprehension, recruit overlapping networks of brain regions.[11,97] Such results suggest that language tasks such as naming or reading emerge from distinct distributions of activation across various brain regions[98] and are consistent with the hypothesis that various language tasks depend on overlapping neural as well as cognitive processes. Most studies also show different patterns of activation depending on the semantic category of stimuli[70] consistent with the hypothesis that semantic representations are distributed across various regions in temporal and perhaps parietal cortex. Difficulty of task and rate of presentation also influence the pattern of activation in both the left and right hemispheres,[99] indicating that some activation in functional imaging may also reflect nonlinguistic aspects of the task, such as the

Table 2 Patterns of errors in naming associated with selective impairments of distinct cognitive processes

Cognitive process	Use of objects	Spoken word comprehension	Oral naming	Written naming	Repetition
Semantics	Errors on low familiarity items	Semantic errors (e.g., dog/cat)	Semantic errors (e.g., dog→cat)	Semantic errors (e.g., dog→cat)	Normal
Lexical-semantics†	Normal*	Semantic errors (e.g., dog/cat)	Semantic errors (dog→cat; dog→bone)	Semantic errors (e.g., dog→cat; dog→bone)	Normal
Modality-independent lexical access	Normal	Normal	Semantic errors (dog→cat; dog→bone)	Semantic errors (e.g., dog→cat; dog→bone)	Normal
Phonologic representations	Normal	Normal	Semantic errors (dog→cat; dog→bone) or phonologically similar words or nonwords	Normal	Normal
Orthographic representations	Normal	Normal	Normal	Semantic errors (e.g., dog→cat; dog→bone) or orthographically similar words or nonwords	Normal
Articulatory planning and programming	Normal	Normal	Variable off-target articulations	Normal	Variable off-target articulations

*Processes that are normal when there is selective impairment of a component may be impaired when the patient has other deficits.
†Lexical-semantics refers to mechanisms for linking a subset of semantic features that define the word to a particular lexical representation (e.g., what makes a dog a dog).

difficulty of response selection[100] or other executive processes. Likewise, some activated regions during picture naming may reflect automatic access to personal memories or emotions connected with the pictured item. As has been frequently discussed, functional imaging studies show areas of the brain that are engaged in a particular task, but cannot determine which of these areas are essential for the tasks.[101] Nevertheless, functional imaging studies have been important in showing that different regions within Wernicke's area[102] or Broca's area[103] subserve different functions, and for showing that the distinct patterns of activation across a number of brain regions support a given language function.[12,95,104]

Lesion studies show that overlapping networks of brain regions are also essential for various language tasks, such as naming or reading. Recent studies indicate that damage to the same regions can disrupt naming, written word comprehension, and spoken word comprehension, but different areas have greater weight in predicting error rates on each of these tasks in regression models.[105] Each underlying component process shared by these tasks might depend on a particular "cog" in the system (a particular brain region) or all components could all depend on the same or overlapping brain regions, but with some areas being more critical to one component or the other. A recent study using discriminant function analysis indicated that disruption of different components of the naming process (depicted in figure 1) could be distinguished by six discriminant functions that reflected distinct distributions of tissue dysfunction across seven left hemisphere Brodmann areas: BA22/Wernicke's area, BA44 and 45/part of Broca's area, BA 38/anterior temporal, BA37/posterior middle–inferior temporal and fusiform gyri, BA 39/angular gyrus, and BA21/inferior temporal.[106a] Other studies have highlighted the importance of a particular region for a given component on naming. For instance, lesions in left BA 37 are associated with modality-independent lexical access,[106,107] and restoration of tissue function in BA 37 is associated with recovery of modality-independent lexical access.[108] Diffusion tensor imaging and tractography are promising methods of identifying white matter tracks that connect various components of the neural network underlying naming and other language tasks.[53,109] To complement the imaging of structural connections, magnetoencephalography can reveal neural networks through the functional connectivity between areas revealed by simultaneous activation.[110]

Some levels of representation computed in naming are likely to be more distributed than others. For example, semantic representations might be widely distributed in the temporal (particular anterior and lateral inferior temporal cortex[14]), frontal, and parietal cortex, with features of some items such as actions represented closer to motor systems, and features of other items, such as colors, represented closer to visual areas. Lesions that affect just part of the distributed semantic representations might cause category-specific semantic impairments. Some areas, such as Wernicke's area, might be critical for linking these widespread semantic represen-

tations—or just the subset of defining features—to specific words for word comprehension and naming.[11,111] Other areas, such as Broca's area or other parts of lateral prefrontal cortex, might be critical for selecting or activating certain types of semantic information to accomplish specific tasks.[103]

RECOVERY A wealth of literature on aphasia recovery demonstrates that most patients make at least some recovery and the majority make substantial or complete recovery. Early recovery is likely to be due to restoration of blood flow and other mechanisms of tissue recovery, while later stages of recovery are likely to depend on reorganization of structure/function relationships, as well as reorganization of cognitive functions and compensatory mechanisms.[67,112] Many functional lesion studies of language recovery have shown increased activation of right hemisphere homologues of language areas, while others show increased activation of perilesional areas of the left hemisphere during recovery.[104,113,114] Several recent studies have indicated that the areas recruited for a particular language task change over the course of recovery, with minimal elicited activation (or hemodynamic response) during the language task in the acute stage of stroke, predominantly right hemisphere activation in the subacute stage, and a return to predominant left hemisphere activation in the more chronic stage in patients who show good recovery of the task.[115]

TREATMENT This review cannot do justice to recent findings in the domain of aphasia treatment. However, a few words are important. First, aphasia therapy can be very useful in improving language and communication in a variety of settings.[116,117] Several recent investigations have shown that intense treatment (e.g., at least 4 days per week, at least 2 hours per day) for a short time is more effective than a similar number of sessions spread out over a longer period.[118] Some treatments focus on treating the underlying impairment, such as improving the component of the naming process that is disrupted or teaching the patient to rely on other components to compensate for the damage process.[119-124] Most of the direct treatments rely on the principle that the more often a patient produces a particular correct response (with as much facilitation as needed), the more often that person will be able to produce that same correct response independently in the future. Other interventions focus on communicative function—how to be successful in a particular communicative task, rather than treating a particular impairment.[125] In both approaches, the treatment must be individualized to the aphasic person's deficits, needs, and goals.

Some current trends in rehabilitation research are to evaluate the effects of pharmacologic augmentation of therapy, with stimulants,[126] cholinesterase inhibitors, dopamine agonists, and other medications that influence availability of particular neurotransmitters.[127,128] There is a paucity of randomized, placebo-controlled trials in this area, but several are under way. There is no evidence that medications are useful in the absence of language therapy, however. Transcranial magnetic stimulation is also being investigated as a method of enhancing aphasia recovery, with some small case series showing some benefit.[129,130]

CONCLUSION The study of aphasia and its associated lesions in the late 19th century led to many insights about the neural organization of language functions. Many of these insights have been confirmed and elaborated in more recent studies using advanced imaging to localize areas of dysfunctional brain tissue associated with particular language deficits or using functional imaging to identify areas of the brain that activated during a particular language task in normal controls[14,103] or in recovering aphasic individuals.[104,131] More detailed theories and computational models of particular language tasks have contributed also to the understanding of how each task might be carried out in the brain.

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