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# Why Is It Difficult to Predict Language Impairment and Outcome in Patients with Aphasia after Stroke?

Andreas Charidimou,<sup>a</sup> Dimitrios Kasselimis,<sup>b,c</sup> Maria Varkanitsa,<sup>d</sup> Caroline Selai,<sup>e</sup> Constantin Potagas,<sup>c</sup> Ioannis Evdokimidis<sup>c</sup>

<sup>a</sup>Stroke Research Group, Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, National Hospital for Neurology and Neurosurgery, London, UK

<sup>b</sup>Department of Psychology, University of Crete, Rethymno, Greece

<sup>c</sup>Department of Neurology, Medical School, National and Kapodistrian University of Athens, Eginition Hospital, Athens, Greece

<sup>d</sup>Division of Psychology and Language Sciences, Department of Linguistics, University College London (UCL), London, UK

<sup>e</sup>Institute of Neurology, The National Hospital for Neurology and Neurosurgery, University College London (UCL), London, UK

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## Correspondence

Andreas Charidimou, MD  
Stroke Research Group,  
Department of Brain Repair and  
Rehabilitation, UCL Institute  
of Neurology, National Hospital  
for Neurology and Neurosurgery,  
Box 6, Queen Square, London  
WC1N 3BG, UK

**Tel** +44 20 34567890

**Fax** +44 20 34484070

**E-mail** charidimou.09@ucl.ac.uk

One of the most devastating consequences of stroke is aphasia. Communication problems after stroke can severely impair the patient's quality of life and make even simple everyday tasks challenging. Despite intense research in the field of aphasiology, the type of language impairment has not yet been localized and correlated with brain damage, making it difficult to predict the language outcome for stroke patients with aphasia. Our primary objective is to present the available evidence that highlights the difficulties of predicting language impairment after stroke. The different levels of complexity involved in predicting the lesion site from language impairment and ultimately predicting the long-term outcome in stroke patients with aphasia were explored. Future directions and potential implications for research and clinical practice are highlighted.

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## Introduction

Stroke causes 9% of all deaths worldwide, second only to ischemic heart disease.<sup>1,2</sup> The prolonged disability experienced by stroke survivors is even more devastating. One of the most severe consequences of stroke is aphasia, a language impairment caused by damage to the brain regions supporting language. However, a clear-cut clinical correlation between lesion sites and specific language deficits has yet to be described.<sup>3</sup> Despite the elucidation of the neural organization of language being the focus of intense research since the 19th century, the functional neuroanatomy of language has proven very difficult to characterize. Nevertheless, advances in neuroimaging [including MRI,

functional MRI, diffusion tensor imaging (DTI), and perfusion imaging] have led to new insights into the identification of the disrupted cognitive processes underlying language after brain damage.

The aim of this paper is to highlight the difficulties of predicting language impairment after stroke. In the next section we summarize the very first efforts to localize language deficits in patients with aphasia, and discuss the importance and the triviality of these efforts in contemporary clinical aphasiology. We then consider Broca's and Wernicke's legacy. In the subsequent section we explore the different levels of complexity that limit the ability to predict a lesion site from language impairment and outcome in stroke patients with aphasia. Finally, we discuss the clinical implications and future directions for research. To better inform our discussion we integrate contemporary knowledge by reviewing the relevant literature when necessary (Table 1). Aphasia studies using functional imaging tools such as functional MRI, PET, and SPECT are beyond the

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scope of this paper.<sup>4</sup>

## Aphasia versus Other Neurological Disorders Affecting Language

There are several disorders that can affect linguistic competence in addition to aphasia. For example, most dementias will eventually affect language. However, while stroke-induced aphasia is characterized by acute language impairment, which often improves over time (from the acute to the chronic stage), patients with dementia demonstrate progressive and diffuse cognitive deficits—not specific to language—and usually deteriorate over time. However, there are three variants of frontotemporal dementia [the syndromes of primary progressive aphasia (PPA)<sup>5</sup>] that are defined by core language deficits, similar to those of stroke-induced aphasias. Nevertheless, the latter are differentiated from PPAs based on the onset of the symptoms and the nature of the damage to the brain (in the case of PPA the onset is gradual, and MRI usually reveals frontal cortical atrophy).

When testing for aphasia it is necessary to also exclude primary sensory or motor deficits in order to establish a definitive diagnosis. Primary sensory deficits, such as hearing impairment or visual fields defects, can result in low performance on language tasks, thus providing misleading results. For example, if a stroke patient has hemianopia, he or she will probably be unable to perform sentence-reading or picture-description tasks, but this impaired performance cannot be attributed to a language deficit. With regard to primary motor deficits, there are various clinical syndromes that resemble nonfluent aphasias [The division of language disturbances into basic aphasia syndromes, including non-fluent aphasia (Broca's aphasia), fluent aphasia (Wernicke's aphasia), is a fundamental and appreciable concept in clinical neurology]. The most common is dysarthria, where articulation is disturbed at a lower, "pure" motor level. In contrast to nonfluent patients with aphasia, who often produce random paraphasic errors and demonstrate various cognitive or linguistic deficits (e.g., in complex sentence comprehension), patients with dysarthria systematically produce articulatory errors with no accompanying language deficits.

Finally, some information-processing deficits that occur after a brain lesion may mimic aphasic manifestations, even if they are not language impairments per se. Verbal short-term and working-memory deficits are associated with left-hemisphere posterior lesions,<sup>6</sup> and can result in impaired performance on comprehension tasks, thus creating a false aphasic phenotype. On the other hand, such processing deficits are often present in aphasia, and their severity is related to the degree of language impairment.<sup>7</sup> Processing and language deficits can therefore coexist, which makes it essential for a complete aphasia exami-

nation to include assessments of the verbal short-term and working memory, since they provide useful information about the underlying cause of the observed comprehension impairment.

## Broca, Wernicke, and Connectionism

In gross anatomical terms, the current views about which brain regions are associated with language function are still based on findings from the late 19th century. However, the first references to aphasic phenomena come from the "surgical papyrus of Edwin Smith" (c. 1700 BC), which made the first association between head injuries and "loss of speech," and in a Hittite text about King Mursilis II (c. 1300 BC), which refers to the temporary "speech paralysis" of King Mursilis.<sup>8</sup> In addition, references in the "Hippocratic Corpus" (c. 400 BC) show that the Hippocratic doctors were aware of the causal connection between damage to the brain and "loss of speech".<sup>8</sup>

An increasing number of more-precise clinical descriptions of aphasia have appeared since the 17th century.<sup>9</sup> A radical change took place at the beginning of the 19th century regarding the relation between language behaviour and brain structure. Two schools of thought had developed: "localizationists" believed that specific areas of the brain are responsible for specific language functions, whereas "holists" believed that the brain works as a unit and that mental ability reflects the total brain volume. While it is possible to distinguish between models belonging to the anatomically based localizationist school and models belonging to the psychologically based holistic school, most contemporary research on aphasia uses both approaches (e.g., Luria's aphasia classification system).

The first modern report on aphasia came from Broca, a Parisian surgeon.<sup>10</sup> The patient that made Broca famous was a man named M. Leborgne who was nicknamed "Tan" due to this being the only utterance he could produce.<sup>11-14</sup> Based on autopsy findings from an analysis of the surface of Tan's uncut brain, Broca suggested that damage on the posterior half of the left inferior frontal gyrus ("the foot of the first frontal gyrus") was responsible for the observed language impairment. Some months later Broca described a second patient who was able to produce only five words.<sup>14,15</sup> The analysis of this second patient yielded essentially similar clinical-pathological inferences as for Tan, verifying Broca's cerebral localization of speech production. Some years later Wernicke described a patient who was speaking unintelligible words, experienced difficulties comprehending speech, and had a lesion in the left posterior temporal lobe.<sup>16-18</sup>

Based on the novel observations of Broca and Wernicke, the cortical area linked to speech production was called Broca's

area, while that involved with speech comprehension was referred as Wernicke's area. The former is typically defined as the pars opercularis and pars triangularis of the inferior frontal gyrus, represented by Brodmann areas 44 and 45, respectively,<sup>19</sup> while the latter is classically defined as the posterior section of the superior temporal gyrus, represented by the posterior part of Brodmann area 22.<sup>3</sup> Based on these definitions, Wernicke and Lichtheim constructed the early scheme for the neural organization of language that was later revitalized and popularized by Norman Geschwind during the 1960s; this model is known as the Wernicke-Lichtheim model. In brief, this scheme postulates that cortical areas (without precise anatomical localizations) for conceptual meanings are connected via transcortical pathways to Wernicke's area (auditory language area) for phoneme processing, and to Broca's area (motor language area) for speech output programming and delivery. In turn, Wernicke's and Broca's areas are connected via a subcortical white matter pathway with a posterior-to-anterior information flow.

While the era of neuroimaging has clearly revealed the limitations of this model, which are mentioned in later sections of this paper, this simple scheme continues to significantly influence contemporary thinking about the neural architecture of language.<sup>20</sup> One of its main historical contributions is that it systematized the main aphasia syndromes that were observed and is considered a practical clinical scheme for aphasia types.

## Going beyond Broca's and Wernicke's Legacy: the First Level of Complexity

As described above, the Wernicke-Lichtheim scheme provides a starting point for aphasia syndromes. If this model were truly representative of language function, predicting a lesion site from language impairment in patients with stroke would be a simple neurological exercise. Even though language assessment at the bedside is not difficult, such predictions are clearly not easy, since the basic types of aphasia are only rarely seen in clinical practice in pure forms. The boundaries between aphasia types are not very clear-cut, and all aphasic patients have some sort of problem with speech production (with various types of error); even patients with a Broca's aphasia syndrome experience problems comprehending complex sentences.

The Wernicke-Lichtheim model fails due to it attempting to categorize a highly complex cognitive function like language into "boxes"; this functioning occurs over a wider spatial area than once thought. Even the two historical Broca's patients-the preserved brains of whom were re-examined using high-resolution MRI-had lesions far beyond the surface lesions identified by Broca (the well-known Broca's area).<sup>13</sup> These damaged areas were spread all over the left hemisphere, not only cortically

but also more deeply.<sup>13</sup> The question therefore arises as to which of these damaged brain areas were responsible for Broca's observations. Obviously the language dysfunction in these cases is attributable to at least some parts of the lesions, but it is extremely difficult to decipher the exact area when a complex pattern of damage is present.<sup>3</sup>

The above-described situation highlights the unreliability of "outlier" single-case studies in deciphering the correlation between lesion sites and language impairment. Single patients with aphasia often represent rare variants that lie at the extremes of the spectrum, and although novel and interesting they are not representative of the general population of patients with aphasia. In the past there has been too much focus on isolated single cases or selected samples of aphasia, including vascular aphasia,<sup>3,21-31</sup> which has stifled research progress in this field for several years.

### Case studies of atypical lesion-deficit correlations

There are many case studies in the aphasia literature demonstrating atypical correlations between lesion sites and language deficits. We conducted a systematic review of the literature in order to find specific case reports of such "unexpected" lesion-to-deficit correspondence (Table 1).

Case studies demonstrating brain lesions linked to unexpected language deficits can be divided in two broad categories: 1) crossed aphasias, referring to cases where the lesion producing the aphasic syndrome is the right homologue of the expected left-hemisphere lesion site, and 2) left-hemisphere lesions with an atypical lesion-to-deficit correspondence. In this paper we focus on the latter category.

There have been several reports of patients with aphasia and unexpected lesion-to-deficit correlations (as summarized in Table 2), such as global aphasia with Wernicke's area being intact, Wernicke's aphasia after extended perisylvian lesions, fluent

**Table 1.** Search strategy and selection criteria for reference identification

Case studies in aphasia literature demonstrating "atypical" lesion-deficit correlations: papers were found through Scopus, using different combinations of the key words "aphasia", "case report", "case study", "lesion", "anatomy", "CT", "MRI", "exceptions".

Population-based studies: we searched Pubmed for papers published during the last 15 years, using various combinations of the key words "aphasia", "stroke", "MRI", "speech", "language", "comprehension", "production", "lesion", "voxel-based" and "VBM". As recently suggested<sup>3</sup> we focused our literature search on studies that looked on the brain as a whole (rather than predefined damaged regions).

The final reference list was chosen on the basis of relevance to the topics covered in this article.

**Table 2.** Case studies in aphasia literature demonstrating “atypical” lesion-deficit correlations

Study	Type of deficit	Reported lesion site
Kuljic-Obradovic et al. (2007)	Anomic aphasia	Right and left thalamus
Fernandez et al. (2004)	Mild conduction aphasia	Wernicke's area, posterior insula, supramarginal gyrus
Love et al. (2002)	Anomic aphasia	Left basal ganglia and surrounding white matter
Selnes et al. (2002)	Mild anomia with preserved repetition	Left arcuate fasciculus
Cereda et al. (2002)	Acute nonfluent aphasia	Left posterior insula
Maeshima et al. (2002)	Mixed transcortical aphasia	Left frontal and parieto-occipital regions, including the inferior frontal and angular gyrus
Hund-Georgiadis et al. (2001)	None (crossed non-aphasia)	Prefrontal, parietal, and temporo-occipital territory of the left middle cerebral artery
Nagaratnam et al. (1998)	Mixed transcortical aphasia	Right occipito-temporal regions, thalamus, internal capsule
Schneider et al. (1999)	Acute Wernicke's aphasia	Left putamen
Nagaratnam and Gilhotra (1998)	Acute mixed transcortical aphasia	Left putamen
Kumar et al. (1996)	Global aphasia	Left thalamus
Maeshima et al. (2002)	Transcortical mixed aphasia	Left frontal and parietal regions
Lazzarino et al. (1991)	Transcortical motor-like aphasia	Left thalamus
Nespoulous et al. (1988)	Broca's aphasia	Left posterior insula, posterior superior temporal gyrus, inferior part of the precentral and postcentralgyri, supramarginal gyrus
Bogousslavsky et al. (1985)	Mixed transcortical aphasia	Left superior and posterior part of the frontal lobe, and parieto-temporo-occipital junction

aphasia after anterior lesions, nonfluent aphasia after posterior lesions, and aphasia resulting from lesions outside the perisylvian language zone.<sup>24</sup> Other researchers have observed similar cases. For example, patients have been reported as having Broca's<sup>32</sup> or conduction<sup>33</sup> aphasia caused by extended perisylvian lesions. Moreover, similar lesion sites have been reported to result in different aphasic syndromes.<sup>34</sup>

On the other hand, some stroke patients do not exhibit aphasia in spite of having a left-hemisphere lesion that affects classical language areas, such as Broca's and Wernicke's areas.<sup>24</sup> Selnes et al.<sup>35</sup> reported a mildly aphasic patient who did not demonstrate any repetition impairment in spite of a lesion affecting the left arcuate fasciculus. Moreover, another patient with a lesion that included the prefrontal, parietal, and temporo-occipital territory of the left middle cerebral artery showed no prominent aphasic deficits.<sup>36</sup>

Subcortical aphasias are of particular interest in terms of outcome. Aphasias resulting from lesions in the basal ganglia and the thalamus are characterized by great variance. Global,<sup>37</sup> anomic,<sup>38</sup> mixed transcortical,<sup>39</sup> and Wernicke's<sup>40</sup> aphasia have been reported in patients with lesions affecting the subcortical nuclei. Lazzarino et al.<sup>41</sup> reported two patients who both suffered from thalamic lesions but had completely different profiles of aphasia: one of them presented with typical thalamic aphasia and the other presented with transcortical motor-like aphasia.

Special reference should be made to transcortical mixed

aphasia. This syndrome was introduced into the aphasiology literature to describe nonfocal lesions, and was referred to as “isolation of the speech area”. Nevertheless, there have been several reports of patients demonstrating transcortical mixed aphasia resulting from focal left-hemisphere lesions affecting frontal and parietal regions,<sup>42</sup> left superior and posterior parts of the frontal lobe and the parieto-temporo-occipital junction,<sup>43</sup> and the left frontal and parieto-occipital regions, including the inferior frontal and angular gyrus.<sup>42</sup> Mixed transcortical aphasia has also been reported in relation to focal lesions in the right hemisphere.<sup>39</sup>

Finally, there are particular aphasic syndromes, such as anomic aphasia, whose localization is rather vague. It could be the case that many regions are involved in the highly complex naming function, meaning that a focal lesion located in one of these regions could result in the same syndrome, namely anomic aphasia. This phenomenon is reflected in several published case reports of anomic patients. An anomic patient with a bilateral lesion of the thalamus has also been reported.<sup>44</sup>

In summary, the review of case studies revealed several patterns of correlations between lesion site and language deficit. The first pattern shows an atypical correlation, in that specific types of aphasia have been linked to damage to brain regions that are not expected to cause these aphasia types. According to the second pattern, patients with similar types of brain damage, such as lesions in the basal ganglia and thalamus, exhibit different language deficits. On the other hand, there are also pa-

tients with the same language impairment caused by different lesions. Finally, the fourth pattern involves patients without any kind of aphasia despite damage to the brain regions thought to be involved in language processing.

### Large population studies

Given the shortcomings of single-case studies and case series, large studies involving modern neuroimaging techniques may provide data that are more representative of the population of patients with aphasia in terms of revealing the relationship between brain damage and language dysfunction. Table 3 summarizes the results of a literature search of large high-resolution MRI studies into the lesion sites associated with impaired speech production or speech comprehension. As recently suggested,<sup>3</sup> we focused our literature search on studies that investigated the brain as a whole rather than only predefined damaged regions.

Several issues concerning the architecture of aphasias are evident from Table 3. Lesions in the vicinity of Broca's and Wernicke's areas in the left hemisphere do seem to be responsible for the deficits in speech production and comprehension, respectively. However, various areas of the brain remote from Broca's and Wernicke's areas can also affect speech comprehension and production.<sup>45-47</sup> Our literature search revealed that both left frontal and left temporal damage is consistently associated with deficits in speech comprehension (Table 3). Also, left insular regions are commonly associated with speech production deficits. In addition, insults restricted to Broca's or

Wernicke's area might not impair language.<sup>27,48</sup> Consequently, damage to many different sites has the potential-individually or in combination-to result in aphasia.<sup>49</sup>

The various MRI studies have led to a rethinking of some essential concepts about the neural architecture of language. The fact that language impairments can arise from lesions in many different brain regions reflects two significant points: 1) language function is a network property and 2) language function has a modular organization, as is also the case for many other brain functions. While the studies reported here (as well as other modern imaging studies) place the neural substrate of this distributed network on the left dominant hemisphere and recognize the importance of the perisylvian region, they consistently implicate specific areas beyond Broca's and Wernicke's areas in comprehension and language production. These results mean that other brain regions might be equally important in language networks.

Whichever the regions are, their interconnections with each other and with additional perisylvian, prefrontal, temporal, and posterior parietal regions constitute a complex network with possible distinct neural subsystems-both within regions and at the network level-subserving different aspects of language.<sup>50-53</sup> This confers a modular organization of language at multiple levels. For example, the intention to speak leads to the action of speaking through multiple processing stages such as conceptualization (the development of an intention to speak and the selection of what will be said),<sup>45,54</sup> message reshaping (involving semantic and syntactic structure) and the retrieval of phonolog-

**Table 3.** Lesion sites and associated language impairments in recent studies involving large populations of patients

Language impairment	Study reference	Lesion sites identified (left hemispheric)
Non-fluent production	1, 2	Inferior frontal gyrus and/or sensorimotor cortex
	3	Inferior frontal gyrus and/or sensorimotor cortex
	4	Posterior and anterior temporal cortex
		Parietal cortex
	5	Insula
		Putamen
Comprehension	6	Superior longitudinal fasciculus
	7	Insula
		Frontal lobe
	8	Parietal lobe
		Putamen
	9	Middle and posterior superior temporal cortex
Middle and posterior superior temporal		
Inferior frontal gyrus and/or sensorimotor cortex		
Parietal, middle and posterior superior temporal cortex		
10	Inferior frontal gyrus and/or middle frontal gyrus	
	Middle and anterior superior temporal cortex	
5	Inferior frontal gyrus and/or middle frontal gyrus	
	Parietal and middle temporal cortex	
6	Posterior superior temporal cortex	

ical codes, selection of the appropriate lexical item, access to articulatory plans, motor programming, and finally the execution of the appropriate physical processes required to produce speech, while the resulting speech output is also self-monitored. The take-home message is that lesions to any (or many) brain region/regions or networks/subnetworks and their interconnections that support these language components could impair the production of language.<sup>3,49</sup> This complexity makes it extremely difficult-or even impossible-to exactly localize a lesion site based on an observed language impairment. We now turn to the dynamics and characteristics of the stroke lesion per se in patients with aphasia after stroke and how these interact with the complex language brain architecture to add another level of complexity.

## Discussion

The aim of this study was to determine why it is difficult to predict language impairment and outcome in patients with aphasia due to stroke. From the very beginning of aphasiology, when the term “aphasia” was not even in use, researchers have tried to localize language impairments. These very first efforts led to several classification systems, such as the Wernicke-Lichtheim model. These systems attempted to link specific language deficits with specific underlying brain damage. However, and despite the importance of classification systems in routine clinical practice, both case studies and large population studies (as systematically reviewed here) have shown that there are not always clear boundaries between different types of aphasia, and that dissociations between lesion sites and language impairments are commonly observed. Below we discuss possible causes underlying this phenomenon, including the special characteristics and dynamics of vascular insults, and individual variability in brain anatomy and language networks.

### Classical aphasia types are vascular syndromes

Since aphasia syndrome in stroke patients is the result of vascular pathology (ischemic or, less often, hemorrhagic) that damages the brain, the characteristics and dynamics of the vascular insult play a crucial role. The neuroanatomical location of the affected vessel is a major determinant of the disorder,<sup>31,46,47,55</sup> however, not only the site of the damage but also the number and combination of lesions are also important determinants. As discussed above, multiple areas of damage may be associated with the same syndrome of aphasia, which makes the clinical localization challenging. In addition to the site and extent of vascular damage, two other important parameters are the degree (completeness) and the geometry of the damage. Neurological vascular damage is not an all-or-nothing phenomenon, and the importance of the percentage of remaining function in

each affected region cannot be overemphasized. As for the geometry of the vascular insult, a larger vascular lesion is more likely to affect a larger functional volume or multiple functional pathways, although the specific location of the damage may be more important; for example, a small lesion strategically positioned at a significant neuronal relay station for a specific aspect of language production could have a greater effect than a larger lesion in a less significant or easily bypassed region.

Language, as a higher cognitive function, is determined not only by processes within single brain areas but also by dynamic interconnections and information flow between and within distributed neural networks. For example, even seemingly simple language tasks (e.g., picture naming, which is frequently tested at the bedside) involve discrete representations and processes, possibly distributed across distinct but overlapping brain regions. This makes it easier to understand the intricate damage distribution, even after a single infarct. Because the human brain is functionally wired, a vascular insult to one region may also affect multiple other adjacent or even remote connected regions, resulting in functional impairments.<sup>28,56-60</sup> Since even a single lesion affects the functional coupling of brain areas outside the lesion per se, multiple lesions could potentially affect language to a greater extent than that predicted from the sum of the effects in each individual region.<sup>28,61-63</sup>

The stroke lesion parameters described above are shaped by cerebrovascular factors. The most significant factors include the location, distribution, and mechanism of the vascular pathology (including the caliber of the affected vessel), the duration of impaired perfusion, the existence and patency of collateral vessels, and the vulnerability of different neuronal populations to hypoxia.<sup>64</sup> Even the extent of ischemia caused by the occlusion of an artery varies within the vascular territory supplied by that artery. There are different zones for the degree of ischemia: the center of the zone (the so-called core of the infarct) is the most severely affected, having the lowest blood supply, while collateral blood delivery at the periphery of the affected territory creates a zone of brain tissue that is dysfunctional but not dead. This latter zone is referred as the ischemic penumbra.<sup>64,65</sup> In general, the state of the perilesional tissue (also that beyond the penumbra) has an important effect on the functional phenotype after stroke. Therefore, the distribution of the damage has multiple determinants: 1) the distribution of the vascular pathology, 2) the resulting distribution of brain pathology (for a given vascular insult), and 3) the distribution of brain functional impairment at the network level. It is important to remember that the vascular territories of the brain do not generally respect the anatomic boundaries of functional areas, and thus the vascular insults do not have a clear-cut relationship with the size and shape of the brain's functional areas.

Stroke is not a static process; instead, it should be viewed as a dynamic and evolving condition. This adds time as an important variable in the language impairment observed after stroke. The affected language function may recover somewhat over time. For example, a patient with a clinical picture of global aphasia may slowly evolve to a clinical phenotype of Broca's aphasia syndrome. A relatively common occurrence in the emergency room is for patients with acute stroke admitted with right hemiparesis and nonfluent aphasia to resolve completely after 1–2 hours. Such a progression of aphasia syndromes over time makes it difficult to correlate language impairment with an anatomic substrate. Further adding individual variability to these parameters means that making any meaningful predictions about affected brain regions and language impairment and outcome seems almost impossible.

### **The role of individual variability: brain anatomy, language networks, and stroke**

Individual structural and functional anatomy differences, and individual variation in stroke damage constitute the two main sources of interindividual variability. All the factors related to stroke as discussed in the previous section may differ between patient populations. For example, patients may exhibit their own specific cerebrovascular factors such as the anatomy of vascular brain territories.<sup>66,67</sup> Moreover, even patients with similar lesion pathologies present with diverse language impairments, which may at least partially be explained by differences in various factors such as age, comorbid conditions, ethnicity, sex, education, perilesional activity, and intervention.<sup>28,68-72</sup>

The second source of possible variation involves (macro- and micro-) structural and functional anatomic brain differences, which have only recently started to be explored.<sup>73</sup> The extent to which the structural anatomy defined by gyri and sulci on MRI are consistently linked is currently unknown, but such knowledge could be used to define relevant functional regions in different patients. The network properties and diffuse connectivity necessary for supporting language, together with the possibility of redundancy in neuronal processing and information flow (a characteristic of many neuronal effector systems), makes it likely that different patients may actually have different and/or alternative neural systems/subsystems and interconnections that serve language.<sup>28,74-76</sup> The presence of such putative alternative pathways might facilitate language recovery after stroke,<sup>77</sup> but they would also further increase the difficulty of localizing them, at least until they have been consistently identified, since they are predicted to be neither random nor unlimited.<sup>77</sup>

## **Implications for Research and Clinical Practice**

Given all these difficulties and controversies, how feasible is it to predict the lesion site and outcome in patients with aphasia after stroke? For a long time aphasiology has considered classical aphasia types to be vascular syndromes, meaning that they reflect damage or dysfunction of brain regions supplied by a particular artery and supporting elements of language function. This approach requires an understanding of the neural circuits that support language. Indeed, studies performed during the last 15 years or so that have attempted to characterize aphasia have focused on identifying the disrupted cognitive processes underlying language, aided by advances in neuroimaging and computing. Recent evidence has converged on the view that even a simple language task depends on a complex set of cognitive processes being supported by an elaborate network of brain regions.<sup>4,49,78,79</sup> Consequently, it is the specific combination of lesions in a patient with aphasia that will determine the language impairments and outcome after stroke.

Given the complexity of the cognitive processes that support language (which remain largely uncharted), a paradigm shift is needed in dealing with the clinical problem of predicting language impairment after stroke. Rather than using a model of language function to make predictions, they could be based on a large amount of data from other patients with similar brain damage after stroke.<sup>3</sup> This will be feasible in the context of an international, multicenter collaboration that utilizes and combines data of a large patient population. The establishment of stroke units in many countries can provide a starting point where large samples of patients could be studied. Reliable conclusions would require large series of patients with aphasia to be phenotyped in detail for demographic and clinical variables, imaging correlates, and extensive language testing.<sup>31</sup>

This information might also help in revisiting the traditional aphasia classification, which seems to be a hot topic in contemporary aphasiology.<sup>80-84</sup> Despite the problems of Broca's and Wernicke's classifications, in clinical practice these classical vascular syndromes remain useful, in that they allow a simple broad categorization of which brain regions are damaged. However, this classification scheme is not especially helpful for prescribing specific therapeutic interventions and making predictions about the language outcome for each patient. A shift from a model-led to a phenotype-led approach may clarify whether any classification scheme is indeed clinically meaningful. Also, aphasia studies using more advanced magnetic resonance neuroimaging techniques and functional imaging tools such as functional MRI, PET, SPECT, and DTI may further elucidate the relationship between lesion site and language impairment in the context of such an approach.<sup>4,78,85</sup>

**Conflicts of Interest**

The authors have no financial conflicts of interest.

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