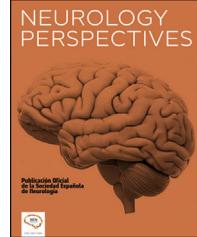




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REVIEW

What have we learned from aphasias in the 21st century? Neuroanatomical, cognitive, and diagnostic implications of the ventral language stream



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KEYWORDS

Aphasia;
semantic dementia;
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Abstract

Introduction: Our understanding of the neural basis of language has grown enormously over the last 2 decades. However, the classical anatomical-lesional model of aphasias, which began with Paul Broca in the late 18th century and culminated with Geschwind in the 1970s, continues to be widely used both in the academic and the clinical contexts.

Development: We discuss the limitations of the classical model from a neuroanatomical, cognitive, and diagnostic perspective. We address in detail the explanatory models of the last 20 years that focus on linguistic processes and neural correlates, including the ventral stream, and analyse the increase in scientific publications that associate this pathway with language, proposing that it may be part of a multimodal association circuit.

Conclusions: This review of the new cognitive and neuroanatomical models of language shows the deficiencies of the classical classification and suggests that some semantic aphasic disorders may be concealed by these categories. There is a need for an assessment based on cognitive processes; we indicate some specific tests for the detection of verbal semantic alterations and guidelines for their rehabilitation.

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PALABRAS CLAVE

Afasia;
Demencia semántica;
lenguaje;
Red ventral;

¿Qué hemos aprendido de las afasias en el siglo XXI?: Implicaciones neuroanatómicas, cognitivas y diagnósticas de la red ventral del lenguaje

Resumen

Introducción: El conocimiento sobre las bases neurales del lenguaje ha experimentado un enorme crecimiento a lo largo de las dos décadas que llevamos del siglo XXI. Sin embargo, el

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Red Dorsal;
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modelo clásico anatómico lesional de las afasias, comenzado por Paul Broca a finales del siglo XVIII y culminado por Geschwind en la década de los 70 del siglo pasado, sigue teniendo un fuerte arraigo a nivel académico y clínico.

Desarrollo: Se señalan las limitaciones del modelo clásico a nivel neuroanatómico, cognitivo y diagnóstico. Se profundiza en los modelos explicativos de los últimos 20 años de los procesos lingüísticos y correlatos neuronales que incluyen la red ventral. Se analiza el incremento de publicaciones científicas que relacionan esta red con el lenguaje, planteando la posibilidad formar parte de un circuito de asociación multimodal

Conclusiones: la revisión actual de los nuevos modelos cognitivos y neuroanatómicos del lenguaje muestran insuficiente la clasificación clásica y plantean la existencia de cuadros afásicos semánticos ocultos en estas categorías. Se plantea la necesidad de hacer una valoración en base a procesos cognitivos, señalando pruebas específicas para una detección de las alteraciones semánticas verbales y pautas de rehabilitación de las mismas.

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Introduction

It has now been over a century since Wittgenstein⁽¹⁾ wrote in his *Tractatus logico-philosophicus* that "the limits of language are the limits of my world." While in this quote, the philosopher referred to language as a mirror reflecting objects in the world, ^(2,3) the idea takes on a very different meaning when applied in the context of aphasia. Over the last 2 decades, new and complex techniques have deepened our understanding of how verbal meaning is represented in the brain. This also invites an integral reflection on how we classify and approach aphasia, which might shed light on how aphasia limits a patient's "world," even beyond language impairment.

The classical Broca-Wernicke model

The first descriptions of the cerebral basis of language arose from anatomical studies of brain lesions by Paul Broca and Karl Wernicke in the late 19th century,^(4–6) which related the posterior part of the third frontal gyrus with expression and the posterior area of the left superior temporal lobe with comprehension. This initial dissociation was further developed with subsequent contributions from Lichtheim,⁽⁷⁾ who indicated the relationship between the arcuate fasciculus and verbal repetition, and Norman Geschwind, ⁽⁸⁾ who associated the angular gyrus with phonological aspects of language, giving rise to the classical model that has constituted the basis for our understanding and classification of aphasias for the last century (Fig. 1).

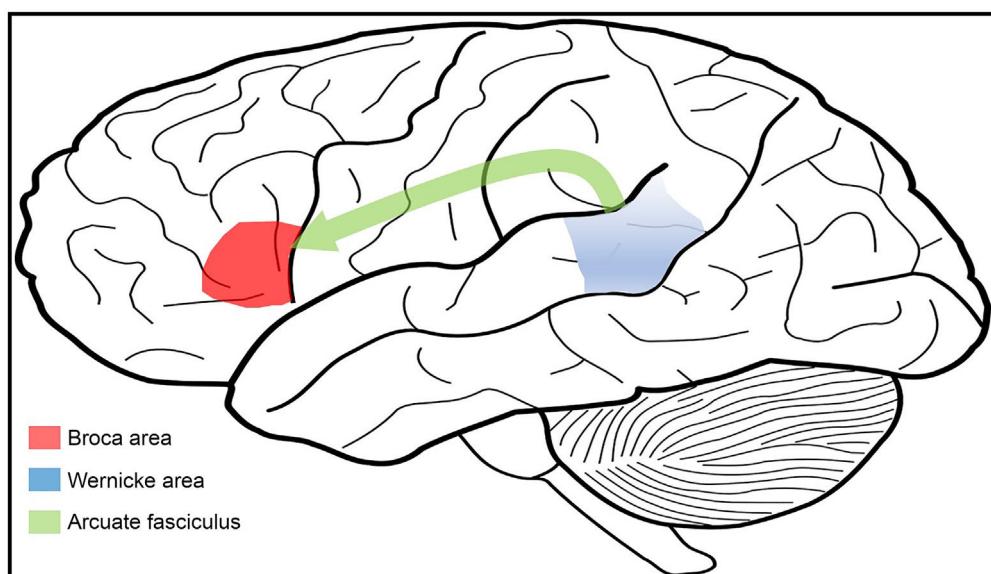


Figure 1 Classical or anatomical model of language, including the Broca area (red), associated with expression, the Wernicke area (blue), associated with verbal comprehension, and the arcuate fasciculus (green), associated with repetition.

Table 1 Diagnostic classification of aphasias according to the classical model.

Expression	Comprehension	Repetition	Naming	Category
Impaired	Intact	Impaired	Partially impaired	Broca
Intact	Impaired	Impaired	Impaired	Wernicke
Intact	Intact	Impaired	Intact	Conduction
Impaired	Impaired	Impaired	Impaired	Global
Impaired	Intact	Intact	Partially impaired	Transcortical motor
Intact	Impaired	Intact	Partially impaired	Transcortical sensory
Impaired	Impaired	Intact	Partially impaired	Mixed transcortical
Partially impaired	Intact	Intact	Impaired	Anomic

The classification of aphasias and its problems

The dissociations that gave rise to this model (expression/comprehension and repetition/non-repetition) enabled the creation of a diagnostic taxonomy of different subtypes of aphasia (Table 1), leading to a series of classical evaluation tools, such as the Western Aphasia Battery and the Boston Diagnostic Aphasia Examination, which aimed to place the patient in the most appropriate category and to measure the severity of aphasia.^(4,5,9–11)

This system remains one of the most widely used approaches in the assessment of aphasia,^(12–15) although a large body of evidence now suggests that it does not accurately reflect the clinical reality. This evidence highlights problems in 3 main areas (Table 2):

-Neuroanatomy. Studies conducted over the last 2 decades have identified numerous regions in the left hemisphere that are essential to language processing but are not recognised in the classical model,^(5,9,15–18) which also neglects the contribution of the right hemisphere.^(19,20)

Moreover, delimitation of the Broca and Wernicke areas is imprecise. For example, Tremblay and Dick⁽¹⁴⁾ compiled the various characterisations of these regions by other

authors, observing that there was significant variability in the sizes reported in different studies, which had clinical and diagnostic implications depending on the definition used.^(21–23)

Finally, from a neuroanatomical perspective, this model does not fully account for the role of subcortical structures in cognition in general and in language in particular.^(24–26)

-Cognition. The dissociations between expression and comprehension and between repetition and non-repetition present certain limitations in the light of advances made in cognitive neuroscience in the late 20th century. Semantic problems do not fit into this model, and many other consolidated entities affecting linguistic processes are not taken into account when establishing a diagnosis.^(27,28)

Another problem is that the model considers language as an isolated cognitive function, when current paradigms of neuropsychological evaluation posit that it is interconnected with other cognitive processes (eg, executive control, working memory, and semantic memory). As a result of this interrelation, problems with verbal expression or comprehension do not necessarily result from a linguistic problem, which may have therapeutic implications.^(29–31)

-Diagnosis. In the light of the issues mentioned above, it seems logical to consider that the diagnostic categories of the classical model may not enable correct delimitation of different profiles of aphasia.

Firstly, a categorical model is unable to explain many of the cognitive alterations observed in patients with aphasia, as they are not relevant to the classical system of classification. For example, we may mention the presence of apraxia, executive dysfunction, or issues related to complex verbal comprehension.^(32–36)

Secondly, several authors report limitations and biases in studies of patients with aphasia diagnosed according to the classical classification. The difficulty of establishing groups of patients with lesions involving specific nuclei and not extending to other areas constitutes a significant limitation for the extrapolation of results.⁽¹⁴⁾ Furthermore, these studies mainly include groups of patients with vascular lesions involving the left middle cerebral artery,⁽³⁰⁾ which is not related to other regions important in language; this also constitutes a significant bias.

Thirdly, some studies highlight the copresence of language alterations from different, supposedly mutually exclusive, diagnostic categories. There is also significant variability in the status of other processes in each diagnostic category, such as reading or writing.^(14,28)

Finally, the classification system as a whole presents numerous inconsistencies. For example, anomia is a feature

Table 2 Critiques of the classical model.

Dimension	Critique	Reference
Neuroanatomy	Incomplete from an anatomical perspective	(17,18)
	Does not account for connectivity	(16,18)
	Purely cortical model	(16–18,24)
	Real delimitation of important nuclei	(15)
Cognition	Some processes not included in the model	(28,29)
	Excludes relationship with other functions	(30–32)
Diagnosis	Clinical signs falling outside diagnostic categories	(35–37)
	Lesions rarely affect a single structure.	(15)
	Overlap of signs between categories	(9)
	Inconsistencies within categories	(38–40)

of practically all types of aphasia, which contradicts the existence of anomia aphasia as a specific entity; this seems to suggest that there may be several currently unrecognised causes of anomia.(12,37) Another example would be global aphasia, which should be understood as simultaneous damage to the Broca and Wernicke areas, despite the fact that many patients with similar clinical alterations present no such lesion.(38,39) Similarly, presence of a sensory verbal issue (discrimination of the stimulus) seems incompatible with unimpaired repetition, as is the case with transcortical sensory aphasia.(40)

In the light of all the issues mentioned above, there is a need for a radical update proposing new forms of evaluating and managing aphasia, especially if we take into consideration studies indicating that, while many academics and clinicians regard the classical model as outdated, no current model proposes a more accurate approach to aphasia.(14)

A new conception of language

-The new cognitive models of language

One critique of the classical model is precisely that it does not account for advances made in the late 20th century in the fields of psycholinguistics and cognitive neuroscience. Since Chomsky's(41) critique of Skinner's(42) radical behaviourist explanation of verbal behaviour, new models have attempted to characterise the processes underlying language.(27,43–46)

A noteworthy example is the model suggested by Ellis and Young,(27) who offer an in-depth analysis of the classical dissociation between expression and comprehension and propose a series of cognitive processes that sequentially form the basis of speech production and comprehension, as well as the execution of such processes as reading and writing (Fig. 2).

This process-based characterisation of language requires evaluation to transcend the use of diagnostic labels. Several tests have been developed to that end, such as the Psycholinguistic Assessment of Language Processing in Aphasia (PALPA),⁽⁴⁷⁾ which converges with more qualitative assessment scales, such as those proposed by the Boston school for general neuropsychological assessment.^(48–50)

-New brain correlates of language

Anatomical-lesional techniques may be considered to have a more limited scope for establishing associations between the brain and language, as they do not account for the functioning of the brain *in vivo* and fail to recognise the role of white matter. Neuroimaging techniques developed in the last 20 years have enabled us to observe and establish relationships between different linguistic processes and their cerebral correlates.

For example, Hickok and Poeppel⁽¹⁶⁾ used diffusion tensor imaging to analyse the connectivity of the Wernicke area, confirming the existence of 2 main pathways (a superior or dorsal stream and an inferior or ventral stream), inferring that these carry information processed in that region. The first route would overlap fully with the classical Broca-Wernicke model, according to which it is related with verbal production. The second route comprises projections from the Wernicke area to the temporal lobe, and particularly the anterior temporal lobe (ATL), a structure not mentioned in the classical models.^(15,16,51,52) This network is related to verbal comprehension, and is often referred to as the "what pathway" (Fig. 3a).

Subsequently, Friederici and Gierhan⁽¹⁷⁾ studied these pathways in greater depth, dividing the dorsal and ventral pathways into 2 new segments (Fig. 3b). The dorsal pathway connects the Broca and Wernicke areas via 2 fascicles, the arcuate fasciculus (included in the classical model) and the superior longitudinal fasciculus (which has important links with the angular gyrus); the authors associate these pathways with grammar and with phonology/repetition, respectively.

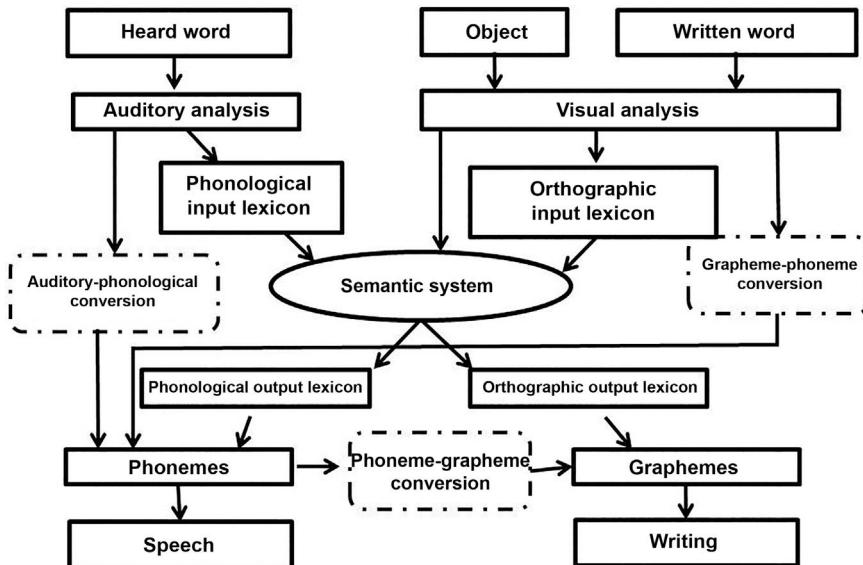


Figure 2 Cognitive model proposed by Ellis and Young.⁽²⁷⁾ This model includes 2 pathways of speech production, one containing a mechanism of auditory-phonological conversion for the repetition of meaningless sounds, and another beginning in the semantic system in order to convert thoughts into words. The authors signal the importance for language comprehension of matching words heard with known meanings, the phonological input lexicon, and the set of known words.

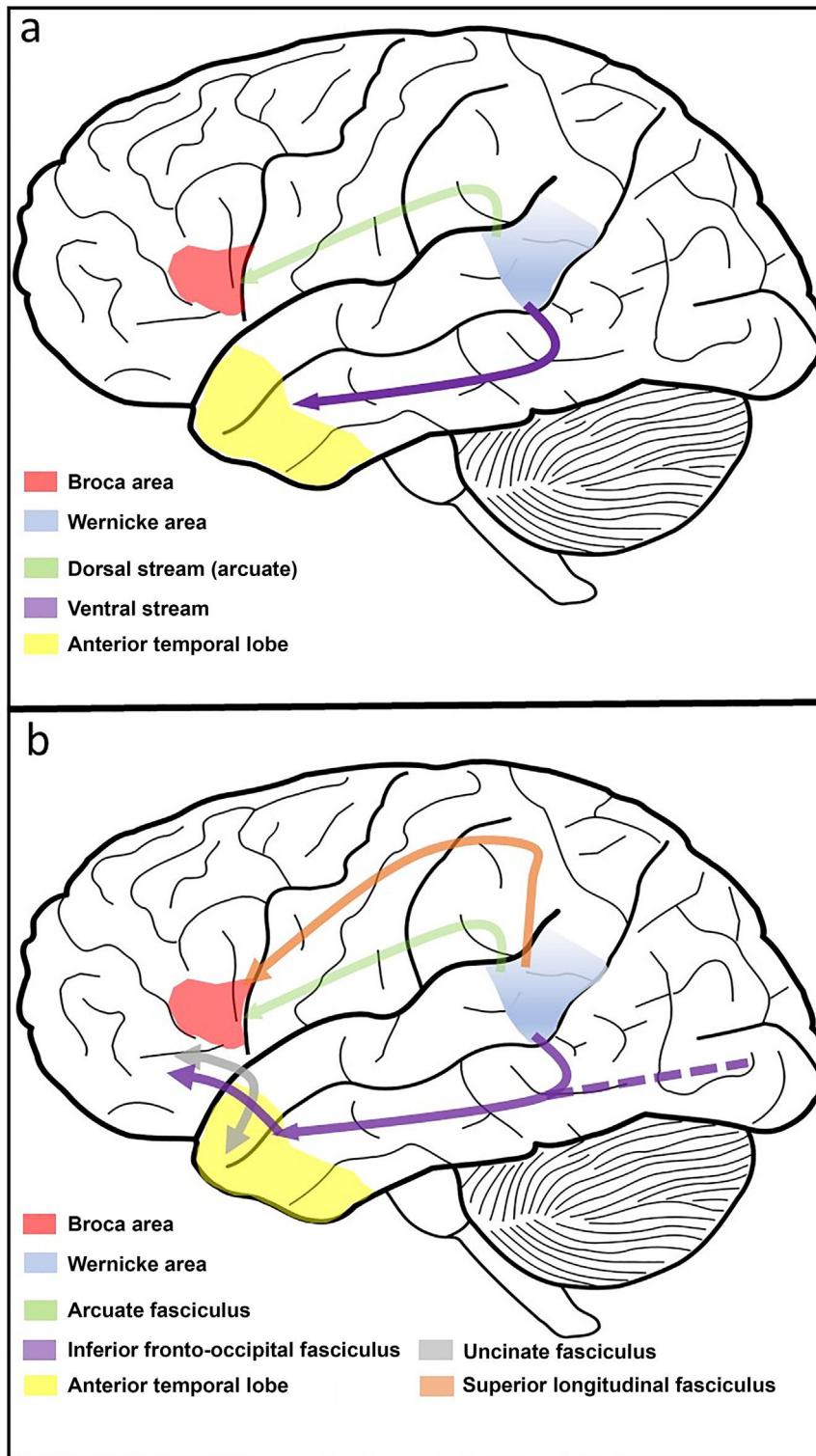


Figure 3 a) Representation of the two-stream model,(16) with a dorsal stream connecting the Broca area to the Wernicke area, related to verbal expression, and a ventral stream connecting the Wernicke area to the temporal lobe, related to comprehension. b) Extended two-stream model,(17) including the superior longitudinal fasciculus and the arcuate fasciculus in the dorsal stream and the uncinate fasciculus and the inferior fronto-occipital fasciculus in the ventral stream.

(17,53–55) The previously overlooked ventral pathway is divided into the inferior fronto-occipital fasciculus (IFOF) and the uncinate fasciculus (UF), related to the comprehension of isolated words and the comprehension of complex sentences,

respectively.(56,57) While this model is more specific, it is somewhat more difficult to establish such a direct relationship between processes and specific brain structures, although there seems to be a reasonable amount of evidence

that this pathway may be highly involved in semantic aspects. (30,31,58,59)

As the dorsal pathway has received more attention overall on account of its overlap with the classical model of language,(14) it would be beneficial to analyse the specific implications of including the ventral pathway in language models, and whether this would enable us to overcome some of the limitations of the classical model.

Further analysis of the ventral pathway

In the last decade, increasing numbers of studies have related language with the ventral pathway, despite it initially being considered to play a greater role in visual processes.(60) A PubMed search of publications including the terms "language" and "ventral stream" in the title or abstract (Fig. 4a) yielded a total of 92 articles published since 1998, 82 of which (88%) were published in the last 10 years. Only 2 were published before the year 2000, but focus on visual function.(61,62) Articles addressing the relationship between the ventral stream and language follow a very broad range of approaches (Fig. 4b), including basic studies of the healthy population to characterise its functioning (63–83) and studies of surgical procedures,(56,84–97) aphasia,(98–112) neurodevelopment,(113–118) and such disorders as Parkinson's disease,(119) multiple sclerosis, (120) and progressive impairment.(121,122) Some studies even address comparative and evolutionary neuroscience. (123–127) This trend has contributed new evidence to change our form of understanding language from the 3 perspectives in which the classical model presents limitations.

Neuroanatomy

From a neuroanatomical perspective, the inclusion of the IFOF and UF is highly relevant. The IFOF connects frontal and occipital areas, running parallel to the medial temporal lobe (17,31,128–130) and connecting to the ATL with projections to the superior temporal lobe. The UF, on the other hand, directly connects the ATL to the posterior inferior frontal cortex, although it presents significant overlap with the IFOF where it crosses the external capsule.(56,129,130) In other words, the ventral pathway connects frontal, temporal, and occipital structures in such a way that, given its extension, it appears to be a multimodal pathway, as has been argued in recent years, rather than solely a language pathway. (131–134)

For example, Leonard Kozlak's research group conducted a detailed study to integrate cortical and subcortical structures in what they call "large-scale brain systems."(24–26) One of the systems they identified is the ventral attention network, comprising the temporoparietal junction, supramarginal gyrus, frontal operculum, anterior insula, and projections to the striatum. This network overlaps with the ventral language stream, connected with subcortical structures involved in the attribution of value to stimuli.(24) This would confirm its role as a multimodal network of semantic processing.

Also related to this idea is the "hub and spoke" theory, (30,131–133) according to which this large ventral pathway would include a structure acting as the central

hub or node, the ATL. The hub would receive information from other cortical regions, distributed across various different routes (spokes) (Fig. 5). Therefore, we may observe either unimodal (if a specific spoke is affected) or multimodal impairment (if the central hub is damaged). An example of unimodal impairment would be associative visual agnosia, in which patients are unable to visually recognise a known object, but are able to copy it and match it with similar objects; IFOF lesions would be involved in this disorder.(135)

This would entail the need to conduct a more detailed assessment of the extent of semantic problems in aphasias, as some patients with apparently speech-related symptoms may in fact present multimodal impairment. Regarding the processes underlying this ventral pathway, one interesting line of research is the study of primary progressive aphasias (PPA), and particularly semantic dementia (SD).

Processes

A recent study by Matias-Guiu et al.(136) identified 5 possible variants of PPA, rather than the 3 types established in the previous consensus classification,(137) by grouping different cerebral metabolic activation profiles (using FDG-PET imaging); these profiles coincided with the linguistic impairment profiles that were clearly distinguished in a process-based assessment of language. This enabled a distinction to be made between 2 forms of nonfluent aphasia (one with more apraxic and another with more agrammatic features), related to the anterior part of the dorsal stream, 2 types of logopenic aphasia (with differences in action naming), related to the parietotemporal region, and SD, related to the predominantly left ATL.

In general, atrophy of the left ATL in patients with PPA is associated with the loss of semantic content, initially with mainly linguistic involvement, with loss of the meanings of previously acquired words.(138,139) It initially affects words requiring greater imageability (abstraction) and progressively affects the semantic network of language, with a loss of more specific content from different categories.(58,59) In this context, language impairment may be considered transversal (Table 3).

However, patients also present other non-linguistic signs, such as prosopagnosia; problems with visual concepts in the context of bilateral ATL atrophy; reduced imageability and future-oriented thought; and potentially reduced daydreams and dream content.(140–143)

In this regard, acute injury to the ATL may cause highly variable impairment of these semantic processes, affecting one or several areas. It is essential to be aware that aphasia may present characteristic signs and impairment of semantic processes that often are not clearly recognised in the classical conception; this is highly relevant in clinical diagnosis and management.

Clinical diagnosis

The study by Mesulam et al.(58) offers valuable insight into the diagnostic implications of the ventral language stream. In a sample of 73 patients diagnosed with SD, the authors studied the function of the Wernicke area and the ATL,

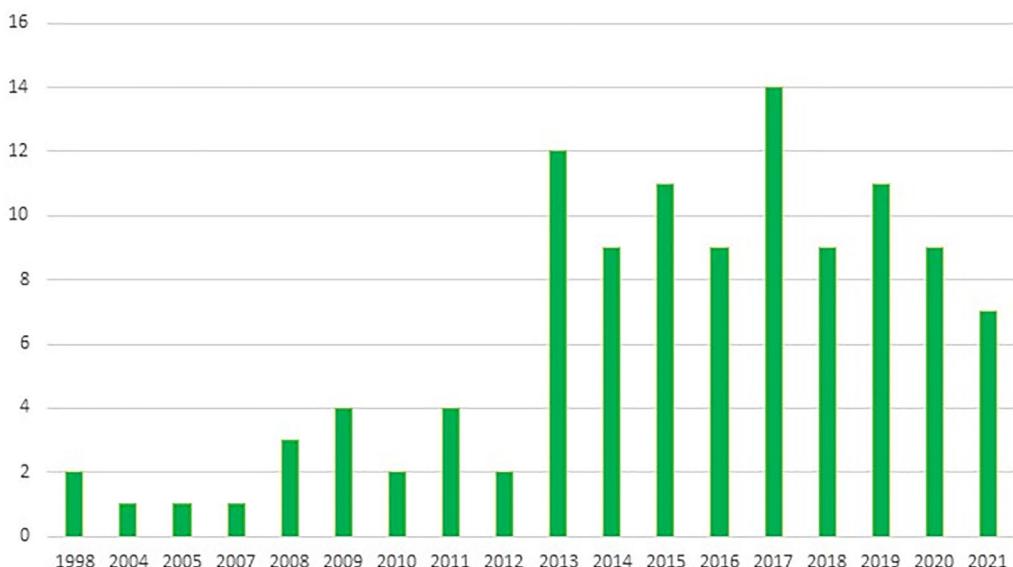
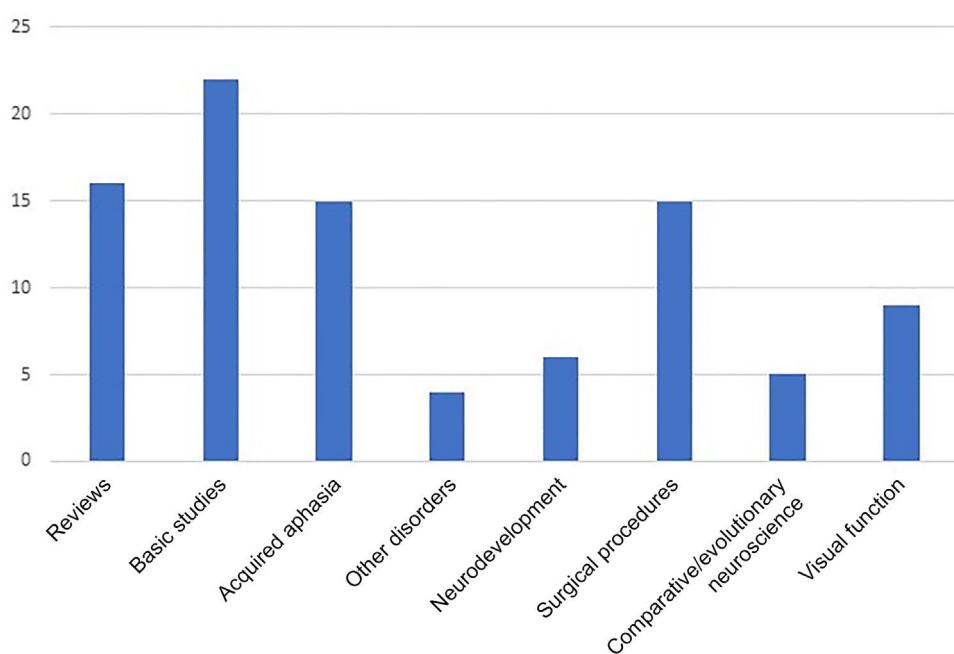
A)**B)**

Figure 4 a) Historical series of publications including the words “language” and “ventral stream” in the title or abstract (PubMed search). b) Distribution of articles identified in the search by topic. The articles addressing visual aspects are those that focus more on visual than on linguistic aspects of the ventral stream (9 in total).

concluding that the Wernicke area is more related to repetition and phonological encoding (auditory discrimination), and has less involvement in verbal comprehension, as had traditionally been believed. On the other hand, the ATL and inferior areas of the temporal lobe represent the neural substrate of this semantic comprehension, which would give

a new meaning to transcortical sensory aphasia, which may be better characterised as a possible acquired semantic aphasia secondary to ventral involvement.

A study by Cuetos et al., (37) in a sample of 28 individuals with aphasic sequelae of acquired brain injury, analyses the pattern of language difficulties in the errors recorded in

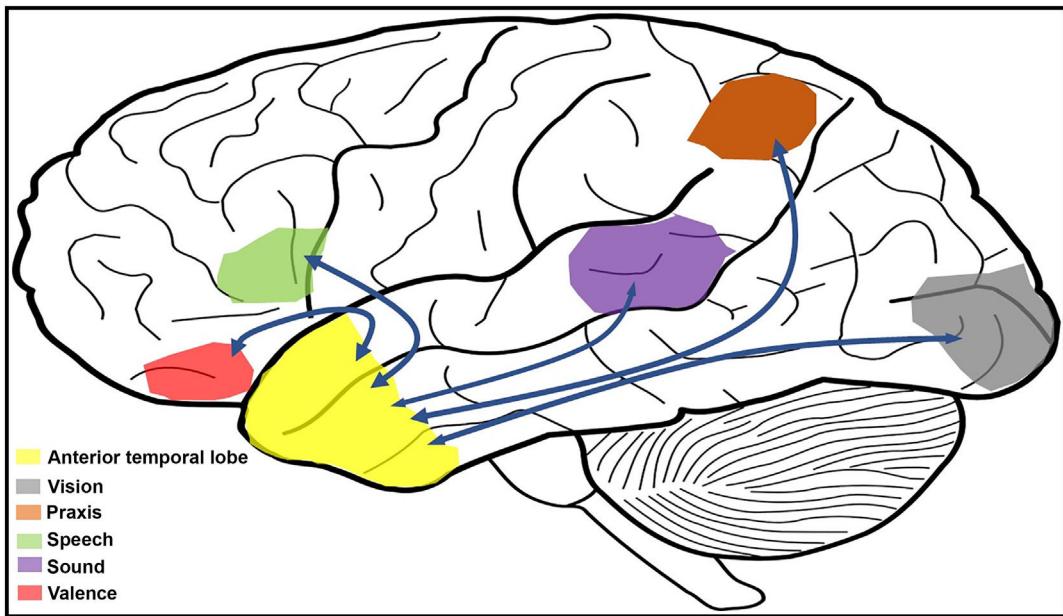


Figure 5 Reproduction of the "hub and spoke" model (adapted from Ralph et al.(30)), showing the different connections between the anterior temporal lobe and other regions responsible for different processes, whose information is integrated in this association area. Information would follow a specific pathway from the primary areas to the association areas; specific alterations of those areas may occur if the corresponding "spoke" is interrupted, and more general alterations may occur if the "hub" is damaged. It is worth noting that many of these areas involved in semantic representation overlap with other more executive areas involved in control.

naming tasks. The authors indicate 3 types of anomia: pure or access anomia, phonological anomia, and semantic anomia. The authors note that while there are no issues classifying access anomia within the category of anomia

aphasia, the phonological and semantic forms do not clearly fall within any of the other classical diagnostic categories, which would not allow for adequate understanding of the problem. This semantic anomia would be a sign of acquired semantic aphasia secondary to ventral stream involvement. In fact, this reduction of vocabulary due to semantic involvement would result in a decrease in verbal expression and comprehension compatible with global aphasia, without damage to the nuclei classically associated with this disorder (Broca and Wernicke areas). These data suggest the existence of profiles of semantic aphasia that overlap with the classical diagnostic labels, which would be difficult to identify without analysing language processes.(28)

Table 3 Profile of possible cognitive alterations within semantic dementia.

Function	Domain	Sign
Language	Expression	Reduced speech
		Reduced complexity
		Perseveration and lack of ideas
	Comprehension	Problems recognising meanings of single spoken words
		Problems understanding complex spoken verbal structures
		Problems naming objects due to limited vocabulary
	Naming	Difficulty pairing words and images
		Problems understanding single written words
		Problems with general comprehension of texts
Learning	Reading	Word-form agnosia: arbitrary loss of spelling
		Prosopagnosia: problems integrating faces
	Writing	Reduced future-oriented thought and daydreams
Visual perception	Face perception	
	Imageability	

Implications for assessment and treatment

Following this line of reasoning, assessment of a possible aphasic syndrome must be based on the analysis of linguistic processes, with specific attention paid to the different processes that rely on the ventral stream. For instance, the PALPA enables discrimination of different processes involved in speech production and comprehension.(47) This does not imply that we should cease to use the classical batteries, but rather that the results should be interpreted according to the signs observed during their administration, as has been proposed for other dementia screening tests.(50)

Furthermore, the multimodal nature of the ventral stream requires us to make distinctions between different processes, such as those that can be made with the Pyramids and Palm Trees test.(144) Involvement of different semantic processes may have an impact on language production and comprehension, and these processes should be appropriately

examined and distinguished. This is also highly important in patients undergoing awake brain surgery, in whom neuropsychological assessment of language processes may significantly reduce the cognitive alterations associated with these interventions, generally based on the evaluation of the status of eloquent areas derived from the classical model (Broca and Wernicke areas).^(90,91,128) Likewise, such new techniques as the analysis of speech production in combination with machine learning may contribute significantly to determining the profile of language alterations⁽¹⁴⁵⁾; the combined use of various neuroimaging techniques may also be valuable, without forgetting the importance of neuropsychological evaluation of linguistic processes.^(136,146)

Proper delimitation of a patient's cognitive profile will enable more tailored treatment approaches. Semantic alterations may often be the underlying problem in patients with impaired language expression or comprehension, and targeted work is key to adequate rehabilitation. This work should focus on the reconstruction of the verbal semantic network, taking advantage of preserved content.^(147,148) Training image-word pairs, association of known words with synonyms and antonyms, and copying dictated words with irregular forms or arbitrary spelling are examples of exercises that promote the recovery of this verbal semantic component, although further studies are needed to properly delimit these deficits and contribute further data on their effectiveness.⁽¹⁴⁹⁾

Conclusions

The new cognitive and cerebral models of language, developed in the last 20 years, underscore the limitations of the classical model of aphasia at several levels.

In terms of neuroanatomy, the entire ventral stream is omitted from the latter model, which overlooks the importance of different fascicles and regions, such as the external capsule or the ATL, in semantic comprehension.^(129,130) The multimodal nature of this pathway forces us to view language as a function that is interdependent with other cognitive processes, rather than as an isolated entity.

In terms of processes and diagnosis, the dissociations between expression and comprehension and between repetition and non-repetition do not accurately describe language processing as it is currently understood. In this classification, and specifically in transcortical aphasias, the integrity of repetition conceals a series of semantic alterations inherent to the ventral stream, whose multimodal nature may lead to the emergence of different subtypes of semantic impairment affecting language. On account of this, it is essential to evaluate the functional integrity of this semantic network, with neuropsychological assessment being key to detecting any alterations.

Understanding the importance of this network in our way of knowing the world in general, and of organising language in particular, brings us back to the famous words of Wittgenstein. Thus, while language may constitute the limits of the world of a person with aphasia, verbal semantic concepts and representations are precisely the world that that person would have constructed through their experience. A world that can be destroyed by many aphasias, which in turn limit language itself.

Conflict of interest

The authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.neurop.2022.01.005>.

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