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PRESIDENTIAL ADDRESS

# 2022 ASSBI PRESIDENTIAL ADDRESS. Reflections on language and primary progressive aphasias

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**Abstract**
Primary progressive aphasias are rare younger-onset dementias. As the label denotes, these dementias are characterised clinically by marked changes in language skills. Evidence over the years has shown that individuals with primary progressive aphasia experience widespread cognitive and behavioural changes that extend beyond language. This evidence, however, seems to be largely ignored or downplayed. This article proposes that linguistic relativity which induces a cognitive bias may be responsible for this omission; it also indicates that a revision of the current diagnostic criteria may need to be revised.

**Keywords:** Dementia; language; diagnosis; social cognition

In Greek mythology, Hermes, messenger of the Gods and Goddesses, is said to have taught language to humans, and, as such, was considered to be the God of languages. Today, it is estimated that as many as 7000 languages exist in the world. India, the second most populous country in the world with its 1.2 billion inhabitants, has 22 official languages and a staggering 450–1200 additional languages that are commonly used by various communities.

Languages are systems of communication comprised of arbitrary signs codified by specific rules, which take the forms of sounds, gestures, or written symbols. In Europe, many of these languages are related and share common roots (e.g., Germanic, Celtic, Slavonic, Latin) either with respect to the meaning of some of the components (words) or of their grammatical structures. Interestingly, a few, such as Basque or, to a lesser degree, Finnish and Hungarian, are, however, unique with little commonalities with their geographically close neighbours. These root differences notwithstanding, what all these systems share is their symbolic nature. For example, the English word 'cat' and associated morpheme [kæt] denote a physical entity, but one that has no relation with its labels. Indeed, were the same cat be in France, it would be identified by the word 'chat' and associated morpheme [ʃɒ]. Another property of languages is that they can also describe and communicate non-tangible things, such as thoughts, feelings, beliefs, emotions, and intentions. In each language, the combination of the units (words) follows highly codified rules (grammar), which regulate how the information is communicated and its meaning. Although complex, these systems of rules are remarkably flexible and enable an unlimited combination of its units into novel meanings.

This capacity for (at least oral) communication in humans appears innate. An extraordinary feat of human cognition is the incredible speed of word acquisition in early life. Children, on average, will utter their first words at ~12 months but with their vocabulary increasing from ~40 words at 16 months to >550 words by 2.5 years, which is paralleled by a marked increase in comprehension, conceptual knowledge and categorisation and grammar acquisition (Bates &

Goodman, 1997; Fenson et al., 1994). From a very young age, children are adept at understanding and extracting general rules of communication, for example, adding 's' to a word to reflect the plural form of the word, or adding 'ed' to verbs to denote the past. This early capacity for flexible application of rules of grammar is exemplified by the errors that children make and using these rules in completely novel situations, for example, "yesterday, I seed (rather than 'saw'), two mouses (rather than 'mice') running in the garden". Most adults are language experts, even if a large interindividual variability exists. We use language effortlessly, to the point that we are only aware of the complexities of functions of language when these become impaired, for example in some neurodevelopmental disorders, following acquired brain injury or in people who have learnt the language as adults.

## Languages: more than tool of communication

Languages, however, are more than a tool of communication or of information dissemination. Beyond the dimension of explicit content delivery (i.e., meaning of words, pronunciation, articulation, etc), as well as rules of construction for content delivery (i.e., grammar and rules of sentence structure; as well as, in writing, punctuation and styles), lies another implicit dimension, which is their central roles in social relations.

Indeed, languages are integral to social interactions. In direct oral language interactions, the content aspect of language comprises only a small portion of its role and functions. The non-linguistic aspects of language play a much more important aspect to this process. Briefly, aspects in oral language interactions can be classified as follows: (i) information carrying that contributes to storytelling (e.g., descriptive, prescriptive, as well as temporality or time travel; or aspect of clarification of content), (ii) information that is not directly relevant to the immediate story telling (e.g., semantic, or nonword fillers, such as 'aarh', 'hmm', 'you know', etc.) and (iii) the social component of the interaction (i.e., emotional, empathic, social rules). These non-information carrying aspects of language can be seen as part of our 'species-wide' (or 'group-wide') expectations, in that the rules relevant to these features of communication are expected to be common, shared and understood, across members of a group. As such they contribute to social bonding.

Again, importantly, it is worth emphasising that these components of language are not explicit and are learnt in a very implicit fashion. Indeed, most individuals are experts at navigating their various social groups and environments. Moving from one social group to another, they effortlessly and flexibly apply social rules of interactions that are relevant to the group. For example, teenagers interact with their peers in a way that is vastly different to the way they interact with others such as parents and teachers. Similarly, in a work situation, we are experts at extracting clues from the environment that will help determine the rules of language engagement with our interlocutor (i.e., is the person a peer, our boss or our employee).

## Language as a tool to define (and constrain) the world

As we saw above, language plays a central role in understanding and defining our environment (our physical world) and our mental world (thoughts, feelings, etc.). Importantly, in there lies a dimension of shared knowledge and, possibly, trust; trust that we are using the language to represent the same thing or reflect the same thought or feeling. Undoubtedly, this is the case in most instances, but this is not necessarily so. For example, my concept/or construct of 'dog' is likely to be similar to yours and to most people: a middle size, furry, four-legged animal, that barks and may or may not be friendly. This general assumption will, however, be sometimes violated, depending on your knowledge of dog breeds and of your personal preferences. Other constructs are less obvious and not as easily sharable. One such example is that of colours. My internal representation of the prototypical colour 'red' is unlikely to be identical to yours. Although tangible and

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part of the external (read 'physical') world, colours are internal representations that arise from changes in neural signals between your retina and your primary visual cortices.

Related to this situation, but independent from it, is something that is less obvious and less studied. Indeed, an unintended consequence of language as a tool to define our external environment and our internal world is that language also constrains and shapes how we apprehend the world. Again, let's think about colours for a minute. Colours are reflected electromagnetic radiations of particular wavelengths (i.e., so called visible spectrum), with red having longer wavelength than blue. In theory, an almost infinite number of colours exist, but our vocabulary is much more limited. For example, many Indo-European languages, including English, have 11–12 'basic' colours (Red, Yellow, Green, Blue, Black, White, Grey, Orange, Brown, Pink and Purple) often represented by the Munsell colour system (Kuehni, 2001). In contrast, Berinmo speakers of Papua New Guinea only have five main colours (Mehi, Wor, Kel, Wap and Nel). Because of these language constraints, the 'reality' of colours in the world for English and Berinmo speakers is very different. When presented with 256 different colour tones that vary in hues and intensity, these speakers will classify them very differently (Roberson and Davidoff, 2000). In other words, the reality is, in part, constructed based on language, a reality that is not ontological or essential (Davidoff, 2001; Masharov & Fischer, 2006). These data have led to the 'linguistic relativity' theoretical model. This model proposes that the structure of a language shapes how people see the world and also affects other cognitive processes. In other words, people's perceptions are relative to their language (Athanasopoulos & Casaponsa, 2020; Wolff & Holmes, 2011).

## Loss of language – Primary progressive aphasias

All this somewhat meandering section was necessary to help address the next issue related to rare progressive neurodegenerative disorders, called primary progressive aphasias. Primary progressive aphasias, or PPAs, are dementia syndromes characterised by progressive loss of language functions that variably affect expressive or receptive language functions, or a mix of both, and which become increasingly pronounced and leads to death within 5–15 years of diagnosis (Kansal et al., 2016). These syndromes were first identified in the mid-80s, where Mesulam reported a series of patients presenting with what appeared to be isolated progressive loss of language functions (Mesulam, 1982). In subsequent years, these syndromes received increasing attention and different presentations were progressively described.

This research led to the publication of the first consensus diagnostic criteria for PPA in 2011, where three main subtypes were described, one fluent presentation - semantic dementia (SD, also referred to as semantic variant of PPA), and two nonfluent presentations – progressive nonfluent aphasia (PNFA or nonfluent variant of PPA) and logopenic progressive aphasia (LPA or also referred to as logopenic variant of PPA). These language syndromes are caused by underlying neuropathological changes associated with frontotemporal lobar degeneration – in the case of SD and PNFA – or Alzheimer's disease – in the case of LPA. Importantly, these neurodegenerative brain conditions do not occur randomly in the brain. Indeed, the neuropathological changes observed in SD are found primarily and essentially in the anterior temporal lobe regions in an asymmetric fashion, generally much more pronounced in the left hemisphere than in the right. In contrast, changes in PNFA are found in the left insular and inferior frontal regions whereas those associated with LPA are present in the left temporo-parietal regions. With disease progression, however, diffuse brain changes are observed progressively encroaching other brain regions in both hemispheres (e.g., Mesulam et al., 2022).

In the past 15 years, work on these rare dementias has been shaped by the diagnostic criteria published in 2011 (Gorno-Tempini et al., 2011). This seminal paper aimed to provide clarification on the core components of the various types of PPA, with the aim to help with early diagnosis and

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management. This laudable attempt to clarify what is a very complex landscape has shown limitations. For example, within each syndrome, profiles of clinical features are relatively variable (Leyton et al., 2011). More recently, Murley et al. (2020) confirmed that aspects of language features are variably affected across the PPA subtypes and with various levels of severity. Indeed, clinical presentations of patients rarely fit a single diagnostic category, with features of other conditions commonly observed, something that becomes increasingly frequent as the disease progresses. In addition, a proportion of individuals presenting with early language disturbance will not fit one of the three syndromes identified (Sajjadi et al., 2012), highlighting the complexity of these clinical presentation and the limitations of the current classification criteria.

## How 'primary' is the language disturbance in PPA?

Importantly, the brain regions involved in these PPA syndromes also support a number of other processes. The insula plays a central role in the integration of body sensation (autonomic and interoceptive information) with information external to the body (i.e., environment: Craig, 2009). Similarly, the anterior temporal region is the hub for semantic information that goes beyond language but supports organisation of conceptual knowledge including that of faces, emotions, living and non-living things, etc. (Wong & Gallate, 2012). Finally, the temporo-parietal junction, is also an integration brain region combining multi-sensory information from various primary cortices, as well as aspects of number processing and arithmetic and body/space orientation. In addition, this region is also heavily involved in aspects of social cognition such as theory of mind (Saxe & Kanwisher, 2003).

As such, it is not surprising that individuals diagnosed with PPA would experience cognitive and behavioural deficits that extend beyond the language domain. This is indeed the case, with evidence in the past 10 years demonstrating that these patients experience changes in most, if not all, aspects of cognition, including attention, working memory, episodic memory, future thinking and imagination, visuoconstruction, executive functions, as well as all aspects of behaviour and social cognition, such as emotion processing, theory of mind and empathy.

## Linguistic relativity and primary progressive aphasia

This knowledge that cognition and behaviour are impacted, however, appears to be somewhat ignored and I will argue that the current terminology and labelling used to describe PPA has constrained the field with regards to diagnosis, and patient management. Indeed, the components of the label constrain the clinical phenomenology. In the first instance, the disorder is defined as disorder of language: 'aphasia' comes from the Greek 'a' – loss, and 'phasia' – language. The use of 'primary', however, is somewhat ambiguous in that it is unclear what the focus of 'primary' should be, is that the loss of language or the progressive nature of this loss? Finally, 'progressive' indicates that the profile will evolve over time, with the implied assumption that it will get worse over time rather than better. This ambiguity aside, most clinicians and researchers will accept that the label of PPA is a disorder of language.

An additional confusion occurs with the use of 'primary'. Indeed, 'primary' has two distinct meanings: It can mean either highest in rank or importance; principal, or it can mean occurring first in time or sequence; earliest. In clinical practice, these two meanings tend to be conflated. A diagnosis of PPA will tend to be established when these two aspects of 'primary' are present; that is, language deficits are the first AND the most prominent features. The consequence of this is that patients presenting with either co-existing deficits in other cognitive domains or where the temporal unfolding is different will tend to be excluded from a diagnosis of PPA. In doing so, the label constrains the external/clinical reality of the complex phenomenology of individuals who

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present to the clinic with disturbances in language that are becoming progressively worse over time.

Focusing on the first meaning of 'primary' (i.e., highest in importance), I contend that this label has had the unintended effect of biasing the classification of patients presenting with progressive language disturbance by excluding those displaying other features. In other words, "is the language disturbance in PPA really 'primary'?" From a cognitive viewpoint, this bias is interesting as it is taking place despite strong evidence to the contrary and with numerous scientific papers reporting changes in other cognitive domains, apart from language. For example, evidence from our group over the years has shown the presence of deficits in aspects of social cognition (emotion recognition, empathy), behavioural changes, attention and working memory, episodic memory, visuospatial abilities and executive functions (Foxe et al., 2021; Goldberg et al., 2021; Piguet et al., 2015; Quang et al., 2021; Ramanan et al., 2021). Importantly, many of these deficits are present even after accounting for the language deficits; in other words, they are not secondary to the language deficits (e.g., due to nature of the verbal instructions) but are an integral part of the clinical profile. Even on a cognitive screening test, such as the ACE-III, presence of cognitive deficits beyond language are already apparent at presentation in PPA patients, and some becoming more prominent as the disease advances (Foxe et al., 2022).

All in all, a recent PubMed search identified about 2000 papers published on PPA. Of these, only 90 examined emotion, 65 examined executive function and 60 focused on attention. I will contend that the linguistic relativity inherent to the PPA criteria have resulted in agnosia (i.e., loss of knowledge). The constraints of the linguistic relativity associated with PPA criteria is even more surprising given the weight of evidence, not only at a behavioural level, but also at the neuroimaging level. Indeed, as described above, the core brain regions undergoing pathological changes in PPA, are known hubs for many cognitive processes beyond those of language (e.g., insula and autonomic system processing and integration; the amygdala and emotion processing; temporo-parietal junction and social cognition: Craig, 2009; Phelps & LeDoux, 2005; Saxe & Kanwisher, 2003).

After more than 10 years of service, it is becoming increasingly apparent that the diagnostic criteria for PPA are in need of a revision to take into account the accumulated evidence about changes that occur beyond language in these progressive brain disorders. It is important to note that the criticisms raised in the previous paragraphs are not isolated to PPA. This phenomenon (evidence blindness) is, in part, due to the difficulty for the brain to apprehend complex systems and complex sets of information and its tendency to reduce complexity to simple, manageable categories. This may be a remnant of evolution, where simple categorisation enables rapid decisions which provided a survival advantage. For example, deciding whether there is a tiger in the bushes is much more important than deciding which species of tiger it may be. In 2022, whilst the environment has changed, how our brain processes information has not. From a clinical and scientific viewpoint, it highlights the importance of remaining curious, and of not ignoring unusual or 'weird' phenomena, and of being critical of common labels. In the case of PPA, a better understanding of ALL the deficits that are part of these syndromes will have significant benefits. They will enable earlier diagnosis, better understanding of disease progression, and need for relevant care support. They also highlight that the language remediation and retraining in PPA patients will be more effective and have greater success when other, non-language deficits, are considered and taken into consideration.

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