The Presentation of Aphasia in Alzheimer Disease and Other Neurological Disorders

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Introduction

Aphasia has been described as a disorder of verbal communication due to an acquired lesion (or lesions) of the central nervous system involving speech production and / or comprehension.[1] Aphasia does not involve deficits in global processes of communication, but only in its linguistic component, as evidenced by patients' ability to communicate through other means (e.g., complex nonverbal gestures).[2] Aphasia is an integral part of the clinical presentation in Alzheimer Disease (AD). It is also an important diagnostic feature of other neurological disorders, which may be distinctive or overlap with AD. Clinicians should have a conceptual understanding of the different forms of aphasia as well as the conditions with which they are associated. The authors will review the diagnosis, assessment and treatment of aphasia, in the context of AD, Primary Progressive Aphasia (PPA), Frontotemporal dementia (FTD) and stroke.

The major types of aphasia can be classified as either fluent or nonfluent. According to Basso and Cubelli (1999),[1] the nonfluent aphasic syndromes include global aphasia, Broca's aphasia and transcortical motor aphasia, while the fluent aphasic syndromes include Wernicke's aphasia, conduction aphasia, anomic aphasia (amnestic aphasia), transcortical sensory aphasia and thalamic / subcortical aphasia.

Alzheimer Disease

Studies of the prevalence of language disturbance in AD have yielded estimates that vary between 30–100 % of patients.[3-6] Estimates of these prevalence rates are confounded by the different criteria used in the various studies to establish the diagnosis of AD, as well as by differences in the staging of the disease process in the samples tested. According to one study, aphasia is present in approximately 30% of individuals with mild AD and 82% with moderate disease.[7] Once the disease reaches the severe stage, aphasia is present in all AD patients.

In general, AD patients initially present with a fluent aphasia and anomia, and progress to exhibit symptomatology characteristic of either transcortical sensory aphasia, or Wernicke's aphasia, with progressive semantic deterioration. The aphasia occurs in association with other characteristic features of AD, including cognitive decline, impaired activities of daily living (ADL) and the development of behavioural symptomatology. The average life span after diagnosis is 10 years. The presence of significant language disturbance in AD has been associated with more rapid deterioration and death.[8,9] Whether later age of onset is associated with a greater level of aphasia is still controversial.[10] Non-fluent aphasia is rare except in cases of severe dementia.[3,10] However, neuropsychological heterogeneity has also been described, with a significant percentage of atypical presentations, such as the occurrence of early-onset nonfluent aphasia.[11-13]

Treatment interventions for AD include the use of acetylcholinesterase (AchE) inhibitors, which delay the progression of aphasia and other symptom domains.[14] Psychosocial interventions for patients and caregivers can also be beneficial.

Primary Progressive Aphasia

Primary Progressive Aphasia (PPA) was first described by Mesulam in 1982[15] and is characterized by a gradual deterioration of language function. It is believed to be the fifth most prevalent type of dementia.[16] Although cognitive deficits are initially absent in PPA, it frequently becomes associated with a gradual decline in cognitive abilities that impact on ADL. However, whether it progresses to dementia in all cases is unclear, leading to controversy regarding whether PPA is truly a distinct condition or a prodrome. It has been noted that, after an average of five years, 50% of PPA patients proceed to dementia.[10] However, in some cases language may be the only area affected for periods as long as 10–14 years.[16] Black described PPA as being a variant of AD or FTD originating in the left perisylvian cortex with the resulting disorder dependent upon the direction of neuroanatomical expansion. Anterior progression is associated with FTD while posterior progression is associated with AD. Post-mortem neuropathological examination has determined that less than 20% of individuals with PPA develop AD, a "nonspecific focal atrophy" accounts for 60% of cases, and Pick's disease occurs in the remaining 20%.[16]

In terms of presentation, PPA can be either nonfluent or fluent, and is characterized by anomia and an impairment of both syntax and semantics. It can be differentiated from AD and FTD because problems with memory, visual processing and personality are uncommon until later stages of the illness. This is especially significant for

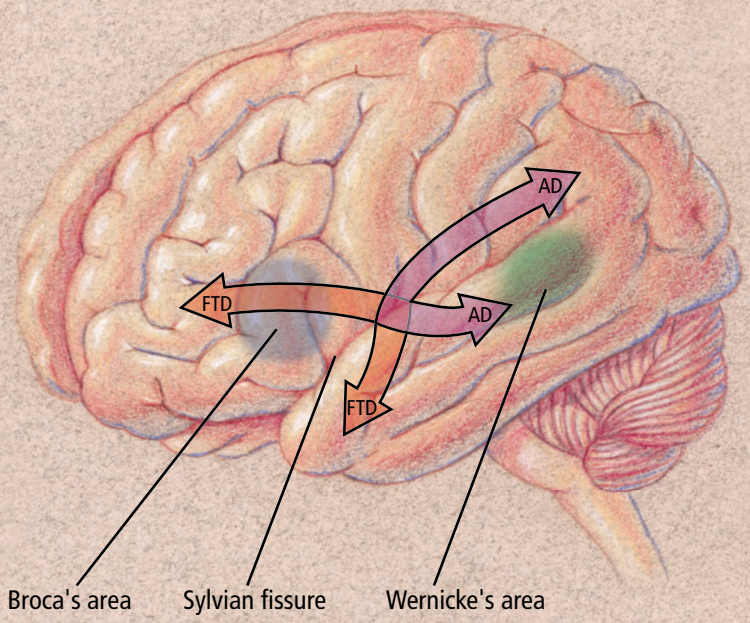
differentiating PPA from AD, given that in one case series of AD patients, 85% initially presented with aphasia.[10] A number of other factors differentiating PPA from AD include an earlier age of onset (typically between 55–65), a greater prevalence in males and independence of apoE4 status.[17] Little is known about risk factors for PPA, although it may be associated with mutations on chromosome 17. Neither pharmacological nor psychosocial interventions have been evaluated to any significant degree for this disorder. Mesulam[16] suggested that speech therapy might be useful, based on the opposite hemisphere acting in a compensatory fashion.

Frontotemporal Dementia

This disorder can present as three major distinct clinical syndromes depending upon the neuroanatomical location of atrophy.[18] In the case of the frontal variant, social, behavioural and personality changes occur, such as disinhibition, problems with impulse control, and antisocial and stereotypical behaviour. It is predominantly the stereotypical behaviours that differentiate FTD from AD. In these patients, the orbitobasal frontal lobe is affected. Where there is anterolateral temporal atrophy, fluent progressive aphasia associated with impairment in the production and comprehension of language occurs. Although this syndrome is sometimes referred to as 'Semantic Dementia' (SD), Mesulam[16] emphasizes that SD initially described a syndrome associated with deficits in visual recognition and non-verbal semantic knowledge, in addition to fluent aphasia and impaired comprehension. More recently, the term SD has been used interchangeably with 'fluent progressive aphasia,' even in the absence of non-verbal semantic impairment; however, it is probably important to differentiate these two groups of patients.[16] Fluent progressive aphasia patients typically complain about having difficulty remembering words and frequently demonstrate substitution of words and phrases. Episodic memory is usually intact, as opposed to AD. Behavioural changes may initially be present, but are mild. In the case of left perisylvian atrophy, progressive non-fluent aphasia occurs, with phonology and syntax being affected. This syndrome tends to be associated with global cognitive decline. Post-mortem pathology in these cases is either that of AD or "Pick-like."[18] The first two syndromes are most common and account for 80% of cases. The current treatment strategies are pharmacological and caregiver-based with a focus on behavioural aspects. At this time, there is no evidence to support the efficacy of treatment with AchE inhibitors.[19]

Primary Progressive Aphasia

A focal dementia syndrome caused by degeneration of the left perisylvian cortex. Progression of the language disorder reflects the nature of the underlying neuropathology and direction of anatomical expansion. Anterior progression is associated with Frontotemporal Dementia (with fluent or non-fluent aphasia), whereas posterior progression is associated with Alzheimer Disease (and fluent aphasia) (10).



Stroke

Aphasia occurs in approximately 40% of acute stroke patients with a significant percentage having residual deficits.[20] Patients with aphasia have a higher incidence of depression and possibly non-verbal cognitive deficits.[21] The presence of aphasia doubles the risk of mortality compared to those without aphasia.[22] However, in the case of patients with mild aphasia, 70% experienced complete recovery, with younger patients doing better than older ones. As with other conditions discussed, individuals who have had strokes do not show progressive deterioration, unless they experience further vascular events. The type of aphasia, as well as associated symptoms, is dependent upon the location, size and number of lesions. Some stroke patients present with a vascular dementia, characterized by a stepwise decline in several domains, including cognition, ADL, behaviour and focal neurological deficits. Diagnostically, stroke patients have a variety of risk factors including hypertension, hypercholesterolemia, cigarette smoking and diabetes.[23] Current treatment focuses on stroke prevention. AchE inhibitors are currently being evaluated in individuals

Table 1

Aphasia in Alzheimer Disease and Other Neurological Disorders

	Type of aphasia	Presentation	Treatment
Alzheimer Disease (AD)	– Early stage: fluent aphasia with anomia – Later stage: transcortical sensory aphasia or Wernicke's aphasia with progressive deterioration in semantic processing	– Aphasia in association with other features of AD such as cognitive decline, impairments in ADL, and behavioural symptoms – Language impairment is associated with more rapid deterioration	– AchE inhibitors – Psychosocial interventions for patients and caregivers
Frontotemporal Dementia (FTD)	– Anterolateral temporal atrophy is associated with progressive fluent aphasia – Perisylvian atrophy is associated with progressive nonfluent aphasia	Three Variants: 1) Frontal Variant: Behavioural and personality changes predominate 2) Semantic Dementia: Impaired memory for words and substitution of words and phrases; episodic memory retained 3) Progressive Nonfluent Aphasia: global cognitive decline	– No evidence to support use of AchE inhibitors in most cases
Primary Progressive Aphasia (PPA)	– Fluent or nonfluent	– Gradual deterioration of language function – Characterized by anomia and impairment in syntax and semantics – Problems with memory, personality, and visual processing uncommon until later stages – 50% of PPA patients proceed to dementia after an average of 5 years	– Speech therapy may be useful – No specific psychosocial or pharmacological interventions have been thoroughly investigated
Stroke	– Type of aphasia and presentation depend on the nature of the stroke	– Aphasic patients have a higher incidence of depression and possibly non-verbal cognitive deficits – Does not progress in the absence of further strokes – Aphasia frequently improves over time – May occur in the context of vascular dementia	– Treatment is focused on stroke prevention – Speech therapy – AchE inhibitors and Piracetam may have some treatment potential

with vascular dementia, and may have a benefit for patients with aphasia. Piracetam, a nootropic, has shown some promise as a treatment for aphasia.[24] Speech therapy is also an integral aspect of rehabilitation.

Diagnostic Evaluation

A thorough clinical assessment is necessary in order to differentiate among the conditions described above. Neuroimaging in the form of CT, MRI and SPECT can play an important role in the identification and localization of lesions or areas of atrophy. It is also critical to evaluate other domains (such as memory, visuospatial skills) before making a diagnosis because deficits that appear to be aphasic disturbances may be secondary to impairment in other domains.

Assessment of Aphasia

The easiest discrimination for the clinician to make is between fluent and nonfluent aphasia. In practical terms, this can typically be done through free conversation with the patient. Patients with nonfluent aphasia will present with halting, agrammatic speech, in which syllables are interrupted with pauses, and sentences are short. Dysarthria or verbal apraxia also frequently accompanies nonfluent aphasia, and phonemic errors are frequent on initial consonants. Patients with fluent aphasia will present with longer sentences (> 5 words), without interruptions or agrammaticism, but the content of the utterance may be incomprehensible (especially in Wernicke's aphasia), and the patient may be unaware of this fact.

Aphasia Batteries versus Individual Tests of Language Function

Neuropsychological assessment of aphasia can take two different forms: specialized aphasia batteries and individual tests of specific language ability. The former can be used when an individual is known to suffer from a disorder of verbal communication and a more detailed analysis is required to determine the exact nature of the deficit. In contrast, specific tests of language ability are more likely to be used within the context of a comprehensive neuropsychological evaluation when the individual is thought to be suffering from a dementing illness of uncertain diagnosis. Many of the specific tests of language ability are incorporated in (or derived from) the more comprehensive aphasia batteries.

Two commonly used batteries for the assessment of aphasia are the Boston Diagnostic Aphasic Examination (BDAE)[25] and the Western Aphasia Battery (WAB).[26] The BDAE is one of the most popular aphasia batteries, and provides a full assessment of an aphasic patient's language skills with special reference to classical, anatomically based aphasic syndromes.[27] The WAB was developed with reference to the BDAE to generate diagnostic classifications and to be suitable for both treatment and research purposes, and incorporates many of the tests from the BDAE.[28] The WAB also quantifies an 'Aphasia Quotient' (AQ) that provides a measure of discrepancy from normal language performance, in addition to providing scores for language subtests.

Individual tests of language function include the Boston Naming test (a test of confrontational naming), the Peabody Picture Vocabulary Test (PPVT-III), designed to assess auditory comprehension of picture names,[28] and the Controlled Oral Word Association test (COWA) to assesses verbal fluency (the patient is required to generate words that begin with a particular letter without using proper names in a one-minute time period).[27] Semantic category fluency assessment (e.g.

Figure 1
Diagnostic Criteria for Primary Progressive Aphasia

1. Insidious onset and gradual progression of word finding, object-naming, or word-comprehension impairments as manifested during spontaneous conversation, or as assessed through formal neuropsychological tests of language.
2. All limitations of daily living activities attributable to the language impairment, for at least two years after onset.
3. Intact premorbid language function (except for developmental dyslexia).
4. Absence of significant apathy, disinhibition, forgetfulness for recent events, visuospatial impairment, visual recognition deficits or sensory-motor dysfunction within the initial two years of the illness. (This criterion can be fulfilled by history, survey of daily living activities, or formal neuropsychological testing).
5. Acalculia and ideomotor apraxia may be present even in the first two years. (Mild constructional deficits and perseveration [as assessed in the go 'no-go' task] are also acceptable as long as neither visuospatial deficits nor disinhibition influences daily living activities).
6. Other domains possibly affected after the first two years but with language remaining the most impaired function throughout the course of the illness and deteriorating faster than other affected domains.
7. Absence of "specific" causes such as stroke or tumour as ascertained by neuroimaging.

generating animal names) complements letter fluency assessment, and may be differentially affected in some disorders. For example, in progressive nonfluent aphasia, semantic category fluency is usually not affected as seriously as letter fluency.[29] The Token Test is designed to assess a patient's capacity to comprehend verbal instructions of increasing complexity,[27] while the Pyramids and Palm Trees task[30] assesses semantic processing. In addition to these specific language-based tests, it is important to assess patients in other cognitive domains, because deficits that appear to be language-based may in fact be secondary to nonverbal factors such as visuospatial compromise.

Conclusions and Summary

Aphasia can present in the context of a number of common neurological disorders. While there is some overlap between AD, PPA and FTD, there are classical and distinctive presentations in each condition. With AD, there is a progressive fluent aphasia in association with specific diagnostic symptoms. PPA is associated with either fluent or non-fluent aphasia, in the absence of other symptoms (frequently for many years). With FTD, either a progressive fluent or nonfluent aphasia occurs. In the case of stroke, the nature of aphasia, as well as associated deficits, is determined by the location of the lesion. In this case, unlike the others, improvement of the aphasia can occur over time. A number of other conditions frequently associated with aphasia such as traumatic brain injury and space occupying lesions have not been discussed, as the focus of this paper has been on disorders that specifically occur in an elderly population.

The nature of aphasia frequently changes as these conditions progress. Atypical presentations are not uncommon and make accurate diagnosis and management challenging. Currently available neuropsychological tests, as well as neuroimaging techniques, are valuable diagnostic tools. It is important for clinicians to have an awareness of the disorders described and existing controversies. There is considerable diagnostic overlap (and debate concerning proper classification) in PPA, temporal lobe FTD variants, and SD,[16,31] indicating that further refinement of the diagnostic criteria and / or understanding of the underlying pathological mechanisms is needed. Limited therapeutic options are available in some cases, and further research in this area is definitely required. Pharmacological interventions used in AD may well have an expanded role in the future. Overall, as our understanding of various disorders associated with aphasia improves, it leads to more accurate diagnosis and better management. ◆

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