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Review

Inflectional morphology in primary progressive aphasia and Alzheimer's disease: A systematic review

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ABSTRACT

Consensus recommendations for three variants of primary progressive aphasia (PPA), the non-fluent/agrammatic, logopenic and semantic variants, were published in 2011 [Gorno-Tempini et al., 2011]. These recommendations describe the most characteristic language impairments for each variant. However, studies using these criteria in larger groups of patients revealed serious limitations concerning their application. Some of these limitations are related to imprecisions in the description of language features, especially for grammatical features. The aim of this review was to examine studies of inflectional morphology in three variants of PPA and in the disease that is the most relevant for differential diagnosis, namely Alzheimer's disease. MedLine, CINAHL and PsycINFO electronic databases were searched to retrieve all relevant peer-reviewed articles published in English language journals. Despite the focus that has been placed on agrammatism by the consensus recommendations, the studies reviewed do not systematically report impairments of inflectional morphology in the non-fluent/agrammatic variant. Studies also show that some individuals with the logopenic variant present with substantial inflection impairments. Contrary to expectations, some studies reveal the presence of morphological difficulties in the semantic variant. These difficulties concern mostly the production of irregular, low-frequency verbs while regular verbs are spared. Similar difficulties are also reported in studies of people with Alzheimer's disease. Overall, the results show the need to more clearly define

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the criteria related to grammar and morphology and to better characterise impairment severity. Future research on primary progressive aphasia and other degenerative diseases with language impairments will help refine our expectations regarding language features that characterise each profile.

1. Introduction

The literature on neurodegenerative impairment with central language features is continuously growing. Warrington (1975) was the first to describe a series of patients with central semantic impairment of degenerative origin. This degenerative profile would later be characterised as semantic dementia (Hodges, Patterson, Oxbury, & Funnell, 1992; Snowden, Goulding, & Neary, 1989). Around the same time, Mesulam (1982) described "slowly progressive aphasia", a syndrome characterised by prominent language impairment of degenerative origins. This paper laid the basis for the description of primary progressive aphasia (PPA) (Mesulam, 2001; Mesulam & Weintraub, 1992). Neary et al. (1998) published consensual criteria for three syndromes of frontotemporal dementia: (behavioural) frontotemporal dementia, progressive nonfluent aphasia and semantic dementia. These criteria did not include a logopenic variant, and implicitly excluded degenerative impairment with aetiologies other than frontotemporal lobar degeneration pathologies. Additionally, according to these criteria, people presenting with associative agnosia could receive a diagnosis of semantic dementia without having a prominent language disorder, which means that they did not necessarily fulfil the core criteria of PPA (Mesulam et al., 2014). This motivated the distinction between fluent PPA and semantic dementia (Mesulam, Grossman, Hillis, Kertesz, & Weintraub, 2003). A turning point was made with the publication of the criteria for three variants of PPA: semantic variant PPA (svPPA), non-fluent/agrammatic variant PPA (nfavPPA) and logopenic variant PPA (lvPPA) (Gorno-Tempini et al., 2011). These criteria require the fulfilment of the core PPA criteria (Mesulam, 2001) prior to the identification of a specific variant. svPPA is characterised by difficulties in word retrieval and single-word comprehension. The supporting features are impaired object knowledge, surface dyslexia or dysgraphia, preserved repetition and preserved grammar and motor speech production. nfavPPA is characterised by agrammatism in speech production and/or apraxia of speech. The supporting features are impaired comprehension of syntactically complex sentences, spared single-word comprehension and spared object knowledge. lvPPA is characterised by impaired single-word retrieval and impaired repetition of sentences and phrases. The supporting features are the production of phonological errors, spared single-word comprehension, spared object knowledge, spared motor speech and an absence of frank agrammatism.

The criteria of Gorno-Tempini et al. (2011) provide complementary information regarding the underlying pathology that is most often associated with each variant. Although no direct association with pathology type was made, Gorno-Tempini et al. (2011) reported results that suggest that in nfavPPA and svPPA, frontotemporal lobar degeneration is the most common underlying pathology, while in lvPPA, Alzheimer's disease (AD) pathology is the most common underlying cause. The 2011 criteria were the result of discussions between experts from several centers and they have been cited extensively since their publication (Mesulam & Weintraub, 2014). However, studies testing their application to fairly large sets of patients have revealed major limitations (Harris et al., 2013; Mesulam, Wieneke, Thompson, Rogalski, & Weintraub, 2012; Mesulam et al., 2014; Sajjadi, Patterson, Arnold, Watson, & Nestor, 2012; Wicklund et al., 2014).

First, studies have shown that not all patients are classifiable using the 2011 criteria. These studies report large proportions of unclassifiable and mixed profiles (Harris et al., 2013; Mesulam et al., 2012, 2014; Sajjadi, Patterson, Arnold, et al., 2012; Wicklund et al., 2014). Second, overlaps in the criteria allow some patients to simultaneously fulfil criteria for more than one variant (Harris et al., 2013; Mesulam et al., 2012, 2014; Sajjadi, Patterson, Arnold, et al., 2012; Wicklund et al., 2014). Third, the association between the underlying pathology and PPA entity is far from systematic. A recent study reporting 58 autopsies of patients with PPA (Mesulam et al., 2014) showed that AD pathology is