



Inflectional morphology in primary progressive aphasia: An elicited production study



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ABSTRACT

Inflectional morphology lies at the intersection of phonology, syntax and the lexicon, three language domains that are differentially impacted in the three main variants of primary progressive aphasia (PPA). To characterize spared and impaired aspects of inflectional morphology in PPA, we elicited inflectional morphemes in 48 individuals with PPA and 13 healthy age-matched controls. We varied the factors of regularity, frequency, word class, and lexicality, and used voxel-based morphometry to identify brain regions where atrophy was predictive of deficits on particular conditions. All three PPA variants showed deficits in inflectional morphology, with the specific nature of the deficits dependent on the anatomical and linguistic features of each variant. Deficits in inflecting low-frequency irregular words were associated with semantic PPA, with lexical/semantic deficits, and with left temporal atrophy. Deficits in inflecting pseudowords were associated with non-fluent/agrammatic and logopenic variants, with phonological deficits, and with left frontal and parietal atrophy.

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1. Introduction

The goal of this study was to investigate the production of inflectional morphology in primary progressive aphasia (PPA). PPA is a neurodegenerative syndrome in which focal degeneration of language areas leads to progressive language deficits, while other cognitive domains remain relatively spared (Mesulam, 1982, 2001). Recent consensus guidelines for the diagnosis of PPA recognize three variants: non-fluent/agrammatic PPA, semantic PPA (also known as semantic dementia), and logopenic PPA (Gorno-Tempini et al., 2011). The three variants differ in terms of which language domains are impacted, distribution of atrophy (Gorno-Tempini et al., 2004) and pathological substrates (Grossman, 2010; Snowden et al., 2011).

Inflectional morphology is the part of grammar that marks words for grammatical features such as tense, aspect, mood, polarity, person, number, gender and case, by means of affixation (e.g. *laugh*, *laughed*) or other modifications of the word (e.g. *come*,

came). Inflectional morphology lies at the intersection of three major components of language: phonology, syntax, and the lexicon (Spencer, 1991). First, inflectional morphology inherently involves phonological processes such as affixation, ablaut or reduplication. When affixes are attached to words, it is often necessary to select the appropriate allomorph based on the phonological context. For instance, the past tense forms of *laugh*, *call* and *want* are [læf-t], [cal-d], and [want-əd], with the past tense suffix surfacing as [-t], [-d] and [-əd] respectively, depending on the phonological features of the final phoneme of the stem. Second, syntax is relevant because it determines many of the grammatical features to be marked. For instance, tense is a syntactic feature that is often instantiated via inflectional morphology, as in the past tense suffix *-ed* in *Yesterday I laughed*. To give another example, grammatical relations such as subject and object are indicated through case marking, so we say *I saw him*, not **Me saw he*. Finally, the lexicon is relevant to inflectional morphology, because in many languages, including English, there are irregularities in inflectional paradigms such that item-specific information about inflected forms must be stored in relation to each lexical item. For instance, an English speaker must store in the lexicon the information that the past tense of *give* is *gave*, not *gived*, and the plural of *mouse* is *mice*, not *mouses*.

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Inflectional morphology lies at the intersection of phonology, syntax, and the lexicon, and these three language domains are differentially impacted in the three variants of PPA. Therefore we may expect deficits in inflectional morphology in each of the three variants. Moreover, the specific nature of these deficits would be expected to differ depending on the particular language domains that are impacted in each variant.

Inflectional morphology has been investigated most thoroughly in the semantic variant of PPA, which is characterized by deficits in lexical and semantic knowledge (Hodges, Patterson, Oxbury, & Funnell, 1992; Snowden, Goulding, & Neary, 1989; Warrington, 1975). Patients with semantic PPA show a selective deficit for inflecting irregular verbs (Patterson, Lambon Ralph, Hodges, & McClelland, 2001; Cortese, Balota, Sergent-Marshall, Buckner, & Gold, 2006; Jefferies, Rogers, Hopper, & Lambon Ralph, 2010; Patterson, Lambon Ralph, et al., 2006), as well as an interaction of regularity by frequency, such that performance is disproportionately poor for low-frequency irregular verbs (Jefferies et al., 2010; Patterson, Lambon Ralph, & Hodges, 2001; Patterson, Lambon Ralph, et al., 2006). Interactions of regularity by frequency are characteristic of a variety of linguistic and non-linguistic domains in semantic PPA (Patterson, Lambon Ralph, et al., 2006). This pattern is thought to be indicative of lexical and/or semantic deficits, because irregular items require item-specific information, and item-specific information is progressively lost, with lower frequency items affected earlier than higher frequency items. There are some indications that patients with semantic PPA show a similar pattern with nominal inflectional morphology: they have been shown to be impaired in selecting the appropriate gender of determiners for nouns whose gender does not match their phonological form, especially for low-frequency items (Lambon Ralph et al., 2011), and noun-verb agreement and noun-adjective agreement were impaired for irregular items in a Hebrew-speaking semantic PPA patient (Kavé, Heinik, & Biran, 2012). Most semantic PPA patients are able to correctly supply regular inflections to pseudo-verbs (Patterson et al., 2001). Taken together, these findings suggest that deficits in inflectional morphology in semantic PPA follow from lexical and/or semantic impairments.

Non-fluent/agrammatic PPA is characterized by agrammatism and/or motor speech deficits (Gorno-Tempini et al., 2011; Grossman et al., 1996; Hodges & Patterson, 1996). Inflectional morphology in non-fluent/agrammatic PPA was investigated in a recent study in which six different verb forms were elicited (Thompson et al., 2013). Non-fluent/agrammatic PPA patients were impaired in producing finite verb forms (i.e. verb forms that mark tense), but they did much better with non-finite verb forms (i.e. verb forms that do not mark tense, e.g. progressive *-ing*). Similarly, quantitative analyses of connected speech have documented the omission and erroneous use of verbal inflectional morphology in non-fluent/agrammatic PPA (Thompson, Ballard, Tait, Weintraub, & Mesulam, 1997; Thompson et al., 2012, 2013; Wilson, Henry, et al., 2010) and, to a lesser extent, nouns (Thompson et al., 2012). Sensitivity to the syntactic factor of finiteness suggests that deficits in inflectional morphology in non-fluent/agrammatic PPA may follow from syntactic deficits. Phonological deficits may also contribute, since non-fluent patients have been shown to produce phonemic paraphasias in connected speech (Patterson, Graham, Lambon Ralph, & Hodges, 2006; Ash et al., 2010; Wilson, Henry, et al., 2010) and to exhibit difficulties on phonological manipulation tasks (Henry et al., 2014; Patterson, Graham, et al., 2006).

Logopenic PPA is associated with core phonological and word-finding deficits (Gorno-Tempini et al., 2004, 2008). In Thompson and colleagues' recent elicited production study, patients with logopenic PPA did not make many morphological errors with either finite or non-finite verbs (Thompson et al., 2013), and they make

few morphological errors in connected speech (Thompson et al., 2012; Wilson, Henry, et al., 2010). Since phonological deficits are a core feature of logopenic PPA, they may be expected to have an impact on inflectional morphology, but there is no evidence to date that this is the case.

To our knowledge, the neural correlates of deficits in inflectional morphology in PPA have not been systematically investigated. Neuropsychological studies in other patient cohorts have provided some evidence suggesting that deficits in regular morphology are associated with frontal and basal ganglia damage, in contrast to deficits in irregular morphology, which are related to temporal lobe lesions (Marin, Saffran, & Schwartz, 1976; Miozzo, 2003; Tyler et al., 2002; Ullman et al., 2005). A number of neuroimaging studies in healthy controls have attempted to identify brain regions differentially involved in regular or irregular morphology, yet findings have been inconsistent (Jaeger et al., 1996; Ullman et al., 1997; see Desai, Conant, Waldron, & Binder, 2006 for review). Any robust differences between these conditions appear to be secondary to phonological, executive, attentional or decision-making factors that differ between regular and irregular items (Desai et al., 2006). Several single case studies of post-stroke aphasic patients have been reported showing clear dissociations between nominal and verbal morphology, though no conclusions were drawn regarding the relevant brain regions (Shapiro & Caramazza, 2003; Shapiro, Shelton, & Caramazza, 2000).

In this study, we sought to characterize spared and impaired aspects of inflectional morphology in the three variants of PPA using an elicited production task. We varied the factors of regularity (regular, irregular), frequency (low, high), word class (verbs, nouns), and lexicality (words, pseudowords). We hypothesized that the specific linguistic and anatomical profile of each PPA variant would impact inflectional morphology in different ways. First, we expected the lexical/semantic deficits that are most prominent in semantic variant PPA to differentially impact the inflection of low-frequency irregular words, regardless of word class, since low-frequency irregular words are most dependent on item-specific information. Second, we predicted that the different kinds of phonological deficits that are seen in non-fluent/agrammatic and logopenic PPA would lead to difficulties inflecting pseudowords, which must be inflected via a productive phonological process. Third, we anticipated that the syntactic deficits that occur in non-fluent/agrammatic PPA would affect all words regardless of regularity, frequency or lexicality, since syntactic deficits reflect sentence- or phrase-level rather than word-level impairment. Therefore syntactic deficits should lead to problems inflecting even high-frequency regular words, which make the least demands on lexical/semantic information. We also investigated the relationships between measures of deficits in particular linguistic domains, and inflection of different types of words, and we used voxel-based morphometry to determine whether atrophy of regions involved in different domains of language impacts different aspects of inflectional morphology accordingly.

2. Methods

2.1. Participants

Individuals with PPA and age-matched controls were recruited through the Memory and Aging Center at the University of California, San Francisco (UCSF). All participants gave written informed consent, and the study was approved by the institutional review boards at UCSF and the University of Arizona. Patients and controls received a comprehensive multidisciplinary evaluation including neurological history and examination, neuropsychological testing, and neuroimaging.

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