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Research report

Patterns of breakdown in spelling in primary progressive aphasia

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ABSTRACT

Introduction: The objective of this study is to determine which cognitive processes underlying spelling are most affected in the three variants of primary progressive aphasia (PPA): Logopenic variant primary progressive aphasia (lvPPA), Semantic variant primary progressive aphasia (svPPA), and Nonfluent variant primary progressive aphasia (nfvPPA).
Methods: 23 PPA patients were administered The Johns Hopkins Dysgraphia Battery to assess spelling. Subtests evaluate for effects of word frequency, concreteness, word length, grammatical word class, lexicality (words *vs* pseudowords), and ''regularity'' by controlling for the other variables. Significant effects of each variable were identified with chi square tests. Responses on all spelling to dictation tests were scored by error type. 16 of the 23 subjects also had a high resolution MRI brain scan to identify areas of atrophy.
Results: We identified 4 patterns of spelling that could be explained by damage to one or more cognitive processes underlying spelling. Nine patients (3 unclassifiable, 4 with lvPPA, 2 with svPPA) had dysgraphia explicable by *impaired access to lexical representations*, with reliance on sublexical phonology-to-orthography conversion (POC). Two patients (with nfvPPA) showed dysgraphia explicable by *impaired access to lexical representations and complete disruption of sublexical POC*. Seven patients (4 with lvPPA, 1 with svPPA, 2 unclassifiable) showed dysgraphia explicable by *impaired access to lexical-semantic representations and/or lexical representations with partially spared sublexical POC mechanisms*. Five patients (1 with nfvPPA, 2 with svPPA, 1 with lvPPA, and 1 unclassifiable) showed dysgraphia explicable by impairment of the graphemic buffer.
Conclusions: Any cognitive process underlying spelling can be affected in PPA. Predominance of phonologically plausible errors, more accurate spelling of regular words than irregular words, and more accurate spelling of pseudowords than words (indicating spared POC mechanisms) may indicate a low probability of progression to nfvPPA.

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1. Introduction

Primary progressive aphasia (PPA) is a neurodegenerative syndrome characterized by progressive impairment of language with sparing of other cognitive domains (except praxis) for at least two years (Mesulam, 2003). PPA has recently been divided into three clinical subtypes based on spoken language comprehension and production that appear to be associated with different regions of cortical atrophy and loosely associated with different pathologies (Posteraro et al., 1988; Gorno-Tempini et al., 2004; Hillis, 2008; Josephs et al., 2008; Mesulam et al., 2008; Gorno-Tempini et al., submitted for publication).

Nonfluent variant primary progressive aphasia (nfvPPA) is classically associated with atrophy in left posterior frontal cortex and insula and is characterized by difficulty with grammaticality of sentence production and apraxia of speech (Gorno-Tempini et al., 2004 and submitted; Rabinovici et al., 2008; Mesulam et al., 2008; Josephs et al., 2008). Many show disproportionately impaired naming of action verbs compared to concrete nouns (Hillis et al., 2004). Writing is sometimes relatively intact compared to speech, and many patients use writing as a primary means of communication (Holland et al., 1985; Hillis et al., 2002). Some patients show a progressive loss of verbs only in speech, while naming of nouns remains normal in speech and naming of verbs and nouns remains normal in writing (Hillis et al., 2002). These patients eventually also develop impaired written naming of verbs (and nouns), but it is often long after they have become mute.

In contrast, Semantic variant primary progressive aphasia (svPPA) is associated with atrophy in the left (more than the right) anterior and inferior temporal lobe and is characterized by deterioration of word and object meanings (Hodges et al., 1992; Mummery et al., 2000). There is often disproportionately impaired naming of nouns (objects) compared to verbs (actions) – opposite to the pattern seen in nfvPPA (Hillis et al., 2004). Comprehension of object meanings is often worse than comprehension of action meanings as well (Rhee et al., 2001). These patients tend to show deterioration in written naming prior to deterioration of spoken naming. Writing and reading often show a reliance on sublexical phonological-orthographic conversion (or the opposite), resulting in phonologically plausible errors (e.g., creature spelled kreechure) (Graham et al., 1995).

Logopenic variant primary progressive aphasia (lvPPA), associated with atrophy in the left posterior, superior temporal, and inferior parietal cortex, is characterized by poor sentence repetition and poor naming of both nouns and verbs (Gorno-Tempini et al., 2004, 2008, submitted for publication; Rabinovici et al., 2008; Hillis, 2008; Josephs et al., 2008). Unlike individuals with svPPA, those with lvPPA have relatively spared word and object meanings. Unlike patients with nfvPPA, they have relatively spared motor speech. Most or all have impaired phonological working memory. In part because this group was recently identified, the spelling performance of these patients has not been studied extensively.

These distinct behavioral patterns also provide clues as to the most likely etiology of the neurological condition. There are three main degenerative neurological pathologies, which can only be diagnosed at autopsy or by brain biopsy that can cause PPA. The three pathologies tend to affect different parts of the brain, so the subtype of PPA (which reflects what part of the brain is affected) allows one to predict the most likely pathology. Most autopsy studies have found that nfvPPA is most commonly associated with corticobasal degeneration or frontotemporal lobar degeneration-tau (''tau-opathies''), while svPPA is most commonly associated with a different abnormal protein inclusion, ubiquitin (Kertesz et al., 2005; Davies et al., 2005; Snowden et al., 2007; Josephs et al., 2008). lvPPA is most commonly associated with the pathology found in Alzheimer's disease (Gorno-Tempini et al., 2008; Rabinovici et al., 2008). These underlying conditions may respond to different medical interventions; therefore, identifying the pattern of language impairment may be useful for deciding on medical treatment. Because writing can be one of the earliest symptoms of language breakdown (particularly in svPPA), the distinct pattern of spelling impairment might predict the subsequent course of language deterioration. However, few studies have examined the breakdown of spelling in various types of PPA.

In this paper, we sought to identify which cognitive processes underlying spelling were impaired in 23 patients with PPA. Previous detailed analyses of spelling performance by patients with focal brain damage such as stroke, along with consideration of the computational demands of the task, have provided evidence for proposing that spelling requires a number of cognitive processes that can be independently disrupted by brain lesions. (Caramazza et al., 1987; Beeson and Hillis, 2001; Rapp, 2002). In brief, spelling can be accomplished either by recognizing the spoken word (phonological representation), accessing its meaning (lexical-semantic representation), and accessing the stored spelling of the word (orthographic representation) or through sublexical (phonology-to-orthography conversion – POC) mechanisms. Accurate spelling may be accomplished through an interaction between these mechanisms, even if one or both are partially impaired (Hillis and Caramazza, 1991, 1995; see also Patterson et al., 1994). Spelling of pseudowords (e.g., frunk) requires sublexical mechanisms, while spelling of irregular words may depend more on lexical and lexical-semantic representations (Rapp, 2002). Whether the spelling is accessed via lexical and semantic representations or assembled through sublexical mechanisms, the sequence of graphemes or abstract letter identities must be stored in working memory while the letters are written or spoken aloud a mechanism known as the ''graphemic buffer''(Caramazza et al., 1987; Posteraro et al., 1988; Hillis and Caramazza, 1989) (see Fig. 1). Written naming requires the same cognitive processes as spelling to dictation of irregular words, except that recognition of the picture, rather than recognition of the spoken word, is required.

To identify the status of each of these cognitive processes underlying spelling in each patient and to determine whether or not there were differences across subtypes of PPA, we administered a battery of spelling tasks to 23 patients with PPA and analyzed their patterns of errors across tasks and stimuli.