Functional neuroanatomy of speech signal decoding in primary progressive aphasias

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The pathophysiology of primary progressive aphasias remains poorly understood. Here, we addressed this issue using activation fMRI in a cohort of 27 patients with primary progressive aphasia (nonfluent, semantic, and logopenic variants) versus 15 healthy controls. Participants listened passively to sequences of spoken syllables in which we manipulated 3-key auditory speech signal characteristics: temporal regularity, phonemic spectral structure, and pitch sequence entropy. Relative to healthy controls, nonfluent variant patients showed reduced activation of medial Heschl’s gyrus in response to any auditory stimulation and reduced activation of anterior cingulate to temporal irregularity. Semantic variant patients had relatively reduced activation of caudate and anterior cingulate in response to increased entropy. Logopenic variant patients showed reduced activation of posterior superior temporal cortex to phonemic spectral structure. Taken together, our findings suggest that impaired processing of core speech signal attributes may drive particular progressive aphasia syndromes and could index a generic physiological mechanism of reduced computational efficiency relevant to all these syndromes, with implications for development of new biomarkers and therapeutic interventions.

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1. Introduction

The primary progressive aphasias (PPAs) have collectively helped establish the paradigm of selective neural vulnerability to neurodegenerative pathologies (Mesulam, 1982; Mesulam et al., 2014). These disorders have been characterized as neurodegenerative pathologies (Mesulam, 1982; Mesulam et al., 2014). Language impairment is the dominant clinical consideration in PPA and enshrined in current consensus diagnostic criteria (Gorno-Tempini et al., 2011). However, a substantial proportion of cases of PPA do not fall clearly into current diagnostic categories, whereas similar linguistic deficits may be prominent in other dementia syndromes such as bvFTD (Hardy et al., 2015; Rohrer and Warren, 2016). A number of studies have documented profiles of nonverbal auditory deficits associated with PPA syndromes (Bozeat et al., 2000; Fletcher et al., 2015; Golden et al., 2015; Gorno-Tempini et al., 2011). Language impairment is the dominant clinical consideration in PPA and enshrined in current consensus diagnostic criteria (Gorno-Tempini et al., 2011). However, a substantial proportion of cases of PPA do not fall clearly into current diagnostic categories, whereas similar linguistic deficits may be prominent in other dementia syndromes such as bvFTD (Hardy et al., 2015; Rohrer and Warren, 2016). A number of studies have documented profiles of nonverbal auditory deficits associated with PPA syndromes (Bozeat et al., 2000; Fletcher et al., 2015; Golden et al., 2015; Gorno-Tempini et al., 2011).
2. Materials and methods

2.1. Participants

The patient cohort comprised 12 patients with nfVPPA (5 female; mean age 70.9 years), 9 patients with svPAPA (3 female; mean age 62.3 years), and 6 patients with lvPAPA (2 female; mean age 62.7 years), each fulfilling consensus criteria for the respective syndromic diagnosis (Gorno-Tempini et al., 2011) and recruited via a specialist cognitive disorders clinic. Brain magnetic resonance imaging (MRI) findings corroborated the syndromic diagnosis in each case; no patient had radiological evidence of significant comorbid cerebrovascular damage. Cerebrospinal fluid tau/alpha profiles were available for 5 of the 6 patients with lvPAPA, all of which were consistent with Alzheimer’s pathology based on local reference ranges (total tau: beta-amyloid1–42 ratio >1). Fifteen healthy older individuals (8 female; mean age 68.8 ± 4.5 years) with no history of neurological or psychiatric illness also participated. All participants had a comprehensive general neuropsychological assessment. Demographic, clinical, and neuropsychological characteristics of participant groups are summarized in Table 1. Peripheral hearing function was assessed in all participants using pure tone audiometry (procedural details in Supplementary Material on-line).

All participants gave informed consent, and the ethical approval for the study was granted by the National Hospital for Neurology and Neurosurgery and University College London Research Ethics Committees, following Declaration of Helsinki guidelines.

2.2. Experimental stimuli

The stimuli presented in the fMRI experiment were based on sequences of spoken syllables comprising consonant-vowel or vowel-consonant phoneme combinations, recorded in a standard Southern English accent by a young adult male speaker. The syllables ‘af’, ‘ba’, ‘da’, ‘ma’, ‘om’, ‘or’, ‘po’, and ‘ro’ were selected for high intelligibility and identifiability, based on pilot testing in 5 young adult listeners in our laboratory. In MATLAB R2012a (https://uk.mathworks.com/), recorded syllables were each edited to duration 240 msec and concatenated with random ordering into