Speech errors in progressive non-fluent aphasia

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\textbf{A R T I C L E   I N F O}

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\textbf{A B S T R A C T}

The nature and frequency of speech production errors in neurodegenerative disease have not previously been precisely quantified. In the present study, 16 patients with a progressive form of non-fluent aphasia (PNFA) were asked to tell a story from a wordless children's picture book. Errors in production were classified as either phonemic, involving language-based deformations that nevertheless result in possible sequences of English speech segments; or phonetic, involving a motor planning deficit and resulting in non-English speech segments. The distribution of cortical atrophy as revealed by structural MRI scans was examined quantitatively in a subset of PNFA patients (\(N = 7\)). The few errors made by healthy seniors were only phonemic in type. PNFA patients made more than four times as many errors as controls. This included both phonemic and phonetic errors, with a preponderance of errors (82\%) classified as phonemic. The majority of phonemic errors were substitutions that shared most distinctive features with the target phoneme. The systematic nature of these substitutions is not consistent with a motor planning deficit. Cortical atrophy was found in prefrontal regions bilaterally and per-Sylvian regions of the left hemisphere. We conclude that the speech errors produced by PNFA patients are mainly errors at the phonemic level of language processing and are not caused by a motor planning impairment.

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1. Introduction

Errors in the production of the segments comprising speech are made by all speakers of a language. For healthy speakers, this happens infrequently and often to humorous effect, evoking reference to the Reverend William Spooner (1844–1930). A more severe impairment of the production of speech sounds is found in pathological conditions. Much of the literature on speech production errors in subjects with an acquired language impairment has focused on patients who have suffered a cerebral vascular accident (Canter, Trost, & Burns, 1985; Dronkers, 1996; Peach & Tonkovich, 2004; Romani, Olson, Semenza, & Grana, 2002). In the last quarter-century, a language disorder resulting from neurodegenerative disease has been described. This is differentiated from the post-stroke syndrome by its progressive nature and so termed “primary progressive aphasia.” The term “progressive non-fluent aphasia” (PNFA) is now widely applied to a group of those patients whose speech is notably dysfluent (Gorno-Tempini et al., 2004; Grossman & Ash, 2004; Grossman, Mickanin, et al., 1996; Hodges & Patterson, 1996; Knibb, Woolams, Hodges, & Patterson, 2009; Snowden, Neary, & Mann, 1996; Thompson, Ballard, Tait, Weintraub, & Mesulam, 1997). This is often a variant of frontotemporal lobar degeneration in which one of the most salient features is effortful speech, with hesitations, retakes, pauses, and errors in the production of words. Patients with this syndrome also characteristically exhibit agrammatism and produce simplified grammatical forms (Ash et al., 2009). They are also impaired in the comprehension of complex syntax (Peelle et al., 2008). Executive resources are impaired as well, but comprehension of single words is relatively spared (Grossman & Ash, 2004; Grossman, Mickanin, et al., 1996; Libon, Massimo, et al., 2007; Libon, Xie, et al., 2007; Snowden et al., 1996).

Little attention has been devoted to the study of speech errors in neurodegenerative disease, even though detailed assessments of speech errors can be quite informative about the nature of the language system and its breakdown in conditions such as PNFA. Discussion of the errors in speech production made by patients with either brain lesions or neurodegenerative disease frequently assumes that the errors are caused by a motor planning impairment (Dronkers, 1996; Duffy, 2006; Gorno-Tempini et al., 2004; Josephs et al., 2006; Peach, 2004) known as apraxia of speech (AOS). The characteristics of AOS that are most often cited are groping towards the articulation of a word, distorted sounds, and dysprosody that often results in the production of a sound that is not part of the speaker’s native language (Croot, 2002; McNeil, Robin, & Schmidt, 1997; Wertz, LaPointe, & Rosenbeck, 1984). While the immediate cause of a speech error must logically be that the speech articula-
tors are not placed in the right place at the right time in the production of a given speech sound or word, the precipitating cause of the production error could occur at a level of implementation upstream from the activation of the articulators (Canter et al., 1985; Romani et al., 2002). A distinction thus is made between AOS and phonemic paraphasias (Canter et al., 1985; Peach & Tonkovich, 2004). Phonemic paraphasic errors are described as phonemes subjected to processes of substitution, deletion, addition (insertion), or transposition (metathesis). These errors are said to involve processes that are more central than activation of the articulators because the speech sounds which are produced are relatively undistorted, actual speech sounds; substitutions and exchanges of speech segments are typically related to the original (intended) speech segments; and displacement in a word suggests that the error occurs at the level of abstract lexical representation, rather than the surface level of articulation. The present investigation examines the nature of speech errors made by patients with PNFA. We sought to determine whether deficits in speech production in this neurodegenerative disease primarily arise from impairments in the language system or impairments of the motor system.

In the characterization of speech errors it is important to distinguish between two levels: the abstract level of the system of speech sounds in a language and the concrete level of the physical realization of speech sounds. The more abstract level is phonemics, the units of which are phonemes. The phoneme /t/, for example, sounds different depending on its position in a word, as illustrated in Fig. 1A; but to the speaker, all the different variants of /t/ are in some sense the same, and the speaker may well not even realize that the /t/ in different positions sound different.

The physical features of the sound that is produced when a person speaks constitute a phone. The different variants of the abstract phoneme, realized as different phones, can be described in terms of their articulatory and acoustic properties, as is illustrated in Fig. 1B. Phonetics is the study of speech sounds at this level.

A phonemic error occurs when a person produces a sound that is a well-formed phoneme of the language but not one that was intended by the speaker or anticipated by the listener, as in Examples 1a and 1b:

1a (a) They have a smole ‘smile’ (smole rhymes with mole).
1b (b) … coming out of the gar ‘jar’ (gar rhymes with bar).

A phonetic error occurs when a speech sound is produced that results in a word which is not a possible sequence of sounds in the speech system of the speaker. This can result from a sound that does not occur in the speech system or from a combination of sounds that does not occur in the language. These productions could be due to an impairment of motor control, or, if produced consistently, they could be caused by an impairment of the mental representation of the phoneme. Examples 2a and 2b show the most frequent type of phonetic error, which results from the lenition of a consonant, that is, the softening of the articulatory force required to produce a well-formed phone. Since these sounds are not part of the inventory of English phonetics, there are no letters of the English alphabet to transcribe them; phonetic symbols borrowed from other alphabets are used. In both examples, the phonetic symbols represent voiced fricatives. The character D in (2a) is not a standard phonetic symbol, but it follows the convention of using barred symbols to represent fricatives (Pullum & Ladusaw, 1986).

In this case, it transcribes a voiced alveolar slit fricative, in contrast to the voiced grooved fricative [zd].

2a (a) kiD ‘kid’.
2b (b) doγ ‘dog’.

It is an empirical question whether the errors of PNFA patients are more often phonemic or phonetic. If the errors are predominantly phonemic, there might be an impairment of language that disturbs the retrieval of the correct phonemes, or there might be an impairment of the executive resources needed to retrieve the appropriate phonemes and assemble them into the correct sequence. If the errors occur at the level of phonetics, this may imply motor difficulty such as an impairment of motor planning. Groping may reflect feedback from an intact phonemic system attempting to guide the motor speech system to produce the correct phonetic segment. If the error occurs consistently, this could imply either the mental representation of the phoneme itself or its manner of articulation.

In a study of single-word processing in two PNFA patients on tasks of naming, repetition, and reading, Croot et al. found better performance on tasks in which the stimulus provided information about the phonological output: both patients performed best on reading, less well on repetition, and least well on naming (Croot, Patterson, & Hodges, 1998). They propose that these patients have difficulty with phonological encoding, so when the task stimulus provides support for that encoding—as do printed or spoken stimuli—performance is improved. In contrast, a stimulus in the form of a picture of an object provides no clues to the phonological form of the target word, which results in the poorest performance among the tasks. These investigators did not distinguish between phonetic and phonemic errors in transcribing the subjects’ speech, but they address the question of whether the impairment occurs at the level of phonological encoding or at the level of articulation, involving the movements and coordination of the tongue, lips, velum, and vocal folds. They acknowledge that the errors they recorded could have been caused by “phonetic disintegration,” thus leaving open the question of whether the speech errors result from an impairment at the cognitive level or the motor level.

With the goal of illuminating the source of speech errors in PNFA, we undertook to classify speech errors as phonetic or phonemic and to characterize these errors in linguistic terms in order to understand the underlying process of deformation of the speech stream. Further, we examined the linguistic and non-linguistic correlates of speech errors as a means of assessing the neurological underpinnings of speech errors in PNFA.

2. Methods

2.1. Subjects

We studied 16 mildly to moderately impaired PNFA patients diagnosed by an experienced neurologist (MG) in the cognitive
neurology clinic of the Department of Neurology at the University of Pennsylvania according to a revision of published criteria (McKhann et al., 2001; The Lund and Manchester Group, 1994). These patients had the clinical diagnosis of frontotemporal dementia (FTD) ($N = 14$) or corticobasal syndrome (CBS) ($N = 2$) assigned prospectively. Criteria for PNFA included the presence of slowed, effortful speech with agrammatic errors and grammatical simplification in conversation as well as the production of segmental speech errors. These patients also demonstrated some difficulty understanding grammatically complex sentences. This pattern of difficulty was insidiously progressive in nature and was the predominant clinical feature for at least 2 years. We also assessed 10 healthy seniors. Exclusionary criteria included other causes of dementia, such as metabolic, endocrine, vascular, structural, nutritional, and infectious etiologies, and primary psychiatric disorders. The patients were mildly impaired according to the Mini Mental State Exam (MMSE) (Folstein, Folstein, & McHugh, 1975). One-way ANOVAs indicated that the two subject groups were matched for age and education, although the PNFA patients had a significantly lower MMSE than controls. All subjects completed an informed consent procedure in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the University of Pennsylvania. Demographic characteristics are summarized in Table 1.

The patients underwent neuropsychological testing within an average of 115 ($\pm$88) days of the date of recording to determine whether speech errors are related to neuropsychological measures of cognition. We calculated Spearman correlation coefficients of subjects’ phonetic and phonemic error rates with their performance on language measures and a range of neuropsychological tests. The tests evaluated three areas of cognitive functioning. These included, first, executive functioning: animal naming (Lezak, 1983), working memory as demonstrated by reverse digit span (Wechsler, 1987), and mental flexibility as demonstrated by time to complete the Trails B test (Reitan & Wolfson, 1985). We also tested semantic memory by means of the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983), and the Pyramids and Palm Trees test (Howard & Patterson, 1992); and we administered two tests of comprehension of syntax (Grossman, D’Esposito, et al., 1996). Performance by PNFA patients and controls on neuropsychological tests is shown in Table 1. PNFA patients are impaired in executive functioning, on semantic measures, and on grammatical comprehension relative to controls.

### 2.2. Materials

The subjects were shown the wordless children’s picture book, *Frog, Where Are You*, by Mayer (1969). The book consists of 24 detailed black-and-white line drawings. All print on the cover and front matter pages was covered with heavy paper stock so that no written words were visible. An outline of the story is given elsewhere (Ash et al., 2006). The elicitation of speech by this means has the advantage of producing a narrative for which the intended content was known, so it was possible to quantify subjects’ performance relative to an externally established standard. The fact that the story was unfamiliar to the subjects prevented the subjects from having preconceived ideas about what was happening or would happen in the course of the story. Extracts from three PNFA subjects’ narratives are given in Appendix 1.

### 2.3. Narrative procedure

The subjects were asked to look through the book to familiarize themselves with the story, then to turn back to the beginning and go through the book again, telling the story as if they were “reading” it to a child. The narrations were recorded digitally and transcribed in detail as described elsewhere (Ash et al., 2006). Seventeen narrations were recorded on a Macintosh Powerbook G3 laptop computer using the Macintosh external microphone (part #590–0670) and the computer program SoundEdit 16, v. 2, with 16-bit recording at a sampling frequency of 44.1 kHz. Five were recorded on a Dell Inspiron 2200 PC using the signal processing software Praat (Boersma & Weenink, 1992–2005) with 16-bit recording at a sampling rate of 22.05 kHz, using a Radio Shack omnidirectional lavalier electret condenser microphone. Four were recorded on a Marantz PMD 670 digital recorder with 16-bit recording at a sampling frequency of 32 kHz, using a Sennheiser MKE2 omnidirectional lavalier condenser microphone.

The narratives were analyzed for phonetic and phonemic errors as defined above. All coding was done by a linguist (SA) with expertise in phonetic and grammatical analysis. They were also coded for linguistic features including editing breaks and hesitation markers. Editing breaks are interruptions in the production of a word, repetitions of whole words, or self-corrections when the speaker switches from saying a word or phrase in order to say something else, as in “The dog–the frog climbed out of the jar.” A portion of these editing breaks constitute efforts at producing a word by successive approximations, which might be a feature of AOS. Therefore we tabulated the occurrences of editing breaks that consisted of successive approximations of a word. Hesitation markers include such items as *um, er, ah, uh*. We coded for additional features of language production as a proportion per utterance: open class words; nouns, total verbs (inflected verbs, participles, and infinitives), complex structures, and percent of well-formed utterances. These terms are defined elsewhere (Ash et al., 2009).

### 2.4. Statistical considerations

Levene’s test of homogeneity of variances revealed that the measures of language production and performance on the neuropsychological tests did not meet the requirement of homogeneity of variances for parametric statistical tests. Therefore nonparametric tests were used to assess the differences between subject groups. Comparisons between subject groups were calculated by the Mann–Whitney *U* statistic, and correlations were calculated using Spearman’s rho.

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### Table 1

<table>
<thead>
<tr>
<th>PNFA</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F</td>
<td>7/9</td>
</tr>
<tr>
<td>Age</td>
<td>69.9 ± 10.9</td>
</tr>
<tr>
<td>Education</td>
<td>15.1 ± 2.8</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>3.4 ± 2.0</td>
</tr>
<tr>
<td>MMSE (max = 30)</td>
<td>24.5 ± 4.4</td>
</tr>
<tr>
<td>Executive functioning</td>
<td></td>
</tr>
<tr>
<td>Animal fluency</td>
<td>9.88 ± 5.02</td>
</tr>
<tr>
<td>Reverse digit span</td>
<td>3.13 ± 1.20</td>
</tr>
<tr>
<td>Trails B time (s)</td>
<td>235 ± 82 (9)</td>
</tr>
<tr>
<td>Semantics</td>
<td></td>
</tr>
<tr>
<td>Boston Naming Test (% correct)</td>
<td>81.9 ± 15.7</td>
</tr>
<tr>
<td>Pyramids and pine trees (max = 52)</td>
<td>46.8 ± 7.2 (12)</td>
</tr>
<tr>
<td>Comprehension</td>
<td></td>
</tr>
<tr>
<td>Short sentence comprehension (max = 12)</td>
<td>9.8 ± 1.5 (9)</td>
</tr>
<tr>
<td>Complex sentence comprehension (max = 48)</td>
<td>34.2 ± 7.8 (11)</td>
</tr>
</tbody>
</table>

* $p < .01$. 

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* S. Ash et al. / Brain & Language 113 (2010) 13–20
2.5. Imaging methods

Structural MRI scans were available for a subset of PNFA patients (N = 7) and a group of age-, education-, and gender-matched healthy seniors (N = 26). MRI images were acquired on a Siemens Trio 3.0T MRI scanner, starting with a rapid sagittal T1-weighted image to determine patient position. Next, high resolution T1-weighted three-dimensional spoiled gradient echo images were acquired with repetition time = 1620 ms, echo time = 3 ms, slice thickness 1.0 mm, flip angle 15°, matrix = 192 × 256, and in-plane resolution 0.9 × 0.9 mm. To quantify grey matter patterns within participants we used a diffeomorphic registration-based cortical thickness (DiReCT) algorithm reported elsewhere (Das, Avants, Grossman, & Gee, 2009). This approach benefits from the use of a prior constrained estimate of the distance between grey matter and white matter which takes into account the contour of the cortical mantle. This approach also benefits from the use of a diffeomorphic procedure which preserves shape-based constraints. The DiReCT algorithm first involves skull-stripping (Smith, 2002) and segmentation using FMRIB’s Automated Segmentation Tool (FAST) (Zhang, Brady, & Smith, 2001), which labels the brain volumes into grey matter, white matter, CSF, and “other,” with inhomogeneity correction. The grey-white matter interface (GWI) is then calculated. It is defined as voxels in which a grey matter voxel and one neighboring voxel have a grey matter probability greater than p < .05, and a neighborhood-connected white matter voxel has a white matter probability of p < .05. We then calculate from the GWI those grey matter voxels which closely estimate an edge of grey matter cortex and use a novel diffeomorphic mapping between the GWI and an optimized template to determine the measure of cortical thickness. The local template was composed of images from 25 healthy seniors and 25 focal neurodegenerative disease patients, collected using the same imaging sequence and scanner. Lastly, the grey matter cortical thickness images were warped into MNI template space and smoothed with a 6 mm FWHM Gaussian filter. Statistical comparisons of significant reduction in whole-brain grey matter cortical thickness were computed using an independent sample t-test in SPMS. We used an explicit mask of grey matter priors to limit comparisons to include only voxels which contained grey matter values greater than zero, and global calculation was omitted. We set a statistical height threshold of p < .0005 and only accepted clusters with an extent of 100 adjacent voxels because a cluster of this size would also demonstrate a consistent effect in a particular neuroanatomical distribution while minimizing false positives (Forman et al., 1995). We only report significant reduction in GM thickness for clusters where a peak voxel survived a statistical threshold of p < .001.

### Table 2

<table>
<thead>
<tr>
<th>Measure</th>
<th>PNFA</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speech output</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time (s)</td>
<td>486 ± 290</td>
<td>255 ± 76</td>
</tr>
<tr>
<td>Words</td>
<td>346 ± 218</td>
<td>586 ± 110</td>
</tr>
<tr>
<td>Words per minute</td>
<td>45 ± 18</td>
<td>143 ± 24</td>
</tr>
<tr>
<td>Mean length of utterance (words)</td>
<td>7.4 ± 2.1</td>
<td>10.3 ± 1.8</td>
</tr>
<tr>
<td>Editing breaks and hesitation markers (per 100 words)</td>
<td>12.8 ± 8.2</td>
<td>2.0 ± 2.0</td>
</tr>
<tr>
<td>Content, structure, grammar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open class words per utterance</td>
<td>2.84 ± .80</td>
<td>4.54 ± .71</td>
</tr>
<tr>
<td>Nouns per utterance</td>
<td>1.48 ± .54</td>
<td>2.08 ± .41</td>
</tr>
<tr>
<td>Total verbs per utterance</td>
<td>1.12 ± .35</td>
<td>1.70 ± .22</td>
</tr>
<tr>
<td>Complex structures per utterance</td>
<td>.14 ± .10</td>
<td>.36 ± .11</td>
</tr>
<tr>
<td>Proportion of well-formed utterances</td>
<td>.62 ± .25</td>
<td>.94 ± .04</td>
</tr>
</tbody>
</table>

*All between-group comparisons are significant at p < .01 except time, which is significant at p < .05.*

### Table 3

<table>
<thead>
<tr>
<th>Measure</th>
<th>PNFA</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phonetic errors</td>
<td>2.7 ± 9.0</td>
<td>0.0 ± 0.0</td>
</tr>
<tr>
<td>Phonemic errors</td>
<td>6.6** ± 10.5</td>
<td>.02 ± .05</td>
</tr>
</tbody>
</table>

**p < .01.

Table 3 presents the frequencies of phonetic and phonemic errors by patients and controls. PNFA patients produced significantly more phonemic errors than controls (p < .01). PNFA patients differed significantly in their production of phonemic vs. phonetic errors (p < .005), producing in total over four times as many phonemic errors as phonetic errors. The preponderance of phonemic errors is illustrated in Fig. 2. Only 5 of the 16 patients made phonetic errors, and the majority were produced by one patient (MF) who was extremely impaired. His clinical diagnosis was FTD with onset 4 years prior to testing. His speech consisted mostly of nouns, with little sentence structure. For the other four patients who made phonetic errors, the frequency per 100 words was 1.16 ± 1.00, while including the case of MF raised the mean frequency of phonetic errors per 100 words to 7.96 ± 15.23. Thirteen of the 16 patients made phonemic errors. For those patients alone, excluding the three who made no errors, the mean frequency of phonemic errors per 100 words was 6.63 ± 9.99, and excluding MF lowered the rate to 3.97 ± 2.99.

![Fig. 2. Phonetic and phonemic errors in PNFA.](image-url)
Most of the patients’ speech was decipherable from either the articulation or the context, but some words were so distorted that it was not possible to tell what the person was trying to say. This was the case for 81 (24%) of the total of 333 errors. Of the 252 interpretable errors, 82% were phonemic: the speaker produced a well-formed speech sound, but it was the wrong sound for that place in that word. In the analyses below, we consider only the errors in words that were interpretable.

A summary of the distribution of error types is displayed in Fig. 3, and some additional detail is provided in Appendix 2. Both consonants and vowels were subject to errors of substitution as well as other processes, including insertion, deletion, lenition (reduction of articulatory force), and metathesis (transposition). The majority of the phonetic errors were the result of non-substitution processes, particularly lenition, as shown in Examples 2a and 2b. In comparison, the majority of the phonemic errors were substitutions. Substitutions in phonemic errors involved the replacement of a segment by one that was a near neighbor in terms of articulation, such as /g/ replacing /k/ or /l/ and /r/ replacing each other. Substitutions were found to be bidirectional. For example, /l/ as a replacement for /t/ occurred, and /t/ as a replacement for /l/ also occurred. The same was found for /m/ and /n/, for nasals and stops, and so on. This implies that these errors are not due to unguided or poorly controlled motor movements, but are made within the phonological system of the speaker. They are not driven by unidirectional processes such as lenition or retraction. Rather, they constitute an incorrect choice of a target phone. Most often, the replacement of one segment by another preserves most of the features of articulation of the intended phoneme. Of the 63 consonant substitutions, 41 (65%) involved a substitution of only one feature; of 60 vowel substitutions, 52 (87%) were substitution by a vowel that was adjacent in articulatory space (that is, differing by only one distinctive feature), for an overall rate of substitution by near neighbors of 76%. Substitution by a phoneme that is not a near neighbor of the intended target or that differs by multiple distinctive features could actually be taken as even stronger evidence that the deformation is not caused by motor difficulty. If, for instance, a voiced velar stop /g/ replaces an alveolar affricate /dʒ/, as in gar for jar in Example 1b, it is evident that the speaker had abundant opportunity to produce a segment that was not well-formed, with all the articulatory distance intervening between the target and the realization. The production of a well-formed phoneme despite this articulatory distance suggests that the speaker’s conception of the target was incorrect, rather than that the speaker’s motor control of the articulators was faulty.

The tabulation of editing breaks involved in successive approximations of a word showed that groping for a word accounted for a low proportion of these disruptions in the flow of speech. For 15 of the 16 patients, the rate of editing breaks that constituted groping for a word was 17%, with an average frequency of 4.1 occurrences out of an average of 23.5 editing breaks per patient. Of these instances of groping for a word, the majority (69%) involved phonemic errors. Phonemic errors accounted for only 11%, and 16% were simple false starts. The 16th patient was an exception, for whom 76 of 147 (52%) editing breaks consisted of groping for words. For this patient too, far more of the segmental speech errors in groping for words were phonemic (22%) than phonetic (3%), but most were false starts (75%). Thus most editing breaks by PNFA patients were the same kinds of false starts and changes of intent that are exhibited by healthy speakers.

Correlations of phonetic and phonemic speech errors with fluency, structural, and content measures of language use are given in Table 4. Phonemic errors occur more when editing breaks and hesitation markers interrupt the flow of speech, although there is no association with speech rate. Both phonetic and phonemic errors occur less in utterances that are grammatically well-formed, but phonetic errors do not correlate significantly with any other aspects of speech production. We also considered a neuropsychological account of speech errors. The correlation analysis revealed no significant correlation of phonetic or phonemic errors with executive functioning, semantic memory, or comprehension of syntax.

Fig. 4A displays the cortical atrophy image for the seven PNFA patients for whom structural MRI scans were available; the Talairach coordinates of the areas of significant atrophy are given in Table 5. The image shows cortical atrophy for PNFA patients bilaterally in frontal regions and in the left peri-Sylvian region. Atrophy in parietal regions may reflect underlying corticobasal syndrome in some of the patients. The area of atrophy is diminished when patients with a diagnosis of CBD are removed from the analysis. Fig. 4B shows a sagittal section through the left insula illustrating significant atrophy in a prefrontal region but no significant atrophy in the insula.

4. Discussion

We studied the production of speech errors in semi-structured speech samples of a cohort of PNFA patients in order to describe the characteristics of these errors and to determine their source. We found that speech errors in PNFA can be phonetic or phonemic, with phonemic errors accounting for more than 80% of errors. These errors are most often substitutions, and they are most often close approximations of the target phoneme, affecting both vowels
speech was extremely impaired in other respects: in almost 8 min of the 46 phonetic errors (70%) were produced by one subject. His articulatory gestures would be expected to produce well-formed segments; poorly controlled articulatory gestures would be expected to produce segments that sound like a well-formed phoneme. For example, a timing error in the onset of voicing, as a consequence of the motor programming of vocal fold vibration, could produce a well-formed segment differing from the target only in voicing. We acknowledge that such an error could occur. If errors of motor programming were the main source of speech errors, then we would expect to hear many more phonetic errors than phonemic errors. It would be unlikely that most of the errors of motor programming were the main source of speech errors, and in his 48 utterances he produced only 6 verbs. Most often, such patients would be regarded as untestable. In a sense, it may not be surprising that a patient whose speech has deteriorated to this extent would suffer in part from an impairment of motor planning or programming. However, there is another possibility. In light of the evidence of the earlier stages in the progression of this syndrome as represented by the other patients, it appears that this patient’s ability to select the features that compose phonemes has deteriorated, in conjunction with the profound breakdown in his ability to represent, identify, and/or select the correct phoneme. Further study is needed to explore this possibility.

We have also found that speech errors do not correlate with features of language structure such as speech rate, frequency of content words, or complexity of grammatical structure. This implies that the phonemic system is dissociable from other components of the language system. The production of speech sounds and the errors produced in PNFA do not appear to be governed by resources related to organization, attention, and other such capacities that are routinely considered in neuropsychological evaluation. Furthermore, the evidence does not point to a motor planning impairment as the cause of the errors. We conclude that phonemic errors in PNFA appear to come from within the neural network for language that supports the system of speech sounds.

Several previous studies have examined speech errors in patients with an aphasia consequent to stroke (Ackermann & Riecker, 2004; Dronkers, 1996; Mumby, Bowen, & Hesketh, 2007; Peach & Tonkovich, 2004; Riecker et al., 2004). Apraxia of speech has been well documented in stroke patients (Dronkers, 1996), and other authors have explicitly compared errors of speech production in patients with fluent vs. non-fluent aphasia due to stroke (Canter et al., 1985; Romani et al., 2002). These studies have generally associated AOS with a non-fluent aphasia, also known as Broca’s aphasia. Canter et al. (1985) suggest that phonemic paraphasias in conduction and Wernicke’s aphasics result from a breakdown of the retrieval of phonological word patterns, while the AOS of Broca’s aphasics follows from an impairment of the encoding of phonological patterns into speech movements.

It has perhaps seemed reasonable to characterize speech errors in PNFA in the same way as in Broca’s aphasia and therefore to attribute them to the same source, i.e. a motor planning impairment. Although PNFA is a non-fluent form of progressive aphasia that partly resembles Broca’s aphasia, there are also important differences between PNFA and Broca’s aphasia following a stroke (Patterson, Graham, Lambon Ralph, & Hodges, 2006). For example, Broca’s aphasia typically is associated with frank motor weakness in the face and right upper extremity, implicating direct involvement of motor regions of the brain, while PNFA is rarely associated with weakness. Limb apraxia and oral apraxia also may be seen in Broca’s aphasia but appear to be much less common in PNFA (Libon, Massimo, et al., 2007). We also find significant executive resource limitations in PNFA that may not be present in Broca’s aphasia, and this may have an impact on the nature of speech and language processing in PNFA (Grossman et al., 2008; Libon, Xie, et al., 2007; Libon et al., 2009). Thus, the presence of AOS in Broca’s aphasia does not necessarily mean that AOS should also be present in PNFA. One PNFA patient in our series nevertheless had prominent AOS without the lateralized motor features of a Broca’s aphasia. We suspect that other PNFA patients may also have prominent AOS, but it is uncommon in our series. Our study thus adds weight to the view that PNFA does not replicate the deficit seen in Broca’s aphasia following stroke.

There have also been reports on the occurrence of phonemic paraphasias in primary progressive aphasia as contrasted with stroke (Patterson et al., 2006) or other syndromes (Weintraub, Ru-
Patterson et al. (2006) concluded that PNFA patients are superior to non-fluent aphasics in phonological processing but are more impaired at producing self-generated speech, consistent with our observation of a high rate of phonemic paraphasias seen in PNFA patients’ self-generated speech. Weintraub et al. (1990) compared primary progressive aphasia (PPA) to probable Alzheimer’s disease (PRAD) in a longitudinal study of four patients and found that the high rate of phonemic paraphasias in PPA was one of the features that most clearly distinguished between the two conditions. Semantic substitutions and circumlocutions were found to be prominent in PRAD but not in PPA. Another study examined errors in spontaneous speech production in patients with the neurodegenerative condition of semantic dementia (SD), characterized by a selective deterioration of semantic knowledge (Meteyard & Patterson, 2009). These authors found that SD patients produced grammatical abnormalities as well as semantic errors, but phonological errors were extremely rare.

In contrast to these studies, other authors do not ascribe the speech errors in PNFA to phonemic paraphasia. Josephs et al. (2006) claim that phonemic paraphasias do not occur in PNFA but state that the term is “probably used to refer to phonetic (i.e., motor) rather than phonemic (i.e. linguistic) distortions” (p. 1386). Gorno-Tempini et al. (2004) suggest that “labored speech,” agrammatism, and impaired production and comprehension of syntax are the defining characteristics of PNFA. However, the definition of AOS is not clearly specified in these studies, and the authors did not distinguish between AOS and phonemic paraphasia. Phonetic errors in our patients were relatively uncommon. This raises the question of an ascertainment bias in the differences between our series and patients reported from other centers, where PNFA patients may have had more pronounced motor impairments associated with movement disorders such as CBS or PSP. Also, these patients may have been evaluated later in the course of their disease (Josephs et al., 2006). Longitudinal studies of patients with well-characterized motor and non-motor disorders would be useful in the future to help resolve these differences.

Another potential source of discrepancy between our reports and those of other authors may be an inconsistency in terminology. Most authors appear to follow the descriptions which define AOS as an impairment of speech production characterized by effortful groping for articulatory gestures, difficulty with the initiation of utterances, distortions of phonemes, impaired transitions between segments, and abnormalities of speech rate, stress assignment, and dysprosody unrelieved by extended stretches of normal rhythm, stress, and prosodic contours (Duffy, 1995; McNeil, Doyle, & Wambaugh, 2000; McNeil et al., 1997; Ogar, Dronkers, Brambati, Miller, & Gorno-Tempini, 2007; Wertz et al., 1984). These features are attributed to a motor impairment. The criterion of “distortions” of speech segments appears to apply to the phonetic errors we observe in PNFA, and thus these errors may also be due to a motor impairment. Likewise, some of the editing breaks we observed appear to correspond to the “groping” characteristic of AOS. Certainly these types of speech errors occur in PNFA, and we have documented this in one patient in particular. However, phonetic errors are far less frequent than phonemic errors in our series, and a detailed analysis of groping indicates that phonetic errors occur no more commonly in groping sequences than in the remainder of the speech sample. Characteristics of AOS thus appear to occur in PNFA speech, but they are not common.

We found little association of speech errors with measures of fluency, content, and syntax in PNFA (Table 4). The correlation of phonemic errors with editing breaks and hesitation markers is unsurprising, as both features stem from difficulty in producing smoothly flowing speech. The correlation of phonetic and phonemic errors with the production of well-formed utterances, among higher-level language measures, seems to reflect the same effect of fluency as editing breaks and hesitation markers: the frequency of these errors of dysfluency is closely correlated with the frequency of well-formed utterances (r = .78, p < .001). We found no relationship between the features of segmental speech production and measures of executive functioning, semantics, and grammatical processing, suggesting that errors in the production of speech segments come from within another component of the language system. Canter, et al. proposes that phonemic paraphasias result from a deficit in retrieval of the phonological pattern. This is an inviting avenue for further investigation in PNFA.

Our imaging findings showed that these PNFA patients have significant atrophy affecting the frontal lobe bilaterally. This is expected in PNFA, based on prior work assessing the distribution of cortical atrophy in these patients (Gorno-Tempini et al., 2004; Grossman & Ash, 2004). The PNFA patients also have some atrophy in a left peri-Sylvian distribution. This may reflect corticobasal syndrome seen in some of our PNFA patients (Gorno-Tempini et al., 2004; Murray, Koenig, Antani, McCawley, & Grossman, 2007).

Some authors have associated left insula disease with AOS in stroke or PNFA. However, reports of insular atrophy in stroke (Dronkers, 1996) may have limited bearing on studies of PNFA, as suggested by Hillis et al. (2004). An imaging study of PNFA (Nestor et al., 2003) found limited left peri-Sylvian atrophy on MRI but significant hypoperfusion of the left insula on PET. These findings are inconsistent with a number of studies that have demonstrated frontal atrophy in PNFA (Gorno-Tempini et al., 2004; Grossman & Ash, 2004; Grossman et al., 2008). CBS is also associated with AOS, albeit less consistently. Additional work is needed to determine whether clinical conditions such as these have an impact on the frequency and nature of speech errors and the anatomic distribution of disease associated with these errors. Further, it appears that up to 30% of PNFA patients have Alzheimer’s disease (AD) as the underlying pathology (Hodges, Davies, Xuereb, Kril, & Halliday, 2003; Knibb, Xuereb, Patterson, & Hodges, 2006). This is also true to some extent in our autopsy series (M. S. Forman et al., 2006; Grossman et al., 2008). AD is associated with peri-Sylvian disease that may have a more posterior anatomic distribution. Additional work is needed with imaging studies in a larger group of patients so that regression analyses can be used to relate speech errors directly to cortical atrophy.

We conclude that errors of word formation at the phonemic level are frequent, and they are a prominent feature of PNFA. We find that speech errors in PNFA are partially systematic in that they most often involve replacement of one phoneme by another phoneme that is similar in articulation. This and other characteristics suggest that speech errors are guided in large part by the linguistic properties of the phonologic system. In contrast to phonemic errors, phonetic errors in PNFA are relatively infrequent. We hypothesize that these errors are more likely to be caused by a motor planning impairment such as AOS.

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Appendix A. Supplementary material


References


