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Research Report

Apraxia of Speech in the Spontaneous Speech of Nonfluent/Agrammatic Primary Progressive Aphasia

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Abstract.
Background: Apraxia of speech (AOS) is a core feature of nonfluent/agrammatic primary progressive aphasia (naPPA), but its precise characteristics and the prevalence of AOS features in spontaneous speech are debated.
Objective: To assess the frequency of features of AOS in the spontaneous, connected speech of individuals with naPPA and to evaluate whether these features are associated with an underlying motor disorder such as corticobasal syndrome or progressive supranuclear palsy.
Methods: We examined features of AOS in 30 patients with naPPA using a picture description task. We compared these patients to 22 individuals with behavioral variant frontotemporal dementia and 30 healthy controls. Each speech sample was evaluated perceptually for lengthened speech segments and quantitatively for speech sound distortions, pauses between and within words, and articulatory groping. We compared subgroups of naPPA with and without at least two features of AOS to assess the possible contribution of a motor impairment to speech production deficits.
Results: naPPA patients produced both speech sound distortions and other speech sound errors. Speech segmentation was found in 27/30 (90%) of individuals. Distortions were identified in 8/30 (27%) of individuals, and other speech sound errors occurred in 18/30 (60%) of individuals. Frequent articulatory groping was observed in 6/30 (20%) of individuals. Lengthened segments were observed rarely. There were no differences in the frequencies of AOS features among naPPA subgroups as a function of extrapyramidal disease.
Conclusion: Features of AOS occur with varying frequency in the spontaneous speech of individuals with naPPA, independently of an underlying motor disorder.

Keywords: Language, phonetics, primary progressive nonfluent aphasia, speech, verbal apraxia

INTRODUCTION

The early modern description of apraxia of speech (AOS) is attributed to Frederic L. Darley et al. [1], who described it as "a disorder of motor speech programming manifested primarily by errors of artic-

[1]Deceased.

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ulation." AOS in adults has been observed as a sequela to stroke, head injury, tumor, and neurodegenerative disease. It is one of the core diagnostic criteria for nonfluent/agrammatic primary progressive aphasia (naPPA) [2], and it may also occur as an independent syndrome, known as primary progressive AOS (PPAOS) [3–7]. There are differing views as to whether it is a disorder of motor programming [8] or motor planning [9] of the speech articulators, but it is agreed that AOS results in inaccurate production of speech sounds due to a motor impairment in the speech production system. This is seen in the presence of effortful, slowed speech, with sound distortions (off-target productions of consonants or vowels), articulatory groping, and prosodic deficits not attributable to dysarthria or cognitive impairment [10–14]. The present report is an examination of the speech of individuals with naPPA with the aim of determining the frequency of occurrence of features of AOS in their spontaneous, connected speech. Studies of AOS frequently include a complete motor examination, with repetition of multisyllabic words and other tasks that challenge the articulatory system. However, in the present study, we examined only speech samples elicited by a picture description task in order to identify and quantify features of AOS that occur in the spontaneous, connected speech of individuals with naPPA. A picture description task is relatively easy for most individuals to perform, as it leaves the speaker free to choose the words s/he can retrieve and produce within the limits of her/his articulatory competence. The description of a scene is similar to the recounting of a first-person narrative in the demands it places on the speaker. This is a speech act that occurs very frequently in everyday life and is therefore valuable in evaluating a person's ability to function effectively. The assessment of spontaneous, connected speech provides more ecologically valid measures of speech production than do structured speech tasks, which may not reflect the complexities and variability of speech production in real-life situations. It can also provide insights into the neural mechanisms underlying motor speech production. This study extends our understanding of AOS in the speech used in everyday life by persons with naPPA.

naPPA is a progressive disorder of language and speech [15]. The core diagnostic criteria for naPPA, of which at least one must be present, are 1) agrammatic language production and 2) "effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)" [2]. Supporting features include impaired comprehension of syntactically complex sentences, spared single word comprehension, and spared object knowledge.

Impairments in the speech sound production of individuals with naPPA have been extensively documented [15–25]. In previous work, we assessed a semi-structured sample of natural, connected speech [18]. We found frequent phonologic errors that could have been due to an impairment in the linguistic representation of abstract phonological forms [26, 27], but only 31% of patients produced the relatively few phonetic (distortion) errors, that is, speech sounds not present in English, which are more transparently attributed to AOS. These findings may be compared to those of a study by Strand et al. [28], which presented a rating scale for assessing the frequency and severity of features of AOS. These authors examined a cohort of naPPA patients through conversational speech, picture description, word and sentence repetition, and tasks that assess diadochokinesis (DDK). They concluded that most (33/35) patients with naPPA also had AOS. They based their assessments of AOS primarily on the pervasiveness, judged perceptually, of features including sound distortions, syllable segmentation, lengthened vowels and consonants, articulatory groping, and slow speech rate. Since the tasks that assess DDK are specifically designed to bring out motor speech deficits, it would be expected that their use would result in the number of individuals judged to have AOS being greater than when individuals are judged only on the basis of everyday connected speech. Moreover, many of the cases from Strand et al. [28] also had an extrapyramidal movement disorder such as progressive supranuclear palsy (PSP) that affects eye movements, gait, and postural stability. There is some uncertainty about whether AOS is an impairment in a general, integrated motor system [29] or whether it is specific to speech [30], as might occur in PPAOS.

To evaluate the possibility that AOS is part of an overall motor programming impairment, we also investigated the contribution of the motor component of AOS by comparing subsets of patients with and without a motor disorder with respect to the presence of features of AOS.

MATERIALS AND METHODS

Participants

We studied 30 patients with naPPA, 22 patients with behavioral variant frontotemporal degeneration (bvFTD) as a brain-damaged control group, and 30 healthy seniors (HC). bvFTD was selected as a brain-damaged control group because these patients share some features of impaired speech with naPPA patients. They exhibit slowed speech, and they have been found to make occasional speech sound errors in our previous work [31]. Their speech is similar to that of controls in many respects, but they are similar to naPPA patients in other respects, including number of words produced, degree of grammatical complexity, and report of content. Thus, bvFTD is an intermediate case compared to naPPA and controls.

Participants with naPPA were recruited sequentially between January 2000 and September 2017. Patients were diagnosed by experienced neurologists (MG, DJI) according to published criteria [2]. Exclusionary criteria included other causes of dementia, such as metabolic, endocrine, vascular, structural, nutritional, and infectious etiologies, and primary psychiatric disorders. Also excluded were patients whose speech was so impaired that they were not able to provide a speech sample that was adequate for analysis. Demographic and clinical characteristics of the participants are summarized in Table 1. The groups did not differ in age, sex, or education, and the patient groups did not differ in disease duration. The naPPA and bvFTD groups did not differ in Mini-Mental State Examination (MMSE) score, but both were impaired relative to HC on this measure of global cognitive status.

Six (20%) of the naPPA patients were also diagnosed with an extrapyramidal disorder, corticobasal syndrome (CBS, N = 4) [32] or PSP (N = 2) [33], and 8 additional patients were noted to have either features suggestive of CBS that did not meet full criteria for this condition or mild features of parkinsonism such as some stooping, with a shortened stride or intermittent lateralized tremor. None of the patients exhibited symptoms of dysarthria, consistent with a review by Duffy et al. [22], which found that forms of dysarthria were not present in a majority of individuals with naPPA. None of the bvFTD patients met criteria for a PPA syndrome or an extrapyramidal disorder, and none of the naPPA patients had changes in behavior and social functioning consistent with bvFTD.

Table 1
Demographic, clinical, and speech characteristics of participants: Mean (SD)

Participants	naPPA	bvFTD	HC
N [% M]	30 [43]	22 [55]	30 [43]
Education (y)	14.6 (3.1)	15.6 (2.5)	15.4 (2.3)
Age (y)	69.7 (9.1)	66.9 (6.1)	67.3 (6.8)
Disease duration (y)	3.0 (1.6)	3.3 (1.8)	–
MMSE	24.2 (5.6)**	24.3 (3.2)**	29.0 (1.1)
Features of AOS			
Sound distortions/100 words	1.12 (2.35)	0.24 (0.78)	–
Articulatory groping/100 words	0.397 (0.892)	0.128 (0.601)	–
False starts and repairs/100 words	8.7 (13.2)*	5.7 (6.9)	2.7 (2.8)
Segmentation of speech: Silences > 150 ms/100 words	36.6 (17.6)**BB	12.6 (6.3)*	9.3 (4.7)
Duration (ms)	894 (402)*	1307 (1469)	707 (258)
Non-AOS speech and language features Speech output			
Sound substitutions/100 words	7.83 (11.82)BB	0.38 (0.87)	–
Total speech errors/100 words	8.69 (13.05)BB	0.62 (1.59)	–
Total time (s)	75 (32)	62 (20)*	78 (23)
Number of words	75 (49)**	96 (46)**	174 (79)
Speech rate (words per min)	61 (28)**BB	94 (40)**	134 (37)
Articulation rate (syllables/s)	2.31 (0.58)**BB	3.88 (0.92)	4.12 (0.59)
Syllables/word	1.126 (0.098)*	1.111 (0.074)**	1.175 (0.059)
Syllable duration (s)	0.462 (0.127)**BB	0.274 (0.074)	0.248 (0.038)
Number of utterances	10.3 (4.9)**	12.3 (4.8)**	17.0 (6.5)
Mean length of utterance (words)	7.0 (2.3)**	7.6 (1.9)**	10.6 (3.5)
Dysfluencies/ 100 words	25.4 (19.6)**B	14.1 (11.7)	10.0 (6.6)
Structure, grammar, content			
Nouns/100 words	22.2 (6.5)*BB	17.4 (4.7)	18.4 (4.4)
Inflected verbs/100 words	14.0 (3.9)	15.0 (4.2)	14.0 (1.9)
Dependent clauses/100 utterances	8.4 (12.6)**	14.9 (14.1)**	47.7 (53.4)
% Well-formed sentences	64.9 (34.6)**	79.0 (23.2)	90.0 (9.3)
Report of contents (max = 9)	4.4 (2.2)**	5.0 (2.1)**	7.2 (1.1)

*Differs from HC, $p < 0.05$; **differs from HC, $p < 0.01$; B differs from bvFTD, $p < 0.05$; BB differs from bvFTD, $p < 0.01$.

Table 2
Clinical diagnosis, CSF, and autopsy pathology for 30 naPPA participants[1]

Case nos.	Clinical diagnosis	CSF-indicated pathology	Autopsy diagnosis
1–9	naPPA	–	–
10–11	naPPA	–	AD
12–14	naPPA	Non-AD	–
15	naPPA	Non-AD	CBD
16	naPPA	Non-AD	PSP
17–18	naPPA +	–	–
19	naPPA +	–	CBD
20–22	naPPA +	Non-AD	–
23	naPPA+	Non-AD	GGT
24	naPPA +	AD	AD
25	CBS	–	CBD
26	CBS	AD	AD
27	CBS	Non-AD	CBD
28	CBS	Non-AD	Pick's disease
29–30	PSP	Non-AD	–

[1]Dash indicates data not available. + indicates medical record note of features suggestive of CBS, mild features of parkinsonism. naPPA, nonfluent/agrammatic primary progressive aphasia; CBS, corticobasal syndrome; PSP, progressive supranuclear palsy; AD, Alzheimer's disease; CBD, corticobasal degeneration; GGT, globular glial tauopathy.

Fifteen of the 30 naPPA participants had a cerebrospinal fluid (CSF) sample available; the samples were collected within a mean of 5.5 months (range 0–20 months) from the time of testing, as described below. Using a validated algorithm to screen for Alzheimer's disease (AD), we identified 13 of those 15 (87%) cases as having a CSF profile (p-Tau/A$\beta < 0.09$) consistent with non-AD FTLD underlying pathology [34, 35]. Eleven of the naPPA participants had a brain autopsy, including 7 of those with a CSF sample. Thus a total of 19 patients had biomarker data. Of those, 15 (79%) had FTLD spectrum pathology, and 4 (21%) had probable or confirmed AD. This is consistent with previous reports finding that about 79% of naPPA patients have an underlying tauopathy and about 21% of naPPA cases have AD pathology [36–38]. The distribution of CSF profiles and autopsy-confirmed pathology by clinical phenotype is summarized for the 30 naPPA participants in Table 2.

All participants completed an informed consent procedure in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the University of Pennsylvania.

Materials and procedures

All participants provided a semi-structured speech sample by describing the Cookie Theft scene from the Boston Diagnostic Aphasia Examination [39]. This task is widely used in studies of speech impairment, which provides a degree of reproducibility across studies, and it reliably elicits a speech sample long enough for a speaker to demonstrate his/her competence in producing natural speech. It requires a diverse lexicon and a certain level of skill in managing pronominal reference. At the same time, it elicits a fairly brief speech sample, which means that features of interest can be extracted relatively quickly. In spite of its brevity, as we demonstrated in a previous publication, the speech characteristics elicited by this brief description of a single picture are equivalent to those elicited by a much longer speech task, the narration of the story in a wordless children's picture book [40].

Participants were asked to describe the Cookie Theft scene in as much detail as they could in about one minute. Prompts were given if the speaker was silent for several seconds, and participants were permitted to continue to speak until they signaled that they were finished. The average (±SD) duration of the speech samples for all participants was 71 (±25) s. The speech samples were analyzed quantitatively for AOS-specific and AOS non-specific speech features, summarized in Table 1, in a manner blinded to other individual patient neurologic characteristics. Features relating specifically to AOS include speech sound distortions and effortful, halting speech, presenting as articulatory groping, including false starts and repairs, and segmented speech, discussed further below. Non-AOS features include sound substitutions, speech rate, mean length of utterance, the grammatical measures of dependent clauses and percentage of utterances that are well-formed sentences, among others, consistent with our previous work [40, 41]. Speech rate was quantified as complete words spoken per minute of recording time, including silences. Articulation rate was quantified as syllables spoken divided by the sum of the periods of continuous speech produced, and syllable duration was calculated as the inverse. The periods of continuous speech were identified and quantified using an automated Speech Activity Detector in order to calculate articulation rate and syllable duration. The speech activity detector is an in-house Gaussian mixture models–hidden Markov models-based speech detector developed at the University of Pennsylvania Linguistic Data Consortium to segment speech samples into segments of speech and silence, allowing the user to derive total speech time with the exclusion of pauses.

Transcription was carried out by a linguist (SA) with extensive experience in phonemic and phonetic transcription of a wide variety of English dialects, in a manner blinded to other individual patient neurologic characteristics. The transcriptions of speech errors were reviewed by a second linguist (GA), who confirmed the transcription of sound distortions, sound substitutions, and uninterpretable words. The earliest speech samples were recorded on cassette tape and subsequently digitized in Praat [42] or recorded on a Marantz PMD 670 digital recorder, while the majority were recorded on smart phones. All recordings were digitized in.wav format (uncompressed) at a sampling rate of 16 KHz and bit depth of 16. The recordings were generally of good quality, and with the aid of high-quality headphones, most of the speech was interpretable and could be transcribed in normal spelling. Some words were readily understandable but were produced with deviations from normal speech, and these were transcribed using phonemic notation, with characters written between slashes. Phonemic notation was also used when an intended word was indeterminate, but the component phonemes were recognizable. Instances where a segment was not identifiable as a phoneme of English were transcribed using phonetic transcription, with characters between square brackets. Speech that was not interpretable was transcribed phonetically or phonemically as needed if ordinary orthography did not adequately indicate the sounds that were spoken. In the entire naPPA corpus, approximately 40/2242 words (1.8%) were not interpretable. Where transcription was not possible, the approximate number of syllables was indicated by sequences of xxx. In the present participant cohort, this occurred only twice, in both cases in the speech of naPPA patients with CBS. Each instance of deviant speech, whether it was a distortion, a phonemic substitution error, an uninterpretable sequence, or a sequence that could not be transcribed, was listed and counted (see Supplementary Material).

Speech errors: Distortions and sound substitutions

The criteria for AOS list "sound distortions" as a core feature [28, 43–46]. This term is used to describe a sound for which the realization "is not quite right" for the target phoneme [43, 47, 48]. In the words of Haley et al. [43], "Segment distortions give the impression that there is something phonetically unusual or incorrect about the sound production." Distortions contrast with phonemic substitution errors, which are correctly articulated phonemes that are not correctly selected for the corresponding word. Distortions seem necessarily to be due to a motor impairment because they arise when the articulators are not positioned in the right place at the right time to produce the intended speech sound or any acceptable American English phoneme. In the present corpus, for example, a patient said, "her water [oßɹ flob]" for "her water overflowed." The beta character in the transcription is the phonetic character for a "b" with incomplete closure. This non-English sound arises by changing the place of articulation from the place for /v/ (labiodental) to the place for /b/ (bilabial), without changing the manner of articulation. This change of place of articulation is a small step, requiring only advancing the lower lip from proximity to the upper teeth to proximity to the upper lip. In this instance, the following /f/ was also incompletely articulated. Thus, this word contained two phonetic distortions, as well as the phonemic substitution of b for d at the end of the sentence.

The patients produced additional phonemic errors that consisted of accurately articulated phonemes which were not close in articulation to the target, such as "meanmaud" for "meanwhile." Some phonemic errors resulted in words that were uninterpretable. For example, one patient said, "Bordgin kid getting cookeds out of the colture jan." It is clear from the picture that *cookeds* means 'cookies' and *colture jan* means 'cookie jar', but the intent of *bordgin* is unknown. Sound distortions in an unidentifiable word were rare, but they were transcribed phonetically and counted. Otherwise, an unidentifiable word was counted as one phonemic error, on the grounds that it was not possible to count the number of sound substitutions, additions, or deletions in such a word. Sound substitutions in naPPA occurred in 98 out of a total of 2,242 words, of which 39 (1.7%) were not recognizable as real words (such as *bordgin*), while 59 were clearly interpretable. Since these words consist of identifiable phonemes, rather than distortions, they only affect the count of sound substitutions and total speech errors, and not the count of features of AOS. Among the bvFTD patients, there were 6/2,107 words with phonemic errors, of which 3 (0.14%) were not recognizable as real words.

In what follows, we consider distortions to represent a motor impairment. We will refer to the set of speech errors consisting of distortions and also phonemic substitutions as "total speech errors." Following Wilson et al. [49], substitution errors were counted as errors even if they were subsequently repaired, but this occurred only once. Incomplete words were not counted as speech errors but rather as false starts. The occurrences of distortions and substitutions were normalized on the total number of complete words spoken by the participant as occurrences per 100 words.

As noted above, major features of AOS other than distortions include the segmentation of speech by brief silences between and within words; lengthened speech segments; and articulatory groping, including false starts and restarts (see below). A feature was judged to count as present in the speech of an individual patient if it occurred with a frequency exceeding an empirically derived threshold. For sound distortions, the threshold was set at 2 standard deviations above the mean of the combined group of bvFTD and HC participants. For the other features, the threshold was set at 2 standard deviations above or below the mean for HC (see below).

Speech segmentation

We measured the frequency and durations of silences between words to address the issue of segmentation of speech in patients. In the present study a threshold of 150 ms was selected empirically, on the basis of the distribution of stop gap durations in the TIMIT database [50], which shows that there are very few (209/20,410, i.e., 1.02%) within-phrase silences greater than 150 ms in duration. To extract the timing information, we used a locally written program to align word boundaries to the speech signal, and the alignment was reviewed and corrected using the signal processing software Praat [42]. Information on downloading the alignment program is given in the Supplementary Material. The durations of all intervals delineated by the alignment procedure were tabulated for each speaker, including both word durations and durations of silences between words, excluding silences between utterances. An utterance is a syntactic unit, defined as an independent clause and all clauses dependent on it [51]. A sentence fragment, missing a subject and/or an inflected verb, was also counted as an utterance if it was not part of any independent clause. Pauses between utterances are not interruptions of the syntactic unit constituted by an utterance and so were not considered to contribute to speech segmentation and were not counted in the assessment of this feature. The number of within-utterance silences was normalized as occurrences per 100 words. Within-word silences were not registered by the alignment algorithm, but they were noted during the process of transcription.

Articulatory groping

The effort to produce a word when the speaker requires multiple attempts to reach the target but does not ultimately succeed in reaching it constitutes articulatory groping, and it may involve either distortions or phonemic substitutions. An instance of articulatory groping is given in Example 1, spoken by an individual with naPPA, age 79, with MMSE = 28, and a disease duration of 3 years. The intended target is given in curly brackets:

(1) I see, cambensen {cabinets}.. camben ness {cabinets}

Another aspect of articulatory groping is the presence of false starts and restarts/repairs [28]. In the present report, we will use the term “repairs” for sequences of words that were repeated or replaced, and we will use the term “false start” to designate a partial word. Example 2, spoken by an individual with naPPA, age 73, with MMSE = 27, and a disease duration of 7 years, illustrates both types. In this example, a false start is shown in italics, and two repaired sequences are underlined.

(2) and one, <u>the man, the kid was, the-</u> the son, was *st-* uh standing <u>on the</u>, on the stool

The entire phrase that is replaced is counted as one repair, so the sentence in (2) contains 2 repairs and 1 false start. The occurrences of groping and of false starts and repairs were normalized on the total number of complete words spoken by the participant as occurrences per 100 words.

Lengthened speech segments

A speech segment is a single speech sound, either a phoneme or a phone, a vowel, or a consonant. Speech segments were judged perceptually to be lengthened if they were heard as having a longer duration than normal relative to the durations of other segments in the word. Discourse markers, such as *and, but, um*, and *well*, were excluded from consideration. The most frequently lengthened segments were the voiceless fricatives /s/ and /f/, as in “ssstool” or “fffinger.” Individual lengthened segments were evaluated perceptually by the first two authors (SA and NN), but quantitative measurement of the duration of each individual segment was beyond the scope of the study.

Each recording was examined in two different ways: 1) For transcription, by the first author, and 2) for perceptual rating of distortion errors, segmentation between and within words, articulatory groping, and lengthened segments independently by the first two authors. The transcription and the perceptual ratings conducted by the first author were performed at different times separated by an interval of at least 2 months.

Statistical considerations

Statistical analyses were conducted using SPSS v. 27, except for Intraclass Correlation Coefficients, which were calculated in R. Levene's test of homogeneity of variances indicated that some language variables did not meet the requirement of homogeneity of variances for parametric statistical tests; therefore, we used nonparametric tests to assess the differences within and between subject groups. Comparisons between subject groups were calculated using the Mann-Whitney U statistic. Comparisons of proportions of speakers between groups were calculated using Fisher's exact test. All reported differences are significant at least at the two-tailed level $p < 0.05$.

RESULTS

Speech errors: Distortions, substitutions, and total speech errors

Distortions were numerically more frequent in naPPA than in bvFTD, but the difference was not statistically significant ($p = 0.095$) (Table 1). The frequencies of both substitutions/100 words and of total speech errors/100 words were significantly greater in naPPA (Table 1). The numbers of individuals who exhibited features of AOS are summarized in Table 5. Eight (27%) of the naPPA patients produced distortions, compared to 2 (9%) bvFTD patients, but this difference in prevalence was not statistically significant. Eighteen (60%) of the 30 individuals with naPPA produced interpretable speech errors, either distortions or substitutions, compared to 3 (14%) of 22 bvFTD patients ($p < 0.01$) and none of the HC participants.

Segmented speech

The quantified frequency of silences ≥ 150 ms between words per 100 words was significantly greater in naPPA than in bvFTD or HC ($p < 0.001$ for both comparisons), and bvFTD produced silences between words more frequently than HC, as shown in Table 1. The differences among groups were also reflected in the number of individuals for whom the quantification of such silences revealed a frequency ≥ 2 standard deviations above the mean for HC: 27/30 (90%) naPPA, 3/22 (14%) bvFTD, and 2/30 (7%) of HC participants (Table 5). The silences between words above the calculated threshold (≥19/100 words) were produced by significantly more individuals with naPPA than by those with bvFTD or HC, but there was no significant difference between the number of individuals with bvFTD and HC who produced silences > 150 ms between words above the threshold. The duration of between-word silences was significantly longer in naPPA than in HC.

In contrast to the frequent segmentation between words just described, there were just 9 occurrences of within-word segmentation in naPPA speech, produced by 5 individuals. These few instances were considered to be too infrequent to count as characteristic of the speech of these patients. Six of the cases were compound words: *over-flow*, *over-flows*, *over-flowed*, *over-flowing*, *drive-way*, and *out-side*; one was a phonemic paraphasia for 'cabinets': *cambenness*; one was a two-syllable word: *wo-man*; and one was a monosyllable: *s-tool*. The duration of the within-word silence in these 9 instances ranged from 155 to 557 ms. Within-word segmentation did not occur in the speech of bvFTD or HC participants.

Articulatory groping

When the recordings were reviewed quantitatively for articulatory groping, as illustrated in Example (1) above, 8 instances of groping were found to have been produced by 6 naPPA patients, and one bvFTD patient produced 2 instances. There was no statistically significant difference between naPPA and bvFTD patients in the quantitative assessment of the frequency of false starts and repairs, but there was a significant difference between naPPA and HC, with naPPA producing significantly more false starts and repairs/100 words than HC (Table 1). The proportion of participants who produced false starts and repairs was similar across all three groups (Table 5).

Lengthened segments

Lengthened segments were judged perceptually to be present with greater than moderate frequency (the midpoint on a 5-point scale from "feature not present"

Table 3
Perceptual judgments of features of AOS in naPPA by 2 judges, rated on a scale of 0 to 4[1]: Mean (SD)

	Rater 1	Rater 2
Sound distortions	0.90 (1.35)	1.10 (1.58)
Segmented speech	2.00 (1.34)	2.17 (1.42)
Lengthened segments	0.23 (0.68)	0.90 (0.99)
Segmentation within words	0.17 (0.38)	0.07 (0.25)
Articulatory groping	0.53 (1.04)	0.67 (1.32)

[1]0 = feature not present, 1 infrequent, 2 moderate, 3 frequent but not severe, 4 severe.

to "severe") compared to controls in 2 of the 30 naPPA speakers. Because they were so infrequent, they were not evaluated quantitatively. A proxy for lengthened segments may be seen in word duration. However, lengthened words are the norm in naPPA, as is reflected by the reduced speech rate of these individuals, and a lengthened word does not necessarily contain individual segments that are lengthened relative to the other segments in the word. A detailed investigation of word duration in these patients and controls is underway in the preparation of a separate paper.

Interrater agreement of judgments of AOS features

Perceptual judgments were made of the essential features of AOS examined for this study: sound distortions, between-word segmentation, within-word segmentation, lengthened segments, and articulatory groping. The judges' perceptual ratings of features of AOS are summarized in Table 3, and the intraclass correlation coefficients for the ratings are presented in Table 4 [52]. For distortion errors, the correlation was qualitatively interpreted as excellent, according to the guidelines of Koo et al. [52]. For segmented speech (between-word segmentation) and articulatory groping, the correlation was good, and for within-word segmentation and lengthened segments, the correlation was moderate.

Other features of speech and language: Speech output, structure, grammar, content

Individuals with naPPA differed in predictable ways from those with bvFTD and HC. Their speech rate in words per minute and their articulation rate in syllables per second were less than those of both bvFTD and HC. The speech rate of bvFTD patients was significantly less than that of HC, but bvFTD did not differ from HC in articulation rate. naPPA patients produced fewer words, and their utterances were fewer and shorter. They were more dysfluent, in that they produced more filled pauses, short pauses within utterances, partial words, and extraneous words. They produced fewer dependent clauses, more grammatical errors, and they expressed less of the content of the picture than HC (Table 1).

Effect of extrapyramidal disease

Speech production measures relevant to AOS in the subsets of naPPA patients with and without a clinical diagnosis or medical record notes suggesting CBS or PSP are summarized in Table 6. This table compares patients with 2 or more of the 4 features of AOS that are examined here to those with fewer than 2 features of AOS. Patients were categorized according to phenotype within 15 months of the time of the recording. They were categorized as "No PSP/CBS" if movement disorder symptoms emerged more than 15 months later than the time of the recording. One individual is excluded from the table because the medical records contemporaneous with the recording were unavailable, although there was autopsy-confirmed CBS. Of those patients with 2 or more features of AOS in connected speech, the only statistically significant difference in the measures of speech production between patients with versus without clinical evidence of CBS or PSP was found for the total time of duration of the speech samples: Patients who had no evidence of CBS or PSP took significantly longer to give their picture description than patients

Table 4
Interrater reliability of judgments of features of AOS in naPPA by two judges

	Intraclass correlation (A,1)	Qualitative interpretation	95% Confidence interval	F-test	*p*
Sound distortions	0.939	Excellent	[0.865, 0.971]	F(29, 21.5) = 35.9	<0.001
Segmented speech	0.851	Good	[0.713, 0.926]	F(29, 29.9) = 12.6	<0.001
Lengthened segments	0.575	Moderate	[–0.026, 0.829]	F(29, 4.25) = 6.89	0.031
Segmentation within words	0.535	Moderate	[0.231, 0.746]	F(29, 28.7) = 3.47	<0.001
Articulatory groping	0.859	Good	[0.727, 0.93]	F(29, 29.9) = 13.3	<0.001

Table 5
Quantitative assessment of AOS-specific and non-AOS specific characteristics by individuals

Participants	naPPA N = 30	bvFTD N = 22	HC N = 30
AOS-specific features			
Individuals with sound distortions[1]	8 (27%)	2 (9%)	0
Individuals with articulatory groping, not reaching target (1 or 2 occurrences)	6 (20%)	1 (5%)	0
Individuals with false starts and/or repairs	23 (77%)	17 (77%)	24 (80%)
Segmentation: Individuals with ≥ 19 between-word silences per 100 words[2]	27 (90%)**[BB]	3 (14%)	2 (7%)
Non-AOS-specific features			
Individuals with phonemic substitutions	18 (60%)[BB]	3 (14%)	0
Individuals with speech errors (all error types)	18 (60%)[BB]	3 (14%)	0
Individuals with WPM < 6[3]	17 (57%)**[B]	5 (23%)	1 (3%)
Individuals with articulation rate < 0.295[3]	25 (83%)**[BB]	4 (18%)	1 (3%)
Individuals with syllable duration > 0.324[2]	26 (87%)**[BB]	6 (27%)	2 (7%)

[1]Cutoff is 2 SD above the mean for bvFTD and HC combined. [2]Cutoff is 2 SD above the HC mean. [3]Cutoff is 2 SD below the HC mean. *Differs from HC, $p < 0.05$; **differs from HC, $p < 0.01$; [B]differs from bvFTD, $p < 0.05$; [BB]differs from bvFTD, $p < 0.01$.

Table 6
Mean frequency (SD) of speech features of naPPA patients with and without at least 2 AOS features and by presence of an extrapyramidal disorder in naPPA[1]

	At least 2 features of AOS		≥2 AOS features[2]	Fewer than 2 features of AOS		<2 AOS features[2]
	PSP/CBS	No PSP/CBS	*p*	PSP/CBS	No PSP/CBS	*p*
N	4	7		6	12	
Sound distortions/ 100 words	2.6 (3.5)	3.3 (3.1)	0.527	0 (0)	0 (0)	1.0
Quantified groping	1.1 (1.3)	0.89 (1.4)	0.788	0.22 (0.54)	0 (0)	0.616
False starts & repairs/100 words	16.8 (15.1)	19.4 (20.6)	1.0	3.3 (2.4)	3.2 (3.8)	0.622
Segmentation: Silences ≥ 150 ms/100 words	39.6 (17.0)	42.7 (16.1)	0.788	26.4 (10.9)	38.1 (21.0)	0.213
Silence duration (ms)	765 (84)	950 (607)	0.927	834 (330)	938 (403)	0.616
Sound substitutions/100 words	18.4 (10.2)	10.6 (10.0)	0.315	1.9 (2.3)	4.8 (14.3)	0.616
Total speech errors/100 words	20.9 (13.0)	13.9 (12.3)	0.412	3.6 (3.9)	4.8 (14.3)	0.250
Total time (s)	60 (17)	105 (29)	0.012	64 (21)	69 (34)	0.750
Number of words	61 (20)	78 (40)	0.648	75 (56)	76 (68)	0.682
WPM	60.7 (10.8)	44.3 (22.1)	0.230	70.8 (27.5)	65.4 (33.2)	0.750
Articulation rate (syllables/s)	2.20 (0.63)	1.94 (0.51)	0.527	2.56 (0.74)	2.37 (0.44)	1.0
Number of utterances	9.8 (4.3)	11.4 (3.3)	0.315	11.0 (3.2)	9.4 (6.7)	0.291
MLU (words)	6.6 (1.7)	6.7 (3.1)	0.788	6.7 (2.2)	7.4 (2.4)	0.820
Dysfluencies/100 words	40.7 (22.4)	41.2 (19.5)	0.927	15.5 (4.5)	17.7 (16.2)	0.820
Nouns/100 words	19.7 (2.8)	24.7 (8.4)	0.527	19.5 (3.5)	23.0 (7.3)	0.140
Inflected verbs/100 words	14.2 (1.9)	13.8 (4.1)	0.927	15.1 (2.0)	13.3 (5.2)	0.180
Dependent clauses/100 utterances	11.1 (15.7)	5.5 (11.3)	0.527	7.8 (10.0)	10.2 (14.8)	1.0
% Well-formed sentences	42.9 (7.0)	45.0 (35.2)	0.927	76.9 (19.8)	75.6 (39.9)	0.385
Report of contents (max = 9)	4.1 (1.9)	3.8 (2.6)	0.927	5.2 (2.7)	4.6 (2.0)	0.335
Disease duration (y)	2.8 (1.5)	3.3 (2.0)	0.527	2.5 (0.5)	3.2 (1.9)	0.616

[1]One individual with autopsy-confirmed CBS is excluded because medical chart notes were unavailable. [2]Significance of comparison of individuals with and without evidence of an extrapyramidal disorder (Mann-Whitney U). WPM, speech rate in words per minute; MLU, mean length of utterance in words.

with evidence of CBS or PSP. This is a surprising finding which may warrant further investigation, but it does not affect the overall result of the comparison between patients with and without evidence of an extrapyramidal disorder. Of those patients with fewer than 2 features of AOS in connected speech, there were no significant differences in measures of speech production between patients with vs. without clinical evidence of CBS or PSP.

DISCUSSION

In this study we conducted a quantitative assessment of spontaneous, connected speech using a semi-structured speech sample in a cohort of naPPA patients to examine the prevalence of features of AOS that could affect everyday communication in these patients. We investigated four characteristics of AOS: 1) speech sound distortions; 2) segmentation of speech within an utterance, both between words and within words; 3) articulatory groping; and 4) lengthened speech segments. The identification of features of AOS in a person's speech is valuable because it supports a diagnosis of naPPA. We found that the incidences of the different characteristics indicative of AOS covered a broad range in the spontaneous, connected speech of the patients' picture descriptions, with speech segmentation being the most frequent (90% of patients) and lengthened segments being the least frequent (7% of patients). We also examined the potential association of extrapyramidal disease with the presence of AOS to assess the hypothesis that a central, praxic deficit gives rise to symptoms of AOS [29]. We found that extrapyramidal disease in naPPA was not related to the presence of AOS features.

Sound distortions

AOS results in alterations of subphonemic detail—that is, sound distortions—in contrast to aphasia, which involves the substitution, addition, or deletion of phonemes and is realized at the level of the mental representation of the linguistic element as a phoneme [43, 53]. Ziegler et al. [54] discuss several possible levels at which apraxia might operate in speech: as a disconnection of phonology (phonological encoding) from motor execution, as a disturbance of learned motor routines (motor planning), or as an impairment of coordination of the temporal and spatial patterning of articulatory movements (motor programming). These authors attribute the uncertainties over the phenomenon of AOS to a "fundamental underspecification of our models describing how stored word form representations are transformed into actual speech movements" (p. S1498).

In the present study, we found that speech errors, including both distortions and sound substitutions, were common, as 18/30 (60%) of the naPPA participants made speech errors. In addition, 3/22 (14%) of bvFTD patients made speech errors, while none of the HC participants produced speech errors in this sample. Of the 18 naPPA patients who made speech errors, only 8 produced distortions at a rate exceeding the threshold of 1.14/100 words calculated for a judgment as a feature of AOS in connected speech. Distortions were observed rarely in bvFTD, in only 2/22 individuals.

The results of this investigation are consistent with those from an earlier study on speech errors in naPPA [18], cited above (p.5). There we found that in a cohort of 16 naPPA patients, 82% of speech errors were sound substitutions, produced by 13/16 patients, and only 18% were distortions, produced by 5/16 patients. These findings were derived from speech samples elicited by asking the participants to narrate the story in a wordless children's picture book, *Frog, Where Are You* [55], which yielded speech samples averaging 346 words for naPPA patients. Although this earlier study included fewer participants, the large quantity of speech provided us with a basis for confirming this level of speech errors in the spontaneous, connected speech of naPPA. The results of prevalence and speech error frequency are similar to those of the present study, confirming the use of a short picture description as a speech sample for studying features of AOS in spontaneous, connected speech.

In another investigation, Knibb et al. [56] characterized quantitatively the conversational speech in a group of naPPA patients. Seven of the 15 patients (47%) had previously been rated as having dysarthria, AOS, or both. The authors did not distinguish types of speech errors, stating that it is not possible to say for an individual speech error whether a distortion is due to dysarthria or apraxia and whether a substitution is a phonemic error or an articulatory error. They found that the patients had a speech error rate of approximately 4.6/100 words, compared to an average for controls of 0.4/100 words. These figures are comparable to those found in the present study, with an overall speech error rate of 5.50/100 words in naPPA, 0.49/100 words in bvFTD, and 0/100 words in HC. Rohrer et al. [57] also examined conversational speech in a cohort of 24 patients with naPPA. Connected speech was elicited by a conversation about the participant's last holiday celebration and a description of the Cookie Theft scene. They reported a frequency of AOS of 14/24 (58%). As in the report of Knibb et al. [56], these authors included all types of speech errors in their assessment of AOS and found a frequency of speech errors of about 6.2/100 words. Again, these frequencies are comparable to our results.

The approach of these two studies, in which all types of speech errors were considered in the assessment of AOS, accords with the view presented by Laganaro [26], who provides evidence for interaction between the phonological and phonetic encoding levels, entailing simultaneous activation of target and nontarget phonemes, triggered by the activation of competing lexical forms. The competition between phonemes may produce either phonetic or phonological errors. The prospect of a phonological impairment giving rise to phonetic errors blurs the line between a phonological impairment and a motor programming impairment as a source of the speech errors that are observed in AOS. Such considerations may account in part for the difference between the quantified assessments evaluated in the present study and clinical impressions in some published reports of the speech of naPPA patients [49, 58, 59], as we discuss below.

Several studies have utilized the Motor Speech Evaluation (MSE) [14] to determine the frequency of AOS. This evaluation instrument includes sections testing DDK, word repetition, and reading of the Grandfather Passage. A number of these studies have reported frequencies of AOS of, for example, 79% [49], 82% [60], 89% [58], and 100% [25]. Tasks in the MSE battery such as alternating motion rate ("papapa") and sequential motion rate ("pataka") can elicit speech errors, even in controls when made adequately difficult, and we expect that speech errors elicited by DDK tasks are likely to overestimate the speech errors that occur in spontaneous connected speech. In contrast to our findings, for example, Wilson et al. [49] assessed AOS on the basis of the MSE, although their study focused on the connected speech of the participants. They report that every naPPA participant in their study produced sound distortions, based on clinical impressions of connected speech elicited by a picture description task, but that phonological errors (i.e., sound substitutions) were produced by only a subset of patients. They arrived at a frequency of distortions in naPPA of 12.6/100 words and a frequency of phonological errors of 1.4/100 words. The corresponding frequencies in bvFTD were 0.4/100 words for distortions and 0.0/100 words for substitutions; for HC, the corresponding frequencies were 0.1/100 words for distortions and 0.1/100 words for substitutions. Their findings for bvFTD and HC are similar to those of the present study, but their results for naPPA give a higher frequency of distortions and a lower frequency of substitutions than the present study. Part of the difference in findings may be attributable to differing definitions of what constitutes a distortion. For example, if "tepping" for "tipping" is heard as a distortion, that would account for much of the discrepancy between our results and those of other authors. In the present study, we judge "tepping" to be a phonemic substitution, not the result of a motor impairment yielding a distortion, since "tepping" is an allowable sequence, which obeys the rules of English word formation and is composed of sounds from the inventory of English speech sounds. Additional work is needed to develop a common set of criteria for speech distortions and phonologic errors across laboratories studying speech. Agreement is also needed on the context of speech– spontaneous or elicited—in order to elucidate the frequency and nature of speech errors in PPA patients.

Segmented speech

The segmentation of speech by silent pauses (>150 ms) between words is a prominent feature in naPPA and contributes to the slow overall rate of speech of these individuals. Speech segmentation is cited as a feature of AOS in qualitative terms, both within words and between words within sentences [28, 59, 61–63]. In the present study, we chose a duration threshold value for silences based on the occurrence of silences in a large corpus of read speech. We found that the frequency of these silences in our sample of naPPA patients was four times the frequency observed in HC and three times the frequency found in bvFTD. Indeed, this feature was almost universal in the naPPA group, which differed significantly from its prevalence in bvFTD and HC. It should however be noted that, while silences between words may be partly attributable to AOS, there are potentially other contributing factors. For example, the non-fluent speech of naPPA patients resulting from prolonged pauses has been related to difficulty in building the grammatical structure of a sentence [17].

In contrast to segmentation between words, we found that segmentation within words was rare, and 6 of the 9 identified instances occurred between syllables that are also independent morphemes, such as *over-flow* and *drive-way*, where segmentation between syllables is similar to segmentation between words. Segmentation within words does not appear to be a significant characteristic of speech in naPPA, at least not in the production of spontaneous, connected speech. This may reflect the fact that spontaneous speech allows the speaker to choose words that s/he is able to pronounce with minimal difficulty.

Articulatory groping, false starts, and repairs

Articulatory groping without reaching the intended target is listed as a characteristic feature of AOS. It did not occur with high frequency in naPPA, but it co-occurred with speech segmentation in every case where it was present. Thus, articulatory groping may be strongly suggestive of AOS when it is detected, despite its relatively infrequent occurrence.

A more detailed examination of articulatory groping in naPPA, taking into account such factors as phrase length and adjacent pauses, may further illuminate this feature. Unlike groping, false starts and repairs were observed in all 3 participant groups. In naPPA, they were produced with high frequency (>2 SD above the HC mean) by 5 patients, all of whom exhibited speech segmentation, and 2 of whom also produced sound distortions above the threshold frequency. However, the percentages of individuals who produced false starts and repairs were the same in naPPA and bvFTD and were almost identical to the percentage in HC (Table 5).

Perceptual judgments of AOS features

Wambaugh et al. [64] investigated the interrater reliability of judgments of features of AOS in 28 post-stroke patients, using the features of Strand et al. [65]. They found good agreement between two raters for phonetic errors, segmented speech, and within-word segmentation, but poor agreement for judgments both of groping and of false starts/restarts. They propose that judgments of those two categories may have been differently assigned by the two raters. In the present study, we found good agreement between the two raters on judgments of groping, as shown in Table 4. False starts/repairs were only assessed quantitatively, based on the transcripts of the recordings, and are shown in Tables 1, 4, and 5. We also found excellent agreement on the perceptual judgments of sound distortions, and we found good agreement on judgments of speech segmentation, the most prominent prosodic feature of AOS. These results support our confidence in the validity of the quantitative measurements. We found only moderate agreement between the raters on the perceptual judgments of lengthened segments and within-word silences. This limited level of agreement may be due to the fact that these two features were found to be infrequent and therefore relatively less reliable in contributing to the impression of impaired speech in naPPA. In addition, these two features are difficult to hear and may be missed in a perceptual assessment; it would be valuable to evaluate them instrumentally for quantitative assessment.

Extrapyramidal disease

naPPA can be seen in the setting of CBS or PSP. It has been suggested that AOS may be an early sign of a motor disorder, as several case studies have found [66–68]. Another case report describes the progression of naPPA with AOS to CBS [69]. In a study of a cohort of patients with a diagnosis of progressive aphasia or AOS and with autopsy confirmation, 9 out of 10 cases that were determined to have had AOS had a pathological diagnosis of PSP or CBD [24]. A review of cases [23] provides further support for the suggestion that a presentation of naPPA with AOS may predict the pathology of CBD or PSP, and a longitudinal study of AOS found that patients may progress over time to show clinical features consistent with PSP or CBS [5]. Another study from our center was designed to test the hypothesis that patients with PSP and CBS exhibit speech impairments found in naPPA. The analysis of speech samples elicited by description of the Cookie Theft scene found that out of 82 cases (selected for the availability of clinical charts) of PSP/CBS, naPPA, or naPPA with co-occurring PSP/CBS, only 5 (6.1%) had documented features that were consistent with AOS. This included 2 patients with PSP/CBS, 1 with naPPA, and 2 with PSP/CBS + naPPA [70].

In the present study, we sought to assess whether the presence of features of AOS in naPPA would be more frequent in the spontaneous speech of patients with extrapyramidal disease than in those without. Contrary to our expectation, our results did not suggest greater frequency of AOS coincident with extrapyramidal disease. Of the 30 naPPA patients, 14 had evidence of a movement disorder during life, and 10 of these individuals had recorded the Cookie Theft picture description within 15 months of exhibiting extrapyramidal symptoms. Comparisons of the groups with and without clinically assessed symptoms of a movement disorder and with and without biomarker or autopsy evidence of CBD or PSP found only one minor, irrelevant difference among the groups in the incidence of features of speech production. These results fail to support the proposal that AOS is part of an overall motor impairment specifically related to extrapyramidal disease. The relationship between AOS and dysarthric features was not evaluated in this study, because the participants with naPPA did not show evidence of dysarthria.

Our study has certain limitations. While we examined a relatively large number of patients with the rare condition of naPPA, several aspects of our study would have benefitted from a larger sample. In particular, the number of cases for which we were able to estimate from biomarkers or know from autopsy the pathology in our cohort was relatively small. We contrasted naPPA with a neurodegenerative control group and found that features of AOS were more frequent in naPPA, but future work should contrast AOS in naPPA with relevant speech features in other variants of PPA. We focused on spontaneous, connected speech in this study, and the value and reliability of this approach can be determined only in the context of a comparative examination with elicited forms such as those in DDK speech.

One factor that may contribute to the frequency of features of AOS in our data could be that a picture description task is less demanding of the speaker than some other tasks. For example, an interview about familiar topics requires more choices about what elements to report and what words to use than does a picture description, where the stimulus is present. The speech samples elicited in this study were rather short, with an average length of 75 words for the naPPA patients. While this may be seen as a limitation of the study, it appeared that the frequency of both speech errors and speech segmentation was great enough so that there was time for both impairments to be manifested, suggesting that the duration of the speech sample was adequate for the speakers to demonstrate their competence in speech production. However, a longer speech sample would increase our confidence in these findings.

Conclusions

With these caveats in mind, this quantitative examination of the speech of patients with naPPA in describing a picture found that at least one feature of AOS was expressed by 90% of the patients, and two or more features were observed in 37% of the patients. We found that some naPPA patients may have an impairment of their ability to assemble the motor program for the accurate production of speech segments, resulting in sound distortions. In addition, speech segmentation is frequent in naPPA and contributes to the presence of AOS in these patients. Articulatory groping and false starts and repairs provide further evidence of AOS in naPPA. We did not find an association of an underlying motor disorder such as CBS or PSP with a motor impairment in speech production. However, our findings do not allow us to specify the precise location(s) in the process of speech production where a breakdown occurs. Further examination of the impairment in naPPA speech would profitably be directed at addressing the “fundamental underspecification” [54] in our understanding of how word forms are selected and assembled to be transformed into speech.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to report.

DATA AVAILABILITY

The data used in this study will be made available upon reasonable request from qualified investigators for research purposes upon approval by the University of Pennsylvania.

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: https://dx.doi.org/10.3233/ADR-220089.

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