Progressive Apraxia of Speech: Might There Be Subtypes?

ABSTRACT

This study examined speech and language characteristics of three groups of individuals with neurodegenerative disease: (1) primary progressive apraxia of speech (AOS) without aphasia (N=18), (2) agrammatic primary progressive aphasia (agPPA) less severe than AOS (N=10), and (3) agPPA more severe than AOS (N=9). Findings indicate that differences in the predominant characteristics of AOS (predominance of articulatory versus prosodic abnormalities) distributed differently among the three groups, independent of AOS severity. Neuroimaging findings also differed among the groups. Results suggest that neurodegenerative AOS may include perceptually distinguishable subtypes that are related to the presence or absence of aphasia and neuroimaging findings.

Proposal (word count, excluding Refs & Tables = 1,190)

Primary progressive aphasia (PPA) has been recognized as an identifiable clinical entity for several decades, and a large body of research has examined its clinical characteristics, neuroimaging correlates, and underlying pathology (e.g., Mesulam, 1982; Gorno-Tempini et al., 2011). More recently, it has been recognized that apraxia of speech (AOS) can also be associated with neurodegenerative disease (e.g., Duffy, 2006; Josephs et al., 2012), an entity that has been called progressive AOS (PAOS). PAOS is often accompanied by aphasia but it can be more prominent than any aphasia and sometimes occurs without aphasia or any other neurologic signs or symptoms, in which case it has been called primary progressive AOS (PPAOS) (Duffy & Josephs, 2012; Duffy & McNeil, 2008; Josephs et al., 2012). The separation of PAOS from PPA is obviously important clinically, but also important because data suggest they are not identical in their localization and may have different underlying pathologies (e.g., (Deramecourt et al., 2010, Josephs et al., 2006).

During a large ongoing study of people with PPA and PAOS we have observed that a substantial proportion of those with AOS and PPA with agrammatic language characteristics are difficult to classify; they do not meet criteria for PPAOS because they have aphasia, and they do not meet criteria for the agrammatic variant of PPA (agPPA) (Gorno-Tempini et al., 2011) because the dominant debilitating feature of the syndrome is AOS (i.e., AOS>aphasia). We have also noted different patterns of motor speech difficulty among those with PPAOS, AOS>aphasia, and agPPA. Some have articulatory distortions and distorted sound substitutions as the predominant AOS characteristics, whereas others' AOS is predominated by slowly produced, syllabically segmented speech with less prominent articulatory distortions and sound substitutions. These different patterns raise the possibility that they might be differentially associated with different clinical syndrome identities (i.e., PPAOS, AOS>aphasia, agPPA).

The purpose of this study was to examine the relationships among the clinical syndromes of PPAOS, AOS>aphasia, and agPPA, and to determine whether differing predominant AOS characteristics were differentially associated with the three clinical syndromes and their neuroimaging correlates. We hypothesized that the clinical syndromes would have distinguishable neuroimaging characteristics and that different patterns of AOS speech characteristics (AOS subtypes) would distribute differently among the clinical syndromes.

Methods

Thirty-seven subjects (Ss) with PAOS and/or aphasia participated in this study. Eighteen had PPAOS without evidence of aphasia, ten had PAOS judged to be more prominent than accompanying aphasia (AOS>aphasia), and nine met criteria for the agrammatic variant of PPA (agPPA) (Gorno-Tempini et al., 2011), in which the aphasia was more prominent than any accompanying AOS. Good interjudge reliability was achieved for these groupings. All Ss had identical imaging sequences: volumetric head MRI, diffusion tensor imaging, f18-fleurodeoxyglucose and C11 labeled Pittsburg compound B PET scanning.

Speech-language assessment included the Western Aphasia Battery (WAB-R; Kertesz, 2007), Part 1; several reading and writing subtests from the WAB-R, Part 2; several word fluency tasks (Loonstra, Tarlow, & Sellars, 2001; Woods et al., 2005); a 15-item Boston Naming Test (Lansing et al., 1999); Token Test, Part V (Wertz, Keith, & Custer, 1971); and a protocol we designed to elicit additional speech responses to help further characterize motor speech deficits. Ss also underwent neurologic and neuropsychological assessments but those results will be addressed only briefly in this presentation.

The diagnosis of AOS was based on the independent judgment of two speech-language pathologists blinded to neuroimaging, clinical neurology, and neuropsychology test results. Agreement about the presence versus absence of AOS was 100%. AOS severity was rated on a 0-4 scale (4=severe) and was also indexed by an AOS rating scale (ASRS) that rates each of 16 speech features that can be associated with AOS on a 5-point scale (0=not present; 4=nearly always present and markedly severe).

Regarding AOS subtypes, a designation of AOS Type 1 was made if distorted sound substitutions or additions (often increasing with increased utterance length or complexity) were judged to clearly dominate the speech pattern. A designation of AOS Type 2 was made if syllable segmentation within multisyllabic words or across words in phrases, and lengthened intersegment durations between syllables, words or phrases, was judged to clearly dominate the speech pattern. If there was no clear predominance of Type 1 or Type 2 features, a designation of AOS NOS (not otherwise specified) was made. Interjudge agreement about AOS subtype for the 36 subjects judged to have AOS was 94% (34/36); the remaining two Ss were ultimately classified by consensus as AOS NOS. AOS presence and type was declared at consensus meetings, independent of the classification of Ss as to PPA presence and type. Agreement about PPA type (i.e., agPPA) was 100%. Other PPA variants were not included in this study.

The presence or absence of dysarthria and its type was rated on a 0-4 severity scale. Consensus about dysarthria presence, type and severity and presence and severity of nonverbal oral apraxia was reached at consensus meetings.

Results

Basic demographic data are summarized in Table 1. Clinical and neuroimaging data are summarized and synthesized in Tables 2 and 3. Composite neuroimaging images will be shown during the presentation and samples of AOS subtype will be played.

The findings to be emphasized in this presentation are summarized as follows:

1. The AOS>aphasia group had more severe AOS than the PPAOS and agPPA groups, but less severe aphasia than the agPPA group.
2. AOS severity in PPAOS and agPPA were similar.
3. Ss with PPAOS and AOS>aphasia most often had AOS Type 2, while those with agPPA mainly had AOS Type 1.
4. Neuroimaging abnormalities were observed predominantly in the left hemisphere in all three groups. Both PPAOS and AOS>aphasia had changes in superior premotor cortex, but those with AOS>aphasia also had abnormalities in inferior premotor cortex. The agPPA group showed widespread involvement affecting premotor, prefrontal, temporal, parietal, caudate, and insula areas.
5. The results suggest that both PPAOS and AOS>aphasia are distinct from agPPA. They suggest that Ss with AOS>aphasia may have more advanced disease than those with PPAOS.

The finding that will be emphasized is the identification of what may be two clinically distinguishable subtypes of progressive AOS. It suggests that the two primary deficits in broad characterizations of AOS - articulation and prosody - can be relatively, although not completely dissociated in some cases, at least in neurodegenerative PAOS. Severity differences probably cannot explain the subtype distinction because AOS severity ratings did not differ between the agPPA group (with Type 1 predominance) and the PPAOS group (with Type 2 predominance). The underlying explanation for the subtype differences are not clear but, because motor speech programming probably involves several stages (more than a single process) that are accomplished within a complex functional anatomic network (more than a single brain location), it is reasonable to hypothesize that subtypes of AOS, manifest as a predominance of some abnormal features over others, might become evident as a function of differential impairment of one or more programming steps that occur in different anatomic locations in the speech-language network. This has implications for our understanding of AOS in general, regardless of its etiology. Further study is obviously required to replicate these findings and identify the relevant explanatory variables.

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Table 1: Summary of demographic and neurological data

	PPAOS	AOS>aphasia	agPPA	p value
N	18	10	9	
Demographics				
[αδ]Female (%)	13 (72%)	1 (10%)	5 (56%)	**0.007**
Handedness (R/L/Ambidex.)	16/1/1	9/1/0	8/1/0	0.85
Disease duration (yrs.)	3.0 (2.0-4.4)	3.8 (2.5 - 4.8)	2.5 (1.5 - 3.5)	0.20
Age at onset	72.0 (61.5-76.3)	69 (63.8 - 74.0)	66 (59 - 70)	0.27
Age at time of examination	74.5 (66.0-79.0)	73.5 (67.0 - 77.0)	70 (62.5 - 71.5)	0.14
Education (yrs.)	15.0 (12.8-17.1)	13 (12 - 17.3)	16 (12.5 - 17)	0.58

[α]Significance achieved comparing PPAOS and AOS>aphasia

[δ]Significance achieved comparing AOS>aphasia and agPPA

Table 2: Summary of speech, language and oral praxis data

	PPAOS	**AOS>aphasia**	**agPPA**	p value
N	18	10	9	
WAB				
[αβ]AQ (/100)	96.9 (95.8-99.0)	85.5 (82.1 - 95.3)	84.1 (64.7 - 89.6)	<0.0001
[αβ]Spontaneous speech (/20)	20 (19-20)	16 (14 - 19)	15.0 (12.5 - 16.0)	<0.0001
[βδ]Aud. Verbal comp (/10)	10 (9.8-10.0)	10 (9.5 - 10)	9.3 (9.2 - 9.7)	0.0008
[αβ]Repetition (/10)	9.7 (9.4-9.9)	9.2 (8.2 - 9.7)	8.8 (4.6 - 9.6)	0.01

[αβ]Naming/word finding (/10)	9.6 (9.3-10.0)	9.1 (8.4 - 9.4)	8.8 (7.1 - 9.0)	<0.0001
[αβ]WAB writing output (/34)	34 (32.8-34.0)	23.3 (17.5 - 31.3)	24.0 (12.3 - 31.5)	0.0004
[αβδ]**Token Test part 5** (/22; 22=best)	21 (19-22)	18.0 (14.0 - 19.0)	12.0 (4.5 - 17.5)	<0.0001
[αβ]Action Fluency	12 (10.8-16.0)	8.0 (6.5 - 9.0)	6.0 (3 - 10.5)	0.009
[β]Letter fluency	23.5 (14.3-33.3)	19.0 (12.0 - 22.5)	10.0 (7 - 13.5)	0.01
[β]Boston Naming Test (/15)	14 (13-15)	13 (12.8 - 15.0)	12 (6 - 14.5)	0.04
AOS				
[αδ]ASRS total score (/64; 0=best)	17.5 (12.8-20.3)	30.5 (21 - 38.3)	13 (6 - 23.5)	0.003
[αδ]Number of abnormal features (/16)	10.5 (9.0-13.0)	13 (11 - 14.5)	11 (6 - 12)	0.03
[αδ]AOS severity				
None	0	0	1 (11%)	0.01
Mild	10 (55.6%)	1 (10%)	5 (56%)	
Moderate	7 (38.9%)	3 (30%)	1 (11%)	
Marked	1 (5.6%)	4 (40%)	0	
Severe	0	2 (20%)	2 (22%)	
[βδ]AOS type				
Type 1	4 (22%)	2 (20%)	5 (63%)	0.01
Type 2	13 (72%)	5 (50%)	0 (0%)	
NOS	1 (6%)	3 (30%)	3 (37%)	
Dysarthria				

None	13 (72%)	5 (50%)	8 (89%)	0.17
Spastic	5 (28%)*†	5 (50%)	1 (11%)	
Severity rating (0-4)	0 (0-1)	0.75 (0 - 4)	0 (0 - 0)	0.08
$^{\alpha\beta\delta}$Non-verbal Oral Apraxia				
None	9 (50%)	1 (10%)	0 (0%)	0.004
Mild	3 (16.7%)	1 (10%)	6 (67%)	
Moderate	2 (11.1%)	5 (50%)	1 (11%)	
Marked	3 (16.7%)	2 (20%)	0 (0%)	
Severe	1 (5.6%)	1 (10%)	2(22%)	
Score (/32; 32=normal)	30 (17.8-32.0)	21.5 (14.8 - 26.8)	28 (15 - 29.5)	0.12

Data shown as median (inter-quartile range) or number (%)

* One case also had questionable hypokinetic dysarthria

† One case has spastic dysarthria versus spasmodic dysphonia

‡ One case had questionable hyperkinetic dysarthria and another had strained voice only

P values across all three groups calculated using Kruskal-Wallis test for continuous variables and chi-square for categorical variables

$^{\alpha}$Significance achieved comparing PPAOS and AOS>aphasia

$^{\beta}$Significance achieved comparing PPAOS and agPPA

$^{\delta}$Significance achieved comparing AOS>aphasia and agPPA

Table 3: Global summary of important characteristic differences across groups.

	PPAOS	**AOS>aphasia**	**agPPA**
Speech & language			
Apraxia of speech	+	+	+/-
Predominant AOS type	**2**	**2**	**1**

Agrammatic aphasia	-	+	+
Spastic dysarthria	+/-	+/-	+/-
Non-verbal oral apraxia	+/-	+/-	+
Neuroimaging*			
Cortical			
Prefrontal	-	-	+
Superior premotor	+	+	+
Inferior premotor	-	+	+
Medial temporal	-	-	+
Lateral temporoparietal	-	-	+
Left frontotemporoparietal	-	-	+
Subcortical			
Caudate	-	+	+
Lentiform	-	-	-
Thalamus	-	-	-
Brainstem/cerebellum			
Midbrain	+	+	-
Cerebellar white matter	-	+	-

* Cortical regions are limited to those in left hemisphere

+ = abnormality present, - = absent, +/- = can be present or absent