

## Dissociations between fluency and agrammatism in primary progressive aphasia

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*Background:* Classical aphasiology, based on the study of stroke sequelae, fuses speech fluency and grammatical ability. Nonfluent (Broca's) aphasia often is accompanied by agrammatism; whereas in the fluent aphasia grammatical deficits are not typical. The assumption that a similar relationship exists in primary progressive aphasia (PPA) has led to the dichotomisation of this syndrome into fluent and nonfluent subtypes.

*Aims:* This study compared elements of fluency and grammatical production in the narrative speech of individuals with PPA to determine if they can be dissociated from one another.

*Methods & Procedures:* Speech samples from 37 individuals with PPA, clinically assigned to agrammatic ( $N = 11$ ), logopaenic ( $N = 20$ ), and semantic ( $N = 6$ ) subtypes, and 13 cognitively healthy control participants telling the "Cinderella Story" were analysed for fluency—i.e., words per minute (WPM) and mean length of utterance in words (MLU-W)—and grammaticality, i.e., the proportion of grammatically correct sentences, open-to-closed-class word ratio, noun-to-verb ratio, and correct production of verb inflection, noun morphology, and verb argument structure. Between-group differences were analysed for each variable. Correlational analyses examined the relation between WPM and each grammatical variable, and an off-line measure of sentence production.

*Outcomes & Results:* Agrammatic and logopaenic groups both had lower scores on the fluency measures and produced significantly fewer grammatical sentences than did

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semantic and control groups. However, only the agrammatic group evinced significantly impaired production of verb inflection and verb argument structure. In addition some semantic participants showed abnormal open-to-closed and noun-to-verb ratios in narrative speech. When the sample was divided on the basis of fluency, all the agrammatic participants fell in the nonfluent category. The logopaenic participants varied in fluency but those with low fluency showed variable performance on measures of grammaticality. Correlational analyses and scatter plots comparing fluency and each grammatical variable revealed dissociations within PPA participants, with some nonfluent participants showing normal grammatical skill.

*Conclusions:* Grammatical production is a complex construct comprising correct usage of several language components, each of which can be selectively affected by disease. This study demonstrates that individuals with PPA show dissociations between fluency and grammatical production in narrative speech. Grammatical ability, and its relationship to fluency, varies from individual to individual, and from one variant of PPA to another, and can even be found in individuals with semantic PPA in whom a fluent aphasia is usually thought to accompany preserved ability to produce grammatical utterances.

*Keywords:* Agrammatism; Frontotemporal lobar degeneration; Fluency; Dementia; Narrative speech.

Primary progressive aphasia (PPA), caused by neurodegenerative brain disease, is a clinical dementia syndrome in which progressive language dysfunction is the salient feature during initial stages of the illness (Mesulam, 1982, 2001, 2003). It is clinically distinct from other profiles of dementia where symptoms of amnesia, behavioural changes, or visuospatial dysfunction dominate the early stages (Weintraub & Mesulam, 1993; Wicklund & Weintraub, 2005). The clinical profile of PPA implicates physiological and structural dysfunction within the left perisylvian language areas measured by structural and functional neuroimaging (Cappa, Perani, Messa, Miozzo, & Fazio, 1996; Chawluk et al., 1986; Gorno-Tempini et al., 2004; Hodges, Patterson, Oxbury, & Funnell, 1992; Mesulam et al., 2009; Rosen et al., 2002; Sapolsky et al., 2010; Seeley, Crawford, Zhou, Miller, & Greicius, 2009; Sonty et al., 2003; Turner, Kenyon, Trojanowski, Gonatas, & Grossman, 1996; Tyrrell, Warrington, Frackowiak, & Rossor, 1990). In all, 60–70% of cases are attributable to one or another of the forms of neuropathology collectively referred to as frontotemporal lobar degeneration (FTLD), with most of the remaining cases being associated with forms of Alzheimer pathology (Knibb, Xuereb, Patterson, & Hodges, 2006; Mesulam & Weintraub, 1992). The presence of agrammatism is particularly associated with FTLD tauopathy (Mesulam et al., 2008) and thus provides a clinical marker for inferring the nature of the neuropathology during the lifetime of the patient.

A common manifestation of PPA is dysfluent speech production that cannot be attributed to dysarthria or speech apraxia alone. In aphasia resulting from stroke, fluency of speech production is a primary characteristic used to classify aphasia type (Goodglass & Kaplan, 1983), with the nonfluent aphasias including Broca's and transcortical motor aphasia and the fluent aphasias including Wernicke's, transcortical sensory, conduction, and anomic aphasia. Research in stroke aphasia has also shown that individuals with nonfluent, Broca's aphasia show deficits in grammatical ability that affect both sentence production and comprehension (Goodglass, 1997; Goodglass et al., 1979; Zurif, Green, Caramazza, & Goodenough, 1976). Conversely, grammatical deficits are not typically associated with fluent aphasia (Caplan, Hildebrandt, & Makris, 1996; Zurif et al., 1976; but see Bastiaanse & Edwards, 2004; Caramazza & Zurif, 1976; Edwards & Bastiaanse, 1998). Hence the terms nonfluent, Broca's, and

agrammatic aphasia often are used interchangeably and the first two implicitly suggest the presence of grammatical deficits (see Thompson & Bastiaanse, in press).

Although there are some clinical similarities between aphasia due to stroke and that associated with PPA, the underlying pathophysiology is distinctly dissimilar. In stroke, areas of damaged neural tissue are associated with the cerebral vascular system and, although adjacent as well as distal tissue may be hypoperfused (Thompson, den Ouden, Bonakdarpour, Garibaldi, & Parrish, 2010), the resulting lesions are focal and completely dysfunctional. In contrast, neurodegenerative disease affects distinctive cell groups and layers in various, but primarily perisylvian, regions of the brain, resulting in incomplete disruption of the language network (Weintraub & Mesulam, 1996). This situation indicates that brain regions associated with language processing, even though compromised by disease, may continue to function in PPA. For example, we demonstrated using fMRI that individuals with PPA show activation of regions of the brain similar to that of healthy controls when they perform language tasks (Sonty et al., 2003) albeit with abnormal patterns of connectivity (Sonty et al., 2007), indicating that these regions are not completely dysfunctional. This could result in aphasia profiles that differ from those associated with stroke and also in unique behavioural dissociations such as those reported for naming and comprehension of words related to living and non-living items (Cardebat, Demonet, Celsis, & Puel, 1996; Hodges et al., 1992)

Interest in PPA has grown since 1982 when the first six cases with “slowly progressive aphasia” were published (Mesulam, 1982) (now called primary progressive aphasia). Subsequently reports emerged showing that individuals with PPA present with different impairment profiles. Therefore researchers adopted, in part, the classification system used for diagnosis of stroke aphasia. That is, Neary and colleagues (1998) classified individuals with PPA as “progressive nonfluent aphasia” and (fluent) “semantic dementia”. Other research in PPA, however, has suggested that the fluent–nonfluent distinction used to classify stroke aphasia is not directly relevant to PPA. For example, analysis of spontaneous discourse in four individuals with PPA, all non-fluent on the basis of the amount and fluidity of speech, revealed distinctly different language deficit patterns across participants and dissociations between fluency and measures of grammaticality emerged as symptoms progressed over time (Thompson, Ballard, Tait, Weintraub, & Mesulam, 1997). Thus some nonfluent patients had features of agrammatism, whereas others did not, motivating a major advance in PPA classification, introducing the *logopaenic* subtype (Gorno-Tempini et al., 2004)

Speech fluency and grammatical ability can both be difficult to quantify in PPA. There often are fluctuations in fluency based on the nature of the discourse task, and changes in fluency over the course of disease are characteristic of PPA (Kertesz, Davidson, McCabe, Takagi, & Munoz, 2003). In addition several factors can interfere with testing of grammatical abilities. For example, sentence comprehension tasks rely on working memory, in particular for processing syntactically complex and/or lengthy sentences, and sentence production tasks are often compromised by word-finding deficits. For these reasons we designed the Northwestern Anagram Test (NAT) (Thompson, Weintraub, & Mesulam, <http://www.soc.northwestern.edu/CCNorthwesternAnagramTest>; Weintraub, Mesulam, et al., 2009), an off-line measure of sentence construction that circumvents speech output and limits the impact of poor working memory on task performance. We demonstrated that performance on the NAT is correlated with performance on other off-line tests of syntactic ability, but not with tests of naming, single word comprehension, or motor speech.

Face validity was also demonstrated by showing that the NAT could be used to identify individuals with the agrammatic subtype of PPA (PPA-G). Correlation with brain atrophy patterns in individuals with PPA also showed that speech fluency and performance on the NAT are influenced by neuronal loss in different parts of the left hemisphere language network (Rogalski et al., 2011). Regions of atrophy associated with NAT performance included anterior aspects of the inferior frontal gyrus (IFG<sub>a</sub>), the posterior IFG, sensory-motor cortex and the inferior parietal lobule including the supramarginal gyrus on the lateral surface, and the superior frontal gyrus (SFG) and paracentral lobule as well as the precuneus on the medial surface. In contrast, fluency, measured by calculating mean length of utterance in words, was correlated with atrophy in the posterior aspect of the middle frontal gyrus (MTG<sub>p</sub>) bilaterally, the left inferior frontal sulcus (IFS), and the right hemisphere superior frontal gyrus.

Analysis of spontaneous speech production provides the most naturalistic characterisation of speech production ability; however, there are only a small number of studies that have attempted to quantitatively describe the narrative language characteristics of individuals presenting with PPA (Ash et al., 2006, 2009; Graham, Patterson, & Hodges, 2004; Knibb, Woollams, Hodges, & Patterson, 2009; Meteyard & Patterson, 2009; Orange & Kertesz, 2000; Patterson, Graham, Ralph, & Hodges, 2006; Thompson et al., 1997; Wilson et al., 2010) and available studies of PPA have methodological limitations. Small participant groups and short speech samples are the major limitations of some of the more rigorous work in this area. Early studies examined only a small number of participants (Orange, Kertesz, & Peacock, 1998; Rogers & Alarcon, 1998; Thompson et al., 1997) and more recent studies, although including a larger number of participants (Graham et al., 2004; Patterson et al., 2006; Wilson et al., 2010) have used picture description tasks, which elicit speech samples of limited size and reduced syntactic complexity. In fact most samples in these studies are no longer than 150 words. It has been argued that a sample size of at least 300 words is required for quantitative analysis (Bastiaanse & Jonkers, 1998; Wagenaar, Snow, & Prins, 1975). In comparison to picture description tasks, narrative tasks elicit larger corpora and more complex syntax and morphology (Armstrong, 2000; Dollaghan, Campbell, & Tomlin, 1990; Prins & Bastiaanse, 2004; Sealey & Gilmore, 2007; Westerveld, Gillon, & Miller, 2004).

Limitations in the coding and analysis methods used in prior studies are also apparent. Some studies have employed analysis methods that either are not specified (Ash et al., 2006; Graham et al., 2004; Meteyard & Patterson, 2009; Rogers & Alarcon, 1998) or are not sensitive enough to investigate important aspects of language production, such as, for example, verb argument structure deficits, which are common in stroke-induced agrammatic aphasia (see De Bleser & Kauschke, 2003; Dragoy & Bastiaanse, 2010; Jonkers & Bastiaanse, 1996; Kim & Thompson, 2000; Kiss, 2000). Additionally, some coding systems either only examine the frequency of occurrence of particular linguistic variables and do not allow close inspection of syntactic and/or lexical errors contributing to the flawed output (Ash et al., 2006; Meteyard & Patterson, 2009; Rogers & Alarcon, 1998) or they do not provide a clear definition of the errors analysed (Graham et al., 2004). Even in studies that have coded for errors, only selected types of omissions have been identified.

To our knowledge, only one study (Wilson et al., 2010) to date has provided a quantitative account of impairments across clinical variants of PPA, including the logopaenic variant (PPA-L). Results from this study showed distinct deficit patterns across PPA subtypes associated with regions of cortical atrophy. However, this study

elicited speech samples by asking participants to describe the *picnic* picture from the Western Aphasia Battery (WAB; Kertesz, 2006). As mentioned, picture description tends to evoke labelling rather than story telling, with instructions to “Tell me what you see.” Further, because all actions are in the present tense, there is little opportunity to use past tense verb markers, an important aspect of production that distinguishes between stroke-induced Broca’s aphasia with agrammatism and other aphasia types. The purpose of the present paper was to investigate the relation between fluency and grammatical ability in PPA, by analysing narrative speech samples acquired using a story-telling task, the “Cinderella Story”, elicited with a wordless picture book. This method provides greater opportunities than are possible using picture description for eliciting different verb forms, as well as adverbials and pronominal references to events that occurred earlier in the story, which add to the syntactic complexity of utterances produced. We also examined the relation between fluency and performance on the NAT.

## METHOD

### Participants

A total of 37 consecutive individuals given a root diagnosis of PPA (Mesulam, 2001, 2003; Mesulam et al., 2009) participated in the study. Individuals were recruited primarily through the Northwestern Cognitive Neurology and Alzheimer’s Disease Center (CNADC) and many of them had inquired about clinical and research opportunities via the CNADC website. Some of the participants were also enrolled in the Clinical Core of the CNADC funded by the National Institute on Aging (NIA) of the National Institutes of Health (NIH), from which 13 cognitively healthy volunteers were also recruited. The study was approved by the Institutional Review Board at Northwestern University and informed consent was obtained from all participants. Control participants had been previously screened for the absence of psychiatric, neurologic, or serious medical diagnoses (e.g., cancer requiring chemotherapy) and no use of psychotropic medications apart from antidepressants for situational reaction. As part of their participation in the CNADC Clinical Core, all control participants had also undergone the procedures of the Uniform Data Set (UDS) (Morris et al., 2003; Weintraub, Salmon, et al., 2009), including a research neurological examination and neuropsychological test battery which demonstrated their normal neurologic and cognitive status.

All participants were Caucasian, had normal hearing for conversation and vision (with correction), and had been recruited and tested between late 2007 and early 2010. With three exceptions (G2, L9, L18, see Table 3) all participants were right-handed. The three non-right-handers scored between  $-35$  and  $-70$  on the Edinburgh handedness scale (Oldfield, 1971). None of the participants was bilingual or polylingual, although one (L9) indicated that she knew how to speak French.

Clinical language tests administered included the Western Aphasia Battery-Revised (WAB-R) (Kertesz, 2006), the Boston Naming Test (BNT) (Kaplan, Goodglass, & Weintraub, 1983), and the Peabody Picture Vocabulary Test-fourth edition (PPVT-IV) (Dunn & Dunn, 2007). A test of motor speech production (repeating syllables of varying complexity; Dabul, 2000) and a 10-item short form of the NAT also were administered. Based on performance on the PPVT-IV and the NAT, the PPA participants were

TABLE 1  
Demographic and language test data (mean, *standard error*) for healthy control and PPA  
participant groups by clinical subtype

	<i>CONTROLS (n = 13)</i>	<i>PPA-G (n = 11)</i>	<i>PPA-L (n = 20)</i>	<i>PPA-S (n = 6)</i>
Age (years)	63.23 (1.63)	63.27 (1.77)	65.90 (2.03)	56.33 (1.52)
Education (years)	16.31 (0.70)	16.82 (0.80)	15.85 (0.49)	16.00 (0.89)
WAB AQ (100)	99.67 (0.20)	79.36 (2.32)	89.43 (1.42)	76.37 (3.52)
BNT (60)	58.62 (0.42)	46.45 (4.10)	46.50 (3.56)	5.67 (1.76)
PPVT (36)	35.58 (0.19)	34.00 (0.54)	34.00 (0.61)	13.33 (1.45)
NAT total (10)	10.00 (0.00)	4.89 (0.20)	8.94 (0.80)	8.80 (0.80)
Motor Speech (50)	50.00 (0.00)	45.00 (5.58)	46.95 (6.66)	40.83 (7.96)

According to Mesulam and colleagues (2009), PPA-G = Primary Progressive Aphasia (PPA) – agrammatic variant ; PPA-L = PPA – logopaenic variant; PPA-S = PPA – semantic variant; WAB AQ = Western Aphasia Battery, Aphasia Quotient; BNT = Boston Naming Test; PPVT-IV = Peabody Picture Vocabulary Test – 4th edition; NAT=Northwestern Anagram Test.

classified as Agrammatic (PPA-G), Logopaenic (PPA-L), and Semantic (PPA-S) subtypes using a previously published algorithm for classifying PPA with these measures (Mesulam et al., 2009).

Table 1 shows demographic data and mean clinical language scores (plus standard error, *SEM*) for all groups. A statistically significant difference was found among the groups for age, (Kruskal-Wallis; K-W),  $\chi^2 = 7.91$ ,  $DF = 3$ ,  $p = .048$ ), with post-hoc pairwise analyses (Wilcoxon Rank Sum test) indicating that the PPA-S group was significantly younger than the PPA-G and PPA-L groups—56.33 years ( $SEM = 1.52$ ), vs 63.27 years ( $SEM = 1.77$ ) and 65.90 years ( $SEM = 2.03$ ), respectively;  $p = .039$  and  $.013$ , respectively. The PPA-S group was also significantly younger than the control participants—63.23 years ( $SEM = 1.63$ );  $p = .018$ . The PPA-G and PPA-L groups did not differ significantly from one another in age, and there was no significant difference between either of these two groups and the control group. Participants within each group were all similarly highly educated with no significant differences among groups ( $\chi^2 = 1.19$ ,  $DF = 3$ ,  $p = .755$ ).

On the WAB AQ, a measure of overall aphasia severity, all PPA participants presented with an AQ score within the mildly to moderately impaired range (76.37 to 89.43). However, the PPA-L group (mean AQ = 89.63,  $SEM = 1.42$ ) was less-severely impaired than either the PPA-G (mean AQ = 79.36,  $SEM = 2.32$ ;  $p = .002$ ) or PPA-S (mean AQ = 76.37,  $SEM = 3.52$ ,  $p = .004$ ) groups. All PPA groups also showed impaired naming, but again there were group differences in performance on the BNT (K-W  $\chi^2 = 27.59$ ,  $DF = 3$ ,  $p = .0001$ ). Post-hoc pairwise comparisons between groups showed that the PPA-S group scored significantly lower (mean total BNT = 5.67,  $SEM = 1.76$ ) than the PPA-G and PPA-L groups (46.45,  $SEM = 4.10$ ,  $p = .001$ , and 46.50,  $SEM = 3.56$ ,  $p = .0005$ , respectively). Similarly, PPVT-IV scores differed significantly among groups ((K-W  $\chi^2 = 21.85$ ,  $DF = 3$ ,  $p = .0001$ ). Pairwise comparisons showed that the PPA-S group scored very poorly (mean = 13.33,  $SEM = 1.45$ ) and significantly lower than the PPA-G and PPA-L groups (mean = 34.00,  $SEM = 0.54$ ,  $p = .001$ , mean = 34.00,  $SEM = 0.61$ ,  $p = .0003$ , respectively). Finally we found a significant group difference on NAT scores (K-W  $\chi^2 = 28.86$ ,  $DF = 3$ ,  $p = .0001$ ), with the PPA-G group [mean = 4.89,  $SEM = 0.20$ ] scoring significantly lower than the PPA-L and PPA-S groups (mean = 8.94,  $SEM = 0.30$ ,  $p = .0003$ , and mean = 8.80,  $SEM = 0.80$ ,  $p = .0101$ , respectively).

Few of the PPA participants presented with any disturbance of motor speech production as indicated by the group mean scores shown in Table 1. Further analysis of the motor speech data indicated a median score for the PPA participants at 48.50 out of a possible 50, with a range of 29 to 50 and a mode of 50. Hence motor speech impairment was not considered to be a major contributor to patterns of narrative production.

All PPA and control participants also were administered a series of non-language tests. Table 2 shows the mean scores on selected measures for the controls and for the PPA group as a whole, as not all patients had all the tests due to changes in study protocol or to lack of time. The healthy control participants performed within normal limits on these tests and on clinical examinations administered as part of the Uniform Data set of the Alzheimer's Disease program of the National Institute on Aging (Beekly et al., 2007; Morris et al., 2006; Weintraub, Salmon, et al., 2009). All control participants also underwent structural MRI, with results showing no abnormalities. The PPA group did not differ from controls on Trail Making Part A (Reitan, 1958) (measure of attention and processing speed), the Visual-Verbal Test (Wicklund, Johnson, & Weintraub, 2004) (measure of reasoning and conceptual flexibility), the Facial Recognition Test (Benton, Hamsher, Varney, & Spreen, 1998) (measure of face perception), and Immediate and Delayed recognition scores on the Faces subtest of the Wechsler Memory Scale (third edition) (Wechsler, 1998) (measure of immediate and delayed memory for faces). In contrast, the two groups differed in performance on part B of Trail Making and on the Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 2004). Language deficits can interfere with the processing of letter stimuli on Part B of Trail Making. In addition we have previously shown that performance on the MMSE in PPA is influenced by the aphasia due to the overwhelmingly verbal nature of this test and thus scores may overestimate dementia severity and functional impairment in these patients (Osher, Wicklund, Rademaker, Johnson, & Weintraub, 2007).

### Narrative data collection and coding

Participants were instructed to review a wordless picture book of the story of Cinderella and then to tell the story to the examiner. Prior to participants beginning their narratives the book was removed, but participants were permitted to look at it to remind themselves of the sequence of events in the story as needed. The entire narrative was recorded using Praat software (version 5.0, <http://www.praat.org>) and "start" and "end" times of each narration were automatically recorded. Interjections by the examiner were kept to a minimum but examiner-generated questions such as "What happened next?" were used to encourage participants to continue their narration when there were long pauses between utterances.

All language samples were transcribed and coded by experienced personnel in the Aphasia and Neurolinguistics Research Laboratory at Northwestern University, with a method developed by Thompson and colleagues (Thompson et al., 1995), used in many studies to quantify the narrative language ability of individuals with stroke-induced agrammatic aphasia and in one of our early studies of conversational speech in four individuals with PPA (Thompson et al., 1997). For each sample, all identifiable words, including phonemic and neologistic paraphasias, were transcribed verbatim with English orthography and segmented into utterances based on semantic, syntactic, and prosodic criteria. For example, a group of words expressing a complete

TABLE 2  
Neuropsychological test scores (mean, *SD*) for controls and PPA participant groups

Group	MMSE* Total (30)	TMT Part A Seconds†	TMT Part B** Seconds	Facial Recognition† (54)	Visual Verbal Shifts† (10)	Visual Verbal Sorts† (20)	WMS-III Faces Immediate† (48)	WMS-III Faces Delay† (48)
NC (N = 13)	29.77	31.77	71.77	46.25	9.00	18.91	37.08	38.92
Mean								
<i>SD</i>	0.44	7.11	20.85	4.16	0.89	1.04	3.92	3.29
PPA (N = 37)	24.97	48.69	141.62	47.00	8.30	18.21	34.72	36.38
Mean								
<i>SD</i>	5.60	31.41	79.17	3.90	1.63	1.85	4.70	4.80

MMSE = Mini Mental State Examination; TMT = Trail Making Tests; WMS-III = Wechsler Memory Scale, 3rd edition; numbers in parentheses beneath test names are maximum scores. *SD* = standard deviation; NC = Normal control group.

\* $t(48) = 3.067, p = .0035$ ; \*\* $t(45) = 3.12, p = .0032$ ; †comparisons not statistically significant.

TABLE 3  
Individual scores for PPA patients and mean scores (SEM) for patients by clinical subtype and controls

Participant, Gender	Off-line grammar	NAT (Max = 100%)	WPM	MLU-W	% Gramm Correct	Narrative measures						% Correct Arg Struc
						Open: Closed	Nouns: Verbs	% Correct Verb Inf	% Correct Noun Morph	% Correct Arg Struc		
<b>CONTROLS</b>												
Mean (SEM)			132.22 (5.22)	11.11 (0.56)	93.02 (1.21)	0.95 (0.03)	1.21 (0.06)	98.88 (0.61)	98.97 (0.79)	98.11 (0.60)		
<b>PPA-G</b>												
G2, M	NA	63.11	6.47	46.67	1.27	1.33	72.73	100.00	100.00	71.43		
G13, M	50	25.22	3.96	40.00	1.47	3.70	100.00	77.27	100.00	14.29		
G14, M	40	55.43	4.97	66.67	0.92	1.32	100.00	100.00	100.00	75.00		
G19, F	50	110.31	7.57	57.50	0.93	1.00	91.43	85.71	100.00	88.00		
G27, F	50	35.95	5.43	66.67	1.14	1.06	93.75	100.00	100.00	100.00		
G31, M	50	77.12	11.33	23.64	0.88	1.51	66.67	94.74	100.00	91.00		
G32, F	NA	74.91	5.85	50.00	0.75	0.92	50.00	100.00	100.00	84.62		
G34, F	50	47.56	7.11	17.86	1.02	1.84	45.95	57.14	100.00	72.97		
G36, F	50	40	6.8	62.50	0.88	1.05	100.00	80.00	100.00	95.45		
G37, M	60	55.32	10.23	71.88	0.99	1.15	81.82	100.00	100.00	96.36		
G39, M	40	63.31	6.74	35.29	1.05	1.81	66.67	91.67	100.00	95.24		
Mean (SEM)	4.89 (0.20)	58.93 (7.03)	6.95 (0.65)	48.97 (5.47)	1.03 (0.06)	1.52 (0.24)	79.00 (6.01)	89.68 (4.14)	80.40 (7.27)			
<b>PPA-L</b>												
L1, M	90	104.45	9.45	92.00	0.97	1.34	97.92	100.00	100.00	97.62		
L3, M	NA	100.75	7.85	76.00	0.91	0.68	97.37	85.71	100.00	97.50		
L5, M	100	141.1	7.86	88.24	1.03	1.21	100.00	100.00	100.00	96.30		
L6, F	NA	98.14	7.83	94.74	0.93	0.93	100.00	100.00	100.00	96.55		
L9, F	NA	127.33	7.36	87.50	0.92	0.46	100.00	100.00	100.00	96.00		
L15, M	70	85.95	6.32	85.71	0.90	0.71	93.75	100.00	100.00	100.00		
L16, M	90	118.68	10.5	81.25	0.95	0.97	100.00	80.00	100.00	92.65		
L17, F	70	19.05	5.36	84.62	0.90	0.78	88.89	100.00	100.00	100.00		
L18, M	100	82.96	7.63	54.55	0.76	0.90	83.33	100.00	100.00	80.00		

(Continued)

TABLE 3  
(Continued)

Participant, Gender	Off-line grammar	Narrative measures									
		NAT (Max = 100%)	WPM	MLU-W	% Gramm Correct	Open: Closed	Nouns: Verbs	% Correct Verb Inf	% Correct Noun Morph	% Correct Arg Struc	
L22, F	100	157.66	13.88	70.37	0.82	1.16	90.00	100.00	93.85		
L25, M	70	58.93	8.63	88.89	0.77	1.30	100.00	100.00	100.00		
L26, M	100	64.3	9.18	60.71	1.00	1.31	94.43	100.00	97.83		
L29, M	100	105.84	10.14	92.31	0.99	1.19	100.00	100.00	95.77		
L30, F	100	94.08	10.69	100.00	0.88	0.90	100.00	100.00	96.92		
L33, M	90	96.57	8.28	93.33	0.85	1.00	100.00	100.00	97.78		
L35, F	90	71.54	6.08	66.67	0.92	1.07	100.00	83.33	88.24		
L40, F	70	99.43	9.85	84.62	0.91	1.10	98.72	88.73	97.26		
L42, F	100	80.38	6.54	81.48	0.98	1.17	91.67	100.00	91.43		
L43, M	80	78.97	10.17	86.67	0.94	0.94	100.00	100.00	100.00		
L44, F	100	153.79	9.52	83.33	0.72	0.63	100.00	100.00	95.71		
Mean (SEM)	8.94 (0.30)	97.00 (7.36)	8.66 (0.44)	82.65 (2.61)	0.90 (0.02)	0.99 (0.05)	96.80 (1.09)	96.89 (1.46)	95.57 (1.06)		
<b>PPA-S</b>											
S10, F	NA	165.29	9.22	95.65	0.79	0.63	100.00	100.00	92.16		
S21, M	100	163.54	13.7	76.92	0.80	0.98	100.00	100.00	93.75		
S24, F	60	122.76	7.83	70.59	0.66	0.67	100.00	100.00	95.83		
S28, F	100	115.65	10.55	90.91	0.67	0.65	100.00	100.00	90.48		
S6, F	100	167.41	9.62	90.48	0.63	0.72	100.00	87.50	100.00		
S45, F	80	76.74	7.63	86.67	0.69	0.81	98.28	100.00	92.50		
Mean (SEM)	8.83 (0.80)	135.23 (14.94)	9.76 (0.91)	85.20 (3.89)	0.71 (0.03)	0.74 (0.05)	99.71 (0.29)	97.92 (2.08)	94.12 (1.38)		

M = Male; F = Female; NAT = Northwestern Anagram Test; WPM = Words per minute; MLU-W = mean length of utterance in words; %Gramm Corr = percent of utterances that are grammatically correct; Open:Closed = ratio of open- to closed-class words; Nouns:Verbs = ratio of nouns to verbs; % Corr Verb Inf = percent of verbs with correct inflection; % Corr Noun Morph = percent of nouns with correct morphology; % Corr Verb Arg Struc = percent of verbs used with correct argument structure; PPA = primary progressive aphasia; G = Agrammatic; L = Logopaenic; S = Semantic; NA = Test not administered.

thought and/or a syntactically complete sentence was considered a single utterance, and falling intonation and/or pauses often suggested its end. Importantly, however, both grammatical and ungrammatical strings of words were considered utterances and pauses alone were not used to segment utterances. When utterance boundaries were unclear, boundaries were placed to create shorter rather than longer utterances. Unintelligible words and utterances (marked with *xs*) as well as interjections (e.g., *uh*, *um*), and repeated words and phrases within an utterance, with exception of repetitions used for emphatic purposes (e.g., *I've been working and working and working*), were coded in brackets (e.g., *I've been [working working working] working*) and were not analysed.

Each transcribed utterance then was coded at four levels: the utterance, lexical, bound morpheme, and verb argument structure level. At the utterance level an utterance code was assigned, denoting whether or not the utterance comprised a sentence or a non-sentence. In order to be considered a sentence, production of a verb in the utterance was required. Each utterance coded as a sentence then was coded as "grammatical" or "ungrammatical". The lexical level identified the grammatical class of all the words produced in each utterance, including both open-class (i.e., nouns, verbs, adjectives, adverbs) and closed-class (e.g., determiners, prepositions, auxiliaries) words. At the bound morpheme level, verb tense (both regular and irregular) and noun plural markers were coded. Omissions, additions, and substitutions of bound morphemes were also indicated using unique codes for each. Finally, at the verb argument structure level, the accuracy of verb argument structure production was coded for each verb produced.

All language samples were independently transcribed and coded by two individuals. The transcriptions were compared in order to determine reliability of word entry and utterance segmentation. Overall inter-transcriber point-to-point agreement was 98% for transcription and 96% for utterance segmentation. Any disagreements were resolved by re-listening to the samples in question and discussion between the transcribers. Intercoder point-to-point agreement also was calculated for each code. Overall agreement ranged from 87% to 90% with an overall mean of 88.5%. Disagreements were resolved by discussion between coders.

## Data analysis

All coded transcripts were entered into the Systematic Analysis of Language Transcripts (SALT) (Miller & Chapman, 2000), which computed the mean length of utterance in words (MLU-W) and the number of words per minute (WPM) for each sample and tallied all examiner-entered codes. These data were then entered into Microsoft Excel for calculation of six dependent measures. The first was a general measure of grammatical integrity: the proportion of grammatically correct sentences produced, computed by dividing the number of grammatical sentences by total sentences. The next two measures constituted the word class level measures: the ratio of nouns-to-verbs (N:V) and the ratio of open-to-closed-class words (O:C). Two morphology measures consisted of the proportion of verbs produced with correct inflections and the percent of nouns produced with correct morphology. Finally the proportion of verbs produced with correct argument structure was calculated.

In order to characterise the performance of each group in a way that is clinically transparent, we computed means (plus standard error, SEM) for each variable (Table 3). However, due to the non normal distribution of test scores, we used

non-parametric statistics (Kruskal-Wallis followed by pairwise Wilcoxon Rank Sum tests) to test for group differences on each of the narrative variables. Because our primary interest was to examine the relation between fluency and grammaticality, we also undertook statistical analyses to examine these relations in the entire sample of PPA participants, regardless of PPA subtype. To accomplish this, Spearman rank correlations were computed comparing fluency to each grammatical variable and to NAT scores. Scatter plots were created showing scores for all individual PPA participants across variables. We also separately computed correlations between fluency and grammaticality *only* for participants with nonfluent speech as evidenced by scores one standard deviation below the WPM mean for the control group.

## RESULTS

Table 3 shows the control mean scores (plus SEM) and PPA individual participant and group mean scores (plus SEM) for all the narrative variables and the NAT. Statistical analyses of these data revealed significant main effects for all narrative variables with the exception of correct noun morphology, which did not differ significantly across groups ( $p = .08$ ). Kruskal-Wallis (K-W) ANOVAs showed significant group effects for WPM (K-W  $\chi^2 = 25.58$ ,  $df = 3$ ,  $p < .0001$ ); MLU-W (K-W  $\chi^2 = 17.60$ ,  $df = 3$ ,  $p = .0005$ ), percent grammatically correct sentences (K-W  $\chi^2 = 28.70$ ,  $df = 3$ ,  $p < .0001$ ), open-to-closed class ratio (K-W  $\chi^2 = 16.10$ ,  $df = 3$ ,  $p = .001$ ), noun-verb ratio (K-W  $\chi^2 = 17.92$ ,  $df = 3$ ,  $p = .0005$ ), percent correct verb inflection (K-W  $\chi^2 = 12.82$ ,  $df = 3$ ,  $p = .005$ ), and correct verb argument structure (K-W  $\chi^2 = 16.15$ ,  $df = 3$ ,  $p = .001$ ).

Summary statistics for follow-up pairwise comparisons between each of the three PPA groups and the control group are presented in Table 4. Notably, we used a significance level of  $p < .008$  (calculated as  $.05/6$ ) to correct for multiple comparisons. These data indicate a significant difference for WPM between PPA-G and PPA-L groups and between PPA-G and PPA-S groups, but not between the PPA-L and PPA-S groups, although quantitatively slower speech was found for the PPA-L compared to the PPA-S group—mean PPA-G = 58.93 ( $SEM = 7.03$ ); mean PPA-L = 97.00 ( $SEM = 7.36$ ); mean PPA-S = 135.23 ( $SEM = 14.94$ ). In addition, both the PPA-G and PPA-L groups, but not the PPA-S group, produced significantly slower speech than the normal controls (PPA-G:  $p < .0001$ ; PPA-L:  $p = .0027$ ; PPA-S:  $p = .6931$ ). Similar differences were noted for MLU-W between PPA groups, with the PPA-G group producing the shortest utterances and the PPA-S group producing the longest—PPA-G mean = 6.95 ( $SEM = 0.65$ ); PPA-L mean = 8.66 ( $SEM = 0.44$ ); PPA-S mean = 9.76 ( $SEM = 0.91$ )—although these differences did not reach significance using our stringent level of statistical significance. However, as with WPM, MLU-W for the PPA-G and PPA-L, but not the PPA-S participants, differed significantly from normal (PPA-G:  $p = .0014$ ; PPA-L:  $p = .0016$ ; PPA-S:  $p = .1047$ ). WPM and MLU-W were significantly correlated with one another (Spearman  $r = .59$ ,  $p < .0001$ ).

With regard to variables associated with grammatical production, the PPA-G group performed significantly more poorly than the PPA-L ( $p < .0001$ ) and the PPA-S ( $p = .0015$ ) groups for the proportion of grammatical sentences, although the PPA-L, but not the PPA-S group, produced significantly fewer grammatical sentences than the normal controls (PPA-L versus normal,  $p = .0028$ ; PPA-S versus normal,  $p = .0714$ ). The PPA-G group was also significantly more impaired in production of verbs with correct argument structure compared to the PPA-L ( $p = .0046$ ), but not the PPA-S

TABLE 4  
Significance values

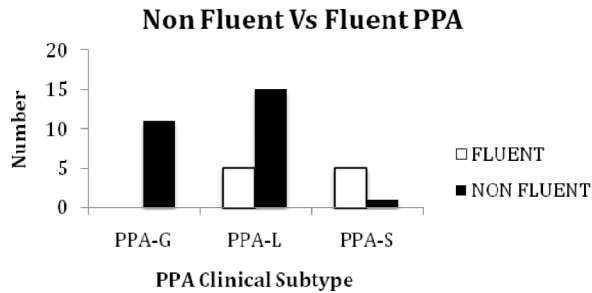
Narrative variable	Comparisons among three PPA groups			Comparison between each PPA group and control group		
	PPA-G vs. PPA-L	PPA-G vs. PPA-S	PPA-L vs. PPA-S	PPA-G vs. CONTROL	PPA-L vs. CONTROL	PPA-S vs. CONTROL
WPM	.0016*	.0022*	.0358	<.0001*	.0027*	.6931
MLU Words	.0335	.0182	.3774	.0014*	.0016*	.1047
% Grammatically Correct Sentences	<.0001*	.0015*	.5838	<.0001*	.0028*	.0714
Open–Closed ratio	.0945	.0022*	.0011*	.3848	.3198	.0010*
Noun–Verb Ratio	.0132	.0015*	.0307	.3690	.0193	.0018*
% Correct Verb Inflection	.0113	.0196	.1647	.0048*	.2421	.4972
% Correct Noun Morphology	.0555	.1435	.8250	.0297	.6028	.8902
% Correct Verb Argument Structure	.0046*	.1911	.1694	.0015*	.0444	.0259

Significance values for pairwise comparisons among the three PPA groups and control participants (based on Wilcoxon Rank Sum Test). Starred and emboldened values are statistically significant based on correction for six pairwise comparisons (i.e.,  $p < .008$ ).

group ( $p = .1911$ ) and the PPA-L and PPA-S groups did not differ significantly from one another ( $p = .1694$ ) or from the normal controls (PPA-L versus normal,  $p = .0444$ ; PPA-S versus normal,  $p = .0259$ ).

For word class production, significant differences between PPA-G and PPA-L were not found (open-to-closed class ratio,  $p = .0945$ ; noun-to-verb ratio,  $p = .0132$ ) and neither group performed significantly differently than the normal controls on either variable (open to closed class: PPA-G versus normal,  $p = .3848$ ; PPA-L versus normal,  $p = .3198$ ; noun-to-verb ratio: PPA-G versus normal,  $p = .3690$ ; PPA-L versus normal,  $p = .0193$ ), although the PPA-G produced numerically more nouns than verbs compared to the PPA-L group—noun-to-verb ratio PPA-G = 1.52 ( $SEM = 0.24$ ) versus PPA-L = 0.99 ( $SEM = 0.05$ ). Significant differences between groups for these variables were found only for comparisons between the PPA-S and the other PPA groups, with the PPA-S group producing significantly fewer open-class compared to closed-class words than the PPA-G group ( $p = .0022$ ), the PPA-L group ( $p = .0011$ ) and the normal controls ( $p = .0010$ )—open-to-closed class ratio: PPA-G = 1.03 ( $SEM = 0.06$ ), PPA-L = 0.90 ( $SEM = 0.02$ ); PPA-S = 0.71 ( $SEM = 0.03$ ); normal controls = 0.95 ( $SEM = 0.03$ ). The PPA-S group also produced significantly fewer nouns than verbs compared to the PPA-G ( $p = .0015$ ) and normal controls ( $p = .0018$ ), noun to verb ratio: PPA-S = 0.74 ( $SEM = 0.05$ ).

Finally, no statistically significant differences were found between the three PPA groups for either verb inflection or noun morphology (verb inflection: PPA-G versus PPA-L,  $p = .0113$ ; PPA-G versus PPA-S,  $p = .0196$ ; PPA-L versus PPA-S,  $p = .1647$ ; noun morphology: PPA-G versus PPA-L,  $p = .0555$ ; PPA-G versus PPA-S,  $p = .1435$ ; PPA-L versus PPA-S,  $p = .8250$ ). However, the proportion of correctly inflected verbs was significantly impaired for the PPA-G group compared to the normal controls—PPA-G = 79.00% correct ( $SEM = 6.01$ ); controls = 98.88% correct ( $SEM = 0.61$ );  $p = .0048$ .



**Figure 1.** Proportion of PPA participants in each clinical subtype group with nonfluent and fluent speech production based on WPM score greater than 1 *SD* below the average for control participants (value = 113.4 WPM).

### Fluency and grammaticality

Because WPM and MLU were significantly correlated with one another we used WPM as the primary measure of fluency. Hence we undertook correlational analyses between WPM and all measures of grammatical production and the NAT score. We also divided the PPA participants into those whose WPM scores were at or below the control mean minus one standard deviation (cut-off = 113.4) (i.e., non fluent) and those whose scores fell above that value (i.e., fluent). Notably, of the 37 PPA participants in the study, 27 were considered nonfluent based on this criterion: all 11 of the PPA-G participants, 15 of the 20 PPA-L and one PPA-S participant (see Figure 1).

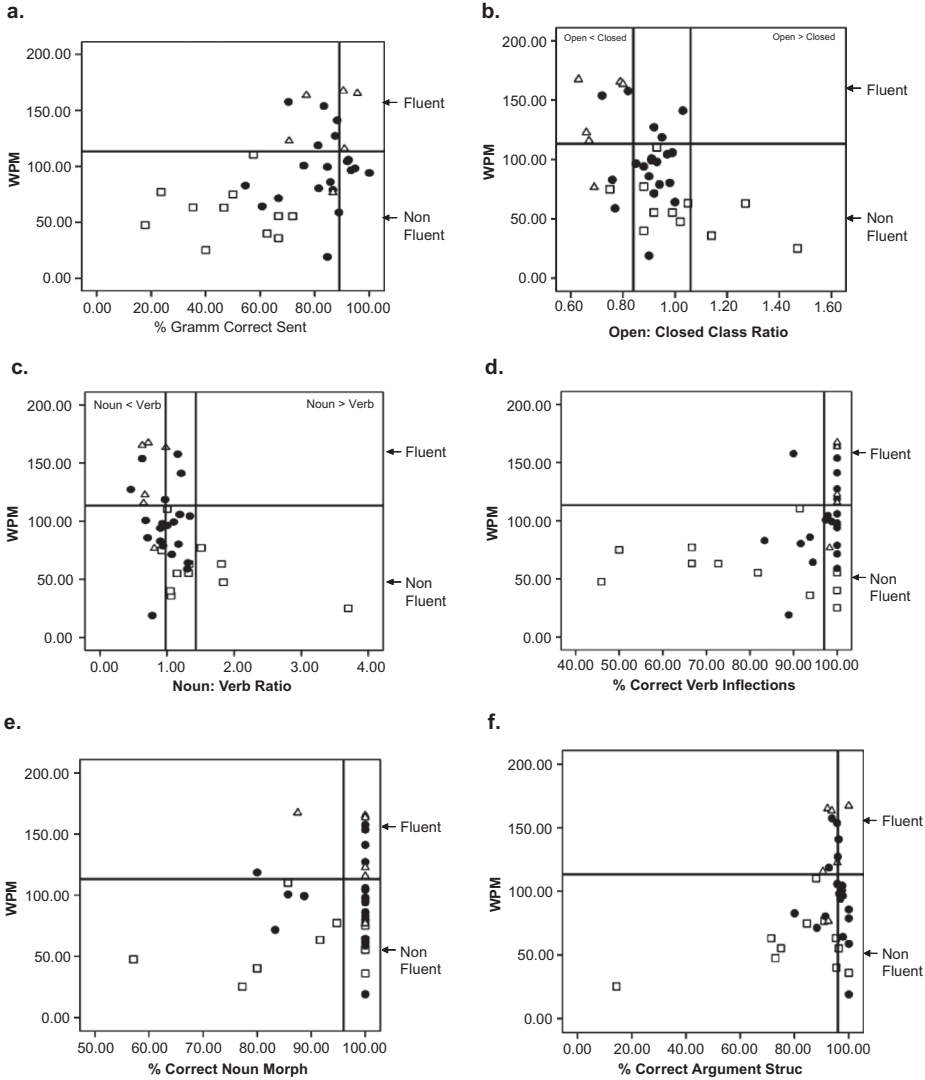
Figure 2a-f shows scatter plots comparing WPM and each grammatical variable derived from narrative analyses. In each plot the horizontal line divides the group into fluent and nonfluent participants and vertical lines represent one standard deviation below the mean for each measure of grammaticality, with the exception of open-to-closed class and noun-to-verb ratios, where vertical lines demarcate one standard deviation above and one standard deviation (*SD*) below the control mean, because both types of deviation are abnormal.

The proportion of grammatically correct sentences produced by each PPA participant is plotted in Figure 2a against WPM around the mean proportion of grammatically correct sentences (minus 1 *SD*) for the control participants (value = 93.02%).

**Figure 2 a-f (opposite).** Scatter plots depicting the relation between WPM and each of six grammatical variables derived from narrative speech analysis. In each, the horizontal line represents the control mean WPM minus 1 *SD* (value = 113.4); vertical lines represent 1 *SD* below (or above) the mean for each variable. □ = PPA-G; ● = PPA-L; △ = PPA-S.

(a) The proportion of grammatically correct sentences produced as a function of WPM. The vertical line represents the control group mean minus 1 *SD* below the mean (89%). All PPA-G participants produced fewer grammatically correct sentences than the normal speakers, whereas the PPA-L speakers showed variable performance. Notably, half of the PPA-S participants also showed lower than normal percent grammatically correct sentences.

(b) Open-to-closed class ratio as a function of WPM. Vertical lines represent 1 *SD* below (0.89) and above (1.06) the mean open-to-closed-class word ratio for the normal control group. Higher scores represent production of fewer closed-class compared to open-class words; lower scores represent production of a greater proportion of closed-class compared to open-class words. All of the PPA-S participants showed lower than normal ratios; whereas only PPA-G participants ( $n = 3$ ) showed higher than normal ratios. The PPA-L participants showed variable performance patterns.



**Figure 2 a–f.** (c) Noun-to-verb ratios plotted for each participant as a function of WPM. Vertical lines represent 1 *SD* below and above the mean noun-to-verb ratio for the normal control group (0.98–1.43, respectively). Values below .98 indicate production of a greater number of verbs compared to nouns, whereas, values above 1.43 indicated the opposite pattern. All seven of the nonfluent PPA-L participants with abnormal scores on this measure produced more verbs than nouns, whereas three of the PPA-G participants produced more nouns than verbs.

(d) Percent of correctly inflected verbs plotted as a function of WPM. The vertical line represents the mean score minus 1 *SD* for the control group on percent of correctly inflected verbs (97%). Although both PPA-G and PPA-L participants showed abnormalities, a greater number of PPA-G, compared to PPA-L participants show below normal production of verb inflection.

(e) Proportion of nouns produced with correct morphology plotted as a function of WPM. The vertical line represents the control mean score minus 1 *SD* (96%). Most of the participants showing low performance on this variable were of the PPA-G subtype.

(f) The proportion of verbs produced with correct verb argument structure plotted as a function of WPM. The vertical line represents the control mean score minus 1 *SD* (96%). The majority of participants with low verb argument structure production were PPA-G whereas most PPA-L participants show preserved argument structure production.

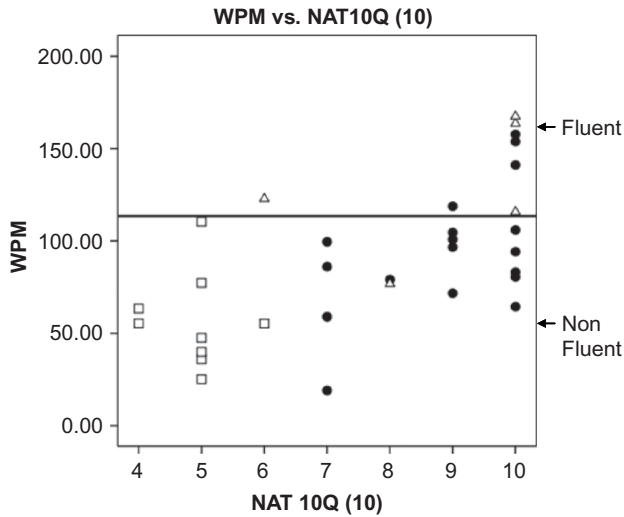
PPA participant G34 produced the lowest proportion of grammatically correct sentences (17.86%) and participant PPA-L30 produced the highest (100%), with WPM ranging from a low of 25.22 (PPA-G13) to a high of 167.41 (PPA-S6). Correlational analysis of these data revealed a significant positive correlation (Spearman  $r = .500$ ,  $p = .002$ ).

In Figure 2b open-to-closed class ratios are plotted around the control mean, plus/minus 1 *SD* (0.84 to 1.06). Scores for the PPA participants ranged from 0.63 (PPA-S6) to 1.47 (PPA-G13), with lower ratios indicating production of a greater number of closed-class compared to open-class words and higher ratios associated with production of a greater number of open-class words in narrative speech. A significant negative correlation between this variable and WPM was found ( $r = -.425$ ,  $p = .009$ ). However, considering only the nonfluent participants, the correlation between WPM and open-to-closed class ratio was not statistically significant ( $r = -.233$ ,  $p = .243$ ).

The relation between fluency and noun-to-verb ratio is plotted in Figure 2c around the mean noun-to-verb ratio for controls, plus/minus 1 *SD* (a normal range of 0.98 to 1.21), with higher values indicating more nouns. Noun-to-verb ratios in all PPA participants ranged from 0.46 (PPA-L9) to 3.70 (PPA-G3), with a significant negative correlation found between this variable and WPM ( $r = .496$ ,  $p = .002$ ). However, a significant correlation between noun-to-verb ratio and WPM was not found when only the nonfluent participants were analysed ( $r = -.310$ ,  $p = .115$ ). Of the nonfluent participants with an abnormally high noun-to-verb ratio, six were clinically agrammatic (PPA-G2, G13, G14, G31, G32, G39), whereas only three were logopaenic (PPA-L1, L25, L26).

Figures 2d and 2e present scatter plots for verb inflection and noun morphology, respectively. For correct verb inflection, scores ranged from 45.95% (PPA-G34) to 100% (participants of all PPA subtypes) correctly inflected verbs, with a statistically significant correlation between this variable and WPM ( $r = -.406$ ,  $p = .013$ ). However, once again, when the data for only nonfluent participants were examined, a significant correlation between percent correct verb inflection and WPM was not found ( $r = 0.176$ ,  $p = .379$ ). The nonfluent PPA participants who evinced below normal scores (i.e., below 98.88%) for verb inflection ( $n = 13$ ) included both agrammatic ( $n = 8$ ) and logopaenic ( $n = 5$ ) individuals. The percentage of nouns produced with correct morphology also did not correlate significantly with WPM for either the group as a whole (Spearman  $r = .160$ ,  $p = .345$ ) or for the nonfluent group ( $r = .123$ ,  $p = .540$ ). Again, both PPA-G ( $n = 6$ ) and PPA-L ( $n = 3$ ) individuals with nonfluent production presented with low noun morphology scores.

Finally, Figure 2f shows the proportion of verbs produced with correct argument structure as a function of WPM. Across participants, scores ranged from 71.43% correct (PPA-G2) to 100% correct (derived from participants of all clinical PPA subtypes), with no statistically significant correlation found between these variables ( $r = .089$ ,  $p = .600$ ). In addition, when we considered only the data derived from the nonfluent participants, the correlation also was not significant (Spearman  $r = -.140$ ,  $p = .485$ ). Notably, however, of the nonfluent PPA participants, a higher proportion of those with PPA-G showed abnormal verb argument structure production (i.e., lower than 96% correct) compared to those with PPA-L (Fisher exact test,  $p = .026$ ).



**Figure 3.** Scatter plot showing the relation between 32 PPA participants' scores on the Northwestern Anagram Test (NAT; 10-item Short Form) and WPM derived from the narrative speech samples. Horizontal line represents 1 *SD* below control WPM mean (113.4). Of the 12 PPA-L participants with abnormal fluency, none overlapped in NAT score with the PPA-G participants and 9 had scores of 80% or more correct.

### Off-line sentence production

Figure 3 presents a scatter plot depicting NAT scores as a function of WPM. Five PPA participants were not administered this measure and results are reported for the remaining 32. NAT scores ranged from 40% correct (PPA-G29) to 100% correct (PPA-L5, 18, 22, 26, 29, 30, 42, 44, and PPA-S 21, 28, 6). Correlational analyses of these data revealed a significant positive correlation between these variables for the entire group of PPA participants ( $r = .64, p < .0001$ ) and for the nonfluent group alone ( $r = .527, p = .008$ ). However, 9 of the 13 nonfluent PPA-L participants performed at or above 80% accuracy on the NAT, whereas the nonfluent PPA-G participants' scores ranged from 40–60% correct.

## DISCUSSION

The present study examined fluency and grammatical ability in individuals with PPA by analysing speech samples derived from Cinderella story narratives. The primary purpose of the study was to determine whether or not these two dimensions of language pattern together in pre-assigned clinical PPA subtypes or if fluency and grammatical production can be differentially impaired within and across PPA subtypes. Results showed that when clinical PPA subtypes were compared with one another and with healthy controls, speech fluency, measured by words per minute and mean length of utterance in words, was disrupted in the agrammatic and logopaenic groups, with significantly reduced scores on both fluency variables compared to the healthy controls. Both the agrammatic and logopaenic groups also produced significantly fewer grammatical sentences compared to the semantic PPA group and the healthy controls. However, only the clinically agrammatic PPA group evinced significantly impaired production of verb inflection and verb argument structure

in their narrative speech. These findings indicate that although fluency is impaired in both agrammatic and logopaenic PPA, individuals with agrammatic PPA show greater impairments in the ability to formulate grammatical speech compared to logopaenic PPA speakers. This indicates that, indeed, fluency and at least some aspects of grammatical production dissociate from one another in the narratives of PPA speakers.

Interestingly, the group analyses also showed that the semantic PPA group, unlike either the agrammatic or logopaenic groups, produced abnormally low open-to-closed class ratios and noun-to-verb ratios. Compared to the normal speakers, the semantic PPA participants also produced fewer open- compared to closed-class words and fewer nouns compared to verbs. This occurred despite the lack of significant differences between the semantic PPA and healthy control groups for either WPM or MLU, our fluency measures. The Semantic PPA participants' diminished production of open-class words, compared with either of the other PPA groups, attests to their primary lexical-semantic rather than grammatical deficits.

In spite of the aforementioned dissociations between fluency and grammatical speech production, close inspection of the fluency data (i.e., WPM) showed that reduced fluency can be seen in individuals presenting with any clinical PPA subtype. All 12 individuals diagnosed with agrammatic PPA, 15 (of 20) with a diagnosis of logopaenic PPA, and 1 of 6 participants with semantic PPA showed WPM at least one standard deviation below the normal mean (i.e., below 113.4 WPM). This finding attests to the fact that fluency is not completely predictive of PPA subtype.

Correlations between fluency, in words per minute, and each grammatical variable further elucidated the relation between fluency and grammatical production in individual PPA speakers. That is, when the relation between fluency and each grammatical variable was computed using the data from all participants, significant correlations were found for all variables, with the exception of the proportion of correct noun morphology. However, when the same computations were undertaken using the data derived from only the nonfluent PPA speakers, no significant correlations were found, indicating that nonfluency and agrammatism are dissociated in many PPA speakers. Reduced fluency was dissociated from overall production of grammatical sentences, with some nonfluent speakers showing normal sentence production ability. This pattern also was found for word class production (i.e., open-to-closed class and noun-to-verb ratios) and for verb-related features, including correct verb inflection and verb argument structure production. Notably, however, examination of the scatter plots illustrated that, although some logopaenic PPA participants with low fluency scores also showed concomitantly low scores on some of the grammatical variables, a greater number of the nonfluent agrammatic PPA speakers showed abnormal grammatical production across variables. Even for production of correct noun morphology, which was not correlated with fluency based either on analysis of the full cohort or only of the nonfluent speakers, a greater number of nonfluent speakers clinically subtyped as agrammatic, compared to nonfluent speakers of other subtypes, showed abnormally low scores on this variable.

Similar patterns were noted with regard to the relation between fluency and sentence production ability as measured by the NAT. Although WPM and NAT performance were significantly correlated when the data from the PPA group as a whole were analysed and also when only the data from the nonfluent speakers were examined, the agrammatic nonfluent speakers performed more poorly on the NAT than the nonfluent logopaenic speakers. That is, the nonfluent agrammatic speakers scored

from 40% to 60% correct on the NAT, whereas, the nonfluent logopaenic participants scored from 70% to 100% correct, with no overlap in scores. These results reflect the fact that our subtyping methods incorporate NAT performance but they also validate the dissociation between speech fluency and grammar in an offline task.

Impairments in grammatical ability can manifest as an initial and highly prominent feature of PPA, which not only has relevance to associated neuropathology, but also has emerged as a key clinical marker for subtyping PPA (Mesulam et al., 2008, 2009). That is, agrammatic PPA (PPA-G) is associated with substantial atrophy in the left inferior frontal region (Mesulam et al., 2009). In addition, an autopsy series from our laboratory showed that PPA-G is most frequently caused by the neuropathology of frontotemporal degeneration with tauopathy (FTLD-TAU) (Mesulam et al., 2008). For example, the following samples of agrammatic output are taken from individuals with PPA who both showed subtypes of FTLD-Tau on post-mortem autopsy. One individual, when asked the reason for her visit to the clinic, said: "Syntax errors and no articles. . . Words in the my head and cut up . . . Writing syntax errors. Edit my work . . . computer." (Mesulam, 2007) and the second individual produced the following email: "I will come my house in your car and drive my car into Chicago . . . You will back get your car and my car park in the driveway. Love, Mom." (Mesulam, 2003). The first individual had Pick's disease; the second showed the pathology of corticobasal degeneration.

Although the importance of agrammatism is widely acknowledged, the term progressive nonfluent aphasia (PNFA), extensively used since its codification by Neary and colleagues (Neary et al., 1994), has encouraged the dichotomisation of the PPA syndrome into fluent and nonfluent varieties, an approach that had enjoyed success for classifying aphasias caused by stroke (Goodglass & Kaplan, 1983). Because fluency is arguably less difficult to measure than grammatical ability, the question has arisen of whether "nonfluent" could be considered a surrogate for "agrammatic", leading to a typology where fluency would be the driving marker for subtyping. Findings from the present study indicate that there is not a straightforward relation between fluency and grammatical ability, and therefore we discourage adopting this dichotomy alone for PPA subtyping. In addition, other work in our laboratories has shown that many individuals with PPA present with intermittent dysfluency caused by word-finding hesitations in the absence of clear agrammatic production patterns (Mesulam, 1982; Mesulam & Weintraub, 2008) and even different patterns of decline are manifest in individuals who show consistent nonfluent patterns, with some evincing increasingly severe patterns of agrammatic speech and others showing no signs of agrammatism per se, but instead gradual decline in lexical access in general (Thompson et al., 1997). These patterns led to the classification of logopaenic PPA, established in 2004 by Gorno-Tempini et al. (2004) and to its inclusion in the newly published consensus recommendations for clinical diagnosis and subtyping of PPA (Gorno-Tempini et al., 2011). Notably, for individuals diagnosed with logopaenic PPA, autopsy has confirmed a high incidence of Alzheimer pathology at post mortem (Mesulam et al., 2008). Hence, the dichotomous fluent-nonfluent distinction in PPA faces two problems: (a) clinically, it oversimplifies the spectrum of the phenotypes and (b) biologically, it mixes groups with different neuropathologic correlates.

Quantifying the speech output seen in PPA can, however, be challenging and debates remain with regard to the precise deficit patterns associated with PPA subtypes. Although most studies agree that the semantic variant is characterised by severe word retrieval and confrontation naming deficits (Gorno-Tempini et al., 2004;

Mesulam et al., 2009; Wilson et al., 2010) studies disagree with regard to the rate of speech production and grammatical complexity. That is, reduced fluency has been found in some studies (Ash et al., 2006, 2009) but not in others (Gorno-Tempini et al., 2004; Wilson et al., 2010), and Patterson and McDonald (2006) found less-elaborate syntax in the semantic variant compared to other PPA types, whereas Wilson and colleagues (2010) did not. The findings from the present study support previous reports of an association between fluent speech production and a high proportion of grammatically correct sentences in semantic PPA. In addition, our findings augment previous characterisations in that our semantic cohort produced few verb inflection or noun morphology errors and presented with normal access to verb argument structure. However, they used more closed-, compared to open-, class words and more verbs compared to nouns in their narrative production.

In contrast, previous studies have failed to completely elucidate linguistic variables that distinguish logopaenic PPA from other PPA variants. Indeed, with the exception of impaired repetition (see Gorno-Tempini et al., 2004, 2008) the basic and unique linguistic properties of logopaenic PPA have yet to be established. Interestingly, in the present study we also did not find any clearly defining characteristics of this clinical population. However, we did show that they may present with either fluent or non-fluent speech production and most, but not all, show a relatively high proportion of grammatically correct sentences even when speech is nonfluent, with a relatively normal distribution of open-class to closed-class words and nouns to verbs, although nouns may be more impaired than verbs. Furthermore, grammatical morphology is relatively spared for both nouns and verbs. Finally, our logopaenic PPA speakers showed relatively normal access to verb argument structure.

The characteristics of the agrammatic variant of PPA, similarly, have not been precisely established and the extent to which the characteristics of agrammatic PPA are similar to or different from those diagnosed as PNFA and/or whether their linguistic deficits are like those seen in individuals with agrammatism caused from stroke is not completely clear. Some studies have shown that individuals with nonfluent agrammatic PPA present patterns similar to those seen in stroke-induced agrammatic aphasia (Ash et al., 2006, 2009; Thompson et al., 1997), whereas other studies fail to find such an association (Graham et al., 2004; Patterson et al., 2006), and yet others suggest that, although most individuals with nonfluent PPA variants produce syntactic errors, these errors are not in line with those produced in aphasia resulting from stroke (Knibb et al., 2009; Wilson et al., 2010). Results of the present study show that the production patterns in our cohort of agrammatic PPA were very similar to those of stroke-induced agrammatic aphasia. The agrammatic speakers' output was invariably nonfluent, characterised by a reduction in the proportion of grammatical sentences produced, and a tendency to produce more open-class compared to closed-class words and more nouns compared to verbs, although not all agrammatic speakers showed this pattern. We also found that most agrammatic speakers present with difficulty in producing inflected verb forms and they show significant, and unique, difficulty with production of verb argument structure. This latter finding indicates that verb argument structure production, an essential component of grammatically correct sentences, is clearly impaired in individuals with PPA clinically subtyped as agrammatic, but it is not impaired in other PPA variants, even those who are similarly nonfluent but not clinically agrammatic, that is, logopaenic.

The findings from the present study suggest that the current tendency to combine agrammatism and nonfluency into a single clinical PPA subtype may result in inaccurate clinical classifications and, in addition, it may lead to variability in research findings because groups characterised as nonfluent may include both agrammatic and logopaenic PPA variants. The present study encourages researchers to consider fluency and grammar as separate variables and to use clinical measures that are sensitive for distinguishing the two. Specifically, we suggest that clinicians and researchers obtain and analyse narrative language samples as part of the diagnostic evaluation using narrative rather than picture description tasks and that, in addition, measures capable of elucidating sentence production patterns (e.g., the NAT, available at <http://www.soc.northwestern.edu/NorthwesternAnagramTest>) as well as grammatical morphology and verb argument structure be administered—for example, the Northwestern Assessment of Verbs and Sentences (NAVS; Thompson, experimental version), and the Northwestern Assessment of Verb Morphology (NAVI; Thompson, experimental version); both available at [www.communication.northwestern.edu/departments/csd/research/aphasia](http://www.communication.northwestern.edu/departments/csd/research/aphasia).

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