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Quantitative assessment of grammar in amyloid-negative logopenic aphasia

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Abstract

Logopenic primary progressive aphasia (lvPPA) typically results from underlying Alzheimer's disease, but subjects have been reported that do not show beta-amyloid (A β) deposition. These subjects do not differ on neurological and speech-language testing from A β -positive lvPPA, but they impressionistically show increased grammatical deficits. We performed a quantitative linguistic analysis of grammatical characteristics in A β -negative lvPPA compared to A β -positive lvPPA and agrammatic PPA, which is characterized by increased grammatical difficulties. A β -negative lvPPA used fewer function words and correct verbs but more syntactic and semantic errors compared to A β -positive lvPPA. These measures did not differ between A β -negative lvPPA and agPPA. Both lvPPA cohorts showed a higher mean length of utterance, more complex sentences, and fewer nouns than agPPA. A β -negative lvPPA subjects appear unique and share

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Author contributions:

JW and KJ were responsible for study design, study supervision and obtaining funding. KT and JW drafted the manuscript, which was revised by KJ, JD, RU, HC, MM, and ES. KT was responsible for the acquisition of linguistic data, data analysis, and statistical analysis. KJ, JD, MM, HC and ES were responsible for acquisition of clinical data. JW was responsible for the neuroimaging analysis. KT, JW, JD, RU, and KJ contributed to interpretation of data.

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linguistic features with both agPPA and A β -positive lvPPA. Quantitative language analysis in lvPPA may be able to distinguish those with and without A β deposition.

Keywords

Aphasia; logopenic; syntax; amyloid; PET; primary progressive aphasia; agrammatism

1.0 Introduction

Logopenic primary progressive aphasia (lvPPA) is a neurodegenerative language disorder that typically presents with language difficulties, including impaired single-word retrieval, difficulties repeating sentences, and phonological errors, which are believed to be caused by an impairment in the phonological loop of the verbal working memory (Gorno-Tempini et al., 2008; Gorno-Tempini et al., 2011; Henry & Gorno-Tempini, 2010; Whitwell, Duffy, et al., 2015).

These language difficulties differ from those found in agrammatic PPA (agPPA), which is characterized by agrammatic and telegraphic language production and grammatical simplification; more specifically, these language impairments include deficits with the production of inflectional morphology, lower proportion or complete omission of function words, higher proportion of nouns compared to other open class words, use of nonfinite (untensed) verb forms, syntactic argument structure errors, and overall reduced sentence and grammatical complexity (Ash et al., 2009; Avrutin, 2001; Grossman et al., 1996; C. K. Thompson, Ballard, Tait, Weintraub, & Mesulam, 1997; C. K. Thompson et al., 2012; Wilson et al., 2010).

The majority of patients who are diagnosed with lvPPA have underlying Alzheimer's disease (AD) pathology, showing beta-amyloid (A β) and tau deposition on PET imaging (M. Mesulam et al., 2008; Rabinovici et al., 2008; Whitwell, Jones, et al., 2015). Because of this, lvPPA is often considered an atypical AD variant. However, some patients do not show A β deposition on PET scanning and are thus believed to have underlying frontotemporal lobar degeneration, likely with TDP-43 pathology, (Josephs et al., 2014; Matías-Guiu et al., 2015; M. M. Mesulam et al., 2014; Santos-Santos et al., 2018; Spinelli et al., 2017; Whitwell, Jones, et al., 2015).

Imaging differences have been reported between lvPPA patients who differ in the presence versus absence of A β deposition: A β -positive lvPPA show increased grey matter atrophy in the right hemisphere, while the volume loss in A β -negative lvPPA is more localized in the left temporal region (Whitwell, Duffy, et al., 2015). Despite these structural differences, very few differences exist between lvPPA subjects who are A β -positive versus those who are A β -negative on neurological and speech-language testing (Whitwell, Jones, et al., 2015). However, a previous case report observed grammatical deficits in one A β -negative lvPPA patient that were uncharacteristic of typical lvPPA language difficulties (Rohrer, Crutch, Warrington, & Warren, 2010). To further investigate this finding of different language impairments in A β -negative lvPPA, we performed a quantitative analysis of the grammatical characteristics of A β -negative lvPPA subjects to determine whether their linguistic

properties differ from those of A β -positive lvPPA subjects and those of agrammatic PPA (agPPA) subjects, who characteristically have grammatical difficulties.

A cohort of 50 lvPPA subjects underwent neurological and speech-language assessments, as well as Pittsburgh Compound B (PiB) PET imaging to assess A β deposition. Six of these subjects were classified as A β -negative, as previously described (Whitwell, Jones, et al., 2015). The neurological, speech-language, genetic, and imaging findings have been previously reported for these six patients (Josephs et al., 2014; Whitwell, Jones, et al., 2015). These six subjects were compared to 15 A β -positive lvPPA and 15 agPPA participants, who were matched by age, gender, and Western Aphasia Battery Aphasia Quotient (WAB-AQ) score (Kertesz, 2007). The picture description task of the WAB was video recorded, and these speech samples were transcribed and coded for quantitative comparison between groups for syntactic structures and errors that have been shown to reveal agrammatic deficits; these included coding all grammatical categories, as well as semantic and syntactic errors, among other language variables (Ash et al., 2010; Tetzloff et al., 2018; Cynthia K Thompson & Mack, 2014). By quantifying their language production in this manner, we were able to compare the grammatical deficits of A β -negative lvPPA to their A β -positive lvPPA counterparts, as well as agPPA patients who are known to have syntactic deficits. We also assessed the patterns of grey matter atrophy in the A β -negative lvPPA, A β -positive lvPPA and agPPA subjects compared to controls to help us understand underlying neuroanatomical abnormalities.

2.0 Results

The three groups did not differ significantly in terms of age, gender, disease duration, education or WAB-AQ score (Table 1). No differences were observed between A β -negative and A β -positive lvPPA in neurological testing. The A β -negative group performed worse than agPPA on tests of verbal memory measured using the Auditory Verbal Learning Test, but did not differ from the A β -positive lvPPA group. However, all three groups performed comparably on testing of visual memory (Wechsler memory scale visual reproduction). The two lvPPA groups performed similarly on speech language testing, with A β -negative lvPPA showing worse sentence repetition than agPPA. Both lvPPA groups showed less Parkinsonism and apraxia of speech than the agPPA subjects. The neurological, neuropsychological and speech/language results of each individual A β -negative lvPPA subjects have been previously published (Josephs et al., 2014).

Upon analyzing the speech samples, A β -negative lvPPA used a smaller proportion of verbs and function words (e.g., determiners, prepositions, etc.), had significantly fewer verbs that were produced with correct morphology, showed fewer utterances that were grammatical and more utterances that lacked a finite (tensed) verb form, and produced more syntactic and semantic errors than A β -positive lvPPA subjects (Table 2). These measures did not differ between c lvPPA and agPPA.

Both A β -negative and A β -positive lvPPA subjects showed a higher mean length of utterance (MLU), a greater proportion of complex utterances, and a smaller proportion of nouns than agPPA subjects (Table 2). Sample transcriptions from each participant group can be found in

the Supplementary Material. Additionally, the grammatical results of each individual A β -negative lvPPA subject are shown in Table 3.

Both lvPPA groups showed grey matter loss in the temporoparietal lobes compared to controls, although the A β -negative subjects showed loss restricted to the left hemisphere and predominantly involved anterior regions of the temporal lobes (Figure 1). The agPPA group showed grey matter loss bilaterally in the frontal lobes, although with greater involvement of the left hemisphere, and particularly targeted inferior frontal and medial frontal regions, with some additional loss observed in the left temporoparietal lobe. The A β -negative lvPPA group did not differ from the other groups after correction for multiple comparisons. However, when assessed uncorrected at $p < 0.001$, they showed smaller volumes in left anterior temporal lobe, but greater volumes in bilateral frontal regions, including the inferior frontal gyrus, compared to agPPA, and greater volumes in scattered regions in the right hemisphere compared to A β -positive lvPPA.

3.0 Discussion

Despite a common diagnosis of aphasia, the presence versus absence of A β deposition may influence the speech characteristics of lvPPA. In our original description, A β -negative lvPPA subjects were not clinically judged to have agrammatism, because their speech output was not what is typically observed in agPPA (e.g., function word omission, subject-object reversal) (Josephs et al., 2014). However, the present quantitative language analysis revealed inadequacies in these subjects that their A β -positive lvPPA counterparts lacked. These included reduced production of function words and correct verbs, more syntactic and semantic errors, and a greater proportion of non-utterances. A β -negative lvPPA did not differ from agPPA on these measures. However, both lvPPA groups produced longer utterances, lower proportion of nouns, and more syntactically complex utterances than agPPA, demonstrating better overall syntactic performance in lvPPA, regardless of A β status. A β -negative lvPPA subjects, therefore, appear to have a unique linguistic profile, sharing grammatical features with both agPPA and lvPPA.

On neuroimaging, the patterns of grey matter loss in the A β -negative lvPPA group were more typical of lvPPA, with both lvPPA groups showing predominant involvement of the temporoparietal lobes; likely underpinning their deficits in naming and sentence repetition. The agPPA group showed more striking involvement of the frontal lobe, particularly the inferior frontal gyrus, as others have previously found (Botha et al., 2015; Gorno-Tempini et al., 2004; Josephs et al., 2006; M. Mesulam et al., 2008). The fact that damage to Broca's area was not observed in A β -negative lvPPA, as previously shown in detail (Whitwell, Jones, et al., 2015), could support a view that the linguistic abnormalities observed in this cohort are fundamentally different, with a different underlying etiology, to those observed in agPPA. It is possible that areas of the language network, aside from Broca's area, may be responsible for the linguistic abnormalities observed in A β -negative lvPPA (Grossman et al., 2013). Sentence production is indeed supported not only by Broca's area but also regions in the temporal and parietal lobes. A functional MRI study that assessed brain regions involved in a picture description task showed that missing verbs, reduced sentence complexity and omission of function words were associated with changes in activation of the left posterior

middle temporal gyrus and inferior parietal lobe, with the inferior frontal gyrus also involved in omission of function words (Schonberger et al., 2014). One structural difference between the lvPPA groups was that the A β -negative lvPPA subjects have significantly more grey matter atrophy in the left hemisphere than the right hemisphere, whereas A β -positive lvPPA show more bilateral patterns of degeneration (Whitwell, Duffy, et al., 2015). It is, therefore, possible that asymmetry of temporoparietal neurodegeneration could play a role in syntactic performance in A β -negative subjects.

Additionally, we previously showed that A β -negative lvPPA shows more hypometabolism on [^{18}F]fluorodeoxyglucose PET in anteromedial temporal regions compared to A β -positive lvPPA (Whitwell, Jones, et al., 2015). This could further explain the higher proportion of semantic errors and the general decreased syntactic performance in A β -negative subjects, as these regions compose part of the language network (Papathanassiou et al., 2000; Stowe, Haverkort, & Zwarts, 2005).

The implications of our findings to the diagnostic classification of our subjects deserve some discussion, as the presence of agrammatism is one of three exclusionary features for lvPPA (Gorno-Tempini et al., 2011). In regards to the consensus criteria for lvPPA, all of the A β -negative lvPPA subjects had a hesitant speech with word retrieval problems, all performed poorly on sentence repetition, and all performed poorly on tests of naming except for one, as previously published (Josephs et al., 2014). All but one subject had phonologic errors, all but one had spared word and object knowledge, and all had spared motor speech. Four of the subjects would meet criteria for lvPPA regardless of whether agrammatism was present or not, and two subjects would only meet criteria for lvPPA if agrammatism was absent. The linguistic analysis presented in this manuscript clearly illustrates that the speech output of the A β -negative subjects is abnormal and different from the A β -positive subjects, but whether these subjects should be labelled as agrammatic could be debated. On one-hand, the A β -negative subjects performed poorly on a number of the linguistic metrics that typically characterize agPPA. However, on the other hand, the speech samples from these subjects look qualitatively different from those produced by agPPA subjects (Josephs et al., 2014), as they produce longer utterances, lower proportion of nouns, and more syntactically complex utterances than agPPA, and they show no evidence for abnormalities in Broca's area on neuroimaging. Given these arguments, it is unclear whether the A β -negative lvPPA subjects should be considered to be agrammatic and hence a mixed variant of PPA (M. M. Mesulam et al., 2014; Spinelli et al., 2017), or whether they should be considered a distinct (Rohrer et al., 2010) or unclassifiable variant of PPA.

Both of the lvPPA groups were impaired on testing for verbal memory, although the A β -negative subjects performed worse. However, both lvPPA groups performed normally on a measure of visual memory suggesting they do have relatively preserved episodic memory, consistent with a root diagnosis of PPA. The diminished verbal memory in these groups is likely due at least in part to disruption of language function rather than a primary memory disorder affecting episodic memory more globally. Furthermore, none of the lvPPA subjects presented with complaints of memory loss, and in all subjects it was the language impairment that was affecting activities in daily living.

It is clear that the presence versus absence of A β deposition in lvPPA subjects corresponds to decreased syntactic performance in speech. These results suggest that quantitative assessment of language production in lvPPA may help identify A β -negative subjects in the absence of PET imaging. Identifying A β -negative cases would be particularly important to guide potential treatment strategies and to provide prognostic information for the patients.

4.0 Methods

All subjects were recruited from the Mayo Clinic, Department of Neurology, into an NIH-funded study investigating speech and language disorders. Each subject underwent a thorough speechlanguage evaluation by a speech language pathologist, and clinical diagnoses of lvPPA or agPPA were rendered by consensus after reviewing the clinical scores and video recordings of each subject, as previously described (Botha et al., 2015; Josephs et al., 2012). As part of the speech language battery, all subjects underwent testing with the WAB (Kertesz, 2007), and a total aphasia quotient (WAB-AQ) was calculated to provide a measure of overall aphasia severity. All subjects underwent a detailed neurological and neuropsychological battery, as previously published (Josephs et al., 2012). All subjects also underwent a Pittsburgh Compound B (PiB) PET scan to assess amyloid deposition and a 3 Tesla volumetric head MRI that included a magnetization prepared rapid gradient echo (MPRAGE) sequence with voxel dimensions of $1.2 \times 1.0 \times 1.0$ mm. A global PiB standard uptake value ratio was calculated for each subjects and of the 50 lvPPA subjects, six were found to be amyloid-negative based on a cut-point of 1.5, as previously described (Josephs et al., 2014; Whitwell, Jones, et al., 2015). These six subjects were then compared to 15 amyloid-positive lvPPA and 15 agPPA subjects for this study, who were matched by age, gender, and WAB-AQ score.

As part of the WAB, subjects were asked to describe a picture of a picnic scene and speak in sentences. The language samples were transcribed and coded in CHAT transcription format for use in the Computerized Language Analysis software (CLAN) (MacWhinney, 2000) by KAT. The transcriptions included word-level codes for various grammatical categories including nouns, verbs, and function words (e.g., articles, prepositions, pronouns, and other closed-class words), in addition to inflectional and derivational morphemes. Semantic errors, including incorrect words and non-specific word substitutes, such as using “thing” or “stuff” instead of the specific noun were marked. Syntactic errors were also coded, which included incorrect verbal morphology, non-finite (untensed) verb forms, and argument structure errors. Utterances were given an additional code of grammatical (0 errors), ungrammatical (1 error), or non-utterance (no finite/tensed verb). The number of utterances and words; mean length of utterance (MLU), which is the average number of morphemes per sentence; verb, noun, and function word counts; number of semantic and syntactic errors, number of complex utterances, and number of each utterance type were calculated using Computerized Language Analysis (MacWhinney, 2000). These variables, which reveal syntactic and agrammatic deficits (Ash et al., 2010; Cynthia K Thompson & Mack, 2014), were calculated as ratios to account for differences in number of utterances and words produced across speakers. Variables were compared between groups using Wilcoxon rank-sum tests, and p-values were corrected for multiple comparisons using false discovery rate (FDR) correction in RStudio (RStudio, 2015).

Patterns of grey matter atrophy were assessed in the three subject groups (lvPPA(-), lvPPA(+) and agPPA) compared to a group of 15 healthy controls that underwent an identical MRI protocol (median [IQR] age at MRI = 56 [59–64], 67% female). All MPRAGE scans were spatially normalized to the Mayo Clinic Adult Lifespan Template (MCALT) (<https://www.nitrc.org/projects/mcalt/>) and segmented using the unified segmentation model (Ashburner & Friston, 2005) in SPM12 with MCALT tissue priors. The custom template space grey matter segmentations were modulated and smoothed at 8 mm full width at half maximum. Voxel-level comparisons were performed using two-sided T-tests in SPM, with results assessed at $p < 0.01$ after correction for multiple comparisons using false discovery rate correction. Age and gender were included in the analysis as covariates.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Amyloid-negative lvPPA subjects have a unique linguistic profile.
- Amyloid-negative lvPPA has some language features similar to amyloid-positive.
- Amyloid-negative lvPPA also shares language features with agrammatic PPA.
- The speech of lvPPA can help distinguish amyloid-negative versus -positive subjects.

Statement of significance:

We found a relationship between the presence versus absence of beta-amyloid deposition and impaired syntactic performance in a group of lvPPA subjects.

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Figure 1: Patterns of grey matter loss in A β -negative lvPPA, A β -positive lvPPA and agPPA compared to controls.

Results are shown on three dimensional brain renderings using BrainNet Viewer (<http://www.nitrc.org/projects/bnv/>), with results shown corrected for multiple comparisons using the false discovery rate correction at $p < 0.01$.

Table 1:

Demographics and clinical results

	A β (-) lvPPA n=6	A β (+) lvPPA n=15	agPPA n=15	A β (-)~A β (+) FDR p-value	A β (-)~agPPA FDR p-value	A β (+)~agPPA FDR p-value
Demographics						
Age at assessment, years	66 (59.5, 68)	66 (58.5, 68)	65 (59, 71.5)	0.30	0.54	0.56
Gender (%female)	0.33	0.60	0.53	0.31	0.44	0.74
Disease duration, years	2 (2, 2.8)	4 (3, 4.8)	2.5 (2, 3.5)	0.22	0.38	0.43
Education	17.5 (14.8, 18)	16 (13, 17)	13 (12, 16)	0.96	0.50	0.67
Age at onset, years	63 (57.3, 65.8)	62 (55, 64.5)	60 (54.8, 69)	0.13	0.34	0.94
Neurological assessments						
Mini-Mental Status Examination (/30)	26.5 (25.3, 27.8)	25 (23.5, 26.5)	28 (25, 29)	0.41	0.40	<0.01*
Montreal Cognitive Assessment Battery (/30)	17 (14, 17.8)	16 (14.5, 20.5)	24 (22, 25.5)	0.45	0.02*	0.06
Clinical Dementia rating sum of boxes (/18)	2.5 (0.5, 3.8)	3.5 (1.8, 5)	0.5 (0, 1.8)	0.99	0.40	0.63
Frontal Assessment Battery (/18)	10 (6.5, 13.5)	13 (11, 14.5)	14 (12.5, 16)	0.11	0.08	0.48
NPI-Q (/36)	2 (1.3, 1.8)	3 (1.5, 4)	2 (1.5, 4)	0.49	0.90	0.04*
WAB limb apraxia (/60)	56.5 (54.5, 58.5)	58 (56, 58)	55 (51.5, 56)	0.49	0.73	0.04*
MDS-UPDRS III (/132)	6 (4, 8)	4 (1, 6.5)	10 (6, 20.3)	0.52	0.04*	0.62
Neuropsychological assessments						
Trail Making Test A MOANS	9 (6.8, 9.8)	6 (3.3, 9)	7 (4.5, 9.5)	0.71	1.00	0.81
Trail Making Test B MOANS	6.0 (2.0, 7.0)	6.5 (3.3, 7.7)	6.0 (4.0, 7.0)	0.67	0.68	0.88
DKEFS card sort scaled score	5 (1.8, 6)	7.5 (4, 8)	8 (5, 9)	0.15	0.13	0.18
WMS III VR % retention scaled score	9.5 (8, 12.5)	10 (7, 11.5)	12 (9.5, 13)	0.66	0.21	0.12
AVLT Trial 5 raw	3.5 (2.3, 4.8)	6.5 (2.3, 8)	9 (6.5, 10.5)	0.50	0.03*	0.23
AVLT long-delay % retention MOANS	5 (3.5, 5.8)	5.5 (3.5, 7.8)	8 (7, 9.5)	0.70	0.03*	0.23
AVLT total learning trials 1 – 5	12.5 (12, 17.5)	25 (18.5, 29)	32 (26.5, 34.5)	0.40	0.02*	0.23
VOSP letters	19 (18, 20)	19 (19, 20)	20 (19, 20)	0.88	0.34	0.19
VOSP cubes	10 (9.3, 10)	9 (4.5, 10)	9.5 (8.3, 10)	0.87	0.38	0.12
Speech and language assessments						
Token Test (/22)	9 (7, 13)	14 (9, 16)	14 (8.5, 17.5)	0.85	0.38	0.51

	$A\beta(-)$ lvPPA n=6	$A\beta(+)$ lvPPA n=15	agPPA n=15	$A\beta(-) \sim A\beta(+)$ FDR p-value	$A\beta(-) \sim agPPA$ FDR p-value	$A\beta(+)\sim agPPA$ FDR p-value
Demographics						
WAB aphasia quotient (/100)	82.3 (75.6, 88.7)	85.2 (83, 88.8)	84.9 (79.7, 87.4)	0.41	0.76	0.40
WAB information content (/10)	8 (8, 8)	9 (8, 10)	9 (8, 10)	0.41	0.67	0.25
WAB fluency (/10)	8 (6, 9)	8 (8, 9)	6 (5.5, 9)	0.90	0.23	0.13
WAB repetition (/10)	7.5 (6.8, 8.1)	8 (7, 8.4)	8.8 (8.4, 9.1)	0.71	0.16	0.07
WAB repetition items 10–15 (/66)	37 (32.5, 44.5)	46 (37, 50.5)	52 (49, 56)	0.44	0.04	0.22
Boston Naming Test (/15)	11 (4.3, 11.8)	8 (5.5, 11.5)	13 (11, 14)	0.68	0.47	<0.01*
Action fluency	6 (4.3, 8.5)	8 (5, 9.5)	10 (7, 12)	0.84	0.61	0.35
Pyramids and Palm Trees (/52)	47 (45.3, 50.3)	49 (46.5, 50)	49 (47.3, 50.8)	0.90	0.47	0.47
Apraxia of Speech Rating Scale (/64)	1.5 (0.3, 3.5)	2 (1, 3.5)	21 (7, 25)	0.98	<0.01*	<0.01*

Data are shown as Median (IQR). Values significant after FDR correction are marked with an asterisk.

NPI-Q = Neuropsychiatric Inventory brief questionnaire version; WAB = Western Aphasia Battery; MDS-UPDRS III = Movement Disorders Society sponsored revision of the Unified Parkinson's Disease Rating Scale; MOANS = Mayo Older American Normative Studies; DKEFs = Delis-Kaplan Executive Function System; WMS-III VR % retention = Wechsler memory scale visual reproduction, percent retention; AVLT = Auditory Verbal Learning Test; VOSP = Visual Object and Space Perception Battery

The MOANS, WMS-III VR % scaled score and DKEFS Card Sort are constructed to have a mean of 10 and standard deviation of 3 in cognitively healthy participants

Table 2:

Linguistic results

Grammatical/language measures	A β (-) IvPPA n=6	A β (+) IvPPA n=15	agPPA n=15	A β (-)~A β (+) FDR p-value	A β (-)~agPPA FDR p-value	A β (+)~agPPA FDR p-value
Utterances	10.5 (8, 13)	11 (8, 12.5)	9 (7, 13.5)	0.842	0.937	0.933
Mean length of utterance (MLU)	12.26 (7.58, 15.00)	12.09 (10.60, 13.21)	7.00 (4.82, 8.44)	0.970	0.036*	<0.0001*
Word count	94.5 (68, 118.75)	112 (79.5, 118.5)	57 (34, 88)	0.622	0.173	0.006*
Ratio of Verbs: total words	0.15 (0.13, 0.16)	0.17 (0.16, 0.19)	0.15 (0.14, 0.17)	0.047*	0.791	0.021*
Ratio of Nouns: total words	0.21 (0.20, 0.23)	0.22 (0.19, 0.25)	0.32 (0.29, 0.41)	0.791	0.001	<0.0001*
Ratio Function words: total words	0.37 (0.34, 0.38)	0.47 (0.43, 0.52)	0.44 (0.37, 0.47)	0.005*	0.213	0.245
Ratio of Correct verbs: total verbs	0.87 (0.85, 0.887)	1 (1, 1)	0.83 (0.44, 0.92)	<0.001*	0.413	<0.0001*
Ratio of Grammatical utterances: total utterances	0.44 (0.33, 0.53)	0.89 (0.74, 0.92)	0.36 (0.21, 0.56)	0.002*	0.559	<0.0001*
Ratio of Ungrammatical utterances: total utterances	0.42 (0.21, 0.49)	0.09 (0.04, 0.22)	0.50 (0.26, 0.66)	0.050	0.436	<0.001*
Ratio of Non-utterances: total utterances	0.10 (0.02, 0.26)	0 (0, 0)	0.14 (0, 0.30)	0.004*	0.968	0.002*
Ratio of Complex utterances: total utterances	0.14 (0.03, 0.56)	0.15 (0.10, 0.38)	0 (0, 0)	0.969	0.013	<0.001*
Ratio of Semantic errors: total words	0.04 (0.02, 0.06)	0.01 (0, 0.02)	0.02 (0, 0.05)	0.008*	0.411	0.090
Ratio of Syntactic errors: total words	0.02 (0.01, 0.04)	0 (0, 0)	0.03 (0.01, 0.06)	0.005*	0.459	<0.0001*

Data are shown as Median (IQR). Values significant after FDR correction are marked with an asterisk.

Table 3:

Individual linguistic results for the six A β -negative lvPPA subjects

Grammatical/language measures	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Subject 6
Utterances	13	8	13	13	5	8
Mean length of utterance (MLU)	11.39	15.63	18.54	6.31	5.2	13.13
Word count	123	106	213	63	24	83
Ratio of Verbs: total words	0.15	0.14	0.13	0.16	0.08	0.22
Ratio of Nouns: total words	0.2	0.23	0.23	0.25	0.17	0.19
Ratio Function words: total words	0.38	0.37	0.38	0.44	0.33	0.33
Ratio of Correct verbs: total verbs	0.85	0.87	0.88	0.87	0.96	0.83
Ratio of Grammatical utterances: total utterances	0.31	0.5	0.54	0.77	0.2	0.38
Ratio of Ungrammatical utterances: total utterances	0.38	0.5	0.46	0.15	0	0.8
Ratio of Non-utterances: total utterances	0.31	0	0	0.08	0.8	0.13
Ratio of Complex utterances: total utterances	0.15	0.13	0.69	0	0	0.75
Ratio of Semantic errors: total words	0.06	0.01	0.03	0.02	0.08	0.05
Ratio of Syntactic errors: total words	0	0.01	0.01	0.03	0.04	0.05