Automated analysis of lexical features in Frontotemporal Degeneration

Sunghye Cho¹, Naomi Nevler², Sharon Ash², Sanjana Shelledi², David J. Irwin², Lauren Massimo², Katya Rascovsky², Christopher Olm²³, Murray Grossman², Mark Liberman¹

¹ Linguistic Data Consortium, University of Pennsylvania, Philadelphia, PA, USA
² Department of Neurology and Penn Frontotemporal Degeneration Center, University of Pennsylvania, Philadelphia, PA, USA
³ Department of Radiology and Penn Image Computing and Science Laboratory, University of Pennsylvania, Philadelphia, PA, USA

Please address correspondence to:
Sunghye Cho
Linguistic Data Consortium
3600 Market Street, Suite 810
University of Pennsylvania
Philadelphia, PA, 19104-2653
e-mail: csunghye@ldc.upenn.edu
voice: 215-898-0464

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Abstract

We implemented an automated analysis of lexical aspects of semi-structured speech produced by three patient groups with Frontotemporal degeneration (FTD): behavioral variant FTD (n=74), semantic variant Primary Progressive Aphasia (svPPA, n=42), and nonfluent/agrammatic PPA (naPPA, n=22). With a natural language processing program, we automatically tagged part-of-speech categories of all words and rated nouns for lexical measures, and computed the cross-entropy estimation, which is a measure of word predictability. Our automated analysis was a valid reflection of manual scoring. For svPPA patients, we found fewer unique nouns and more pronouns and wh-words than in the other patient groups and the controls; high abstractness, ambiguity, frequency, and familiarity for nouns they produced; and the lowest cross-entropy estimation among the groups. These measures were associated with cortical thinning in the left temporal lobe. In naPPA patients, we found increased speech errors, which were associated with cortical thinning in the left middle frontal gyrus. bvFTD patients were similar to the controls. Our results underline distinct word use profiles in subgroups of PPA patients and validate our automated method of analyzing FTD patients’ speech.

Keywords

Frontotemporal degeneration, semantic measures, Primary Progressive Aphasia, Part-of-speech
1. Introduction

Speech production is a complex, intentional, planned activity. Speakers select appropriate words from their lexicon that are consistent with the meaning of an intended message, arrange words into a specific order following syntactic rules of the language, plan their articulations, and articulate the prepared message following the phonological rules of the language. This involves multiple brain regions and we can expect that patients with degenerative brain conditions to show impaired speech compared to healthy adults. Moreover, depending on the form of disease, we can expect distinct impairment profiles. In this study, we investigate linguistic impairments in patients with frontotemporal degeneration (FTD), by implementing a fully automated method of lexical analysis.

FTD refers to a group of disorders caused by atrophy in the brain’s frontal, temporal, and parietal lobes which is related to the underlying accumulation of abnormal Tau or TDP proteins. The disorders we are investigating include different forms of primary progressive aphasia (PPA), in particular semantic variant PPA (svPPA), nonfluent/agrammatic variant PPA (naPPA), and also behavioral variant frontotemporal dementia (bvFTD). Patients with svPPA, also known as semantic dementia, are characterized by semantic impairment and difficulties in confrontation naming and lexical retrieval (Amici et al., 2007; Hodges & Patterson, 2007). Previous studies reveal that svPPA patients have difficulty in processing words denoting concrete objects (Bonner, Price, Peelle, & Grossman, 2016; Bonner et al., 2009; Breedin, Saffran, & Coslett, 1994; Cousins, York, Bauer, & Grossman, 2016; Cousins, Ash, Irwin, & Grossman, 2017; Macoir, 2009), but their prosody and syntax are less disrupted (Adlam, Bozeat, Arnold, Watson, & Hodges, 2006, Ash et al. 2006; Ash et al., 2009; Nevler, Ash, Irwin, Liberman, & Grossman, 2019; Thompson & Mack, 2014). It has also been observed that svPPA patients’ lexical retrieval is related to word familiarity and frequency (Bird et al., 2000; Hodges & Patterson, 2007; Rogers, Patterson, Jefferies, & Lambon Ralph, 2015). Patients with naPPA, also known as progressive non-fluent aphasia, present with effortful speech, slow speech rate, grammatical simplification, and speech errors or apraxia of speech (AoS) (Ash et al., 2009; Grossman, 2012; Grossman et al., 1996; Josephs et al., 2006; Ogar, Dronkers, Bramati, Miller, & Gorno-Tempini, 2007). These patients may also have difficulty retrieving verbs (Hillis, Oh, & Ken, 2004; Hillis, Tuffiash, & Caramazza, 2002; Rhee, Antiquena, & Grossman, 2001). Patients with bvFTD undergo changes in personality, behavior, and social cognition, and may present impairments in behaviors, such as apathy and lack of motivation. Previous studies have reported that bvFTD patients have subtle linguistic deficits with reduced retrieval of abstract words, reduced speech rate, tangential speech with irrelevant subject matter, and limited narrative expression (Ash et al., 2006; Cousins et al., 2017; Farag et al., 2010; Gunawardena et al., 2010; Hardy et al., 2016).

While valuable, most previous studies have relied on subjective, manual assessments of speech, which require a substantial amount of time, labor, and cost. There are also potential difficulties with manually coding the part of speech (POS) categories of every token, so previous studies on the POS analysis have rarely examined every word of an utterance. This is a problem in studying language use of patients with dementia, because many previous studies have shown that patients with dementia tend to produce fewer words than controls (e.g., Ash et al. 2013; Slegers et al., 2018; Tappen et al., 2002), but failed to show in detail which POS categories were reduced in which patient groups due to the efforts required for manual POS tagging. Because of the effort
involved, large-scale studies are rarely performed. The present study describes implementation of a novel, quantitative, reproducible, automated approach to studying lexical characteristics of patients with FTD. We show that the results from our novel methods are reliable and comparable with validation of previous manual findings. We also provide novel findings by directly examining all POS categories from a semi-structured speech sample elicited during a picture description task. Few groups beyond ours have compared FTD subgroups on various language measures and studied part of speech expression in behavioral variant frontotemporal degeneration (bvFTD), and this is the first comprehensive assessment of part-of-speech expression in bvFTD of which we are aware. Also, a picture description task provides a more natural source of speech than repetition or confrontation naming and imposes fewer task-related resource demands than highly controlled experimental studies. The use of a picture to guide speech facilitates judgments of accuracy compared to free conversational speech. We further focus on lexical-semantic aspects of FTD patients’ speech because the lexicon is important in verbal communication where the goal is to convey meaningful messages to interlocutors. Our novel, automated technique for text analysis is based on a modern natural language processing (NLP) program and examines speech samples in a large cohort of FTD patients. Based on previous findings, we hypothesize the following:

- Frequencies of POS categories from an automated POS tagger and lexical ratings are valuable measures in distinguishing naPPA, svPPA and bvFTD patient groups.
  - In particular, we expect that svPPA patients would produce fewer nouns but more pronouns than the other patient groups due to their impairment in confrontation naming. We also expect patients with svPPA would produce more wh-words (e.g., “What is this?”), since they have difficulties in retrieving the names of objects. We also expect that their nouns are different in various lexical measures from those produced by the other patient groups due to their semantic impairment. Furthermore, we expect these language features will be related to regions of cortical thinning in svPPA patients.
  - We expect that naPPA patients would differ from the other patient groups in their frequency of speech errors and partial words and verbs due to AoS and their difficulties in retrieving verbs. We also expect these measures will be related to cortical thinning in naPPA patients’ brains.

2. Methods

2.1 Participants

We examined 138 patients with FTD diagnosed by experienced neurologists (M.G., D.J.I.) in the Department of Neurology at the Hospital of the University of Pennsylvania according to published criteria (Gorno-Tempini et al., 2011; Rascovsky et al., 2011). This includes 74 patients with bvFTD, 22 patients with naPPA, and 42 patients with svPPA. Among the svPPA patients, we included 32 cases with concomitant mild behavioral features, a common co-occurrence. These patients did not significantly differ from the other 10 svPPA patients without behavioral impairment in terms of demographic characteristics or their linguistic performance. We also included 37 healthy seniors as a control group. The Institutional Review Board of the Hospital of
the University of Pennsylvania approved the study of human subjects, and written consent was obtained from all participants.

All participants (n=175) were native speakers of English. The participants were matched on education level, but not on age and sex ratio (Table 1). bvFTD patients were significantly younger than naPPA patients and controls (vs. naPPA: p=0.002, vs. control: p=0.007). svPPA patients were also significantly younger (vs. naPPA: p=0.007, vs. control: p=0.029). There were more females in the control group than in the bvFTD group (p=0.006) although the sex ratio was not different among the patient groups. Patient groups were matched on disease duration (p=0.24) and Mini Mental State Exam (MMSE, p=0.47).

We also measured patients’ performance on neuropsychological assessments (Table 1) with the Boston Naming Test (BNT, Kaplan, Goodglass, & Weintraub, 2001), Pyramids and Palm Trees Test (PPT, Howard & Patterson, 1992), and Animals and Tools Category Naming Fluency (Lezak, Howieson, & Loring, 1983) to assess semantic knowledge. As expected, in BNT, where participants were asked to name an object, svPPA patients had significantly lower scores than the other groups (p<0.001 for all three pairwise comparisons). Patients with bvFTD also significantly scored lower on the BNT than healthy controls (p=0.01). On PPT, where participants were asked to choose one of two words that was more closely related to a target word, svPPA patients had lower scores than controls (p<0.001) and naPPA patients (p=0.012), and bvFTD patients also scored lower than controls (p<0.001). All patient groups performed poorly in the category fluency tasks, where participants were asked to name items in a given category (either animals or tools), compared to controls (p<0.001 for all three pairwise comparisons). The difference in the fluency task scores between bvFTD and svPPA patients was also significant (p<0.001). The participants’ demographic and neuropsychological characteristics are summarized in Table 1.

Table 1: Clinical and demographic characteristics of all participants.

|                         | control (N=37) | bvFTD (N=74) | naPPA (N=22) | svPPA (N=42) | p-value |
|-------------------------|----------------|--------------|--------------|--------------|---------|
| **Sex**                 |                |              |              |              |         |
| Female (N, percent)     | 24 (64.9%)     | 26 (35.1%)   | 11 (50.0%)   | 23 (54.8%)   | 0.019   |
| Male (N, percent)       | 13 (35.1%)     | 48 (64.9%)   | 11 (50.0%)   | 19 (45.2%)   |         |
| **Education: Mean, (SD)** | 15.9 (2.5)     | 15.8 (2.8)   | 15.3 (3.1)   | 15.1 (2.8)   | 0.437   |
| **Age (years): Mean, (SD)** | 68.5 (7.9)     | 63.1 (8.7)   | 70.4 (9.4)   | 63.3 (7)     | <0.001  |
| **Disease duration (years): Mean, (SD)** | -              | 4.4 (3.5)    | 3.2 (1.9)    | 3.9 (2)      | 0.239   |
| **Time between MRI & cookie theft (months): N**  | -              | 42           | 8            | 26           | 0.326   |
| Mean (SD)               | -              | 2.2 (1.9)    | 1.7 (1.7)    | 2.8 (2.6)    |         |
| **Mini mental state exam (0-30): N**  | 31             | 68           | 20           | 38           | <0.001  |
| Mean (SD)               | 29.2 (1)       | 23.6 (5.5)   | 22.7 (6)     | 22.1 (6.3)   |         |
| **BNT (0-30): N**       | 23             | 68           | 16           | 40           | <0.001  |
Mean (SD) | 27.9 (2.5) | 23.8 (5.8) | 24.7 (4.6) | 7.5 (6.4) \\
---|---|---|---|---
Animals and Tools (Max 60 sec): N | 23 | 65 | 16 | 39 | <0.001 \\
  Mean (SD) | 16.8 (4.6) | 9.2 (5.2) | 8.2 (4.4) | 5.1 (3.8) \\
---|---|---|---|---
PPT (0-52): N | 18 | 35 | 7 | 19 | <0.001 \\
  Mean (SD) | 50.8 (1.9) | 42.9 (7.9) | 48.4 (2.9) | 39.6 (6.6) \\

2.2 Picture description procedure

The participants were asked to describe the Cookie Theft picture from the Boston Diagnostic Aphasia Examination (Goodglass & Kaplan, 1983), and descriptions were digitally recorded. Patients were prompted to continue describing the picture after several seconds of silence up to 60 seconds after the beginning of the description. Recordings were transcribed by a linguist (S.A.) blinded to the clinical features and group membership of the participants, and further reformatted and time-stamped by trained, blinded annotators at the Linguistic Data Consortium (LDC) of the University of Pennsylvania. We note that no part of the study procedures or analyses were pre-registered prior to the research being conducted.

2.3 POS tagging

We employed spaCy (Honnibal & Johnson, 2015; https://spacy.io), an NLP library in Python, to automate the POS tagging process. spaCy has two different schemes of POS tagging. One is the OntoNotes 5 (Weischedel et al. 2013) version of the Penn Treebank tag set (Marcus, Santorini, & Marcinkiewicz, 1993). spaCy also maps the Penn Treebank tag to the simpler Google Universal POS tag set (Petrov, Das, & McDonald, 2012). Here we mainly reported the Google Universal POS tag results, and the Penn Treebank tag results were used only to calculate the number of tense-inflected verbs (see below). The POS lists are included in the Appendix (Table A).

We wrote a Python program (S.C.) so that spaCy automatically tokenized each utterance in the transcripts with its default language model and annotated the POS category and the lemma for each word. We had 21,990 POS tokens in total. The token count of each POS category was tallied for each participant, and the number of each POS category per 100 words was calculated.

The POS annotation scheme of spaCy uses “X” to tag words that do not exist in its language model. For example, sprtkljlgl would be tagged as X, since the word is not a valid English word. Patients did not produce many non-English words during the picture description task, but they produced many partial words and speech errors, which looked like non-English words. For example, in an utterance, “There’s a pu- um a plate,” produced by one of our patients, pu- was tagged as X by spaCy, since it is not an English word. We compared the frequency of this category by group in order to evaluate the frequency of speech errors and partial words in naPPA patients.

We also calculated the number of tense-inflected verbs per 100 words, the number of unique nouns per 100 words, the number of w/h-words per 100 words and the total number of words in each speech sample, using the POS tags and lemma counts. First, we summed all tokens
produced by each participant for the total number of words. This measure included partial words and speech errors. The number of tense-inflected verbs was calculated by summing the number of modal auxiliary verbs, the number of past tense verbs, and the number of present tense verbs, using the Penn Treebank tags. This sum was used to compute the number of tense-inflected verbs per 100 words. We counted the number of unique lemmas in each speech sample and calculated the number of unique nouns per 100 words, controlling for the total number of words. We also counted the number of wh-words, “what” and “who”, using a Python script, and calculated the number of wh-words per 100 words to examine clinical observations that svPPA patients use more wh-words to ask objects’ names than the other groups due to their impairments in object knowledge. To see if the ratio of POS categories differed by group, we calculated the ratio of content words to function words per each participant. The calculated measures were used for between-group comparisons, covarying for age and sex.

2.4 Lexical parameters

We performed additional analyses of nouns because of their potential value in distinguishing FTD patient groups. We rated nouns for abstractness on a continuum from concrete to abstract (Brysbaert, Warriner, & Kuperman, 2014), semantic ambiguity (number of a given word’s meanings in a context, Hoffman, Lambon Ralph, & Rogers, 2013), word frequency (defined as word frequency per million words in a log10 scale, Brysbaert & New, 2009), age of acquisition (Brysbaert, Mandera, & Keuleers, 2018) and word familiarity (z-standardized measure of the number of people who know a given word, Brysbaert et al., 2018). We wrote a Python program (S.C.) to automatically rate these parameters for all nouns that spaCy annotated. We built a pipeline in the program which (1) rated a word if a word was listed in the published database and (2) rated the lemma of a word if a word was not listed in the published database but its lemma was (e.g., overflowed ⇒ overflow). The program excluded a word if neither the word nor its lemma was included in the lists (e.g., countertop, Mary Jane). The abstractness ratings ranged from 1 to 5, where the most concrete was 5 and the most abstract was 1. For clearer representation, we inverted the scale so that the most concrete was 1 and the most abstract was 5.

Along with these measures, we also computed cross-entropy estimation using all the words of the participants’ speech. Cross-entropy estimation is a measurement to estimate the predictability of all words of a document with respect to their predictability in a larger language sample. For example, high cross-entropy (uncertainty) is observed in a document that uses surprising words given the source language sample. A computational linguist (M.L.) computed the cross-entropy estimation of the speech samples by patients, based on a 1-gram language model of three large-scale corpora: the SUBLEXTus (Brysbaert & New, 2009), Fisher English Training Speech (Cieri, Graff, Kimball, Miller, & Walker, 2004), and Switchboard (Godfrey & Holliman, 1997).

We also calculated lexical diversity to see how diverse a patient’s vocabulary usage was. Traditionally, lexical diversity has been measured using the type/token ratio, where type is the number of unique words and token is the number of instances of all words. However, type/token ratio has the disadvantage that the measure is affected by the total number of words. To cope with this challenge, various approaches have been suggested by previous studies (e.g., Covington & McFall, 2010; Jarvis, 2002; McKee, Malvern, & Richards, 2000; Moscoso del Prado Martín, 2017; Tweedie & Baayen, 1998). In this study, we used the moving-average type/token ratio (Covington & McFall, 2010), which has been reported to be a stable measure for lexical diversity.
(Cunningham & Haley, 2020). This measure calculates a type/token ratio for a fixed-length window, moving one word at a time from the beginning to the end of a text document, and averages type/token ratios from all windows. We varied the length of windows from 20 to 35 words by 5-word increments. Since the results were the same regardless of the window size, we only reported results from 20-word windows.

2.5 Imaging methods

High resolution T1 volumetric brain MRI data that were collected on a Siemens 3.0T Trio scanner at 1mm isotropic resolution was available for a subset of our patients (n=94): 18 controls, 42 bvFTD, 8 naPPA, and 26 svPPA patients. The mean time interval between MRI and speech sample collections was 1.95 months (SD=2.11 months). Clinical and demographic characteristics of this subset of patients matched those of the patients in the full dataset (Table 1) and did not differ by group. The linguistic measurements of these patient groups are summarized in the Appendix (Table B).

Sixty-five images were collected in an axial plane with repetition time=1620 msec, echo time=3.87 msec, slice thickness=1.0 mm, flip angle=15°, matrix=192x256, and in-plane resolution=0.9766x0.9766 mm. Twenty-nine images were collected with a sagittal acquisition with repetition time=2300 msec, echo time=2.95 msec, slice thickness=1.2 mm, flip angle=9°, matrix=256x240, and in-plane resolution=1.05x1.05 mm. Briefly, whole-brain MRI volumes were preprocessed using the antsCorticalThickness.sh processing pipeline, implemented using the Advanced Normalization Tools (ANTs) (https://github.com/ANTsX/ANTs; Tustison et al., 2014). Cortical thickness was estimated at each voxel of the cortex using the DiReCT algorithm (Das, Avants, Grossman, & Gee, 2009). easy_lausanne (https://github.com/mattcieslak/easy_lausanne; Daducci et al., 2012) was run on our local template, which was created based upon data from the Open Access Series of Imaging Studies (OASIS) (Marcus, Fotenos, Csernansky, Morris, & Buckner, 2007), to create a standard cortical parcellation. The template parcellation was then spatially normalized to each participant’s native T1 space using the template-to-native T1 warps generated by ANTs, and then we calculated the mean cortical thickness in each region of interest (ROI) of the Lausanne250 scale, which we used for our analysis.

To identify regions of atrophy in svPPA and naPPA patients, we compared cortical thickness of all patients in each patient group with those of the controls for all cortical regions of interest (ROIs), and selected our specific ROIs per patient group, where patients’ cortical thickness was significantly thinner than that of the controls (p<0.01 for svPPA and p<0.05 for naPPA patients; both uncorrected p-values). We applied a more lenient p-value threshold in selecting ROIs for naPPA patients due to the small number of patients with MRI data.

2.6 Statistical considerations

We standardized patient performance with a z-score scale relative to control performance for the lexical measures, such as concreteness, except for the frequency of the POS categories per 100 words. This standardization process enabled us to compare the various linguistic measures directly despite different scales. Levene’s test for homogeneity of variance, residuals and Q-Q plots were employed to validate the requirements for parametric tests. Group comparisons were performed with Analysis of Covariance (ANCOVA) for the frequency of the POS category per
100 words or the lexical measures as a dependent variable and phenotype as an independent variable. We introduced age and sex as covariates (Sections 4.1–4.2), as the groups were not matched on these factors. For those linguistic parameters where the requirements for parametric tests were not met, we performed the rank-based inverse normal transformation (Conover, 1980) on the values of a given linguistic parameter, and the transformed values were used as the dependent variable in an ANCOVA. When there was a significant group effect, pair-wise group comparisons were conducted with the lsmeans package (Lenth, 2016) in R to adjust for multiple comparisons with false discovery rate. When the group difference from ANCOVA was marginal, we performed logistic regressions with age and sex as covariates to compare the number of patients who had a z-score < -1 by group, where the z-score scale was computed based on the controls’ mean and standard deviation. For the supplementary analysis for noun counts, we coded participants who produced fewer nouns (z-score < -1) as 1 and others as 0 for a dependent variable, and ran a logistic regression with svPPA patients as a reference group and phenotype as an independent variable, controlling for age and sex. For the supplementary analysis of adverb counts, we coded participants who produced fewer adverbs as 1 and others as 0, with the naPPA group as our reference. We selected these reference groups based on our hypotheses. A separate linear regression analysis was performed to relate the cross-entropy estimations to the lexical measures.

Linear regression analyses were used to relate the lexical measures to the patients’ cortical thinning. Since the lexical features were rated for each noun, we averaged those values per individual and used the mean values of the participants in the regression analyses. We implemented univariate multiple regression analyses, covarying for potential confounding factors: the pulse sequence type used for MRI acquisition, patients’ age and disease duration. We did not covary for sex because the participants with MRI data did not significantly differ in the sex ratio and there was no consistent evidence of the effect of sex on cortical thinning. The regions selected for svPPA and naPPA patients were used to relate their regions of cortical thinning to linguistic measures that significantly differed between groups. We reported t-statistics at a significance level of 0.05 (two-tailed, uncorrected) for these regressions. All statistical analyses were performed in R (R Core Team, 2019) version 3.5.2 and RStudio (RStudio Team, 2016) version 1.1.456 (S.C.).

3. Accuracy validation

Despite the fact that the accuracy of POS tagging reported by spaCy is very high (about 97%; https://spacy.io/models/en), it was not clear how well it would perform for a clinical dataset with abnormal speech. The training data (OntoNotes 5; Weischedel et al., 2013) of spaCy included natural conversations, but the ratio of conversational speech to written texts was only around 8.3% (120K out of 1.4 million words) and the conversations were between healthy adults. To validate the accuracy of the spaCy tags on natural speech of a clinical population with abnormal speech, a linguist (S.A.) who was blinded to the automated analysis manually tagged a random subset of the transcripts comprehensively (6 Controls, 5 naPPA, 7 svPPA, and 7 bvFTD; 25 cases in total) to generate a gold standard dataset. We compared the results of spaCy to our gold standard dataset to calculate the error rates.
The error rate was generally low in all groups. The overall accuracy of spaCy on this subset of the picture description data was 91.1%, and the variances between the groups were not significantly different (Levene’s test for homogeneity of variance: F(3,21)=2.69, \( p=0.072 \)). Also, a one-way ANOVA test revealed that the difference in error rates between the groups was not significant (F(3,21)=2.695, \( p=0.075 \)). The mean error rate of the control group was 5.4% (SD=1.7%). The error rates of individual svPPA, naPPA, and bvFTD patients were slightly higher than the controls’ (svPPA: 8.8 ± 2.8%; naPPA: 13.3 ± 9.2%; bvFTD: 9.0 ± 3.0%), but the difference among the patients groups was not significant (F(2,16)=1.32, \( p=0.3 \)). While the error rates for svPPA and bvFTD did not differ from that of controls, the difference between naPPA patients and the controls was significant (\( p=0.049 \)). This was expected, given that naPPA speech contains the largest number of speech errors (see below) and thus differs most from the training data of spaCy.

For further validation, we correlated the token counts of nouns, tense-inflected verbs, and speech errors/partial words from spaCy with the counts that a linguist manually coded for all 175 participants. For the correlation between the noun counts of each individual, we used all NOUN tokens in the Universal tag set. Modal auxiliaries (MD), past (VBD) and present (VBP, VBZ) tense verbs in the Penn Treebank tag set were used for the correlation with tense-inflected verb counts. As for speech errors, we compared the X category in the Universal tag set with the counts of manually coded speech errors. We found that the noun and inflected verb counts of spaCy and counts of those categories in our manual coding were strongly correlated (nouns: \( r=0.958, p<0.001 \); verbs: \( r=0.973, p<0.001 \)). Also, the correlation of counts of X with our manual coding of speech errors was significant (\( r=0.43, p<0.001 \)), suggesting that the POS tags produced by spaCy were reliable.

4. Results

We first present the results of automatic POS tagging (Section 4.1). Next, we show the group differences in abstractness ratings, semantic ambiguity, word frequency, word familiarity, and age of acquisition in nouns produced by patients and cross-entropy estimations and lexical diversity in all words (Section 4.2). In Section 4.3, we present the regression results with MRI data.
4.1 POS categories and derived measures

Figure 1: Median, 1SD, 25th-75th percentile and outliers in number of POS categories and derived measures per 100 words by phenotype.

Table 2 summarizes the statistical results of the POS measures. Groups significantly differed in the number of unique nouns (Fig. 1Aa). svPPA patients produced fewer unique nouns than naPPA patients (p=0.022) and marginally than bvFTD patients (p=0.056). Noun production marginally varied by phenotype after controlling for age and sex (Fig. 1Ab). However, group-wise paired comparisons failed to reach significance (svPPA vs. bvFTD: p=0.062; svPPA vs. naPPA: p=0.062). A supplementary analysis with a logistic regression revealed that there were significantly more svPPA patients who produced fewer nouns (z-score < -1) compared to bvFTD patients (z=-2.01, p=0.044) and controls (z=-2.75, p=0.006) but not compared to naPPA patients (z=-1.67, p=0.096). Pronoun production (Fig. 1Ac) significantly differed between groups; pronouns were significantly more frequent for svPPA patients than for the other groups (svPPA vs. control: p=0.016; svPPA vs. naPPA: p=0.005; svPPA vs. bvFTD: p=0.002). Also, the groups significantly differed in the number of wh-words per 100 words (Fig. 1Ad). Patients with
svPPA produced more *wh*-words than the other groups (*p*<0.001 for all three pairwise comparisons).

The number of tense-inflected verbs per 100 words significantly differed by group (Fig. 1Ae). Pairwise group comparisons revealed that naPPA patients produced fewer tense-inflected verbs than svPPA patients (*p*=0.006). Similarly, the group difference in the total number of verbs was significant (Fig. 1Af). naPPA patients produced fewer verbs than svPPA patients (*p*=0.008) and bvFTD patients (*p*=0.016). The groups were also different in the counts of speech errors and partial words (Fig. 1Ag). naPPA patients produced this category significantly more frequently than the controls (naPPA vs. Control: *p*=0.005). Adverb production also differed by group (Fig. 1Ah). naPPA patients tended to produce fewer adverbs than svPPA patients (*p*=0.052). A supplementary analysis with a logistic regression showed that the number of naPPA patients who produced fewer adverbs (z-score < -1) was greater than the number of svPPA patients (z=-3.05, *p*=0.002) and controls (z=-3.57, *p*<0.001) but not greater than the number bvFTD patients (z=-1.8, *p*=0.07).

The total number of words participants produced during the picture description significantly differed by group (Fig. 1Ai). Controls produced significantly more words than any of the patient groups (vs. bvFTD: *p*<0.001; vs. naPPA: *p*<0.001; vs. svPPA: *p*=0.006). Similarly, adjective production per 100 words significantly varied by group (Fig. 1Aj), and all patient groups used fewer adjectives than controls (vs. bvFTD: *p*=0.013; vs. naPPA: *p*=0.003; vs. svPPA: *p*=0.002). Also, the group difference in prepositions (Fig. 1Ak) was significant. Each patient group produced fewer prepositions than controls (vs. bvFTD: *p*=0.004; vs. naPPA: *p*<0.001; vs. svPPA: *p*=0.004). The differences among the patient groups for these categories were not significant.

Lastly, the productions of conjunctions, determiners, fillers and the ratio of content to function words did not differ by group (Fig. 1B).

**Table 2**: Mean (SD) and group differences of the POS categories of all participants.

| Category                  | Control          | bvFTD            | naPPA            | svPPA            | F    | p     |
|---------------------------|------------------|------------------|------------------|------------------|------|-------|
| Unique nouns              | 14.7 (3.19)      | 14.87 (5.93)     | 16.73 (5.96)     | 12.21 (5.19)     | 3.46 | 0.018 |
| Nouns                     | 20.32 (4.4)      | 20.16 (6.48)     | 21.92 (8.7)      | 17.49 (5.3)      | 2.52 | 0.058 |
| Pronouns                  | 7.33 (2.41)      | 7.13 (3.77)      | 6.46 (3.2)       | 9.74 (3.9)       | 7.66 | <0.001|
| *wh*-words                | 0.34 (0.53)      | 0.6 (1.12)       | 0.34 (0.99)      | 1.61 (1.72)      | 9.26 | <0.001|
| Tense-inflected verbs     | 12.47 (1.83)     | 12.94 (3.68)     | 11.26 (3.2)      | 14.14 (2.98)     | 3.92 | 0.01  |
| Verbs                     | 22.56 (3.42)     | 23.59 (4.86)     | 20.22 (4.42)     | 24.44 (4.06)     | 3.86 | 0.011 |
| Speech errors/partial words| 0.48 (0.89)     | 1.42 (2.26)      | 3.67 (3.4)       | 0.89 (1.54)      | 4.18 | 0.007 |
| Adverbs                   | 5.59 (2.07)      | 6.04 (4.36)      | 4.37 (3.61)      | 7.05 (3.36)      | 2.82 | 0.041 |
| Adjectives                | 5.54 (1.82)      | 3.98 (3.16)      | 3.17 (2.03)      | 3.69 (2.04)      | 5.87 | <0.001|
| Total words               | 174.38 (66.38)   | 109.99 (62.35)   | 91 (55.8)        | 127.57 (66.5)    | 11.37| <0.001|
| Prepositions              | 9.96 (1.94)      | 7.63 (4.06)      | 5.98 (3.19)      | 7.24 (3.72)      | 7.66 | <0.001|
Determiners 14.16 (2.48) 14.85 (4.33) 14.34 (5.4) 13.35 (4.98) 0.97 0.41
Conjunctions 4.43 (1.91) 5.12 (2.69) 5.9 (4.68) 4.85 (2.88) 1.41 0.24
Fillers 5.5 (2.56) 5.89 (3.9) 10.03 (10.3) 6.27 (4.83) 1.46 0.23
Ratio of content to function words 1.32 (0.22) 1.36 (0.33) 1.3 (0.6) 1.32 (0.36) 0.7 0.55

4.2 Lexical-semantic features

Figure 2: Mean and standard error range of abstractness scores, semantic ambiguity ratings, word frequency, word familiarity, and age of acquisition of nouns, cross-entropy estimation and lexical diversity with all words. We used a z-score scale relative to controls’ performance for better visual representations.

Table 3: Mean (SD) and group differences of the lexical measures of all participants.

|                  | Control   | bvFTD     | naPPA     | svPPA     | F       | p       |
|------------------|-----------|-----------|-----------|-----------|---------|---------|
| Abstractness (noun) | 1.52 (0.76) | 1.55 (0.83) | 1.4 (0.59) | 1.92 (1.14) | 9.27    | <0.001  |
| Ambiguity         | 1.65 (0.25) | 1.64 (0.26) | 1.64 (0.23) | 1.74 (0.28) | 8.04    | <0.001  |
All participants produced nouns that were not abstract in the picture description task, which is not surprising given the task of describing a picture that contains concrete objects. Yet, the group difference was significant (Fig. 2A). svPPA patients produced nouns that were more abstract (i.e., less concrete) compared to bvFTD patients ($p=0.003$), naPPA patients ($p<0.001$), and controls ($p=0.004$).

Semantic ambiguity ratings of nouns also significantly differed by group (Fig. 2B). Nouns produced by svPPA patients showed significantly higher semantic ambiguity than those produced by the other groups (vs. bvFTD: $p<0.001$; vs. naPPA: $p<0.001$, vs. controls: $p=0.017$).

Patients tended to use more frequent nouns than controls ($z$-score $>0$), and the group difference in the frequency of nouns was highly significant (Fig. 2C). svPPA patients produced more frequent nouns than bvFTD patients ($p<0.001$), naPPA patients ($p=0.001$), and controls ($p<0.001$).

The familiarity of nouns also significantly differed by group (Fig. 2D). svPPA patients used more familiar nouns than bvFTD patients ($p=0.003$) and controls ($p=0.003$).

All patients tended to produce nouns acquired at an earlier age than controls ($z$-score $<0$, Fig. 2E), and the group difference in the age of acquisition of nouns was significant. naPPA ($p=0.015$) and svPPA patients ($p=0.004$) produced nouns that were acquired later than controls.

The cross-entropy estimation differed significantly by phenotype (Fig. 2F); the cross-entropy estimation of svPPA patients was lower than that of bvFTD patients ($p=0.006$), naPPA patients ($p<0.001$), and controls ($p<0.001$). In other words, words produced by svPPA patients were more predictable than those produced by the other patient groups. To further examine why svPPA patients’ cross-entropy estimation was lower than those of the other groups, a linear regression analysis was performed to relate cross-entropy estimation in svPPA patients with all lexical semantic measures. We found that word frequency and semantic ambiguity were significantly related to cross-entropy estimation in svPPA (word frequency: $\beta=-1.72, p<0.001$; semantic ambiguity: $\beta=-0.93, p=0.019$).

There was a significant group difference in lexical diversity that was measured by moving-average type/token ratio with a window size of 20 words (Fig. 2G). Elderly controls showed higher lexical diversity than all patient groups (vs. bvFTD: $p<0.001$, vs. naPPA: $p=0.021$, vs. svPPA: $p=0.031$). We also tried different window sizes (25 words and 30 words) and found the same group differences.
4.3 MRI results

Since svPPA and naPPA patients showed significant linguistic differences, here we examined their brain regions with cortical thinning and relations between cortical thinning and specific linguistic features in each group. We found distributions of cortical thinning that were representative of each group (Ash et al., 2012, 2009; Cousins et al., 2016). Specifically, the MRI results showed that svPPA patients have significant cortical thinning in the anterior temporal and orbital frontal cortex areas of both hemispheres, but cortical thinning is more prominent in the left hemisphere than the right hemisphere ($p<0.01$; Fig. 3A). naPPA patients have significant cortical thinning that is most prominent in the left middle frontal, inferior temporal and middle temporal regions, but also apparent in the left supramarginal gyrus, right temporal gyrus, and right pars opercularis ($p<0.05$, Fig. 3B). We examined patients’ speech production in relation to cortical thinning in greater detail. The results are summarized in Table 2, and the associations are illustrated in Figure 3.

![Image of cortical thinning in svPPA and naPPA patients](image-url)

Figure 3: Cortical thinning in svPPA (A) and naPPA (B) patients, and example areas with cortical thinning that were significantly related to linguistic measures ($p<0.05$, uncorrected) in svPPA (A1-3) and naPPA (B1) patients.

We selected the linguistic features that were distinctive of svPPA patients in our main analyses outlined above. These showed significant associations with cortical thinning in anterior and middle temporal regions of the left hemisphere (Table 2, Fig. 3A1-3).

We also found that the production of speech errors and partial words was related to cortical thinning in the left rostral middle frontal gyrus for naPPA patients (Fig. 3B1), suggesting that speech errors are related to impairment in frontal executive functions. We also related verb, tense-inflected verb, and adverb counts to cortical thinning in naPPA patients, but the results were not significant.

Table 2: Results of regression analyses with cortical thinning in svPPA and naPPA patients.

| svPPA               | Estimate | Std. Error | t-value | p-value |
|---------------------|----------|------------|---------|---------|
| Noun L inferior temporal | 0.059    | 0.021      | 2.85    | 0.01    |
| Region                          | Z Score | p Value | T Value | p Value |
|--------------------------------|---------|---------|---------|---------|
| L. middle temporal             | 0.054   | 0.026   | 2.09    | 0.049   |
| L. superior temporal           | 0.045   | 0.021   | 2.18    | 0.041   |
| L. insula                      | 0.035   | 0.016   | 2.19    | 0.04    |
| **Pronoun**                    |         |         |         |         |
| L. inferior temporal           | -0.098  | 0.038   | -2.54   | 0.019   |
| L. parahippocampal             | -0.059  | 0.028   | -2.16   | 0.043   |
| L. entorhinal                  | -0.104  | 0.05    | -2.08   | 0.049   |
| **Wh-words**                   |         |         |         |         |
| L. inferior temporal           | -0.219  | 0.08    | -2.6    | 0.021   |
| L. middle temporal             | -0.244  | 0.11    | -2.14   | 0.044   |
| L. superior temporal           | -0.19   | 0.087   | -2.2    | 0.039   |
| L. fusiform                    | -0.303  | 0.108   | -2.818  | 0.01    |
| L. insula                      | -0.142  | 0.065   | -2.207  | 0.04    |
| **Abstractness**               |         |         |         |         |
| L. temporal pole               | -0.582  | 0.228   | -2.55   | 0.019   |
| L. inferior temporal           | -0.531  | 0.218   | -2.42   | 0.025   |
| L. middle temporal             | -0.652  | 0.225   | -2.89   | 0.011   |
| L. superior temporal           | -0.51   | 0.189   | -2.69   | 0.019   |
| L. fusiform                    | -0.597  | 0.243   | -2.49   | 0.027   |
| R. superior temporal           | -0.309  | 0.14    | -2.21   | 0.038   |
| **Semantic ambiguity**         |         |         |         |         |
| L. inferior temporal           | -2.609  | 0.833   | -3.11   | 0.007   |
| L. middle temporal             | -2.617  | 0.896   | -2.96   | 0.011   |
| L. bank superior temporal      | -1.795  | 0.572   | -3.13   | 0.006   |
| L. superior temporal           | -1.946  | 0.693   | -2.8    | 0.013   |
| L. supramarginal               | -1.722  | 0.601   | -2.86   | 0.018   |
| L. insula                      | -0.5    | 0.205   | -2.39   | 0.026   |
| L. lateral orbito-frontal      | -1.182  | 0.564   | -2.1    | 0.048   |
| **Word frequency**             |         |         |         |         |
| L. inferior temporal           | -0.627  | 0.258   | -2.46   | 0.024   |
| L. middle temporal             | -0.685  | 0.264   | -2.58   | 0.019   |
| L. bank superior temporal      | -0.379  | 0.176   | -2.16   | 0.043   |
| L. superior temporal           | -0.49   | 0.208   | -2.34   | 0.031   |
| L. fusiform                    | -0.593  | 0.267   | -2.22   | 0.037   |
| **Word familiarity**           |         |         |         |         |
| L. inferior temporal           | -0.755  | 0.29    | -2.61   | 0.016   |
| L. middle temporal             | -0.83   | 0.247   | -3.41   | 0.009   |
L superior temporal  -0.53  0.182  -2.98  0.018
L rostral middle frontal -0.821  0.216  -3.8  0.001
R rostral middle frontal -0.608  0.222  -2.72  0.014
L precentral  -0.599  0.163  -3.67  0.001
L supramarginal -0.517  0.19  -2.72  0.013
L lateral orbitofrontal -0.365  0.163  -2.24  0.001
R superior frontal  -0.592  0.218  -2.72  0.013
R pars opercularis  -0.549  0.192  -2.86  0.009

Cross-entropy estimation
L inferior temporal  0.451  0.187  2.4  0.027
L middle temporal  0.419  0.199  2.1  0.048
L bank superior temporal  0.348  0.143  2.45  0.026
L superior temporal  0.392  0.156  2.51  0.02
L fusiform  0.713  0.224  3.18  0.004

naPPA

|                          | Estimate | Std. Error | t-value | p-value |
|--------------------------|----------|------------|---------|---------|
| Speech errors / Partial words |          |            |         |         |
| L rostral middle frontal | -0.194   | 0.044      | -4.39   | 0.022   |

5. Discussion

In this study, we examined word production and lexical characteristics of speech in FTD patients with a novel, automated method that is objective, comprehensive and reproducible. Lexical semantic measures derived from the automated method were highly correlated with manually coded linguistic measures (Section 3). Moreover, distinct measures were associated with each patient group (Sections 4.1–4.2). We found that svPPA patients produced fewer unique nouns than naPPA patients, and these nouns were more ambiguous, abstract, and frequent than those of naPPA and bvFTD patients. Correspondingly, svPPA patients produced more pronouns and wh-words. A new linguistic measure of cross-entropy estimation showed that their word selection in general was more predictable from its context than that of the other groups, and this was related in part to noun ambiguity and frequency. Patients’ words were less diverse than those of controls, but there was no significant group difference among the patient groups. naPPA patients, by comparison, produced fewer adverbs and more speech errors and partial words than the other groups. We also found significant associations between our lexical measures and cortical thinning. Cortical thinning in left anterior inferior and middle temporal gyri was associated with disrupted lexical and semantic features in svPPA, and cortical thinning in the left middle frontal gyrus was associated with speech errors and partial words in naPPA. We discuss these findings in turn below.
5.1 Word use in svPPA

svPPA patients produced fewer unique nouns than other groups in the current study. Moreover, there was a large number of individual patients who produced fewer nouns in the svPPA cohort than in the other patient groups. There has been some inconsistency in this observation across reports (Ash et al., 2009; Cousins et al., 2016; Riello et al., 2018; Wilson et al., 2010), and this may be due in part to the source of nouns and how these were ascertained in various studies. Here we examined a semistructured speech sample elicited during a picture description task and assessed by an automated analysis. We also noted that the profiles of svPPA patients’ nouns exhibited semantic characteristics that significantly differed from those of the other groups. They displayed high abstractness, semantic ambiguity, word frequency, and word familiarity. This is in line with other findings consistent with the hypothesis attributing the deficit in svPPA in part to the degradation of visual feature knowledge associated with object concepts (Bird, Lambon Ralph, Patterson, & Hodges, 2000; Bonner et al., 2016, 2009; Cousins et al., 2016; Cousins et al., 2017; Cousins, Ash, Olm, & Grossman, 2018; Hoffman et al., 2013).

We previously argued that the semantic deficit in svPPA patients is due in part to their cortical atrophy in the anterior inferior temporal region, because this is a portion of visual association cortex which may contribute to the representation of visual feature knowledge associated with object concepts (Bonner et al., 2016, 2009; Cousins et al., 2016; Cousins et al., 2017, 2018). This may also explain in part why svPPA patients produced nouns with high abstractness in our results: abstract nouns are less dependent on visual feature knowledge to derive their meaning, thereby reducing the need to activate the anterior and inferior temporal regions of the brain. We also found that an increase in the abstract rating of nouns is related to cortical thinning in the left anterior temporal region. Our MRI results are in line with previous findings with smaller number of patients using manual analyses of nouns (Cousins et al., 2017). In the context of concrete noun difficulty due to degraded representations of visual objects, it is not surprising that svPPA patients may also substitute more pronouns, and this was also reflected in associations with cortical thinning in the left temporal lobe and pronoun usage. In sum, we argue that difficulty with the representation of visual feature knowledge associated with object concepts that is the key deficit in svPPA.

Pronouns are frequent, ambiguous, and familiar, and we also found that svPPA patients produced nouns with higher frequency, ambiguity, and familiarity. Previous observations have showed that svPPA patients’ lexical retrieval is strongly graded by word familiarity and frequency (Bird et al., 2000; Hodges & Patterson, 2007; Rogers, Patterson, Jefferies, & Lambon Ralph, 2015). These observations suggest that at least some proportion of svPPA patients’ picture description deficit is due in part to a lexical retrieval deficit that extends beyond their degraded semantic representations of object knowledge. As for semantic ambiguity, Hoffman et al. (2013) argue that this feature is highly correlated with abstractness ratings (|r| = .51, p < 0.001; Hoffman et al. 2013), suggesting that abstract words, such as set or time, are more ambiguous than concrete words, such as desk or orange. Given the high correlation of ambiguity and abstractness, it is not surprising that svPPA patients produced more nouns that were abstract and ambiguous. Another possibility is that svPPA patients produce nouns such as furniture, object, or thing that are superordinate in a hierarchically organized semantic network. These possibilities need to be further studied in future work.
Previous work describing the hub-and-spoke model (Patterson, Nestor, & Rogers, 2007) claims that disease in the anterior temporal lobe is responsible for a universal semantic deficit in svPPA. We found in the present study that svPPA patients used verbs more frequently than patients with naPPA. A frequent use of a specific POS category does not necessarily reflect the integrity of the meaning of this word class. However, on the assumption that patients use words with which they are more familiar in a semistructured speech sample, the more frequent use of verbs than nouns in svPPA would be contrary to the claim that the meaning of all words is degraded in svPPA. Likewise, we showed that the meaning of words for abstract nouns is relatively preserved in svPPA (Bonner et al., 2016; Cousins et al., 2016) and that the meaning of words dependent on number knowledge is relatively preserved in svPPA (Ash et al., 2016). In a longitudinal study of lexical expression in svPPA, we found progressively reduced use of concrete words relative to abstract words (Cousins et al., 2018). Findings such as these are more consistent with a relatively more selective degradation of the lexicon in svPPA. Additional work is needed to assess these claims.

5.2 Word use in naPPA

A distinguishing feature of naPPA is that they produced more speech errors and partial words. The increased speech error and partial word rate in naPPA conforms to previous findings that naPPA patients exhibit effortful and non-fluent speech (Ash et al., 2013, 2009; Croot, Ballard, Leyton, & Hodges, 2012; Gorno-Tempini et al., 2004; Grossman et al., 1996; Weintraub et al., 1990). We related increased partial words and speech errors to cortical thinning in the left middle frontal gyrus, which is in line with previous findings (Ash et al., 2009; Gorno-Tempini et al., 2004; Grossman et al., 1996). An important characteristic of naPPA patients is their AoS, that is, the poor coordination of the motor articulators during speech production (Ash et al., 2009; Gorno-Tempini et al., 2011; Grossman et al., 1996, 2005; Josephs et al., 2006; Ogar et al., 2007). It is claimed that a subset of naPPA patients has AoS errors without grammatical impairment, and that this differs from naPPA patients with grammatical impairments who have AoS (Josephs et al., 2013, 2012). A major challenge to this area of investigation is the ability to detect speech errors in an objective, reliable and reproducible manner. A rating scale based on subjective judgments has been developed, but reliability is challenging (Josephs et al., 2012; Strand, Duffy, Clark, & Josephs, 2014). Another challenge is that increased partial words in naPPA patients are not explained solely by AoS. Additional work is needed to confirm the identification of speech errors and partial words in an naPPA cohort, to extend this observation to patients with movement disorders such as progressive supranuclear palsy and corticobasal syndrome, and to distinguish this from speech errors in patients with bulbar disease such as amyotrophic lateral sclerosis.

Patients with naPPA in our study produced fewer verbs than the other groups. Decreased verb use in naPPA patients has also been observed in previous studies (Ash et al., 2013, 2009). Several accounts have been forwarded to explain this finding. One suggestion is that naPPA patients have difficulty in producing tense-inflected verbs and constructing complex sentence structures due to a syntactic deficit, which leads to a reduced use of verbs in their speech (Ash et al., 2013, 2009; Grossman et al., 1996; Grossman, Rhee, & Moore, 2005). Alternatively, disease in naPPA may also affect motor association regions of the frontal lobe and interfere with the representation of action knowledge associated with verbs of action (Hillis et al., 2004, 2002). Yet another possibility is that the class of verbs is associated with a richer and more demanding set of
features—including not only its semantic attributes but also a rich set of grammatical and thematic properties—and nPPA patients have limitations in executive functioning that may make verbs more difficult for nPPA patients to process (Kramer et al., 2003; Libon et al., 2007; Weintraub, Rubin, & Mesulam, 1990). Previous work based on a smaller cohort of patients has suggested that the latter explanations are less likely than the grammatical one (Gunawardena et al., 2010), and we could not provide further evidence on these competing claims since the verb counts were not associated with cortical thinning in nPPA patients in our results. Additional work is needed to assess these claims.

5.3 Word use in bvFTD

bvFTD patients were a purely behavioral group without obvious aphasia, and they were the most similar to the controls among the patient groups. They did not differ from controls in most of the POS productions. bvFTD patients did differ from controls in their reduced number of adjectives, prepositions, total words, and lexical diversity, but this deficit was evident not only in bvFTD patients but was present in all patients. This seems to suggest that reduced production of adjectives, prepositions, total number of words, and low lexical diversity might reflect general linguistic impairments and may be sensitive to disease state but not specific to each phenotype. We did not confirm our previous observation that bvFTD patients tend to produce relatively more concrete words than abstract words (Cousins et al., 2017). Additional work thus is needed to evaluate the deficit in abstract word use in bvFTD.

5.4 Validating an automated lexical analysis of PPA patients’ speech

An important strength of our study is that we were able to validate the use of an automated method for analyzing lexical production in a semi-structured speech sample produced by patients with speech deficits. An automated analysis is reliable in normal, healthy speakers. Here we were able to show that there was over 90% agreement between the automated analysis and the judgment of a linguist for speakers with abnormal speech. Our automated analysis is reproducible, accessible, and non-invasive, making it an ideal screening biomarker for neurodegenerative disease. Indeed, the results of the present study are in line with many previous findings, suggesting that our novel, automated method is valid in studying FTD patients’ speech. Speech is central to human daily functioning and our approach has potential to serve as a clinical endpoint for treatment trials. While the present study focuses on cross-sectional data, work in progress assesses objective analyses of our longitudinal speech samples. Language production is a multifaceted process that requires a large expanse of brain tissue and is a sensitive marker for capturing even very early stages of neurodegeneration. Semi-structured speech data such as a picture description is inexpensive to collect on a large scale, when compared to MRI or lumbar puncture for cerebrospinal fluid which are expensive and/or invasive. However, it is nearly impossible to utilize and analyze large-scale speech data in a reproducible manner without an automated method. We believe that the method proposed in this paper can facilitate analyzing large-scale speech data in a quantifiable, automated, easy, and reproducible way and can be used in automatic prescreening for neurodegeneration in the future (e.g., Cho et al. 2020).
6. Conclusion

While our study has many strengths, there are also some limitations that should be kept in mind when interpreting our results. One limitation is that the accuracy of the POS tagging for naPPA patients was not quite as high as for the other groups. Thus, the results of naPPA patients will need to be interpreted with caution. This is an expected result for a POS tagger, since all existing POS taggers are trained with speech/text data of healthy adults. Accuracy could be improved if we trained a POS tagger using our patients’ speech samples with speech errors and other abnormalities as a training dataset. Also, since our automated methods rely on texts, there might be, for example, minor speech errors that were transcribed with regular spellings and our pipeline might have missed tagging those tokens as speech errors. A related limitation is that we could not assess the simplified syntactic structures of naPPA patients with a syntactic dependency parser due to its low accuracy, even though it is a more direct way of looking at sentence structures than looking at verb counts with a POS tagger. We used an open-source POS tagger in the present study, but we plan to develop NLP tools, including a POS tagger, a syntactic dependency parser, and an automated speech recognition system for automatic transcription, that will be trained with patients’ speech in the near future. Another limitation is that we had a relatively small number of digitized speech samples, and a small number of MRI samples for naPPA patients, and this limited our ability to perform statistically robust regression analyses in this patient group. We collect data on a regular basis and future studies will contain more speech samples.

Appendices

Table A: List of POS categories and mapping between the Google POS tag set and the Penn Treebank tag set

| Google POS | Penn Treebank | Gloss |
|------------|---------------|-------|
| NOUN       | NN            | noun, singular or mass |
|            | NNS           | noun, plural |
| VERB       | MD            | verb, modal auxiliary |
|            | VB            | verb, base form |
|            | VBD           | verb, past tense |
|            | VBG           | verb, gerund or present participle |
|            | VBN           | verb, past participle |
|            | VBP           | verb, non-3rd person singular present |
|            | VBZ           | verb, 3rd person singular present |
| ADJ (adjective) | AFX         | affix |
|            | JJ            | adjective |
|            | JJR           | adjective, comparative |
|            | JJS           | adjective, superlative |
|            | PRP$          | pronoun, possessive |
|       | Controls  | bvFTD     | naPPA     | svPPA     |
|-------|-----------|-----------|-----------|-----------|
| Nouns | 19.42 (4.67) | 21.67 (6.94) | 23.65 (7.33) | 17.43 (5.12) |
| Unique nouns | 14.4 (3.37) | 16.26 (6.27) | 19.44 (3.84) | 12.24 (4.6) |
| Pronouns | 7.64 (2.33) | 6.21 (3.58) | 5.55 (1.86) | 9.4 (3.89) |
| $wh$-words | 0.63 (0.35) | 1.3 (3.04) | 1.16 (1.81) | 0.9 (1.32) |
| Tense-inflected verbs | 12.02 (1.56) | 12.26 (3.8) | 11.28 (3.88) | 13.71 (3.2) |
| Verbs | 22.46 (3.1) | 22.67 (4.56) | 20.81 (4.67) | 24.11 (4.68) |
| Speech errors/Partial words | 0.81 (1.16) | 1.17 (1.86) | 3.36 (3.93) | 0.73 (1.12) |
| Adverbs | 5.61 (1.79) | 5.46 (3.31) | 3.51 (2.88) | 7.94 (4.69) |
| Adjectives | 6.01 (1.68) | 3.89 (2.38) | 3.35 (2.28) | 3.3 (2.6) |
| Prepositions | 10.81 (1.52) | 8.34 (4.07) | 5.48 (2.73) | 7.78 (3.96) |
| Total words | 194.22 (75.56) | 112.23 (67.5) | 85.75 (50) | 121.88 (66.49) |
| Determiners | 13.6 (2.16) | 15.6 (3.93) | 16.5 (4.24) | 12.76 (5.3) |
| Conjunctions | 4.38 (1.82) | 5.01 (2.78) | 4.36 (3.24) | 5.02 (3.31) |
| Interjections | 5.02 (2.43) | 5.7 (3.83) | 8.9 (4.78) | 6.45 (5.43) |
| Ratio of content to function words | 1.31 (0.26) | 1.36 (0.35) | 1.28 (0.24) | 1.32 (0.32) |
| Abstractness (noun) | 1.54 (0.24) | 1.48 (0.26) | 1.35 (0.21) | 1.86 (0.51) |
|                  |        |        |        |        |
|------------------|--------|--------|--------|--------|
| Ambiguity (noun) | 1.69 (0.05) | 1.66 (0.06) | 1.63 (0.09) | 1.77 (0.13) |
| Frequency (noun) | 3.58 (0.17) | 3.61 (0.28) | 3.49 (0.4) | 4.01 (0.44) |
| Familiarity (noun) | 2.36 (0.03) | 2.35 (0.05) | 2.36 (0.03) | 2.41 (0.07) |
| AoA (noun)       | 4.4 (0.38) | 4.21 (0.42) | 4.14 (0.5) | 4.1 (0.46) |
| Cross entropy    | 9.75 (0.52) | 9.66 (0.74) | 10.21 (1) | 9.18 (0.58) |
| Lexical diversity| 0.85 (0.04) | 0.79 (0.09) | 0.8 (0.06) | 0.8 (0.1) |

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