Computational speech markers of negative symptoms show evidence of being robust to antipsychotic dose and extrapyramidal symptoms in schizophrenia

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Competing interests statement

MJS, JR, MX, WS are full-time employees of Winterlight Labs and Cambridge Cognition. SXT owns equity and serves as a consultant for North Shore Therapeutics, received research funding and serves as a consultant for Winterlight Labs, and is on the advisory board and owns equity for Psyrin. All other authors have no conflicts of interests to declare.

Abstract

There is increasing interest in using computational speech and language analysis for the objective assessment of symptom severity in schizophrenia spectrum disorders (SSD), including negative symptom severity. However, the extent to which antipsychotic side effects influence speech markers of negative symptoms is unclear. This study investigated associations between computational speech and negative symptom severity, and examined whether speech features are associated with antipsychotic dose and extrapyramidal symptoms (EPS). Sixty-seven participants with SSD completed speech-focused tasks and clinical assessment. Seventeen speech features capturing relevant acoustic, timing, and linguistic characteristics were extracted from participant responses and examined for associations with negative symptoms, EPS, and antipsychotic dose. Eight timing features and one linguistic feature were significantly correlated with negative symptom severity ($p < .05$, false-discovery-rate-corrected; FDR), and these relationships were specific to negative symptoms rather than overall psychiatric symptom severity. No features were significantly correlated with antipsychotic dose or EPS after FDR correction, and Bayesian analyses provided moderate evidence for the null hypothesis (i.e., absence of an association) for most features. Two features showed Bayesian evidence for the alternative hypothesis, however; the association between speech and negative symptoms remained significant after removing the clinical covariate effects. The results provide support for computational speech markers of negative symptom severity, and both frequentist and Bayesian evidence that these speech markers are generally not confounded by antipsychotic side effects. The results help advance the clinical validation of computational speech assessment and analysis for measuring negative symptom severity in SSD.

Keywords: antipsychotic medication, computational speech, extrapyramidal side effects, natural language processing, negative symptoms, schizophrenia

Introduction

Quantitative speech and language analysis is increasingly being investigated as a tool to objectively measure symptom severity in schizophrenia spectrum disorders (SSD), with the goals of improving assessment reliability, enhancing routine symptom monitoring across settings, increasing sensitivity to treatment response, and reducing barriers to clinical care (DeSouza et al., 2023). These approaches use acoustic signal analysis and natural language processing (NLP) to objectively quantify the speech- and language-based manifestations of the symptoms of SSD, including positive symptoms (e.g., disorganized speech, delusional thought content), negative symptoms (e.g., alogia, blunted affect), and cognitive deficits (e.g., dysfluency, interpersonal communication difficulties) (see Hitczenko et al., 2021, for a review).

The speech and language alterations in SSD are hypothesized to reflect underlying disorder psychopathology, and in addition to demonstrating relationships with clinician ratings of language dysfunction (Krell et al., 2022; Tang et al., 2023), quantitative speech measures have shown associations with symptom domains more broadly (e.g., global positive and negative symptom severity; de Boer et al., 2023; Girard et al., 2022; Nikzad et al., 2022; Vail et al., 2018) and with symptoms of schizophrenia not traditionally defined in terms of alterations in speech (e.g., anhedonia; Buck et al., 2015; Cohen et al., 2009). These speech measures have further demonstrated utility in predicting psychosis risk (Bearden et al., 2011; Bedi et al., 2015; Corcoran et al., 2018; Rezaii et al., 2019) and functional outcome in SSD (Voleti et al., 2023).

Given that quantitative speech features have high sensitivity to subtle changes in diverse aspects of speech and language (Tang et al., 2021), determining the extent to which other relevant clinical factors influence these variables is crucial to evaluating the clinical validity of these metrics for their appropriate use in clinical practice. Of particular relevance is whether

speech-based markers of negative symptoms are influenced by antipsychotic dosage and extrapyramidal symptoms (EPS). First, negative symptoms are of high clinical relevance: they are important predictors of functional outcome (Milev et al., 2005); yet, no existing treatments yield sustained improvement in negative symptoms (Fusar-Poli et al., 2015), underscoring the need to improve the way negative symptoms and assessed, understood, and targeted (Daniel et al., 2023; Galderisi et al., 2018). Second, evidence is emerging for several objective speech-based markers of negative symptoms such as alogia and flat affect, including features that capture the acoustic (e.g., increased pitch variability), timing (e.g., reduced speech rate, increased pause duration), and verbal output (e.g., reduced speaking time) properties of speech (however, cross-study heterogeneity for other features has also been noted; Cohen et al., 2014; Parola et al., 2020). Third, antipsychotic medication side effects can resemble negative symptoms and impact behaviour, including speech. For example, sedation is one of the most common side effects of antipsychotics, which can mimic negative symptoms through decreased motor and voluntary goal-directed activity (Leucht et al., 2013; Saavedra-Velez et al., 2009). Additionally, antipsychotics have been associated with adverse effects on cognition, including language abilities, both through the occupancy of dopamine D2 receptors and their anticholinergic properties (Haddad et al., 2023; Joshi et al., 2021; Sakurai et al., 2013). Finally, EPS are common antipsychotic-induced adverse effects, including several movement disorders such as parkinsonism (bradykinesia, rigidity, tremor) and akathisia (inner tension and motor restlessness) that are known to impact motor speech (Bär et al., 2004; Caroff et al., 2011; Ekhart et al., 2021; Pierre, 2005; Stroup and Gray, 2018).

Despite the potential for antipsychotic effects to impact speech and motor activity, few studies have examined the extent to which these effects influence the computational speech

markers of negative symptoms in SSD. An early study reported no significant relationships between bradykinesia and four acoustic speech features in a small schizophrenia inpatient sample; however, no additional speech features or EPS were examined (Alpert et al., 2002). Another study (de Boer et al., 2020) examined speech characteristics in SSD participants grouped into those taking high vs. low dopamine D2 receptor occupancy antipsychotics. The high D2 group displayed significant differences from a healthy control group on multiple speech features, while the low D2 group showed an intermediate pattern between the high D2 and control groups. However, in a follow-up study with a larger sample (de Boer et al., 2023), no significant associations between antipsychotic dosage and acoustic speech features were observed, and there were no significant differences in speech between subgroups of low vs. high D2 receptor occupancy; however, post-hoc analyses indicated a group difference on mean pause duration.

Based on the findings from the three studies described above, the evidence remains mixed and incomplete regarding whether antipsychotic medication and EPS influence relevant speech features in SSD. Furthermore, these studies examined speech from participant responses during open-ended interviews, and the findings may not generalize to other tasks commonly used to elicit speech in studies of schizophrenia (e.g., picture description). Therefore, the current study employed computational analysis of speech elicited from a range of speech tasks to: 1) confirm the relationship between negative symptom severity and speech features, and 2) determine whether these features are additionally sensitive to the effects of antipsychotic dosage and EPS.

Methods

Participants

Participants were 67 English-speaking individuals with SSD recruited from inpatient psychiatric units and participating in a longitudinal study of predictors of psychosis outcomes. SSD diagnoses (specifically: schizophrenia, schizophreniform disorder, schizoaffective disorder, unspecified psychotic disorder, brief psychotic disorder, bipolar disorder with psychotic features) were confirmed with the Structured Clinical Interview for DSM-IV (SCID-I; First and Gibbon, 2004) and Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5; APA, 2013) criteria. Exclusion criteria were age below 15 or above 40 in order to minimize potential age-related effects, a psychotic disorder that was substance-induced or due to a general medical condition, intellectual disability, significant risk of suicidal or homicidal behavior, disorders or significant physical impairments affecting speech or language (e.g., aphasia, tardive dyskinesia), and serious neurological, endocrine, or other medical condition or treatment known to affect the brain and/or language. All participants provided informed consent before participating and the study protocol was approved by the Institutional Review Board of the Feinstein Institutes for Medical Research.

Procedure

Participants completed up to four assessments in total (baseline assessment during inpatient admission, discharge assessment, 3- and 6-month follow-up assessments). For the current investigation, baseline data were analyzed unless assessments were incomplete for a given participant, in which case the next available assessment was used instead. There were 55 participants with available clinical ratings of EPS, while antipsychotic medication dosage and clinical ratings of negative symptoms were available for the full participant sample (n = 67; see Table 1).

At each visit, participants underwent a semi-structured clinical assessment administered by trained clinical assessors. In addition to the SCID-I, measures relevant to the current investigation were the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1989), the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962), and the Extrapyramidal Symptom Rating Scale (ESRS; Chouinard and Margolese, 2005), which provides Global Impression scores for parkinsonism, akathisia, tardive dyskinesia, and dystonia. The ESRS was administered in person by trained physicians (SXT & AHN) who assessed participants jointly until reliability was achieved. Missing datapoints resulted from clinical staff being unavailable to assess participants at the time of the research visit or restrictions due to the COVID pandemic; no participants declined assessment for EPS. Antipsychotic medication dosage was obtained through patient report and medical chart review, and a chlorpromazine equivalent (CPZE) dose was computed (Leucht et al., 2016).

Participants completed five speech- and language-focused tasks ranging from structured to open-ended: 1) a paragraph reading task requiring participants to read a passage of text out loud; 2) a semantic fluency task prompting participants to name as many animals as they could think of in 1 minute; 3) a phonemic fluency task asking participants to say as many words they could think of that begin with the letter “F” in 1 minute; 4) a picture description task in which participants were asked to describe everything they could see in a presented picture (three trials with unique pictures were administered); and 5) an open-ended narrative (“journaling”) task in which participants had to respond to an open-ended prompt (two trials were administered: “Tell me about yourself?” and “How have you been spending your time recently?”). All tasks were administered in a quiet room through the Winterlight Assessment App (winterlightlabs.com) on an iPad tablet computer, which recorded participants’ spoken responses.

Table 1. Participant characteristics

N	67
Age (*M*, *SD*)	26.5 (5.2)
Sex	
Female (n, %)	20 (30%)
Male (n, %)	47 (70%)
Race (*N*, %)	
Asian	12 (18%)
Black	30 (45%)
White	15 (22%)
Mixed	3 (4%)
Other	7 (10%)
Years of completed education (*M*, *SD*)	14.1 (1.9)
SANS Total (*M*, *SD*)	27.7 (12.7)
Alogia	5.6 (5.9)
Anhedonia/Asociality	6.9 (4.8)
Avolition	11.2 (3.8)
Blunted affect	5.6 (5.9)
BPRS Total (*M*, *SD*)	46.6 (11.6)
ESRS[a]	
Akathisia (% with symptoms)	20%
Dyskinesia (% with symptoms)	2%
Dystonia (% with symptoms)	7%
Parkinsonism (% with symptoms)	60%
CPZE units (*M*, *SD*)	303.4 (222.9)

Note. BPRS = Brief Psychiatric Rating Scale; ESRS = Extrapyramidal Symptom Rating Scale; SANS = Scale for the Assessment of Negative Symptoms.

[a]Percentages are for the 55 participants with ESRS ratings.

Data processing and analysis

Speech processing

Participant speech recordings were transcribed by trained transcriptionists, and recordings and accompanying text transcripts were analyzed through the Winterlight analysis platform (winterlightlabs.com), which uses Python-based standard acoustic and language processing libraries (e.g., spaCy, Stanford parser, Praat/Parselmouth) and custom code to extract over 700

individual feature variables quantifying the linguistic (i.e., language use) and paralinguistic (i.e., acoustic and timing) properties of speech.

The current investigation focused on 17 key paralinguistic features (8 acoustic, 9 timing) and two related linguistic features capturing speech production (total words and the mean length of utterances) (Table 2). These features were selected a priori to characterize the aspects of speech most relevant to the goals of examining markers of negative symptom severity and the potential influence of antipsychotic and motor symptoms.

Rates of missing data and feature value distributions were examined on a within-task basis to exclude speech features where the feature value could not be computed for over 50% of participants and/or features with identical values in over 50% of participants, which resulted in the exclusion of the filled pauses feature for the analysis of paragraph reading speech. Speech feature values from multiple trials within tasks were averaged prior to statistical analysis.

Table 2. Description of speech features

Feature	Category	Description
MLU	Linguistic	Mean length of utterances, in words
Total words	Linguistic	Total number of words
F0 mean	Acoustic	Mean fundamental frequency, in Hz
F0 variance	Acoustic	Variance of the fundamental frequency, in Hz
HNR (mean)	Acoustic	Mean harmonic-to-noise ratio (ratio of the period and non-periodic component), in dB
HNR (variance)	Acoustic	Variance in the harmonic-to-noise ratio (ratio of the period and non-periodic component), in dB
Intensity (mean)	Acoustic	Mean of the intensity curve (perceived loudness), in dB
Intensity (variance)	Acoustic	Variance in the intensity curve (perceived loudness), in dB
Jitter	Acoustic	Perturbation in the fundamental frequency from one cycle to the next, as a percentage
Shimmer	Acoustic	Perturbation in the amplitude from one cycle to the next, as a percentage
Articulation rate	Timing	Number of syllables per second
Filled Pauses	Timing	Fraction of annotations that are filled pauses
Hesitation	Timing	Fraction of utterances that begin with a pause
Pause duration (mean)	Timing	Mean duration of pauses, in seconds

Pause-word ratio	Timing	Number of pauses divided by the number words
Phonation rate	Timing	Ratio of voiced to unvoiced audio
Speech duration	Timing	Total duration of speech, in seconds
Speech rate	Timing	Number of words per minute
Unfilled pauses	Timing	Fraction of annotations that are unfilled pauses

Statistical analyses

Frequentist statistics

Associations between speech features and SANS negative symptoms severity scores were examined separately within each task using non-parametric Kendall's tau partial correlations, adjusted for participant age and biological sex. These correlations were also performed on BPRS Total scores to examine the specificity of findings to negative symptoms vs. overall clinical severity. Similar analyses examined relationships between speech features and CPZE dose, and between speech features and EPS. As tardive dyskinesia and dystonia symptoms were absent in over 90% of participants, this analysis focused on parkinsonism (present in 60% of subsample) and akathisia (present in 20% of subsample) (Figure 1). For all correlation analyses described above, the threshold for statistical significance was set at $p < .05$ (two-tailed), and a false-discovery rate (FDR) correction was applied within each task and clinical score.

Bayesian statistics

Following the correlation analyses, Bayesian statistics were employed to evaluate the strength of the evidence for the absence of an association between identified speech features and clinical covariates of interest (ESRS and CPZE scores). These analyses focused on speech features that had significant (FDR-corrected) correlations with negative symptom scores or significant (uncorrected) correlations with parkinsonism, akathisia, or CPZE dose, and focused on speech from the specific tasks showing these associations.

As a Bayesian implementation of non-parametric partial correlations was not available, these analyses employed zero-order Kendall's tau correlations. Differences in the correlation coefficient between the partial and zero-order correlation coefficients were small across variables on average (mean difference in Kendall's tau ≤ 0.02); see Supplementary Table S1. Analyses were performed using the default prior distribution (stretched beta prior width = 1). Bayes Factors (BF) for the null hypothesis (BF_{01}) were interpreted according to published guidelines (van Doorn et al., 2021): strong: BF01 = 10-30; moderate: BF01 = 3-10; anecdotal: BF01 = 1-3; no evidence: BF01 = 1. BF values for the alternative hypothesis (i.e., an association between speech and clinical covariates; BF10) are simply the inverse of BF01.

Mediation analysis

Finally, for any Bayesian correlation indicating moderate or above evidence for the alternative hypothesis, a causal mediation analysis was performed to examine whether the clinical covariate (parkinsonism, akathisia, CPZE dose) mediated the observed relationship between the associated negative symptom and speech feature, with confidence intervals for average causal mediation effects computed using non-parametric bootstrapping with 1000 simulations. Statistical analyses were conducted with R version 4.2.1 in RStudio (using the following packages: tidyverse, stats, mediation) and with JASP version 0.16.4.

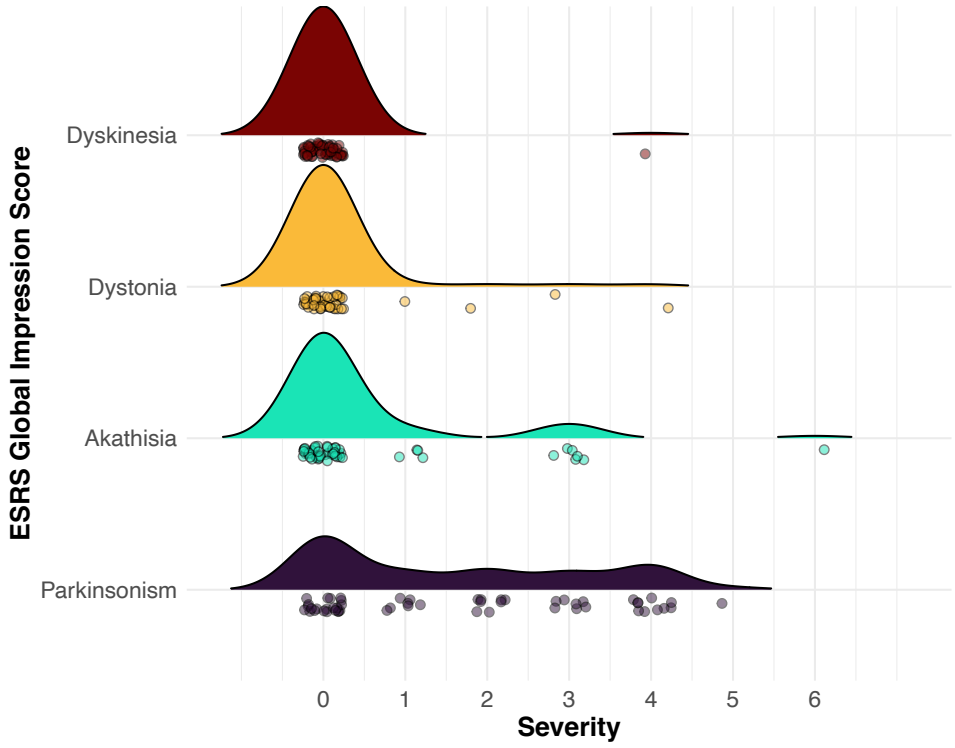

Figure 1. ESRS Global Impression score distributions in the participant sample.

Results

Speech correlates of negative symptom severity

The results of the correlational analysis between speech and negative symptom severity are summarized in Figure 2 and the full set of significant results are reported in Supplementary Table S2. Eight of the nine timing features and one of two linguistic features (total words) were significantly correlated with negative symptom severity, with the magnitude of effects ranging from *tau* = 0.21 to 0.42 (comparable to Pearson *r* values = 0.32 to 0.61; Gilpin, 1993). There were no significant correlations for any of the acoustic features.

Associations were generally not specific to a particular negative symptom domain: all significant features were associated with SANS Total scores, and most features showed additional associations with one or more SANS domain score. However, there was variability in the number of SANS domains associated with each feature. For example, slower speech rate

indexed greater negative symptom severity across all SANS scores. In contrast, a greater pause-word ratio was only significantly associated with greater SANS Total scores.

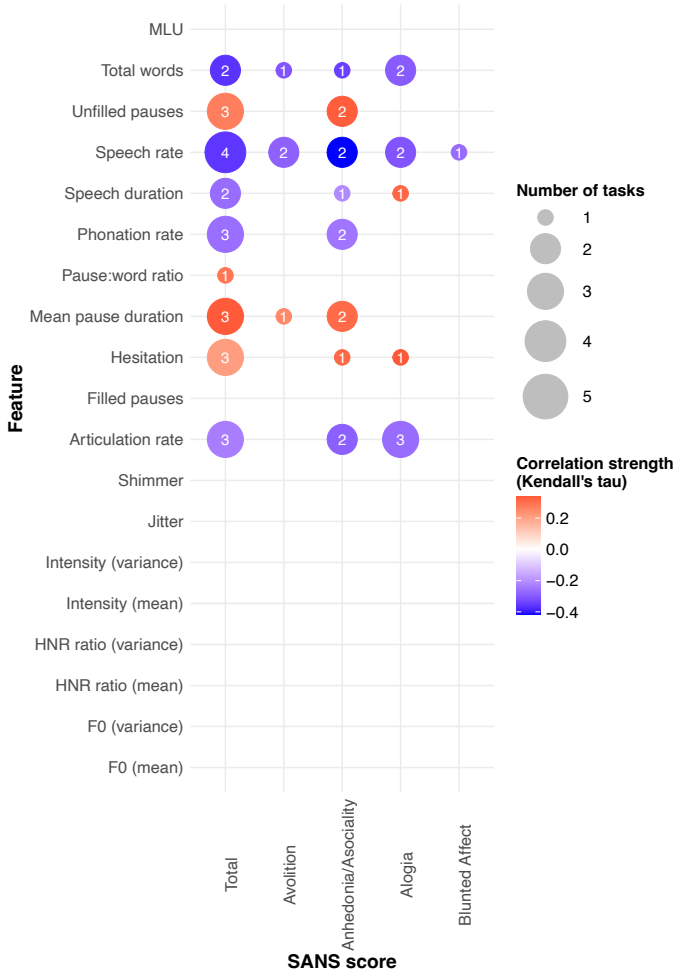

Figure 2. Significant correlations between speech features and negative symptom scores. Heatmap denotes correlation strength and number/size denotes the number of tasks in which the significant correlation was observed.

Speech feature associations with SANS Total scores were observed across multiple speech tasks, whereas several associations with SANS domain scores were only observed on a single task. The direction of the relationship between speech features and negative symptom

severity was consistent across tasks (except for speech duration, where the direction of the relationship was consistent with the specific demands of each task).

The semantic fluency (18 of 51 significant correlations) and picture description (14 of 51 significant correlations) tasks appeared most sensitive to the association between speech and negative symptom severity overall. However, there was some variability across negative symptom domains (Figure 3): speech features from the paragraph reading task showed the largest number of associations with SANS Alogia, and the journaling task (speech rate) had the only association with Blunted Affect, while journaling speech also showed a large number of associations with Total scores.

In contrast, no speech features had significant relationships with BPRS Total scores (p_{FDR}-values > .124), suggesting that the identified speech features were specifically capturing severity of negative symptoms rather than overall clinical severity.

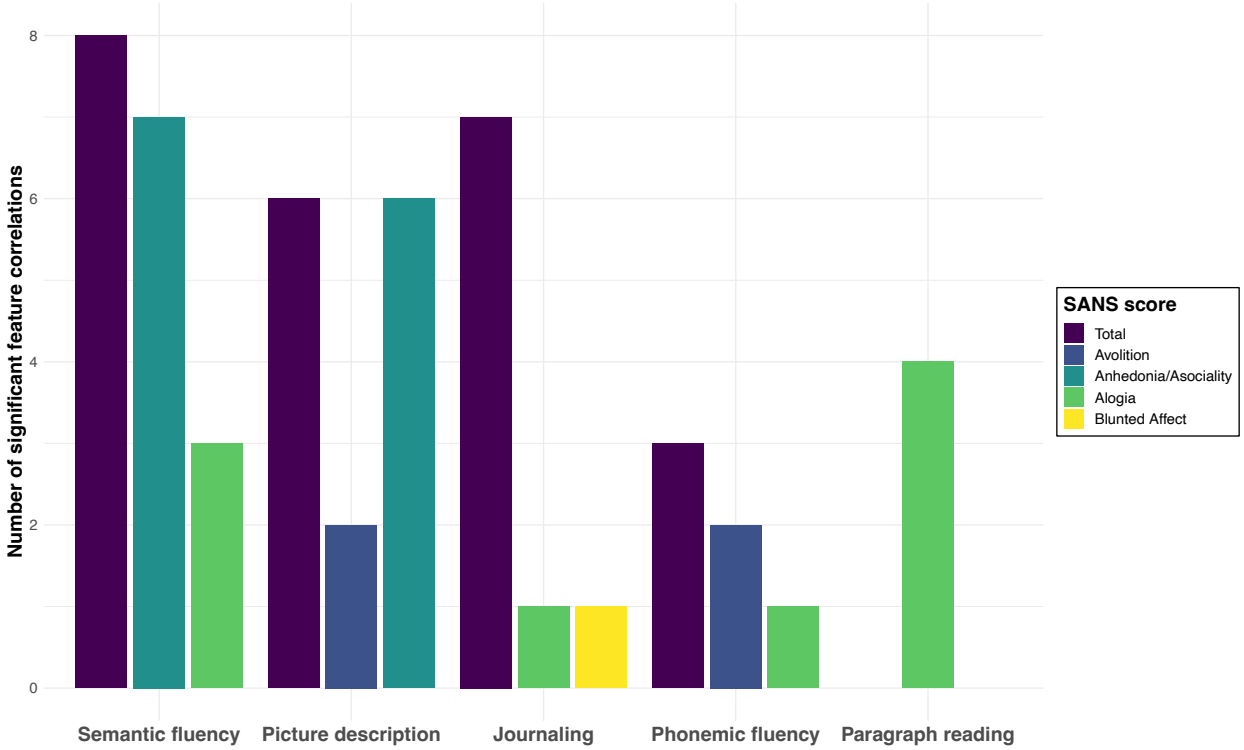

Figure 3. Number of significant correlations between speech features each negative symptom score as a function of task.

Speech associations with motor symptoms and antipsychotic dosage

No correlations between speech and ESRS scores (akathisia: p_{FDR}-values > .16; parkinsonism: p_{FDR}-values > .48) or between speech and CPZE dose (p_{FDR}-values > .05) were significant after FDR correction, suggesting no strong evidence that speech features of interest are influenced by antipsychotic dose or motor side effects. However, several correlations were significant prior to FDR correction: parkinsonism severity with greater unfilled pauses during phonemic fluency (p = .03); akathisia with reduced HNR variance during paragraph reading (p = .01), and with greater total words (p = .01) and speech duration (p = .03) during picture description; and CPZE dose showed associations with speech rate (p = .003-.01), total words (p = .003-.02), mean length of utterances (p = .02), and pauses (p = .04) on one or more tasks.

Bayesian analyses provided moderate support for the null hypothesis (i.e., the absence of an association) for the majority of features (52 of 90 examined feature-score associations), consistent with the frequentist hypothesis testing results (Supplementary Tables S3-S5). However, Bayes Factors for two features indicated at least moderate evidence for the *alternative hypothesis*. A higher CPZE dose was associated with fewer total words (phonemic fluency BF_{01} = 0.30 (moderate); semantic fluency BF_{01} = 0.08 (strong), picture description BF_{01} = 0.10 (moderate)) and slower speech rate (semantic fluency BF_{01} = 0.26 (moderate); picture description BF_{01} = 0.07 (strong)). Additionally, more severe akathisia was associated with greater total words (picture description BF_{01} = 0.16 (moderate)); however, the direction of this association was opposite to the one observed between total words and negative symptom

severity. There was no more than anecdotal evidence for an association between examined speech features and parkinsonism severity.

Mediation analysis results

Mediation analysis indicated a significant partial mediation for total words during the semantic fluency task only, such that CPZE dose partially mediated the relationship between total words and SANS Alogia scores (estimate = -0.30, p = .046) while the direct relationship between SANS Alogia and total words remained significant after removing the effect of CPZE dose (estimate = -0.91, p = 0.02). For all other relationships, mediation effects were nonsignificant (p-values ≥ .08) and direct effects between SANS scores and speech features remained significant after removing the effect of the clinical covariate (p-values ≤ .002).

Discussion

This study investigated associations between computational speech features and negative symptom severity in inpatient participants with SSD, and examined whether these features are influenced by antipsychotic dose and EPS. The results confirmed our expectations for relationships between negative symptoms and computational speech features. Speech features quantifying the timing characteristics of speech (e.g., slower speech rate, greater number of pauses) and amount of speech production (fewer total words) were significantly associated with the severity of overall negative symptoms, corroborating previous findings (Parola et al., 2020) and extending the associations to related features not previously included in prior analyses (e.g., articulation rate, phonation rate, pause-word ratio, hesitation). These features were additionally associated with individual negative symptom domains, including both speech-based symptoms (alogia, blunted affect) and symptoms not traditionally defined in terms of speech (avolition, anhedonia), suggesting the sensitivity of these features to multiple aspects of negative symptom

severity. However, associations with individual symptoms were variable across tasks and no speech feature showed selectivity for a particular symptom domain. Importantly, these speech features were not significantly associated with BPRS total scores. Taken together, the results suggest that the identified computational speech features are markers of negative symptom severity specifically, rather than reflecting overall psychiatric symptomatology in SSD.

Despite significant associations with negative symptoms, there was little evidence that these features were associated with antipsychotic dose or EPS, as indicated by nonsignificant correlations, and further confirmed by Bayesian support for the null hypothesis. These results build on previous studies reporting nonsignificant associations between computational speech and either EPS (Alpert et al., 2002) or antipsychotic dosage (de Boer et al., 2023), and provide further support that speech-based markers of negative symptoms are generally not confounded by these relevant clinical variables.

Our findings should be interpreted in the context of earlier findings of de Boer and colleagues (2020), who reported greater speech differences relative to healthy control participants in SSD participants taking high compared to low D2 dopamine receptor occupancy antipsychotics. Of note, the sample sizes of the SSD groups were limited, and the SSD groups significantly differed from each other on only two features reflecting total words and lexical diversity. These findings raise the potential for a differential influence of antipsychotic medication D2 action on speech, such as greater detrimental effects of a higher D2 receptor occupancy or greater beneficial effects of low D2 receptor occupancy drugs (de Boer et al., 2020). Alternatively, the findings could be influenced by other factors influencing clinical decision making, since medication choice was not randomized. It is possible that, in both the de Boer et al. (2020) study and the current study, patient clinical presentation (e.g., more chronic

course, greater treatment resistance) influenced both the medication prescribing patterns and the observed speech associations. We did not directly evaluate D2 receptor occupancy groups in the current study because many participants were taking low (e.g., clozapine) and high (e.g., aripiprazole) D2 receptor occupancy drugs concurrently.

Nonetheless, despite the overall absence of significant associations between speech and both antipsychotic dose and EPS, several correlations between speech and these variables were significant prior to FDR correction, and Bayesian analyses indicated at least moderate support for these associations for two features: total number of words and speech rate. Fewer total words and slower speech rate were associated with greater antipsychotic dose, particularly for speech from tasks with a greater cognitive focus such as verbal fluency and picture description, suggesting that these findings may reflect cognitive effects of antipsychotic medication (Joshi et al., 2021; Sakurai et al., 2013), consistent with the pattern reported by de Boer et al. (2020). However, mediation analysis indicated that these features continued to show an association with negative symptom severity after removing the effect of antipsychotic dose, and there was only a significant partial mediation effect of antipsychotic dose for the relationship between total words during semantic fluency and alogia severity. Therefore, although there was some evidence for an association between antipsychotic dose and specific speech features, these did not appear to significantly account for or confound the relationship between speech and negative symptom severity.

The total words feature was additionally associated with akathisia; however, the relationship was opposite to the one observed for negative symptoms, with *greater* total words indicating more severe akathisia. Moreover, there was no strong evidence for an association

between speech and parkinsonism. Overall, the severity of EPS did not appear to be significantly associated with speech markers of negative symptom severity in SSD.

In contrast to negative symptom associations with timing features and total words, acoustic speech features (e.g., variance in fundamental frequency) were not significantly correlated with negative symptom severity. Although previous reports have linked acoustic features to negative symptoms such as alogia and blunted affect, heterogeneity has also been noted across studies (Parola et al., 2020). Conceptually, these features are believed to map onto the symptom of blunted affect (i.e. monotone speech absent of variation in intensity and pitch) (Cohen et al., 2014). One possibility is that acoustic features, due to being computed by averaging across the entire speech recording, may be insensitive to whether vocal changes (e.g., in fundamental frequency) are occurring in tandem with changes in valence (e.g., speaking about a happy vs. sad topic). In the current study, only speech from the journaling task had a significant association with blunted affect. Compared to the other speech tasks, the journaling task is designed to elicit speech with greater and more varied affective content, suggesting that the sensitivity of computational measures of blunted affect may also depend on the elicited speech, such as the amount or variation of affective content.

Although associations between speech features and negative symptom severity were observed across tasks, variability was also noted, such that the semantic fluency, picture description, and journaling tasks appeared most sensitive for the speech-based assessment of overall negative symptom severity relative to the phonemic fluency and paragraph reading tasks. However, despite being insensitive to global negative symptom severity, speech from the paragraph reading task had the largest number of significant associations with alogia, suggesting that a highly structured speech task where all participants are required to read an identical text

passage may facilitate the assessment of alogia severity. Additionally, the journaling task had the only significant association with blunted affect, suggesting the utility of eliciting self-referential and/or affective speech content for assessing blunted affect. Additional research directly comparing a range of speech tasks and further manipulating task structure may help develop task-specific recommendations for the speech-based assessment of negative symptoms in SSD. Overall, the current results suggest that speech elicited even from brief speech tasks can serve as a marker of negative symptom severity, similar to the results of studies using longer speech recordings of interviews (Alpert et al., 2002; Cohen et al., 2021; Kliper et al., 2016).

Several limitations must be considered when interpreting the results of this study. The participant sample was not enriched for EPS. As expected for patients undergoing treatment with modern antipsychotic medications and current clinical best practices, dyskinesia and dystonia were very rare, and analyses were limited to symptoms of akathisia and parkinsonism. While additional research including participants with more severe and varied EPS will help further rule out the influence of EPS on speech markers of negative symptoms, the current study is relevant for most realistic clinical situations where automated detection of psychosis symptoms through speech and language are likely to occur. Moreover, the directionality of findings cannot be conclusively determined; for example, whether a greater CPZE dose alters speech or is more likely to be prescribed to patients with more severe symptoms. As a measure, CPZE was designed to indicate potency against psychosis symptoms (Atkins et al., 1997) and may not necessarily represent the magnitude of expected antipsychotic-related side effects. Additionally, analyses did not distinguish between classes of antipsychotic medications (e.g., typical vs. atypical) and receptor binding profiles (e.g., high vs. low dopamine D2 receptor occupancy). Future studies examining specific drug properties may help identify the mechanisms of action

most likely to impact speech in SSD. The analyses were limited to acoustic/timing features and speech production linguistic features due to their putative link to negative symptoms and motor speech, and because we hypothesized that these relationships were most likely to be sensitive to antipsychotic side effects; future studies including a more diverse range of linguistic features may reveal novel markers of negative symptoms. Finally, although the speech assessment was conducted in a quiet recording environment, the influence of environmental noise or device placement on the measurement of acoustic speech features cannot be conclusively ruled out.

In summary, the current results provide support for several computational speech markers of negative symptom severity and both frequentist and Bayesian evidence that these speech markers are generally not susceptible to antipsychotic medication side effects. Computational speech assessment and analysis may therefore help to provide a low-burden and objective measure of negative symptom severity to facilitate and improve symptom monitoring; for example, through remote, high-frequency assessment. Future studies focused on the development of normative data for speech profiles may additionally enable the use of computational speech to improve negative symptom screening and patient stratification to advance personalized treatment.

Data availability

The deidentified dataset for the current analysis is available upon request from the corresponding author.

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