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Utilizing Speech Analysis to Differentiate Progressive Supranuclear Palsy from Parkinson's Disease

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Abstract

Introduction: Distinguishing Parkinson's disease (PD) from Progressive supranuclear palsy (PSP) at early disease stages is important for clinical trial enrollment and clinical care/ prognostication.

Methods: We recruited 21 participants with PSP(n=11) or PD(n=10) with reliable caregivers. Standardized passage reading, counting, and sustained phonation were recorded on the BioDigit Home tablet (BioSensics LLC, Newton, MA USA), and speech features from the assessments

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Competing interests

Ram Kinker Mishra, Jose Casado, Rylee Cole, Adonay S. Nunes, Marc Derhammer, Gregory Barchard and Ashkan Vaziri are employees of BioSensics LLC.

Bijan Najafi, a co-author of this paper, serves as a consultant for BioSensics LLC. However, he did not participate in patient recruitment, and his contribution to the study was limited to interpreting data and providing guidance on data analysis.

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Supplementary material

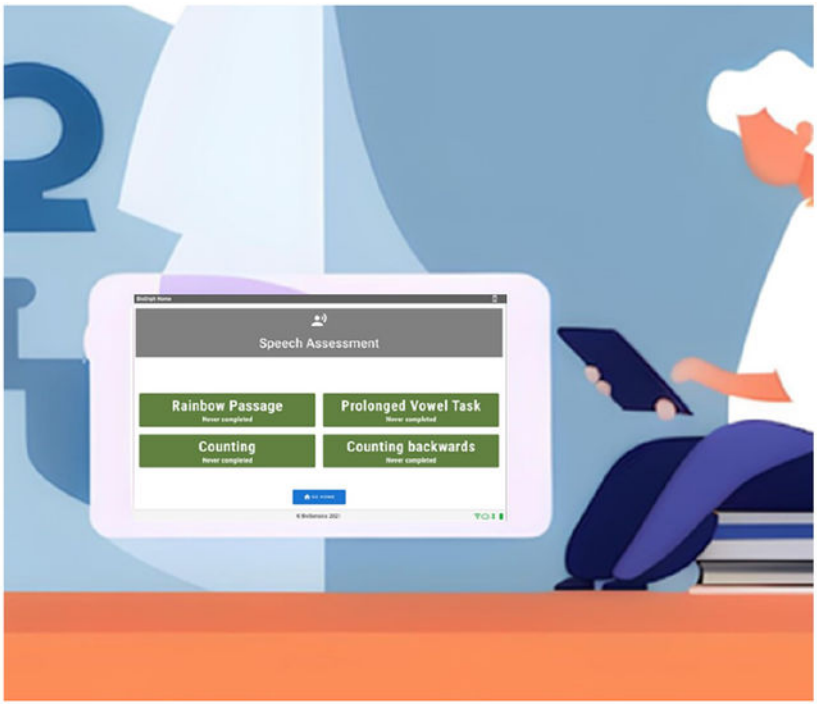
Supplementary material is available at *Parkinsonism and Related Disorders* online.

were analyzed using the BioDigit Speech platform (BioSensics LLC, Newton, MA USA). An independent t-test was performed to compare each speech feature between PSP and PD participants. We also performed Spearman's correlations to evaluate associations between speech measures and clinical scores (e.g., PSP rating scales and MoCA). In addition, the model's performance in classifying PSP and PD was evaluated using Rainbow passage reading analysis.

Results: During Rainbow passage reading, PSP participants had a significantly slower articulation rate (2.45(0.49) vs 3.60(0.47) words/minute), lower speech-to-pause ratio (2.33(1.08) vs 3.67(1.18)), intelligibility dynamic time warping (DTW, 0.26(0.19) vs 0.53(0.26)), and similarity DTW (0.43(0.27) vs 0.67(0.13)) compared to PD participants. PSP participants also had longer pause times (17.24(5.47) vs 8.45(3.13) sec) and longer total signal times (52.44(6.67) vs (36.67(6.73) sec) when reading the passage. In terms of the phonation '*a*', PSP participants showed a significant higher spectral entropy, spectral centroid, and spectral spread compared to PD participants and no differences were found for phonation '*e*'. PD participants had more accurate reverse number counts than PSP participants (14.89(3.86) vs 7.36(4.67)). PSP Rating Scale (PSPRS) dysarthria (r=0.79, p=0.004) and bulbar item scores (r=0.803, p=0.005) were positively correlated with articulation rate in reverse number counts. Correct reverse number counts were positively correlated with total Montreal Cognitive Assessment scores (r=0.703, p=0.016). Machine learning models using passage reading-derived measures obtained an AUC of 0.93, and the sensitivity/specificity in correctly classifying PSP and PD participants were 0.95 and 0.90, respectively.

Conclusion: Our study demonstrates the feasibility of differentiating PSP from PD using a digital health technology platform. Further multi-center studies are needed to expand and validate our initial findings.

Graphical Abstract



Keywords

Digital biomarkers; Machine learning; Remote patient monitoring; Speech assessments; Parkinsonism

Introduction

Progressive supranuclear palsy (PSP) is a rare neurodegenerative disease and an atypical parkinsonian disorder (APD) that shares some clinical features with Parkinson's disease (PD) including bradykinesia and other symptoms: tremor, rigidity, postural instability (typically later in the disease course), anxiety/depression, speech difficulties, cognitive impairment, and sleep disturbances, to name a few[1]. However, there are important clinical differences between the two conditions such as vertical eye movement abnormalities, early balance loss, changes in speech and swallow function, and cognitive (typically frontal executive) abnormalities[2], [3].

Previous studies suggest speech assessment can be useful in differentiating between PD and PSP, as these two conditions often exhibit distinct speech characteristic[4]. PSP patients exhibit weaker overall voice quality and speech reproduction ability compared to patients with PD[4], [5]. To distinguish the two diagnoses more accurately, it may prove useful to examine both temporal[6], [7] and spectral acoustic features[8] and their relationship to clinical symptoms.

To improve the care and treatment of people with PD and PSP, quantitative, observer-independent, real-time, and validated measures with noninvasive monitoring are crucial. Thus, this study utilized a digital health technology platform to compare speech parameters between PD and PSP. We considered both temporal and spectral acoustic features of speech as well as their relationship to clinical symptoms to obtain complementary information about speech characteristics in classifying PD and PSP.

Methodology

Participants

The study protocol was approved by the Mass General Brigham Human Research Committee and the Johns Hopkins Medicine Institutional Review Board. All procedures were in accordance with the Helsinki Declaration of 1975, as revised in 1983. Participants with probable PSP or PD (Supplementary Table 1) with a caregiver able to assist with all study-related procedures were recruited at Massachusetts General Hospital and Johns Hopkins from November 2021-November 2022.

Data Collection and Analysis

BioDigit Home (BioSensics LLC, Newton, MA USA) was used to measure motor, speech, and cognitive function in participant's homes using digital assessments and wearable sensors. It provides visual and audio instructions, as well as reminders to ensure consistent and timely collection of data.

A study-specific version of the BioDigit Home was developed to include measures relevant to PSP and PD, including a fall diary, the PSP Rating Scale (PSPRS), MDS-Unified PD Rating Scale (MDS-UPDRS), and Montreal Cognitive Assessment (MoCA). These were collected either virtually (19 participants; Zoom, San Jose, CA) using the modified version of the rating scales (modified MDS-UPDRS Part III [9]; modified PSPRS [10], or during in-person visits (2 participants).

Participants performed five digital assessments of speech:(1) passage reading, (2) counting forward from 0 to 20, (3) counting backward by 3 from 50 to 0, and (4,5) sustained vowel phonation *e* and *a*. For all tasks, participants were in a quiet environment and outside noise was kept to a minimum.

Speech data were analyzed using BioDigit Speech (BioSensics LLC, Newton, MA USA) (Supplementary Figure 1). BioDigit Speech uses automated speech recognition (ASR) to transcribe the speech and provides timestamps for segments, rather than at the word level. Dynamic time warping (DTW) was used to compare the transcribed reading and the original passage. Rather than encoding words, letters were encoded as numbers as this better captures speech alterations. Rather than encoding words, letters were encoded as numbers as this better captures speech alterations [11]. Similarity DTW represents the 1/(1 + DTW distance) between the original passage and the transcribed reading. Higher values indicate greater similarity between the two encoded signals. Intelligibility DTW represents the similarity between a transcription from a medium-size ASR model and a small-size ASR model. The pre-processed audio was then analyzed to extract phonatory, articulatory, prosody and intelligibility features relevant to each assessment including passage reading, counting, and sustained phonation.

Statistical Analysis and Machine Learning

An independent *t*-test was performed for each feature. The effect size of the differences between PSP and PD was calculated with Cohen's *d*. For each task, features were correlated with the dysarthria and dysphagia items from the PSP rating scale (scale items 12 and 13, correlated both individually and as part of a summed "bulbar" subscale score) and total MoCA scores. Spearman's correlation was used to evaluate for associations between speech measures and clinical scores. False discovery rate with a $q = 0.1$ was used to correct for multiple comparisons.

Model performance to classify subjects with PSP and PD was assessed using features from the passage reading, given that this task had the most significant differences between groups. A Gaussian process classifier with a radial basis function kernel was trained for classification and evaluated with a leave-one-subject-out (LOSO) cross validation. All the available visits per subject were used (total of visit = 31; 10 PD visits and 21 PSP visits). Performance was assessed with area under the curve (AUC), accuracy, sensitivity and specificity. For estimating clinical scores, a stochastic gradient descent regressor with an elasticnet penalty was used and evaluated with a LOSO cross validation. Performance was assessed with the mean squared error, mean absolute error and explained variance. A permutation-based method was used to estimate the contribution of the features by removing a feature at each iteration and measuring the difference in model performance[12].

Results

Twenty-one participants were enrolled, including PSP (n=11) and PD (n=10). There were no significant differences between the groups in age (PSP = 67.6 (1.30); PD = 70.30 (1.80) years, p = 0.53), and years of education (PSP = 17.60 (0.80); PD = 18.00 (0.80), p = 0.07). However, duration of disease (PSP = 14.00 (3.50); PD = 87.90 (16.90) months, p = 0.003) and MoCA scores (PSP = 23.10 (1.50); PD = 26.5 (0.60), p = 0.03) were significantly different between the 2 groups (see Supplementary Table 2).

Rainbow Passage Reading

We found a significant slower articulation rate in PSP (2.45 (0.49) words/second) compared to PD participants (3.60 (0.47), p < 0.001) (Figure 1A). In terms of the accuracy, PSP showed less similarity between the original passage and the transcribed reading (i.e., similarity dynamic time warping or DTW) (0.43 (0.27) vs 0.67 (0.13), p = 0.022) (Figure 1B) and less similarity between a transcription from an automatic speech recognition (ASR) model of size medium and a mode of size small (i.e. intelligibility DTW) (0.26 (0.19) vs 0.53 (0.26), p = 0.017) compared to PD participants (Figure 1C).

The speech to pause ratio was also significantly lower in PSP (2.33 (1.08)) compared to PD participants (3.67 (1.18), p = 0.016) (Figure 1D), indicating that PSP participants tended to be more hesitant when reading the passage. Accordingly, PSP had significantly longer pause times (17.24 (5.47) vs 8.45 (3.13) sec, p < 0.001) (Figure 1E) and significantly longer total signal times (52.44 (6.67) vs (36.67 (6f.73) sec, p < 0.001) than PD participants (Figure 1F).

For the acoustic features, PSP participants' reading was louder (90.49 (12.37)) than PD participants' (75.04 (18.70), p = 0.043) (Additional data are available in the Supplementary Table 3).

3-n Back Counting

PD had more accurate reverse number counts than PSP participants (PD: 14.89 (3.86) vs PSP: 7.36 (4.67), p = 0.001). There were no significant differences in acoustic measures between PSP and PD for 3-n back counting (Additional data are available in the Supplementary Table 4).

Sustained Phonation 'a' and 'e'

For sustained phonation 'a', there were significant differences between PSP and PD participants in spectral entropy (PSP: 4.63 (0.39) vs PD: 4.15 (0.35), p = 0.007), spectral centroid (2310.60 (722.20) Hz vs 1602.30 (398.00) Hz, p = 0.013), and spectral spread (2848.60 (793.40) Hz vs 2070.10 (517.00) Hz, p = 0.016 (Additional data are available in the Supplementary Table 5). These spectral differences indicated that PSP participants' frequency content of the phonation was more complicated and broader, and contained higher frequency shifts.

The data for a sustained vowel 'e' phonation are provided in Supplementary Table 6.

Correlation between Speech Outcomes and Clinical Scores in PSP

In Rainbow Passage reading, bulbar scores were negatively correlated with similarity DTW (r= −0.80, p= 0.010), but positively correlated with the ratio of extra words (r= 0.80, p= 0.01) and the ratio of missing words (r= 0.91, p< 0.001) (Supplementary Figures 2A, 2B, 2C, respectively). The PSPRS dysphagia score was negatively correlated with DTW similarity (r= −0.74, p= 0.014) and positively correlated with the ratio of extra words (r= 0.82, p= 0.004) and the ratio of missing words (r= 0.78, p= 0.007 (Supplementary Figures 2D, 2E, 2F, respectively). PSPRS dysarthria (r= 0.79, p= 0.004) and bulbar scores (r= 0.803, p= 0.005) were positively correlated with articulation rate in reverse number counts. Moreover, total MoCA scores were positively correlated with correct reverse number counts (r= 0.703, p= 0.016). Table 1 indicates the correlation between speech outcomes and clinical scores.

Spearman rho correlation analysis between MoCA scores and PSPRS dysphagia/bulbar scores showed a significant negative correlation (dysphagia: r= −0.43, p= 0.008; bulbar: r= −0.39, p= 0.018), indicating that lower MoCA scores were associated with worse PSPRS dysphagia/bulbar scores.

Model Performance (Machine Learning)

A model trained using speech features from passage reading achieved an AUC = 0.93 with an accuracy of 0.94 in differentiating between PD and PSP. The sensitivity in correctly classifying PSP participants was 0.95 and the specificity of correctly identifying PD participants was 0.90. To further explore the contribution of the features in the classification, a permutation approach was used. The results are presented in Supplementary Figure 3. Articulatory rate was the most highly contributing feature followed by total signal time, mean pause length and total pause length. These were also the most significantly different features in the statistical analysis.

Meaningful models are the ones with a positive explained variance, thus dysarthria and MoCA did not significantly predict the scores. mPSPRS-21 showed a positive explained variance, but with a low value. However, dysphagia and bulbar scores were predicted with an explained variance of 0.53 and 0.61, respectively. This translates to a mean absolute error of 0.50 and 0.78 points and a mean absolute error of 0.48 and 0.85, respectively. The predicted and actual score correlations were 0.74 and 0.79, respectively (Supplementary Table 7). Supplementary Figures 4A, 4B, and 4C (Top) show the predicted vs clinical scores from the regression model trained with passage features. As in the classification, the feature importance was calculated for the models with larger than zero explained variance and shown in Supplementary Figures 4D, 4E, and 4F (Bottom).

Discussion

The findings of this study support and extend previous studies that reported a decreased net speech rate (total speech time minus total pause time) and an increased pause ratio (percentage of speech time consumed by pauses) in PSP compared to PD[15]. Multiple temporal and spectral speech features were differentially affected in PSP and PD. It has

been suggested that dysarthria in PSP may be linked to spastic components associated with reduced speech rate and articulation[13], [14]. This was supported by our findings of a significant correlation between dysarthria and articulatory rate.

It is crucial to identify the most important features that differentiate PSP from PD. Group classification using speech features achieved an accuracy of 94% with a sensitivity of 95% and specificity of 90%, and this high performance was expected based on the strong significant differences between the groups despite limited sample size. Rusz *et al.* reported an accuracy of 95% for classifying PD and APD and 75% accuracy in classifying Multiple system atrophy and PSP [4]. A recent study reported an accuracy of 80% classifying the latter groups using features from multiple speech assessments[15].

This study's strengths include analyzing both temporal and spectral speech aspects, correlating speech features with clinical outcomes, employing machine learning to classify group disorders and predict clinical scores in PSP, utilizing 2-site study design, and implementing a digital health platform. This platform facilitated convenient and efficient data collection for both participants and study team members and is likely to translate well to the home environment. Furthermore, the digital assessments were highly customizable based on initial piloting and user feedback.

Study limitations included small sample size, a PSP sample limited to the Richardson syndrome variant, and lack of pathological confirmation of PD/PSP diagnosis. Additionally, the patients' prior and current speech therapy experience were not documented. Though unlikely given the simplicity of the digital assessments, differences in cognitive performance (PD average MoCA =26.5; PSP average MoCA=23.1) may have impacted our results (particularly 3-n back counting, which has an attentional component). Lower MoCA scores were also associated with worse PSPRS dysphagia/bulbar scores, but these correlations do not diminish the strength of our approach to differentiate between PSP and PD by analyzing brief speech samples. Despite the notably shorter duration of disease in individuals with progressive supranuclear palsy (PSP) compared to those with PD, our study revealed distinct speech features that indicate the potential for distinguishing between PSP and PD speech features, where PSP patients exhibited more pronounced speech impairments despite having a shorter disease duration. Future comparisons of PSP and PD earlier in the disease course (where a lesser degree of impairment in PD is expected) will likely yield even greater differences than those observed in our study.

We estimated sample sizes based on our key findings (Supplementary Table 8) for future considerations. Longitudinal monitoring of these speech features to track disease progression is also needed and is underway at our centers. Ultimately, we hope that using these digital speech assessments will enable earlier accurate disease detection and prompt appropriate referral to clinical trials and interventions such as speech therapy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

The data that support the findings of this study are available only for non-commercial applications from the corresponding author, upon reasonable request.

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Highlights

- Distinguishing PSP from PD can be challenging
- Digital health technology may distinguish speech patterns in PSP vs. PD
- Found greater impairments in reading, phonation, and reverse counting in PSP
- PSP digital measures correlated with clinical rating scale scores

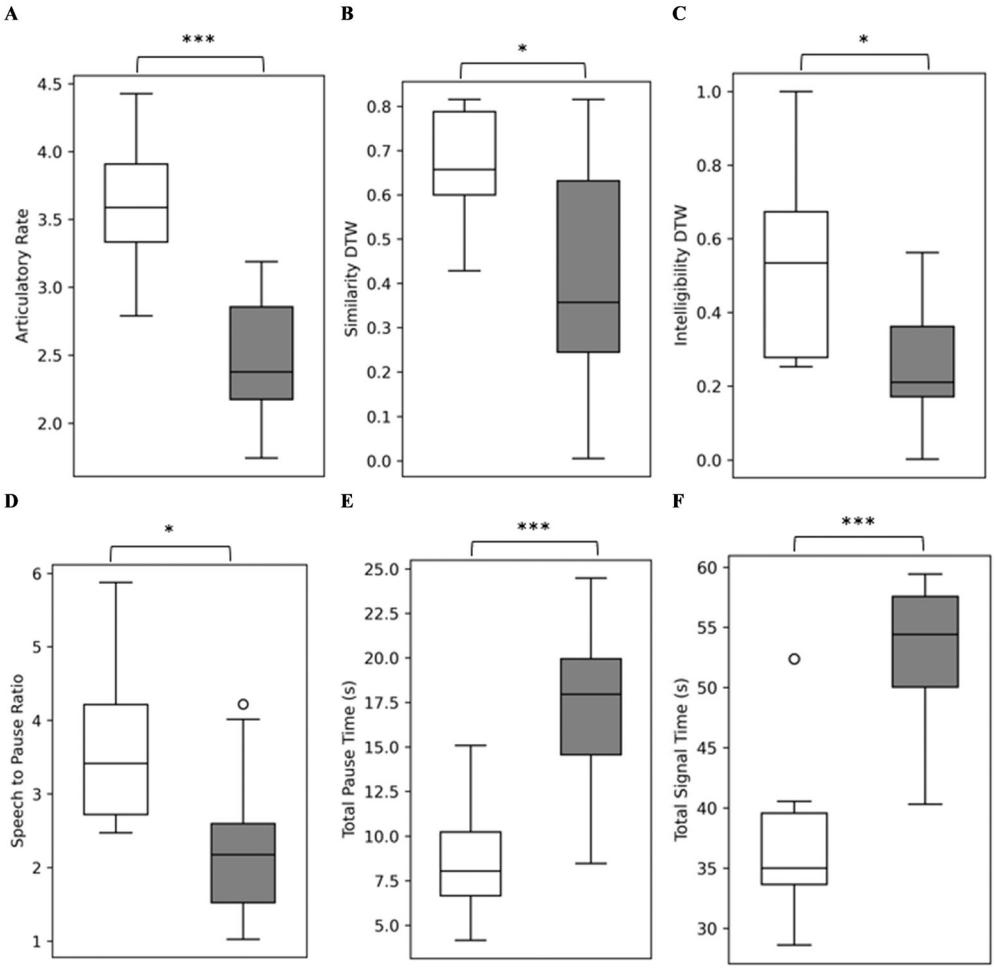

Figure 1. Whisker box plots of rainbow passage speech features significantly different between groups.

(A) articulatory rate (words/minute), (B) similarity DTW, (C) intelligibility DTW, (D) speech to pause ratio, (E) total pause time (sec), (F) total signal time (sec). * p-value <.05, ** p <.01, *** p <.001 DTW, dynamic time warping

Table 1.
Correlation between speech outcomes and clinical scores in PSP.

Speech outcomes were computed from Rainbow Passage reading, 3-n back counting and sustained '*a*' vowel phonation.

	PSPRS Dysarthria			PSPRS Dysphagia			Bulbar Subscale Score			MoCA Total Score	
Rainbow passage	**r**	**p-value**		**r**	**p-value**		**r**	**p-value**		**r**	**p-value**
loudness	−0.333	0.347		0.091	0.803		−0.051	0.896		0.025	0.946
similarity DTW	−0.539	0.108		**−0.742**	**0.014**		**−0.799**	**0.01**	*	0.006	0.986
intelligibility DTW	−0.624	0.054		−0.363	0.302		−0.46	0.213		−0.02	0.959
articulatory rate	−0.354	0.316		0.467	0.173		0.247	0.522		−0.17	0.633
total voiced time	−0.132	0.717		−0.688	0.028		−0.672	0.047		−0.05	0.892
total pause time	0.132	0.717		−0.065	0.859		0.085	0.828		0.056	0.879
total signal time	0.305	0.391		−0.519	0.124		−0.306	0.423		0.222	0.537
speech to pause ratio	0.104	0.775		−0.195	0.59		−0.213	0.582		−0.09	0.799
number of pauses	0.083	0.819		−0.599	0.067		−0.363	0.337		0.167	0.644
mean pause length	−0.118	0.746		0.532	0.113		0.341	0.37		0.123	0.734
pitch	−0.097	0.79		0.078	0.831		−0.094	0.811		0.161	0.658
pitch SD	−0.368	0.296		−0.013	0.972		−0.332	0.383		0.253	0.48
ratio extra words	0.437	0.207		**0.817**	**0.004**	*	**0.8**	**0.01**	*	−0.04	0.919
ratio missing words	0.597	0.069		**0.783**	**0.007**	*	**0.906**	**<0.001**	*	0.009	0.98
3-n back counting	**r**	**pval**		**r**	**pval**		**r**	**pval**		**r**	**pval**
loudness	−0.163	0.632		−0.072	0.834		−0.148	0.683		0.221	0.513
correct counts	0.046	0.893		0.014	0.966		−0.009	0.98		**0.703**	**0.016**
incorrect counts	0.256	0.447		0.163	0.632		0.282	0.43		0.016	0.962
ratio correct counts	−0.46	0.155		−0.35	0.292		−0.517	0.126		0.46	0.155
articulatory rate	**0.79**	**0.004**	*	0.617	0.043		**0.803**	**0.005**		−0.08	0.819
total voiced time	−0.336	0.312		−0.158	0.643		−0.247	0.492		0.341	0.305
total pause time	0.082	0.812		0.234	0.488		0.167	0.645		−0.34	0.312
total signal time	−0.392	0.233		0.072	0.834		−0.123	0.734		−0.32	0.341
pause to speech ratio	0.133	0.698		0.311	0.352		0.259	0.469		−0.26	0.444
mean pause length	0.066	0.847		0.081	0.812		0.019	0.959		−0.3	0.379
pitch	−0.515	0.105		−0.33	0.322		−0.537	0.109		0.258	0.444
pitch SD	0.025	0.941		−0.387	0.24		−0.34	0.337		0.088	0.798

In bold, correlations with a p-value <.05, * = significant after FDR correction.