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Altered speech with migraine attacks: A prospective, longitudinal study of episodic migraine without aura

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Abstract

Background and Objective: Some individuals with migraine report the presence of speech changes during their migraine attacks. The goal of this study was to compare objective features of speech during the migraine pre-attack, the migraine attack, and during the interictal period.

Methods: This was a prospective, longitudinal, observational study of adults with episodic migraine and healthy nonmigraine controls. Participants provided speech samples three times per day using a speech elicitation tool included within a mobile app. Six complementary speech features that capture articulation and prosody were extracted from speech samples. Participants with migraine maintained a daily headache diary using the same app. A mixed effects model and t-tests were used to investigate differences in speech features between controls, the migraine pre-attack phase, the migraine attack, and the interictal period.

Results: In total, 56,767 speech samples were collected, including 43,102 from 15 individuals with migraine and 13,665 from matched healthy controls. Significant group-level differences in speech features were identified between those with migraine and healthy controls and within the migraine group during the pre-attack vs. attack vs. interictal periods (all $p < .05$). Most consistently, speech changes occurred in the speaking rate, articulation rate and precision, and phonatory duration. Within-subject analysis revealed that seven of 15 individuals with migraine showed significant change in at least one speech feature when comparing the migraine attack vs. interictal phase and four showed similar changes when comparing the pre-attack vs. interictal phases.

Conclusions: Changes in speech occurred in almost half of the individuals during migraine attacks. Once confirmed in subsequent studies, speech changes could be considered a feature of the migraine attack.

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Keywords

Migraine; speech; headache; premonitory; language; analytics

Introduction

Difficulties with speech and language have been documented during the aura phase of migraine. Although changes in speech during other phases of the migraine attack are reported by patients, objectively measured changes in speech associated with migraine have been inadequately investigated during the non-aura phases of the migraine attack. We hypothesized that subtle changes in speech, changes that an individual may or may not notice but that can be detected objectively, are present during the pre-attack phase (defined as 0–12 hours prior to an individual recognizing the start of a migraine attack) and headache phases of the migraine attack.

Changes in speech patterns during migraine attacks might be expected given the relatively widespread alterations in brain function and functional connectivity that occur during migraine attacks. The ability to share our thoughts and ideas through spoken communication is a complex and fragile process. Even the simplest verbal response requires a complex sequence of events. It requires thinking of the words that best convey the message, sequencing these words in an order that is allowed in the language, and then sending signals to the muscles required to produce speech. Even the slightest disturbance to the brain areas that orchestrate these events can manifest in speech problems.

The aims of this study were to determine if there are objectively measured changes in speech during the 12 hours prior to an individual recognizing that they are having a migraine attack (referred to as the “pre-attack” phase hereafter) and during the migraine attack compared to the interictal period.

Methods

Research participants

This Mayo Clinic IRB-approved study was conducted between January and December 2017. All participants completed an informed consent process. Participants were required to be 18 years of age or older, native English speakers, and willing to record speech samples three times per day. Potential participants were excluded if they had a known speech or language disorder, if they drank more than two alcoholic beverages per week, if they used illicit drugs, and if they used prescription drugs that could impact speech and language patterns (e.g. topiramate). Healthy controls had no personal history of migraine. Participants with migraine reported having between four and 10 migraine attacks and fewer than 15 headache days per month on average over the 3 months prior to enrollment. Use of migraine preventive and abortive therapies was allowed, except for those therapies that in the investigator’s opinion could impact speech and language (e.g. topiramate). Potential participants were interviewed by the headache specialist (TJS), and those who had ever had a migraine with aura attack were excluded from participating in this study. Migraine

diagnoses were made according to the diagnostic criteria of the International Classification of Headache Disorders 3rd edition (beta version) (1). Healthy controls were age and sex-matched to the participants with migraine.

Baseline study visit

During a single baseline study visit, data were collected on participant demographics, headache and migraine attack frequency, migraine attack features, and premonitory symptoms (Table 1). Participants reported whether they had premonitory symptoms and, if so, selected their symptoms from a list (see Tables 1 and 2) and reported how often their migraine attacks were preceded by premonitory symptoms. Participants were provided with a tablet that contained a headache diary mobile app with integrated speech elicitation tasks. Participants were trained on how to use the app and practiced doing so under the supervision of the research team.

Follow-up telephone calls

Participants were contacted by telephone every two weeks to determine if there were any time periods during which their speech may have been impacted by factors other than migraine (e.g. laryngitis). When such conditions were present, speech samples collected on those dates were excluded from analysis.

Headache diary

Participants with migraine were asked to maintain a daily electronic headache diary for a minimum of 3 months. If a participant did not experience at least 20 migraine attacks by the conclusion of 3 months, they were asked to continue their participation until they had 20 migraine attacks, up to a maximum of 6 months of participation. Each day, participants were asked to input whether they had a headache that day. When they experienced a headache, they provided information on start and stop times, headache severity, location, quality, and presence of light sensitivity, sound sensitivity, nausea, vomiting, and worsening of pain with routine physical activity. Participants indicated all premonitory symptoms that they experienced by choosing from a list of potential symptoms (Table 2).

Speech sampling, processing and analyses

Healthy controls were asked to provide speech samples three times per day, equally dispersed throughout waking hours, for one month. Participants with migraine also provided speech samples three times per day and they were asked to provide an additional speech sample during migraine attacks. Participants with migraine recorded speech samples for at least 3 months, up to 6 months or until they had recorded 20 migraine attacks in their headache diary.

Speech samples were collected via the same mobile app that contained the headache diary. While recording, participants were instructed to hold the device 12 inches from their mouth and speak in a normal conversational manner. The speech paradigm consisted of reading and reciting five sentences, enunciating four vowel sounds for as long as possible, and repeating the word “buttercup” as many times as possible in one breath. The recorded samples were automatically uploaded to a secured site.

Speech analytics

For those with migraine, diary information was used to identify which speech samples were collected during migraine attacks. Speech samples were categorized to the pre-attack phase if they occurred 0–12 hours before a reported migraine attack onset and interictal if they occurred 48 hours before the start and 48 hours after the end of a migraine attack.

Six complementary feature sets that represent physical characteristics of speech were extracted from participant speech recordings:

- **Articulation entropy:** A proxy measure of articulatory precision, or the accuracy with which articulators (e.g. tongue, lips, palate) achieve their targets. Articulation entropy accomplishes this measurement by estimating the number of distinct sounds a speaker is capable of producing. The articulation entropy was measured using the algorithm in Jiao 2016 (2).
- **Rate features – speaking rate, pause rate, articulation rate:** Speaking rate measures the rate at which a speaker enunciates syllables in a sentence, including time spent pausing between words. Similarly, articulation rate measures the rate of syllable enunciation after removing pauses from the speech. Removing pauses provides an estimate for the speed at which the articulators are moving. Lastly, the pause rate measures the percentage of a sentence that a speaker spends pausing in between words. The rate measures were estimated using the algorithm in Jiao 2015 (3).
- **Vowel space area:** The area of the quadrilateral in vowel space formed by the first and second formants of the four English corner vowels (4). Because formants – resonant peaks in the frequency spectrum of speech – relate to the kinematics of speech production (e.g. tongue position, mouth cavity size and shape), vowel space area can be used to measure changes in articulatory control. The vowel space area was estimated using the algorithm in Sandoval 2013 (5).
- **Energy decay slope:** During a sustained phonation, we measure the rate at which a speaker's volume decreases over time. A large energy decay slope can be an indicator of fatigue.
- **Phonatory duration:** During a sustained phonation, we measure the length of time a speaker can produce a vowel sound (phonation) before stopping to take a breath.
- **Average pitch:** The fundamental frequency of a speaker's voice averaged across the duration of five sentences.

Data analyses

Descriptive statistics are provided for participant demographics, baseline headache characteristics and daily headache diary data (Tables 1 and 2). Descriptive statistics for each speech feature by migraine phase (including healthy controls) are also provided (Table 3). A mixed effects model approach was used to determine the differences in speech over the time course of a migraine attack, with comparisons to speech from healthy controls. Given the

nested structure of the data, a three-level model was constructed to account for the multiple speech measurements (level 1) nested within a day (level 2) and the multiple days of measurements nested in a subject (level 3). For each speech feature, a multi-level mixed effect model was constructed with migraine phase as the fixed effect, and subject ID and day as the random effects. The fixed effect included the control phase and all three migraine phases: Pre-attack, migraine, and interictal. The temporal nature of the data (speech measured as a function of time) was adjusted for by including a rank order variable as a covariate. The working correlation structure for the models was set as independent to account for the different subject-level variances, and the unbalanced number of speech samples (i.e. not an equal number of samples per subject). A regression slope was calculated for each migraine phase group relative to controls; the *p*-value for the slope is reported here (see Table 4). Similarly, the differences between migraine phases (excluding controls) were estimated and the *p*-values are reported here (Table 4).

Data from migraineurs were further analyzed to examine speech changes at the subject level. The paired t-test (or nonparametric analog) was used to compare speech features between a) the interictal and migraine pre-attack phases, b) the interictal and migraine attack phases, and c) the pre-attack and migraine attack phases. To control for the increased false discovery rate, we used the Benjamini-Hochberg adjustment (10).

For all analyses, statistical significance was defined as alpha of 0.05. Analyses were performed with STATA 13.1 (College Station, TX).

Results

The 15 healthy control and 15 migraine participants were well balanced for age and sex. Both the healthy control and migraine group contained 13 female and two male participants. The average participant age was 44.5 ± 13 years in the migraine group and 43.1 ± 14 years in the control group.

1426 days of headache diary data, including 424 headache days, of which 323 days met criteria for migraine/probable migraine, were collected from the 15 migraine participants.

Between the individuals with migraine and the 15 healthy controls, 56,767 speech samples were collected (11 samples per recording session), including 13,665 speech samples from healthy controls and 43,102 from individuals with migraine. Amongst those with migraine, 11,253 were collected during the interictal phase, 2,475 were collected during the pre-attack phase, and 2,079 were collected during a migraine attack.

Table 1 includes headache and migraine frequency reported by participants according to their retrospective recall at the baseline study visit and prospectively recorded in headache diaries. At baseline, average headache frequency was reported as 9.3 days per month and average migraine attack frequency was 6.2 per month. Per headache diaries, average headache frequency was 8.9 days per month and average migraine attack frequency was 6.8 per month.

Information about premonitory symptoms is found in Tables 1 and 2. At baseline, all individuals with migraine reported having premonitory symptoms with at least some of their attacks. On average, they reported that 90% of their migraine attacks were preceded by premonitory symptoms and that when they noted symptoms thought to be premonitory in nature, 86.7% of the time a migraine attack followed. According to headache diaries, 72.1% of migraine attacks were preceded by premonitory symptoms. At baseline, the most commonly reported premonitory symptoms based upon participant recall included (in descending order of frequency): Light sensitivity, neck stiffness, fatigue/tiredness, generalized feeling of being unwell, and sound sensitivity. Problems speaking were reported by 20% of the individuals with migraine. According to prospective headache diaries, the most commonly reported premonitory symptoms included (in descending order of frequency): Generalized feeling of being unwell, fatigue/tiredness, neck stiffness, mood changes, and light sensitivity. Problems speaking were reported by 27% of participants.

Speech features

Table 3 contains average values and standard deviations of the speech feature sets.

Comparing individuals with migraine to healthy controls.—We compared speech patterns of those with migraine against the group of age-and-gender-matched healthy controls (Tables 3 and 4). There were several group-level differences that indicated a loss in articulatory precision, a change in speech rhythm, and phonatory fatigue during migraine attacks and during the pre-attack phase compared to healthy controls. For example, migraineurs had significantly lower values of phonatory duration and higher energy decay slopes during the migraine attack, pre-attack phase, and interictal phase when compared to healthy controls. There were additional group-level differences between healthy controls and those with migraine in the interictal phase. Healthy controls were shown to have significantly higher speaking, articulation rates, and lower average pitch compared to migraineurs during the interictal period. These results are shown in Tables 3 and 4.

Comparing migraine pre-attack, migraine attack and interictal phases.—At the group level (Table 4), there were no statistically significant differences in speech features between the migraine and pre-attack phases. This indicates that with respect to the speech features, the migraineurs in this cohort had speech characteristics up to 12 hours prior to a migraine that were indistinguishable from speech characteristics during a recognized migraine attack. A decreased speaking rate, articulation rate, and articulation entropy were all statistically significant characteristics of the pre-attack and migraine phases compared to the interictal phase. A statistically significant decrease in average pitch was also a feature of migraine compared to the interictal phase.

Changes in speech features were also investigated within individual subjects using paired t-tests. Seven of the 15 migraine participants showed statistically significant changes in speech patterns between interictal and migraine attack phases. Of these seven patients, three experienced a statistically significant change in more than one speech feature (Table 5). Figure 1 illustrates the observed speech changes for these subjects with migraine.

Additionally, four of the 15 migraine participants showed a statistically significant change in the speech features between the interictal and pre-attack phase (see Table 6 and Figure 2).

Relationship between self-reported changes in speech to objectively measured changes in speech.—At the baseline visit (prior to beginning the research headache diary and speech elicitation task), three of 15 individuals with migraine self-reported that they experienced speech changes during their “pre-attack” phase. Among these three individuals, none experienced a statistically significant change in speech when comparing their pre-attack to interictal phases. Two had a statistically significant change in speech when comparing their migraine attack to interictal phases. Among the four individuals who self-reported a change in speech during the pre-attack phase, at least once while prospectively providing data in the headache diary, none had a statistically significant change in speech when comparing their pre-attack to interictal phases. Within this same subgroup, two subjects displayed a statistically significant change between the migraine and interictal phases. Amongst the four individuals who had significant objectively measured changes in speech when comparing the migraine pre-attack to interictal phases (Table 6), none self-recognized such speech changes.

Discussion

This study investigated objective changes in speech that occur prior to and during migraine attacks. The study showed that close to half of participants had objective changes in speech during the migraine attack compared to their interictal phase. The most common changes were slowing of speaking rate and a decrease in articulatory precision, indicating a measurable decrease in speech motor excursions during a migraine attack. Significant changes in speaking rate and articulatory precision were observed at the group level and within the seven participants who exhibited speech pattern changes. Additionally, significant speech pattern changes were observed during the migraine pre-attack phase in four of 15 participants with migraine. Furthermore, there were group-level differences in speaking rate, articulation rate, articulation entropy, energy decay slope, phonatory duration, and average pitch between interictal migraineurs and healthy controls. These differences can most likely be explained by idiosyncratic differences in speaking style between the two groups. Despite the fact that we took great precaution in matching subjects by gender and age, there can still be differences in speaking style between the two groups. However, it is also possible that individuals with migraine have persistent speech changes even during the interictal period. This further motivates our within-subject analysis.

Difficulties with speech and language have been documented during the aura phase of migraine (6–9). However, self-reported speech alterations and objectively measured alterations in speech associated with migraine have been inadequately investigated during the non-aura phases of the migraine attack and during the interictal period.

Subjective self-reported changes in speech during premonitory and headache phases of a migraine attack have been reported within a few studies. Patient-reported speech difficulties were reported during 9% of recorded migraine premonitory phases and 19.9% of recorded migraine headache attacks in an electronic headache diary study of 97 individuals (11).

Furthermore, identification of speech difficulties during the premonitory phase was strongly associated with an oncoming migraine attack (11). In a prospective study of 100 episodic migraine patients, 17% reported speech difficulties as a premonitory symptom (12). In our study, 20% of participants retrospectively recalled having speech problems during the premonitory phase and 27% reported such symptoms prospectively, frequencies that are more-or-less consistent with those reported in prior publications.

The frequency of objectively measured changes in speech during migraine attacks and in the pre-attack phase was previously unknown. In contrast to the relatively low frequency of self-reported speech changes reported in the literature and by the subjects in our study, 46% of participants in our study had significant changes in speech during migraine attacks while 26% of participants had speech changes within the 12 hours preceding self-recognition of a migraine attack starting. It is important to note that these percentages are likely underestimates, since this was only a 3-month study. The rate-limiting factor in analyzing the effects of an oncoming migraine attack on speech is the relatively small number of migraine attacks we captured for each study participant during the 3-month study. Had the study captured a larger number of migraine attacks, it is likely that a greater proportion of participants would have been found to have significant changes in speech. Despite this, according to our work, changes in speech are a common symptom during a migraine attack, perhaps almost as common as nausea and unilateral headache (as opposed to bilateral), and more common than vomiting, key features for defining a migraine attack. If our findings are confirmed in subsequent studies, speech changes might be considered a common feature of migraine and thus should be assessed when collecting information about symptoms from migraine patients.

However, there was a weak relationship between self-reported changes in speech and objectively measured changes in speech that occur with migraine attacks. In fact, none of the four individuals who had significant objectively measured changes in speech when comparing the migraine pre-attack to interictal phases self-recognized such speech changes. These results suggest a poor relationship between actual changes in speech and one's self-perception of speech changes associated with migraine attacks. Patient self-report of speech changes might be inadequate for detecting subtle changes in speech that occur in some patients with migraine attacks. User-friendly methods of objectively measuring speech, like the method used in this study, might be necessary for accurately detecting speech changes associated with migraine attacks.

An interesting extension of our work includes joint analysis of speech production and language processing as potential early indicators of migraine. We were able to find one published study that analyzed the language processing abilities in a group of migraineurs who had speech disturbances with migraine attacks (reported by the patient or their relative) and in a matched group who did not report speech disturbances (13). The study showed that the group reporting speech disturbances had increased language processing reaction times when tested during the interictal phase.

Limitations of this study include: a) Migraine symptoms are variable from patient to patient and from attack to attack. We expect that speech changes are present in some patients with

migraine, and in those patients might only be present with some attacks. Although we collected information from a number of migraine attacks, our migraine participant sample size was relatively small. b) As a strength of this study design, individuals who have migraine with aura were excluded. However, it is possible that speech or language changes that occur late in the pre-attack phase could be manifestations of a subtle migraine aura rather than being premonitory symptoms. c) Although participants with migraine were asked about problems speaking during the premonitory phase of migraine and 100% of the patients reported having premonitory symptoms, they were not asked about problems speaking that might occur during the headache or interictal phases of migraine. d) Only 20–27% of participants reported having problems speaking during the premonitory phase of their migraine attacks. We purposefully did not limit enrollment into this study to individuals who reported that they have speech problems associated with migraine attacks since we hypothesized that objective measures of speech would be more sensitive for detecting changes than self-report, a hypothesis that proved correct in this study. However, only enrolling individuals who report speech difficulties might enhance the objective differences detected in this study. e) Participants were asked to provide speech samples three times per day and during migraine attacks. More frequent collection of speech samples would have allowed for investigation of migraine pre-attack speech changes that occur even closer to the time of migraine attack onset (e.g. within 60 minutes of attack onset). However, from a research feasibility perspective, it was important to limit the number of required speech samples provided each day.

In conclusion, migraine is associated with alterations in speech. Alterations in speech may be present in individuals with migraine between migraine attacks compared to healthy controls and further speech changes occur during the migraine pre-attack and migraine attack phases compared to the interictal period. These changes in speech can be difficult to ascertain subjectively. The relative ease with which speech samples can be collected using mobile technology makes it appealing as an objective marker for oncoming or existing migraine attacks.

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References

1. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* 2013; 33: 629–808. [PubMed: 23771276]
2. Jiao Y, Berisha V, Liss J, et al. Articulation entropy: An unsupervised measure of articulatory precision. *IEEE Signal Process Lett* 2016; 24: 485–489.
3. Jiao Y, Berisha V, Tu M, et al. Convex weighting criteria for speaking rate estimation. *IEEE/ACM Trans Audio Speech Lang Process* 2015; 23: 1421–1430. [PubMed: 26167516]
4. Berisha V, Sandoval S, Utianski R, et al. Characterizing the distribution of the quadrilateral vowel space area. *J Acoust Soc Am* 2014; 135: 421–427. [PubMed: 24437782]
5. Sandoval S, Berisha V, Utianski RL, et al. Automatic assessment of vowel space area. *J Acoust Soc Am* 2013; 134: EL477–EL483. [PubMed: 24181994]

6. Sjaastad O, Bakketeig LS and Petersen HC. Migraine with aura: Visual disturbances and interrelationship with the pain phase. Vaga study of headache epidemiology. J Headache Pain 2006; 7: 127–135. [PubMed: 16767529]
7. Petrusic I, Zidverc-Trajkovic J, Podgorac A, et al. Underestimated phenomena: Higher cortical dysfunctions during migraine aura. Cephalalgia 2013; 33: 861–867. [PubMed: 23430982]
8. Petrusic I, Pavlovski V, Vucinic D, et al. Features of migraine aura in teenagers. J Headache Pain 2014; 15: 87. [PubMed: 25496701]
9. Jensen K, Tfelt-Hansen P, Lauritzen M, et al. Classic migraine. A prospective recording of symptoms. Acta Neurol Scand 1986; 73: 359–362. [PubMed: 3727912]
10. Benjamini Y and Hochberg Y. Controlling the false discovery rate: A practical and powerful approach to multiple testing. J Royal Stat Soc 1995; 57: 289–300.
11. Giffin NJ, Ruggiero L, Lipton RB, et al. Premonitory symptoms in migraine: An electronic diary study. Neurology 2003; 60: 935–940. [PubMed: 12654956]
12. Quintela E, Castillo J, Munoz P, et al. Premonitory and resolution symptoms in migraine: A prospective study in 100 unselected patients. Cephalalgia 2006; 26: 1051–1060. [PubMed: 16919055]
13. Crisp AH, Levett G, Davies P, et al. Cerebral hemisphere function and migraine. J Psychiat Res 1989; 23: 201–212. [PubMed: 2635218]

Key findings

- Nearly half of individuals with episodic migraine had objectively measured changes in speech associated with migraine attacks compared to their interictal period.
- Changes in speech can be objectively measured even in individuals who do not report having speech changes during migraine attacks.

Figure 1. Means and standard errors for speech features that significantly differed during interictal vs. migraine attack phases. Within subject changes for the six speech measures that showed significant changes between interictal and migraine attack phases are demonstrated. Each line represents a single participant with migraine.

Figure 2.

Means and standard errors for speech features that significantly differed during interictal vs. migraine pre-attack phases. Within-subject changes for the six speech measures that showed significant changes between interictal and migraine pre-attack phases are demonstrated. Each line represents a single participant with migraine.

Table 1.

Migraine characteristics.

	Migraine (n = 15)
Headache frequency in days/month: Baseline report (mean $\pm$ sd)	9.3 $\pm$ 2.8
Headache frequency in days/month: per diary (mean $\pm$ sd)	8.9 $\pm$ 4.1
Migraine attack frequency per month: baseline report	6.2 $\pm$ 2.3
Migraine attack frequency per month: per diary	6.8 $\pm$ 4.3
Patients reporting premonitory symptoms (%)	100
Migraine attacks with premonitory symptoms reported at baseline (mean $\pm$ sd) (%)	90 $\pm$ 14.9
Migraine attacks with premonitory symptoms per diary (%)	72.1

Baseline data are retrospective self-assessments obtained during the baseline research visit. Diary data are derived from prospectively maintained daily headache diaries. sd: standard deviation.

Table 2.**Premontory symptoms.**

	Premontory symptom reported at baseline (% of patients with symptom)	Premontory symptom reported in diary (% of patients with symptom)
Light sensitivity	67	73
Neck stiffness	67	80
Generalized feeling of being unwell	60	87
Fatigue/tiredness	60	87
Sound sensitivity	53	47
Mood change	47	80
Odor sensitivity/distortions	40	27
Dizzy/lightheaded	40	67
Temperature change (e.g. chills, sweats)	40	67
Yawning	33	67
Muscle pain	27	60
Vision change	27	53
Nausea	27	67
Problems speaking	20	27
Facial flushing/pale face	13	33
Food cravings	13	40
GI symptoms	7	33
Increased urination	0	33

During the baseline office visit, participants were asked if they experienced any premonitory symptoms and to select premonitory symptoms that they had ever experienced from a written list. In the headache diary, participants were asked if they experienced any of the premonitory symptoms each time they recorded an episode of headache. In this table, a patient was considered to experience a premonitory symptom if they recorded having that symptom with one or more migraine attacks.

Table 3.

Speech features for healthy controls and those with migraine during interictal, migraine pre-attack, and migraine attack phases.

	Healthy controls (mean/sd)	Interictal phase (mean/sd)	Pre-attack phase (mean/sd)	Migraine attack (mean/sd)
Speaking rate (syllables/s)	4.995/0.719	5.301/0.757	5.035/0.824	5.054/0.728
Pause rate (% of recording length)	1.1/1.9	1.4/4.9	1.8/4.7	1.7/4.0
Articulation rate (syllables/s)	5.049/0.697	5.413/1.510	5.144/0.894	5.149/0.745
Articulation entropy	97.68/16.47	98.36/17.48	91.00/17.45	90.52/19.91
Vowel space area (Hz ²)	$2.186 \times 10^5/1.529 \times 10^5$	$2.152 \times 10^5/1.734 \times 10^5$	$2.579 \times 10^5/4.433 \times 10^5$	$2.337 \times 10^5/1.738 \times 10^5$
Energy decay slope (dB/s)	-0.304/0.605	-0.354/0.508	-0.500/0.450	-0.377/0.520
Phonatory duration (s)	12.794/5.865	9.423/3.291	9.123/3.294	8.834/3.839
Average pitch (Hz)	172.56/32.81	174.21/36.31	171.54/32.57	171.05/34.87

s: second; sd: standard deviation.

Table 4.

Slopes and *p*-values for speech feature comparisons.

Comparisons within migraine group		Migraine vs. healthy control		
	Slope <i>p</i> -value	Interictal vs. pre-attack	Pre-attack vs. healthy control	Migraine attack vs. healthy control
Speaking rate	-0.309	-0.290	0.187	0.022
	<0.001	<0.001	0.692	<0.001
Pause rate	0.006	0.003	0.006	0.004
	0.086	0.390	0.100	0.012
Articulation rate	-0.298	0.287	0.237	0.053
	<0.001	<0.001	0.825	0.761
Articulation entropy	-8.35	-7.831	-7.089	-3.382
	<0.001	<0.001	<0.001	<0.001
Vowel space area	-1945.7	-7478.5	-7422.8	-5879.3
	0.823	0.145	0.805	0.258
Energy decay slope	-0.021	-0.030	-0.140	-0.063
	0.731	0.421	<0.001	<0.001
Phonatory duration	-0.319	-0.253	-3.782	-1.953
	0.052	0.191	<0.001	<0.001
Average pitch	-6.413	-3.95	0.106	-0.858
	0.008	0.054	0.045	0.186

The table shows slopes and *p*-values for every speech parameter compared across different conditions. As a group, those with migraine had alterations in several speech parameters during their interictal, migraine pre-attack and migraine attack phases compared to healthy controls. Furthermore, there were changes in speech parameters during the migraine pre-attack and migraine attack phases compared to the interictal period. Bolded slopes and *p*-values are significant after a multiple comparisons correction.

Table 5.

p-values for migraine attack vs. interictal phase.

Subject	01	05	06	09	13	18	19
Speaking rate	0.023	0.004	0.003	0.542	0.003	0.048	< 0.001
Pause rate	0.909	0.321	0.416	0.126	0.501	0.926	0.078
Articulation rate	0.089	0.001	0.002	0.359	0.039	0.027	< 0.001
Articulation entropy	0.892	0.696	< 0.001	0.002	0.912	0.035	0.037
Vowel space area	0.550	0.464	0.002	0.018	0.749	0.373	0.292
Energy decay slope	0.087	0.027	0.062	0.810	0.663	0.298	0.055
Phonatory duration	< 0.001	0.666	0.857	0.025	0.194	0.011	0.027
Average pitch	0.705	0.120	0.020	0.134	0.333	0.003	0.001

Seven of 15 individuals with migraine had changes in speech parameters during migraine attacks compared to their own interictal periods. Bolded *p*-values are significant after multiple comparisons correction.

Table 6.

p-values for migraine pre-attack vs. interictal phase.

Subject	06	09	18	19
Speaking rate	0.000	0.579	0.020	0.488
Pause rate	0.132	0.293	0.366	0.402
Articulation rate	0.000	0.398	0.007	0.644
Articulation entropy	0.000	0.038	0.124	0.397
Vowel space area	0.192	0.005	0.012	0.528
Energy decay slope	0.161	0.343	0.288	0.000
Phonatory duration	0.274	0.075	0.009	0.100
Average pitch	0.000	0.411	0.200	0.835

Four of 15 individuals with migraine had changes in speech parameters during migraine pre-attack phases compared to their own interictal periods. Bolded *p*-values are significant after multiple comparisons correction.