Acoustic monitoring of speech impairment in motor neuron disease associated with frontotemporal dementia: a case series

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Abstract

Frontotemporal dementia is the second most common form of younger onset dementia. A subset of people with this disorder develop motor neuron disease (MND) with associated speech impairment (dysarthria). Here, we aim to measure the progression of dysarthria in a case of FTD-MND with acoustic analysis. Four individuals with FTD (one developing concomitant MND) were longitudinally assessed over two years. Two acoustic measures demonstrated capacity to objectively monitor dysarthria in FTD-MND. These preliminary data highlight potential for the clinical use of these methods to identify the initial signs of bulbar onset motor neuron disease.

Index terms: acoustics, disease monitoring, dysarthria, frontotemporal dementia, motor neuron disease.

1. Introduction

Frontotemporal dementia (FTD) is a form of non-Alzheimer's dementia caused by neurodegenerative atrophy in the frontal and temporal lobes of the brain [1, 2]. The behavioural variant of FTD (bvFTD) is one of three subtypes of FTD which is characterised by changes in behaviour and personality such as disinhibition, apathy, executive dysfunction and stereotypic behaviours [2]. While speech abnormalities have been noted in some people with bvFTD [3, 4], speech impairment is not regarded as a diagnostic feature of bvFTD [2].

Motor neuron disease (MND) is a neurodegenerative disorder characterised by progressive paralysis resulting from impaired functioning of the both upper and lower motor neurons [5]. The disorder can have a limb or bulbar onset, the latter affecting the muscles responsible for speech and swallowing [5]. Features of dysarthria in MND may include decreased speech rate, distortions of consonants and vowels, increased nasal resonance, reduced respiratory capacity, and a hoarse, strained voice quality [6].

While traditionally considered to be distinct disorders, MND and FTD can now be conceptualised on a clinicopathological continuum, with the pure motor involvement of MND at one end and the frontal lobe cognitive deficits of FTD at the other [7]. As many as 13-25% of MND patients meet criteria for bvFTD, while a greater proportion (up to 45%) experience some cognitive and/or behavioural changes consistent with FTD [8, 9]. Similarly, motor dysfunction which is sufficient to meet criteria for MND has been identified in 10-15% of people with FTD, while up to 36% show some signs of motor dysfunction, such as wasting, fasciculations or weakness [10]. Evidence of overlapping clinical features are supported by pathological overlap for each disorder, with the TDP-43 protein associated with a majority of familial and sporadic MND cases, and a subgroup of FTD cases [11]. Furthermore, there is a strong genetic link with the *C9orf72* intronic repeat mutation having been identified in about one third of FTD cases, half of MND cases, and the majority (70-80%) of FTD-MND cases [7, 12-14].

Assessment of bulbar involvement in MND is commonly performed by neurological examination or listener-based speech assessment, despite evidence of bulbar dysfunction occurring prior to observable changes in speech intelligibility [15]. Objective and quantifiable measures have been evaluated to identify the onset of bulbar involvement in MND and for monitoring disease progression. Acoustic correlates of bulbar involvement in this population relate to voice instability [16], temporal measures such as utterance duration and segment duration [17], and measures of the articulatory subsystem, such as vowel space area and formant trajectories [17, 18]. Rong and colleauges identified changes in articulation, in particular velocities of lip and jaw movement, and phonation (fundamental frequency at participant's highest possible pitch on a sustained vowel) which occurred prior to a discernible change in speech and intelligibility. [19] These measures are hypothesised to correlate with decreased strength of lip and jaw musculature and vocal fold weakness [19].

Accurate and early identification of disease parameters that can lead to changes in diagnosis have significant clinical and empirical value for informing disease trajectory. Data may also act as a surrogate marker for treatment response in future clinical trials. Here we present a unique longitudinal case series comparing objective speech outcomes in MND and bvFTD.

2. Method

2.1. Participants

Four participants with a diagnosis of bvFTD were recruited from the Eastern Cognitive Disorders Clinic, Melbourne (see Table 1 for demographic information). One of these cases, VP, presented with concomitant dysarthria associated with MND.

All participants were assessed at two time points, two years apart.

2.1.1. VP

At his initial assessment, VP was a 71 year old man, who had been referred to a tertiary assessment clinic for investigation of his suspected frontotemporal dementia and dysarthria. He had been symptomatic for approximately four years. He had changes to his behaviour of four years duration and signs of dysarthria in the 12 months prior to the first assessment. His wife also described gait and balance changes at the first assessment.VP satisfied criteria for bvFTD and was diagnosed as such by a neurologist with expertise in behavioural neurology. The presence of dysarthria suggested potential MND. Kennedy's disease was raised as a possible differential diagnosis. Genetic testing for Kennedy's disease was offered but declined by VP's family.

2.1.2. bvFTD case 1

bvFTD case 1 is a male participant who underwent his first speech assessment at age 59. He had a four year history of personality and behavioural change. Language, motor speech and visuospatial function were intact.

2.1.3 bvFTD case 2

bvFTD case 2 is a male participant who underwent his first speech assessment at age 70. He had received a diagnosis of behavioural variant frontotemporal dementia at age 65, following a 4 – 6 year history of behavioural and personality change. His speech was fluent and grammatical, however hesitant due to word finding difficulties.

2.1.4 bvFTD case 3

bvFTD case 3 underwent his first speech assessment at age 76, with a 15 year history of slowly progressing bvFTD. A neuropsychological assessment conducted at age 76 revealed impairments of executive functioning, naming, word comprehension, semantic knowledge, and memory retrieval.

Table 1 *Participant demographics*

	VP	bvFTD Case 1	bvFTD Case 2	bvFTD Case 3
Gender	M	M	M	M
Age time 1	71	59	70	76
Age at onset	67	54	59 – 61	61

2.2. Speech sample recording and stimuli

Participants provided four speech samples: (i) a one minute monologue about something that they enjoyed; (ii) saying the days of the week; (iii) producing a sustained /a/ vowel on one breath (maximum phonation time); (iv) repetition of multisyllabic words; (v) diadochokinetic rate (DDK; saying "pataka" repeatedly as quickly and clearly as possible). All tasks were produced twice, with the exception of the monologue, and the second iteration was used in all analyses in order to mitigate the effect of unfamiliarity on the novel tasks [20]. The tasks have been shown to have reliability and sensitivity to impairment for measures of speech timing [20, 21]. The speech samples were recorded using a Marantz PMD671 solid state recorder with an AKG C520 condenser cardioid head mounted microphone positioned 8 cm from the participants' mouth at a 45° angle. Recordings were sampled at 44.1 KHz and quantized at 8 bits.

2.3. Speech analysis

Speech was quantified objectively using acoustic analysis and subjectively via listener based evaluations at both first and second time points. Details of these methods and the stimuli utilised are outlined below.

2.3.1. Acoustic analysis of speech

Measures of speech timing, vowel articulation (the vowel articulation index), and voice (harmonics to noise ratio) were conducted. Speech timing measures (syllables per second, mean pause length (MPL), proportion of pause time (PPT)) were calculated for the days of the week stimulus using automated scripts, derived from the methodology of [22] in Praat [23]. The days of the week stimulus was selected for timing measurement as it was hypothesised to be less influenced by cognitive and behavioural impairment compared to the monologue, due to its automaticity. The vowel articulation index (VAI) was calculated by measuring the first two formants (prominent resonant frequencies) of the /a/, /i/ and /u/ vowels [24]. The /a/ and /i/ vowels were taken from repetition of the word 'artillery', and the /u/ vowel from 'Tuesday' in the days of the week task. First (F1) and second formant (F2) frequencies were calculated in Praat, and the VAI was calculated with the following formula: VAI = (F2/i/ + F1/a/)/(F1/i/ + F1/u/ + F2/u/ + F2/a/). Decreasing VAI values indicate centralisation of the vowel formants, which is indicative of impaired vowel articulation [25]. The harmonics to noise ratio (HNR) quantifies the amount of additive noise in the voice signal relative to the harmonic component [26] to provide an objective evaluation of the degree of hoarseness in a person's voice.

2.3.2. Listener-based speech assessment

The participants' speech was rated by two speech pathologists (MLP & APV). The raters were blinded to participant, diagnosis and time point. Speech samples were rated independently by each rater and disagreement was resolved by consensus. Samples were assessed on a range of speech domains with a five point severity rating scale (0 = no impairment, 1 = sub-clinical, 2 = mild, 3 = moderate, 4 = severe impairment). Twenty-five speech features were assessed for severity within the domains of pitch, respiration, loudness, prosody, voice, articulation, resonance and DDK production.

3. Results

3.1. Acoustic analysis of speech

3.1.1. Speech timing

The degree of change in participants' MPL at time points 1 and 2 is presented in Figure 1. VP presented with an MPL at the first time point of 0.058 and 0.323 at the second. This change exceeded two standard deviations of the bvFTD group mean change (0.036 at time 1, and 0.063 at time 2). Figure 2 shows the magnitude of change for proportion of silence time in each sample. At the second time point, the mean decrease for the bvFTD group was 15% (from 10.28 to 8.68). VP's proportion of silence increased by 22% (from 27.26 to 33.13),

which was greater than two standard deviations of the bvFTD group mean change. Degree of change in speech rate is presented in Figure 3. The rate of change for VP was similar to that of the bvFTD group.

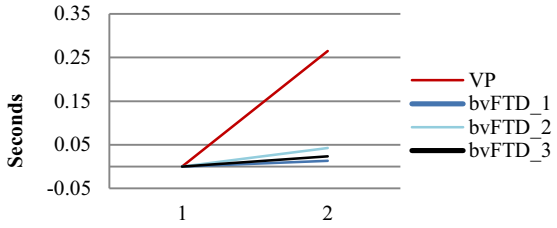

Figure 1: *Degree of change for MPL between two time points*

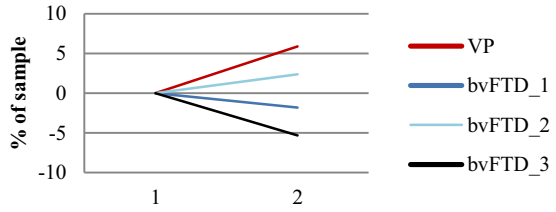

Figure 2: *Degree of change for PPT between two time points*

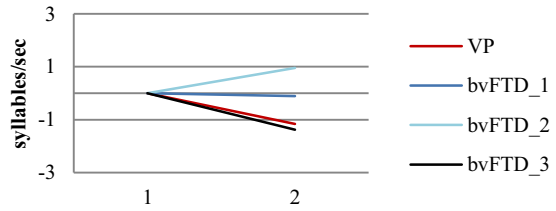

Figure 3: *Degree of change for speech rate between two time points*

3.1.2. Vowel articulation index

VAI values for each participant are presented in Figure 4. On average, the bvFTD participants' VAI changed by 1% between the two time points (0.734 to 0.733). VP showed a 15% decrease (0.861 to 0.730) in VAI which indicates a reduced qualitative distinction between the /i/ ("ee"), /u/ ("oo"), and /a/ ("ah") vowels. This change was greater than two standard deviations of the bvFTD participants' mean change.

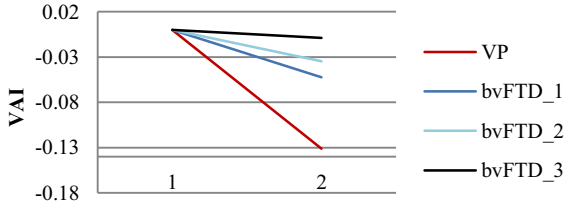

Figure 4: *Degree of change for VAI between two time points*

3.1.3. Harmonics to noise ratio

Participants' harmonics to noise ratios are presented in Figure 5. There was a high degree of variance within the bvFTD group for this measure, and VP was within one standard deviation of the control group mean change.

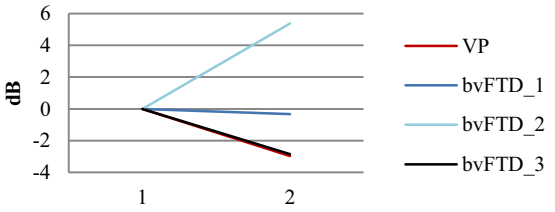

Figure 5: *Degree of change for HNR between two time points*

3.2. Listener-based speech assessment

VP had impairments of prosody, articulation and voice at the first assessment. His second assessment revealed deterioration of prosody, articulation and pitch variation. There was minimal change in perceptual ratings for the bvFTD participants.

4. Discussion

The use of acoustic measures allowed accurate detection of the accelerated change caused by the motor speech impairments of MND as opposed to the cognitive-linguistic and behavioural impairments of bvFTD. Consensus ratings from two speech pathologists blinded to participant and time point confirmed a perceptual change to VP's speech across multiple speech sub-systems, predominantly those of pitch, articulation and prosody. Deterioration of speech quality was also observed in the bvFTD participants; however, these were restricted to changes to voice quality and prosody. The study is limited as participants are recorded only at two timepoints, and further longitudinal follow up would enhance the study by demonstrating consistent change over time. These features will be discussed in relation to the acoustic correlates of timing, vowel articulation and voice quality.

4.1.1. Timing

Mean pause duration was the most effective timing method for identifying changes of speech secondary to motor dysfunction, as demonstrated by the large increase in VP's MPL relative to the bvFTD participants.

The increase in VP's MPL is consistent with the change in his speech rate (syllables per second), for which VP was shown to have a reduction of approximately one syllable per second. Two bvFTD participants experienced changes of similar magnitude, which suggests that this measure is also sensitive to behavioural and cognitive change.

Investigation of these timing measures in MND and FTD at a single time point has shown that the PPT has been shown to differentiate MND patients with predominantly respiratory symptoms [27] from bulbar onset MND, bvFTD and progressive nonfluent aphasia, and may act as a measure of respiratory function deterioration [19]. The significant increase in VP's MPL in this study may indicate that this measure has utility in measuring within-individual change.

4.1.2. Vowel articulation

Deterioration of articulation was quantified with the vowel articulation index. VAI has been shown to be effective in identifying and monitoring dysarthria in Parkinson's disease [25, 28], even prior to perceptual identification of vowel distortions [29]. Smaller vowel space areas, as demonstrated

for VP, have been previously documented as a feature of dysarthria in MND in comparison to healthy controls [30, 31]. These findings suggest that vowel articulation index may be valuable for identifying and measuring articulatory change in the FTD-MND continuum.

4.1.3. Voice quality

There was variation in harmonics to noise ratio (HNR) for both VP and the bvFTD participants, with bvFTD participants experiencing both increases and decreases in HNR. Deterioration of HNR is expected in healthy ageing [32], and this is consistent with known changes to vocal fold physiology in older adults [33]. In this case series, HNR declined with increased breathiness over time, however it was not useful in identifying change that was specific to motor dysfunction as opposed to changes associated with ageing.

5. Conclusions

Several quantitative speech measures have demonstrated capacity to monitor change in both MND and bvFTD. Measures of mean pause rate and VAI were shown to be sensitive to the greater magnitude of change associated with motor speech dysfunction, in comparison to more general behavioural and cognitive changes related to FTD. These quantitative measures were largely consistent with listener-based ratings of speech changes, and therefore have potential for objective monitoring which could be utilised as an adjunct to listener-based ratings in clinical settings. In particular, such measures have potential to assist in the early identification of bulbar onset MND in the FTD population. Future longitudinal studies with larger cohorts could allow for the sensitivity and specificity of these measures to be established. A focus on assessing speech changes over shorter time periods would further clarify their potential as clinical measures.

6. References

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