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A protocol for identification of early bulbar signs in amyotrophic lateral sclerosis

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Abstract

The purpose of this project is to identify characteristics that may be of assistance in establishing the diagnosis and monitoring early progression of bulbar dysfunction in patients with Amyotrophic Lateral Sclerosis (ALS). Early identification of bulbar dysfunction would assist in clinical trials and management decisions. A database of 218 clinic visits of patients with ALS was developed and formed the basis for these analyses. As a framework for the description of our methodology, the Disablement Model [World Health Organization. WHO International classification of impairment, activity, and participation: beginner's guide. In: WHO, editor. Beta-1 draft for field trials; 1999] was utilized. Our data identified that the strongest early predictors of bulbar speech dysfunction include altered voice quality (laryngeal control), speaking rate, and communication effectiveness. A protocol for measuring these speech parameters was therefore undertaken. This paper presents the protocol used to measure these bulbar parameters. © 2001 Elsevier Science B.V. All rights reserved.

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With the advent of novel pharmacological treatments through clinical trials and introduction of additional clinical trials aimed at the treatment of ALS, early definitive diagnosis is imperative [1,2]. As M. Swash has stated, "earlier diagnosis and earlier treatment is likely to result in a better outcome in terms of length of survival, survival at a good quality of life, with less stress on social services and on the quality of life..." [3].

The purpose of this project is to monitor progression of early speech dysfunction and to identify communication factors that may be utilized in early diagnosis and clinical decision-making. Traynor et al. [4] reported that, in the bulbar-onset population of ALS patients, dysarthria was eight times more common than dysphagia as an initial symptom. Bulbar disorders that result from disturbed neuromuscular control involve impaired execution of movements for speech production. The goal of this project is to develop a standard assessment protocol to monitor the early progression of bulbar symptoms, with a focus on speech impairments.

MND is a progressive neurodegenerative disorder involving neurons in the cerebral cortex, brainstem, and spinal cord. There are no clinical laboratory tests that confirm or rule out the diagnosis of ALS, and the disease progresses at different rates for each individual patient. Physicians typically describe early diagnosis of MND as difficult, based upon the tools currently available.

In an effort to establish diagnostic standards, guidelines were determined (1990 El Escorial Criteria (EEC) [5], 1999 Airlie House Criteria [6], and World Federation of Neurology [7]).

Some authors [4] have indicated that although the established clinically based diagnostic systems are suitably specific to diagnose ALS, the EEC [1] and Airlie House Criteria [6] lack sensitivity, particularly at early stages of the illness. Early diagnosis is not possible based upon the currently established criteria.

The Disablement Model: International Classification of Impairment, Activity and Participation [8] was selected to provide a framework to systematically delineate the health consequences resulting from ALS. This model focuses on three levels of this disorder: (1) *Impairments* occur at the level of the body and can be structural or functional in origin; (2) *Activities* occur at the level of the person and reflect the overall capability of a person to eat, walk, or

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communicate and are typically assessed in decontextualized situations, such as a clinical setting; and (3) *Participation* occurs at the societal level and reflects how well a person participates in social contexts or situations.

1. Methods

1.1. Participants

Data was recorded from clinical visits of ALS patients who were seen in a regional neuromuscular clinic in the Midwestern USA. One hundred and sixty seven clinic visits by $N = 49$ different ALS patients were documented in a database for analysis. Participants were diagnosed with ALS by a neuromuscular clinician (4th author) using the El Escorial criteria and were diagnosed with either ALS-probable or ALS-definite. Eighteen participants were diagnosed with bulbar onset, twenty participants were diagnosed with spinal onset, and eleven participants were diagnosed with mixed onset ALS. All patients with ALS documented in this study completed the full assessment protocol, requiring approximately 15 min. This project received prior approval from the University of Nebraska Medical Center Institutional Review Board for investigation involving human subjects. Informed consent was obtained from each participant.

1.2. Procedures

Assessment was completed at each level of the ICIAP disablement model. Clinical outcomes-based speech assessments were utilized to identify bulbar involvement and provide clinical decision-making strategies. The goal was to identify items to be included in the assessment protocol that were:

- sensitive to early changes in speech mechanism control,
- measurable in a clinical setting in terms of complexity, time, and patient fatigue, and
- include some speech impairments not routinely detectable by the human ear alone.

1.3. Activity level

Individuals with ALS express varying degrees of disability at the activity level. The person's overall ability to communicate was assessed by examining their intelligibility of speech and rate of speech production.

1.3.1. Intelligibility and rate of speech

Speech intelligibility has traditionally been a measure of the presence and severity of dysarthria [9]. The concept of speech understandability has been relatively easy for patients, their families, and clinicians to understand. Historically, intelligibility was measured using a perceptual rating scale; however, more recently, transcription intelligibility strategies have been used to objectively measure the understandability of speech. In our protocol the Sentence Intelligibility Test (SIT) [10], a widely used standardized clinical transcription test, was used to measure speech intelligibility. Normative data associated with this assessment indicate no influence of fatigue on productions of typical speakers [10].

The SIT was used to obtain a sample of sentence production from each patient with ALS. This clinical measure consists of a series of 11 randomly generated sentences. Standard administration and measurement procedures were employed. Each succeeding sentence increases in length by one word, from a 5- to a 15-word sentence. The participants read each sentence as presented. If a patient was unable to read the sentences, he/she was instructed to repeat them imitatively following presentation by the examiner. Production of the entire test required approximately 2 min, although the duration was variable (as described in the Results). It was observed clinically that duration (or speaking rate) was primarily associated with (or affected by) the individual patient's dysarthric speech productions rather than reading difficulties. Speech productions were digitally recorded using an I-Book Mackintosh laptop computer, the SoundEdit audio software program, and an Andrea (ANC-550) headset microphone. A listener, who was unfamiliar with the speaker and with the stimuli sentences, transcribed the recorded speech samples using broad transcription techniques. Transcription analysis resulted in a percent of intelligible productions in sentences. Following transcription, speech samples were timed to obtain a measure of speaking rate in words per minute (wpm).

1.4. Impairment level

In the case of individuals with ALS, examination of the impairment level involves examination of the active disease processes. Items incorporated in the speech assessment included evaluation of velopharyngeal (VP) functioning, tongue strength, voice quality, and respiratory pressures during speech (intraoral pressures) production. Research by Dworkin et al. established a strong correlational relationship between tongue force and dysarthria in persons with ALS [11]. In addition, Kent et al., Forrest and Weismer, and Tomik et al. have examined the commonly observed acoustic characteristics of speech in persons with ALS [12–14].

1.4.1. Pattern of velopharyngeal closure

Warren et al. [15] indicated that these measures provide an accurate description of speech deficits, assist in devel-

opment of new treatment approaches, and demonstrate quantifiable changes in physiologic responses. Measures were taken using an air flow meter (pneumotachograph with a nasal mask) and an air pressure transducer with a flexible tube placed laterally across the tongue. Each participant produced less than 2 min of speech, producing "puh" [pʌpʌpʌpʌpʌ] for approximately 10 s, and repetition of the sentence "Buy Bobby a puppy" two times. Normal measures indicate minimal (less than 10 cm^3/s) nasal airflow present on production of pressure consonants (e.g., /p, b, t, d/) and 4–8 cm H_2O pressure orally.

Printouts obtained from the aerodynamic speech measures were examined by the first and third authors with patterns of velopharyngeal (VP) closure observed.

1.4.2. Graded tongue movement

Assessment of tongue strength for production of movements for speech was completed using a format from the Clinical Examination for ALS [16]. Tongue movements were graded on a five-point scale, with "5" indicating movements within normal limits and "1" indicating minimal to absent tongue movement. The examiners (1st and 3rd authors) rated graded tongue movements in the clinical setting.

1.4.3. Volitional cough

Respiratory function can be measured clinically for speech and swallowing by examining volitional cough force [17]. Volitional cough was rated on a five-point scale of observed weakness, with "2" representing within normal limits and "6" representing absent volitional cough. The lead author rated volitional cough in the clinical setting.

1.4.4. Vocal quality change

A review of literature found frequent mention of breathiness, hoarseness, vocal stridor, and reduced loudness of voicing in the ALS population [9,18]. In this protocol, vocal quality was rated by consensus of the lead author and the participant on a seven-point scale with "0" representing normal and "6" representing severe impairment. The lead author made judgments of vocal quality from speech samples produced during the Sentence Intelligibility Test and sustained phonation.

1.5. Participation level

1.5.1. ALS Severity Speech Scale

The ALS Severity Scale was developed as a staging system to rate the level of functional performance of someone with ALS. The evaluator assigns numerical values to performance in four areas: speech, swallowing, upper extremity, and lower extremity [17]. Each of the four subscales provides a choice of 10 scores based upon progressive decline in function [16]. On this scale, scores of "9" or "10" indicate essentially normal functioning, "7" or "8" indicate detectable abnormalities, "5" or "6" indicate a need for behavioral modification, "3" or "4" indicate a need for technical modifications, and "1" of "2" indicate a loss of function. The speech subscale was used in our profile to obtain information specific to speech deterioration. The lead author rated each patient on the ALS Severity Speech Scale based upon clinical observation of the participant's speech productions.

1.5.2. Communication effectiveness

The Communication Effectiveness Index (CETI) [19] was developed to document communicative interactions. Persons with aphasia and their spouses generated CETI items as a result of interactions within daily communication situations. The CETI was valid as a measure of functional communication and was responsive to changes in performance over time [19].

The modified communication effectiveness index implemented for the current study was described by Yorkston et al. [20] and uses a visual analog and Likert scale involving 10 contextual situations. Assessment of communication effectiveness completed by both the patients with ALS and their significant others provides personalized evidence on communication performance. For this project, the communication effectiveness ratings were made on a seven-point scale by the "significant other" for one situation (conversing with familiar persons in a quiet environment).

1.6. Analyses

The relationship between selected variables will be analyzed using correlational statistics. This analysis was selected because no attempt has been made to control or manipulate these variables, but rather they have been observed as they exist naturally in the clinical setting. The resulting analyses will be presented in graphic form.

2. Results

2.1. Activity level

2.1.1. Intelligibility

A review of our data reveals that reduction in speech intelligibility is not an early bulbar symptom in ALS. In fact, ALS patients produce speech intelligibility within normal limits long after the onset of bulbar ALS symptoms. Typically, the reduction in intelligibility occurs over a relatively brief period of time during the middle phases of disease progression, regardless of type of ALS onset. Therefore, speech intelligibility alone is not an effective early identifier of the speech symptoms associated with bulbar ALS.

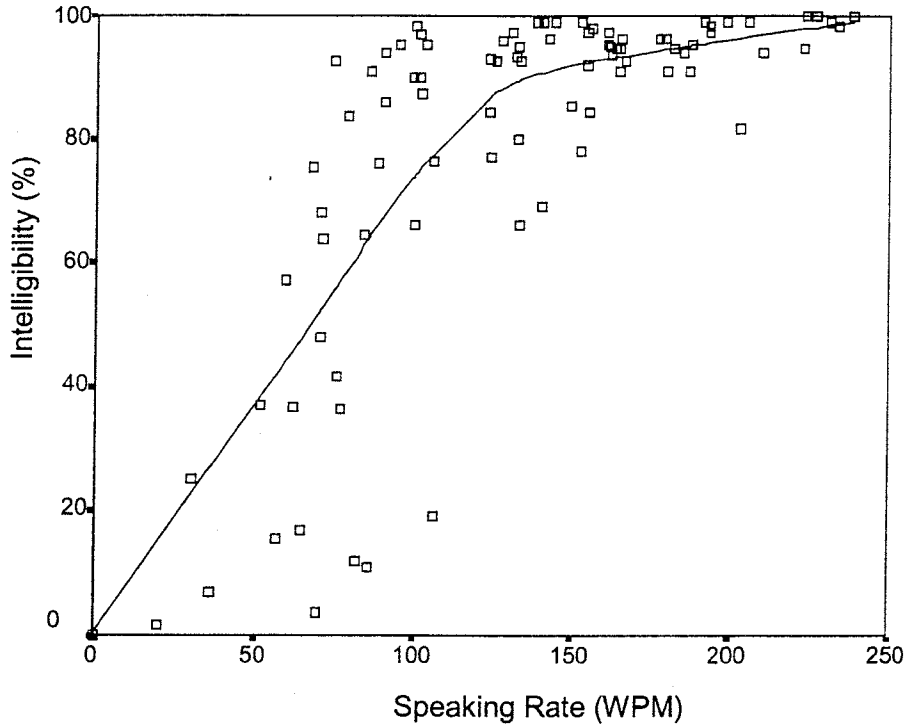

Fig. 1. This scatter plot includes percent of speech intelligibility and speaking rate (words per minute). A Lowess line is superimposed to demonstrate a line of best fit for the data.

2.1.2. Speaking rate

In this protocol, speaking rate is measured using the SIT [10] and is reported in words per minute. In Fig. 1, speaking rate is plotted against speech intelligibility. A review of this graph reveals that decreases in speaking rate are observed much sooner following onset of ALS symptoms than reductions in speech intelligibility. Partial correlation data analysis indicated that with type of onset

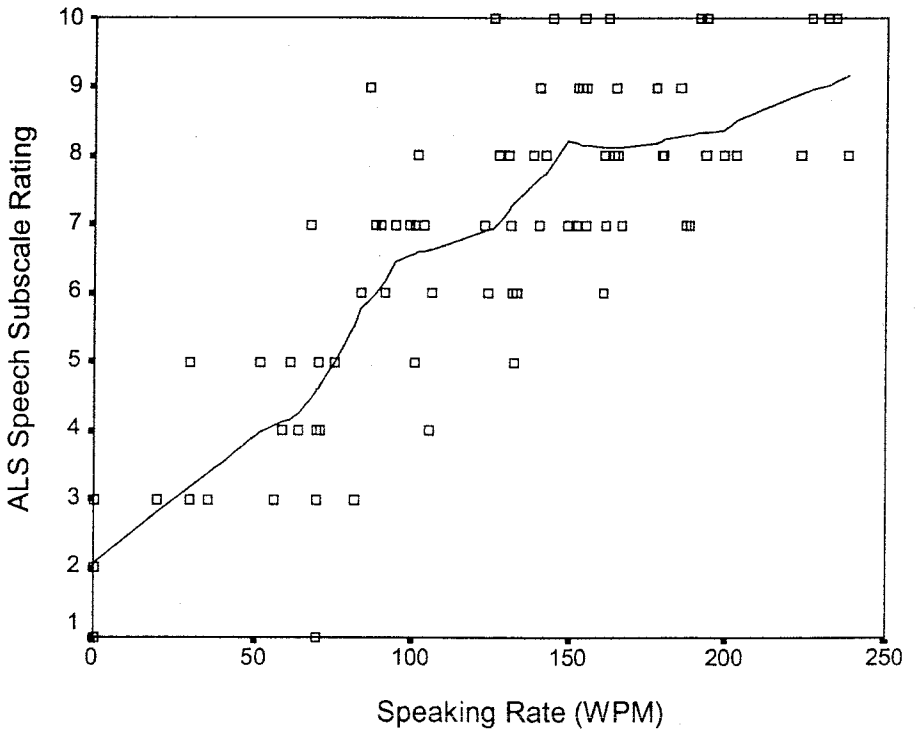

Fig. 2. This scatter plot contains ALS Speech Severity Subscale (10-point scale) and speaking rate (words per minute) data. A Lowess line is superimposed to demonstrate a line of best fit for the data.

controlled, $R^2 = 0.72$, $p = 0.000$ rate of speech and intelligibility of speech were highly correlated in this sample. Consistent with previous research [21], when rate decreases to 60% of normal, or approximately 100 wpm on the SIT (non-disabled speakers average 190 wpm), persons with ALS can expect a precipitous decline in intelligibility. Therefore, we have included a measure of speaking rate in our protocol to identify early speech changes and to predict the timing of Augmentative and Alternative Communication (AAC) intervention that is necessary to support communication as intelligibility decreases.

2.1.3. ALS Speech Rating Scale

The ALS Speech Rating Scale [16] follows a continuum from "10" indicating normal speech production and "1" representing speech limited to rare vocalization only. Fig. 2 displays the ALS speech scale score plotted against speaking rate. A review of this figure indicates that the ALS speech score declines as speaking rate declines. It appears that the rate of decline in the ALS speech scale score is somewhat more precipitous when speaking rate is less than 150 wpm. The overall correlation between ALS speech scale score and speaking rate is $R^2 = 0.845$, significant at the $p = 0.000$ level. The ALS speech scale appears to be sensitive to early changes in speech performance.

2.2. Impairment level

2.2.1. Pattern of velopharyngeal (VP) closure

A review of the literature reveals reports of early velopharyngeal dysfunction (hypernasality) as an early symptom of ALS [21]. In our protocol we have included two measures of VP dysfunction: ratings of hypernasality and aerodynamic measures of VP closure patterns. Five patterns of VP function were recorded. As ALS progresses, each of the patterns are typically observed. *Pattern 1 (normal)* is consistent with a normal VP closure pattern exhibited by complete closure of the velopharyngeal mechanism during production of pressure consonants. *Pattern 2 (inconsistent)* indicates inconsistent closure or approximation of VP closure on production of pressure consonants. *Pattern 3 (gradual closure)* demonstrates initial VP insufficiency, with the patient with ALS attaining closure by the end of the production. *Pattern 4 (gradual insufficiency)* demonstrates initial VP closure on produc-

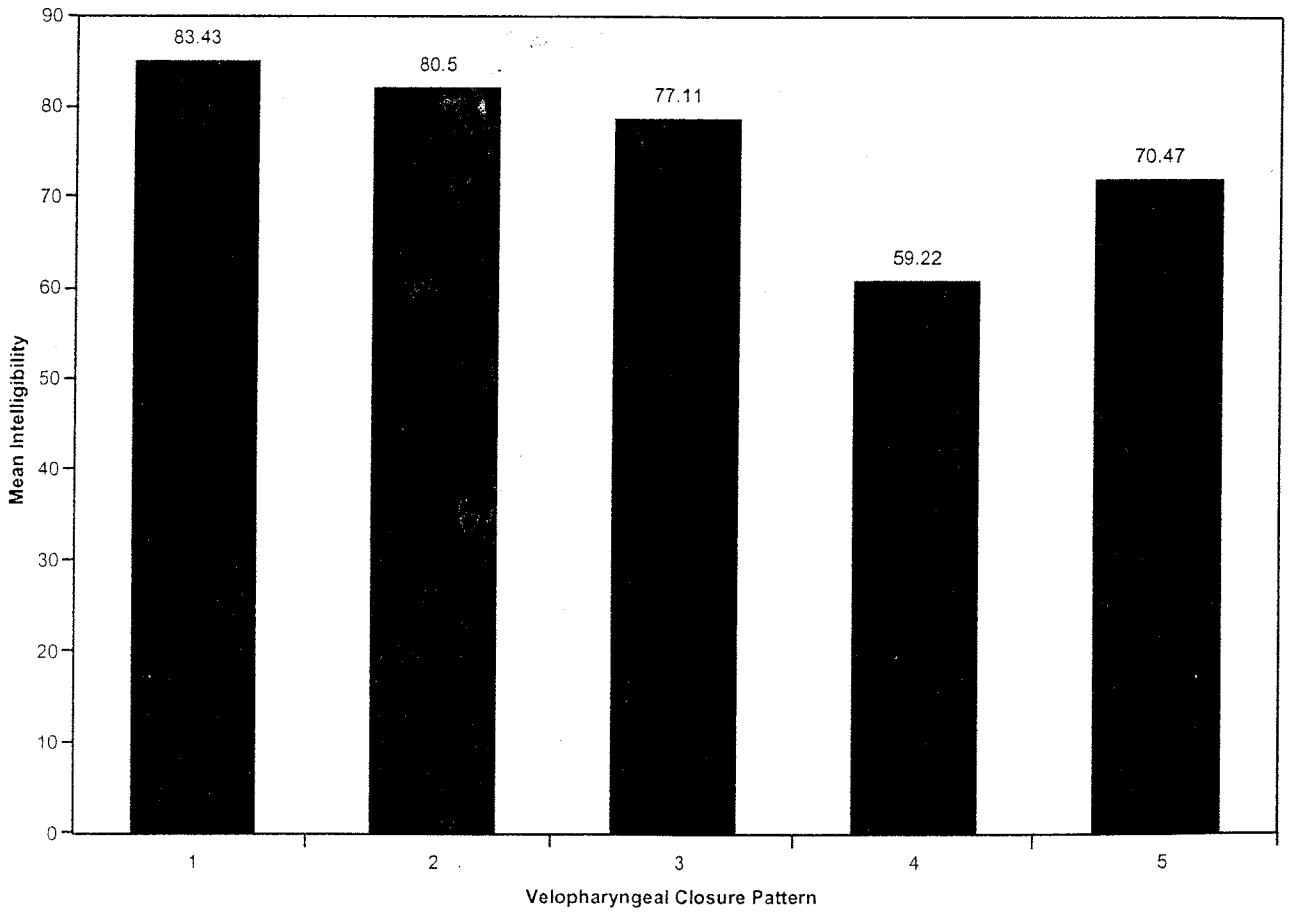

Fig. 3. Graph of speech intelligibility (%) by velopharyngeal closure pattern. Pattern 1—velopharyngeal closure on all pressure consonants. Pattern 2—Intermittent velopharyngeal insufficiency. Pattern 3—Initial velopharyngeal insufficiency eventually closes. Pattern 4—Initial velopharyngeal closure beginning inefficient by end of utterance. Pattern 5—Excessive velopharyngeal insufficiency on all pressure consonants.

tion of pressure consonants, with the patient with ALS becoming insufficient by the end of the utterance production. *Pattern 5 (insufficiency)* is consistent with lack of VP closure on all pressure consonants.

In Fig. 3, average intelligibility scores were computed for participants in each of the pattern groupings. Consistent with intelligibility and speaking rate measures, VP closure pattern and intelligibility measures remain steady until the ALS patient completely and consistently loses VP closure ($R^2 = -0.393$, $p = 0.005$).

In Fig. 4, average rate scores were computed for participants in each of the VP pattern groupings. A decline in speaking rate was noted at the earliest VP pattern groupings indicating an extant change concurrent with "normal" VP ratings. VP closure does exhibit a marked decline at the 100 wpm mark and again at the 60 wpm mark.

2.2.2. *Vocal quality change*

In this protocol, vocal quality was rated on a seven-point scale, with "0" representing vocal quality within normal limits and "6" representing severe vocal quality changes. In Fig. 5, vocal quality change is plotted against speaking rate. A review of this figure reveals a highly linear relationship, in that as speaking rate slows, there is an increase in vocal quality impairment. The correlation between these two variables was significant ($R^2 = -0.765$, $p = 0.000$). These results confirm that voice quality changes are a bulbar speech sign in persons with ALS.

2.2.3. *Graded tongue movement*

Tongue movements were graded on a five-point scale, with "5" indicating movements within normal limits and "1" indicating minimal to absent tongue movement. Fig. 6 displays graded tongue movement against speaking rate. Tongue movements were within normal limits until speaking rate was reduced to 150 wpm. As speaking rate was further reduced, the graded tongue movements followed a linear decline. The correlation between speaking rate and graded tongue movement was $R^2 = -0.724$, significant at the $p = 0.000$ level. The correlation between graded tongue movement and speech intelligibility was $R^2 = 0.792$, significant at the $p = 0.000$ level.

2.2.4. *Volitional cough*

Volitional cough was rated on a five-point scale, with "2" representing within normal limits and "6" representing absent volitional cough. In Fig. 7, volitional cough is plotted against speaking rate. A review of this figure indicates that ratings of volitional cough remain stable until speaking rate is reduced to approximately 150 wpm.

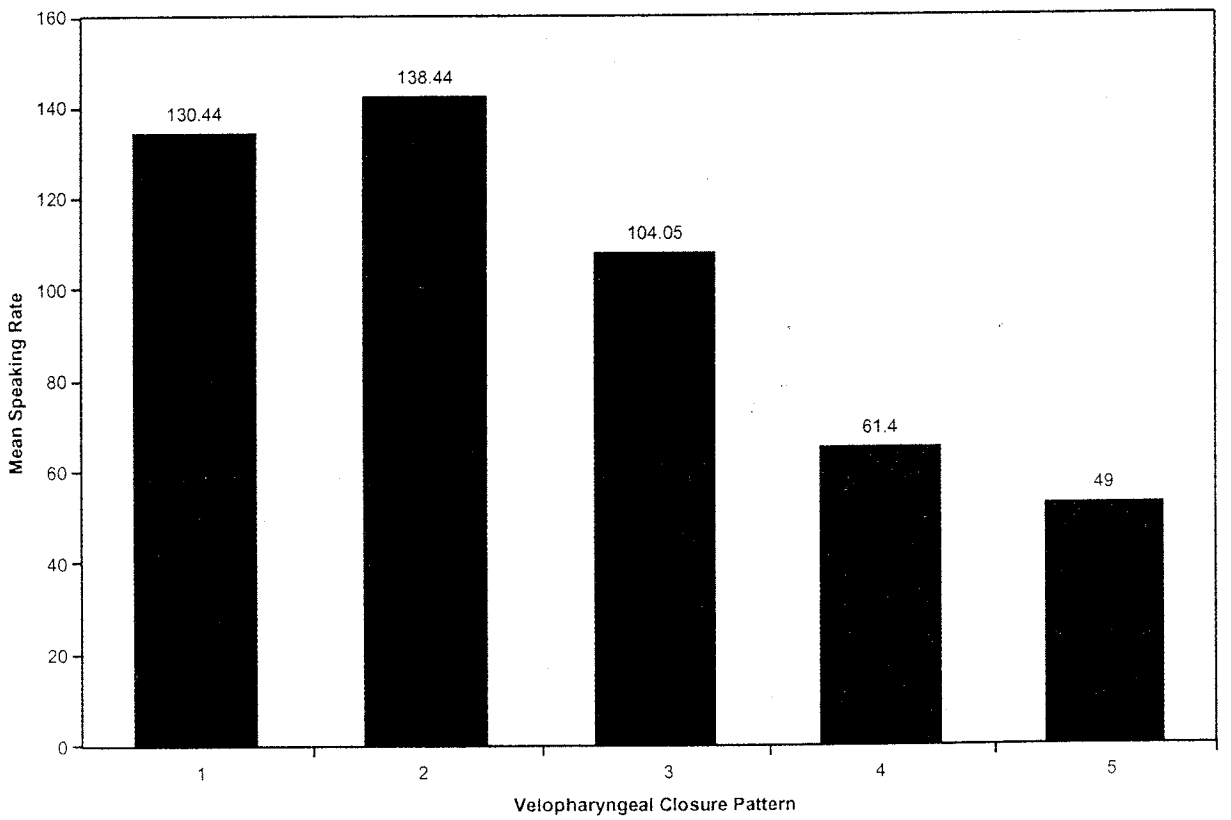

Fig. 4. Graph of speaking rates (words per minute) by velopharyngeal closure pattern. Pattern 1—velopharyngeal closure on all pressure consonants. Pattern 2—Intermittent velopharyngeal insufficiency. Pattern 3—Initial velopharyngeal insufficiency eventually closes. Pattern 4—Initial velopharyngeal closure beginning inefficient by end of utterance. Pattern 5—Excessive velopharyngeal insufficiency on all pressure consonants.

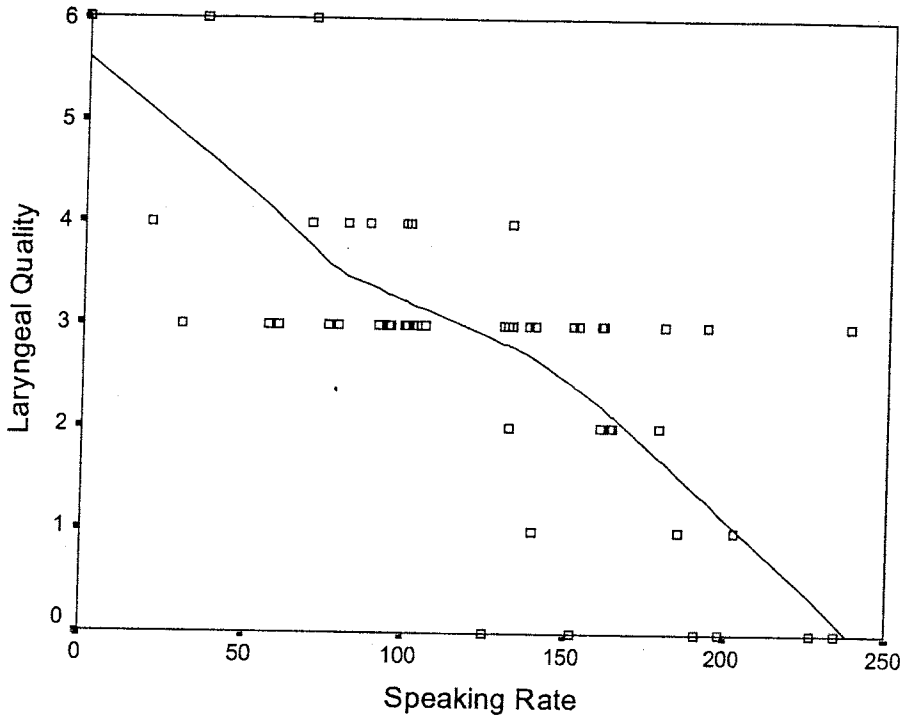

Fig. 5. This scatter plot contains vocal (laryngeal) quality change (seven-point scale) and speaking rate (words per minute) data. A Lowess line is superimposed to demonstrate a line of best fit for the data.

Further reductions in speaking rate are accompanied by a nearly linear reduction in volitional cough rating. These data suggest that ratings of volitional cough are a more sensitive early indicator of bulbar symptoms than intelligibility, but not as sensitive as speaking rate changes or voice quality changes. The overall correlation between volitional cough and speaking rate is $R^2 = -0.520$, significant at the $p = 0.001$ level.

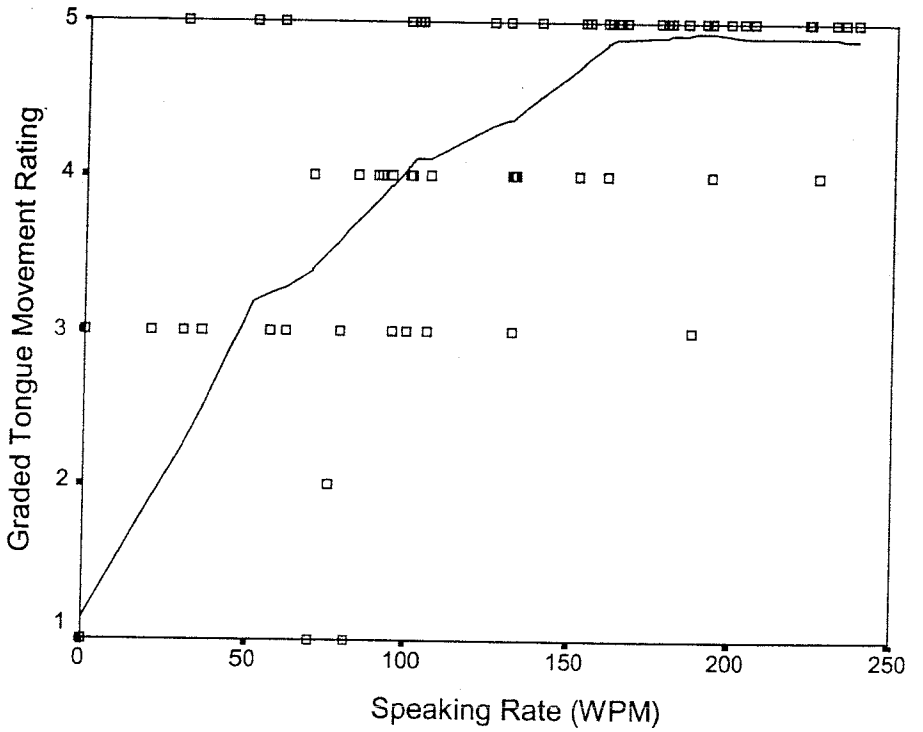

Fig. 6. This scatter plot contains graded tongue movement (5-point scale) and speaking rate (words per minute) data. A Lowess line is superimposed to demonstrate a line of best fit for the data.

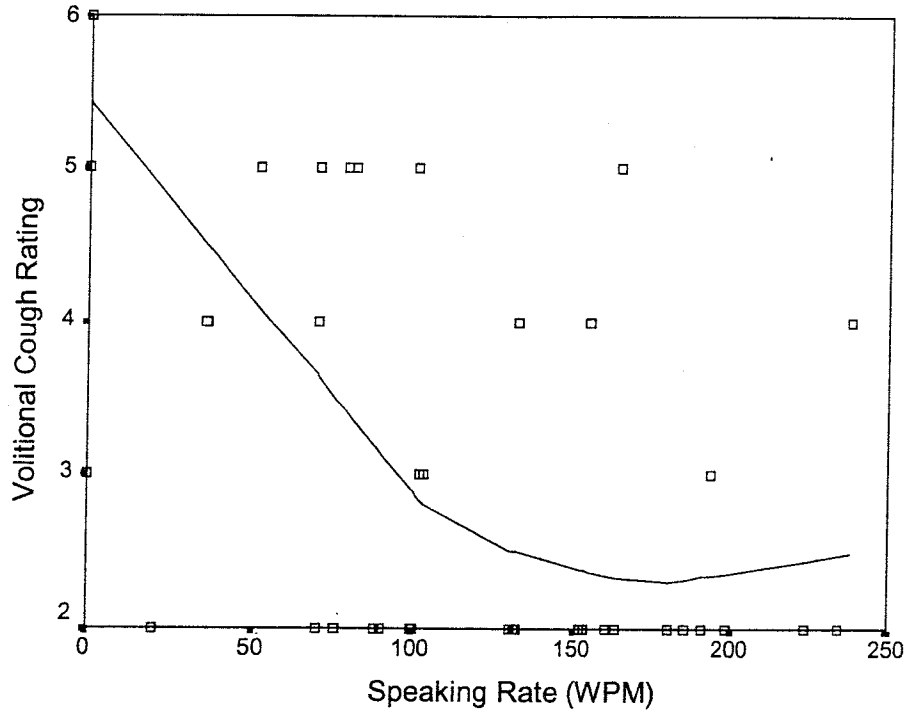

Fig. 7. This scatter plot contains volitional cough (five-point scale) and speaking rate (words per minute) data. A Lowess line is superimposed to demonstrate a line of best fit for the data.

2.3. Participation level

2.3.1. Communication effectiveness

The modified CETI [19] scale was used to measure the societal limitation perceived by the ALS patient when communicating. When communicating with a familiar partner in a quiet environment, communication effectiveness was rated on a seven-point scale with "1" representing inability to communicate in a situation and "7" representing very effective communication in a situation.

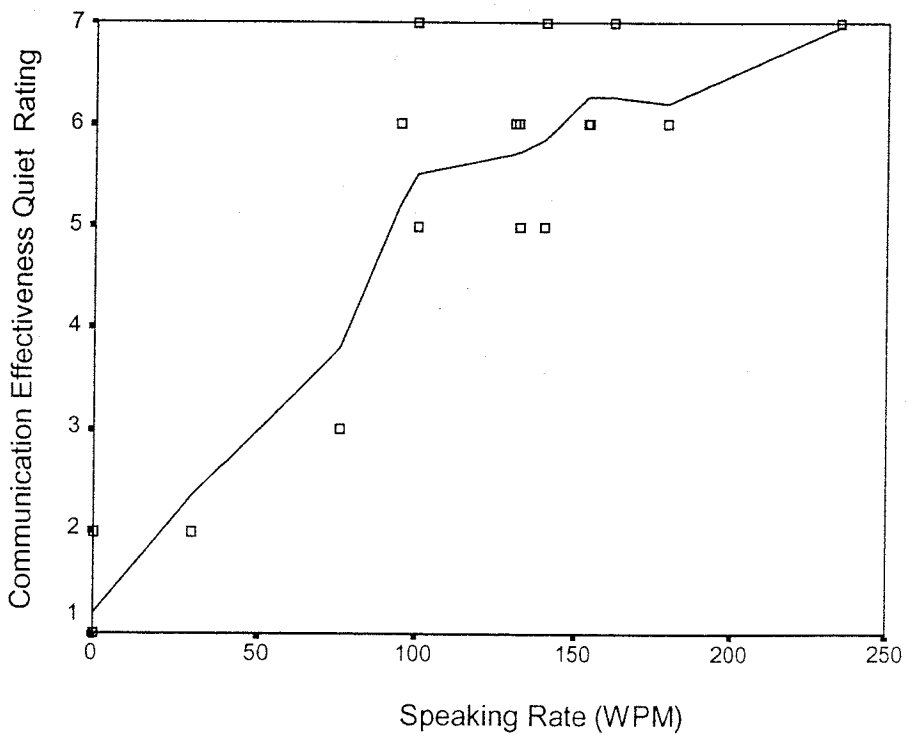

Fig. 8. Scatter plot contains communication effectiveness ratings (seven-point scale) and speaking rate (words per minute) data. A Lowess line is superimposed to demonstrate a line of best fit for the data.

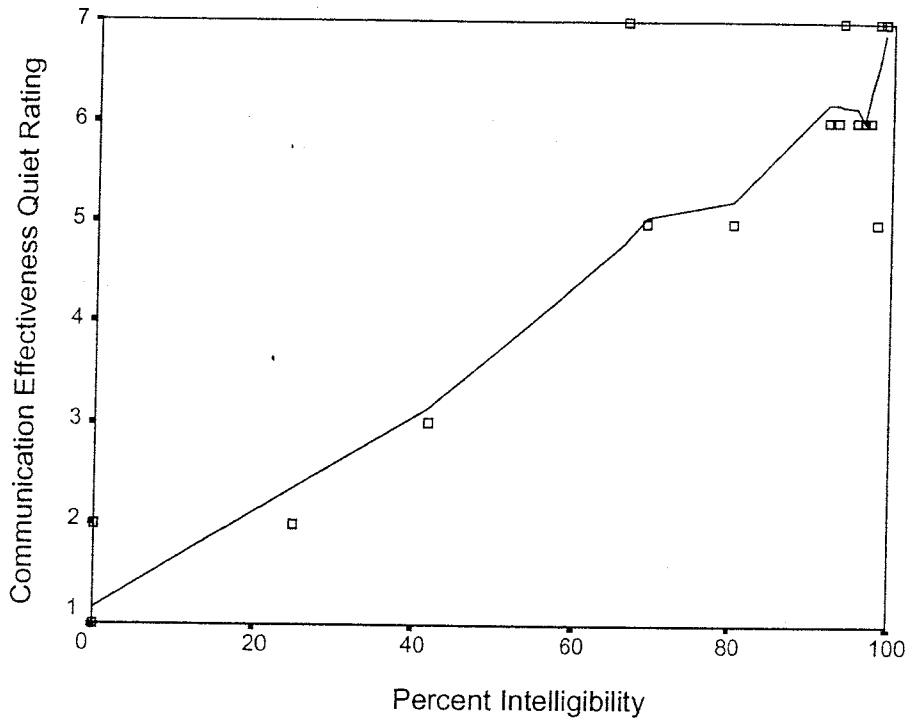

Fig. 9. Scatter plot containing communication effectiveness rating (seven-point scale) and speech intelligibility. A Lowess line is superimposed to demonstrate a line of best fit for the data.

Fig. 8 displays communication effectiveness plotted against speaking rate. A review of this figure indicates that communication effectiveness demonstrates a linear decline beginning at normal speaking rates. Consistent linear decline is noted, with a plateau observed from approximately 180 to 150 wpm. This plateau is followed by a precipitous decline to approximately 140 wpm at which time a second plateau is revealed. At 100 wpm, communication effectiveness takes another precipitous decline that proceeds until the individual is unable to communicate.

Fig. 9 displays communication effectiveness plotted against intelligibility of speech. Evident from this graph is the presence of a linear decline in communication effectiveness that precedes reduction in speech intelligibility, that is, while speech intelligibility is still within normal limits, a decline in communication effectiveness rating is apparent. The overall correlation between communication effectiveness and speaking rate is $R^2 = 0.882$, significant at the $p = 0.000$ level. The correlation between communication effectiveness and intelligibility is $R^2 = 0.929$, significant at the $p = 0.000$ level. The ratings of communication effectiveness appear to be sensitive to early changes in speech performance.

3. Discussion

The Disablement Model [8] was used as a framework to monitor early speech symptoms associated with ALS. This framework was used to categorize and select measures to identify and stage early signs of bulbar speech involvement upon which clinical management decisions can be based.

Results of this project indicate that early bulbar speech dysfunction is apparent across all levels of the Disablement Model. The Disablement Model identifies on three levels of a disorder: *impairment*, *activity*, and *participation*. There are a number of clinical measures that are sensitive to detection of early speech changes. The strongest early predictors appear to be subjective measures at the *impairment* level including vocal (laryngeal) control as reflected in voice quality, objective measures at the *activity* level involving speaking rate, and more subjective measures at the *participation* level including listener ratings of communication effectiveness. All of these parameters show considerable change before objectively measured reductions in speech intelligibility occur. Specific tasks are associated with early identification of bulbar dysfunction at each level of disability.

Tasks at the *impairment* level of disability assessment included examination of vocal quality change, graded tongue movements, volitional cough and aerodynamic speech measures with the pattern of VP closure. Results indicated that changes in vocal quality were an early bulbar speech sign. In addition, graded tongue movement and effective volitional cough followed a linear decline at the 150 wpm speaking rate, indicating observable impairment prior to changes in intelligibility. When compared to intelligibility, VP closure pattern remained steady until the participants completely and consistently lost VP closure.

When compared to speaking rate, a decline in VP closure is noted at approximately 130–140 wpm, and again at 104 wpm, indicating an early bulbar speech sign noted prior to changes in intelligibility.

Tasks at the *activity* level of disability assessment included examination of intelligibility of speech, speaking rate, and the speech subtest of the ALS Severity Scale. Our data do not support intelligibility as an early bulbar speech symptom. The sharp and rapid decline in intelligibility is observed over a brief time frame and may remain within normal limits long after the onset of other observed bulbar symptoms. Our data do indicate that ALS patients will demonstrate a sharp decline in intelligibility associated with a decline in speaking rate to approximately 100 wpm. While intelligibility may not prove useful in early identification, it plays a key role in determining augmentative and alternative communication intervention for communication specialists. Speaking rate is a key determinant in early bulbar measures. It is highly correlated with several measures and is used in conjunction with these to determine presence of bulbar symptoms. The ALS Severity Scale (Speech Subtest) [17] scores decline as speaking rate declines, with a somewhat sharper decline with speaking rates below 105 wpm. This indicates that the ALS Severity Scale (Speech Subtest) is an adequate predictor of decline in speech functioning.

Tasks at the *participation* level of disability assessment included examination of communication effectiveness judged by frequent communication partners of ALS patients. The modified CETI [19] was found to be an adequate predictor of changes in speech noted by frequent communication partners at speaking rates at 200, 140, and 100 wpm. This assessment also demonstrated a marked decline immediately from 100% intelligibility levels, again at 90% and again at 65%. Although patients were objectively judged to have 100% understandable speech, communication effectiveness was in decline.

In examination of the results, it is indicated that future research is needed to identify the frequency with which each of the most sensitive predictors is the initial sign of bulbar involvement. The individual scales included in the current protocol would be strengthened through additional evaluation to establish reliability and validity with the population of persons with ALS as well as with persons with other neurological impairments and those with no known neurological impairments. In addition, research is needed to identify the rate of progression observed in bulbar involvement associated with these parameters and to examine the time frame during which the voice, rate, intelligibility, and communication effectiveness reduction occurs. The association between date of onset or date of diagnosis and rate of bulbar decline should be assessed. The addition of more objective measures, including functional vital capacity, phonation time, tongue strength with the Iowa Oral Performance Instrument [22] may be added to future iterations of the protocol.

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References

[1] Brooks BR. Diagnostic dilemmas in Amyotrophic Lateral Sclerosis. Journal of the Neurological Sciences 1999;165(Suppl.):S1–9.
[2] Pongrantz D. The diagnostic process in ALS. Journal of Neurological Sciences 1999;165(Suppl.):S10–3.
[3] Swash M. Early diagnosis of ALS/MND. Journal of Neurological Sciences 1998;160(Suppl.):S33–6.
[4] Traynor B, Codd M, Corr B, Forde C, Frost E, Hardiman O. Clinical features of Amyotrophic Lateral Sclerosis according to the El Escorial and Airlie House diagnostic criteria. Arch Neurol 2000:57: 1171–6.
[5] Brooks BR. El Escorial World Federation of Neurology criteria for the diagnosis of Amyotrophic Lateral Sclerosis. Journal of Neurological Sciences 1994;124(Suppl.):S96–107.
[6] Miller R, Munsant T, Swash M, Brooks B. Consensus guidelines for the design and implementation of clinical trials in ALS. Journal of Neurological Sciences 1999;169:2–12.
[7] Brooks B. Defining optimal management in ALS: from first symptoms to announcement. Neurology 1999;53(8 Suppl. 5):S1–3.
[8] World Health Organization. WHO International classification of impairment, activity, and participation: beginner's guide. In: WHO, editor. Beta-1 draft for field trials; 1999.
[9] Darley F, Aronson A, Brown J. Motor speech disorders. Philadelphia: W.B. Saunders, 1975.
[10] Yorkston K, Beukelman D, Tice R. Sentence intelligibility test. 1.0 edn. Lincoln, NE: Tice Technology Services, 1991.
[11] Dworkin J, Aronson A, Mulder D. Tongue force in normals and in dysarthric patients with Amyotrophic Lateral Sclerosis. Journal of Speech and Hearing Research 1980;6:828–37.
[12] Kent R, Kent J, Weismer G, Sufit R, Brooks B, Rosenbek J. Relationships between speech intelligibility and the slope of second-formant transitions in dysarthric subjects. Clinical Linguistics and Phonetics 1989;3:347–58.
[13] Forrest K, Weismer G. Acoustic analysis of dysarthric speech. In: McNeil M, editor. Clinical management of sensorimotor speech disorders. New York, NY: Thieme 1997:63–79.
[14] Tomik B, Wszolek W, Glodzik-Sobanska L, Krupinski J, Bala-Slodowska M, Lechwacka A, et al. Acoustic speech analysis in ALS patients. 10th International Symposium on ALS/MND: 17 November 1999. Vancouver, Canada: Motor Neuron Disease Association 1999:76–7.
[15] Warren D, Roche A, Hinton V. Aerodynamics. In: McNeil M, editor. Clinical management of sensorimotor speech disorders. New York: Thieme 1997:81–106.
[16] Yorkston K, Miller R, Strand E. Management of speech and swallowing in degenerative diseases. Tucson, AZ: Communication Skill Builders, 1995.
[17] Hillel A, Miller R, Yorkston K, McDonald E, Norris F, Konikow N. ALS severity scale. Journal of Neuroepidemiology 1989;8:142–50.
[18] Weismer G, Jeng J, Laures J, Kent R, Kent J. Acoustic and intelligibility characteristics of sentence production in neurogenic speech disorders. Folia Phoniatrica 2001;53(1):1–18.

[19] Lomas J, Pickard L, Bester S, Elbard H, Finlayson A, Zoghaib C. The communication effectiveness index: development and psychometric evaluation of a functional communication measure for adult aphasia. Journal of Speech and Hearing Disorders 1989;54(1):113–24.

[20] Yorkston K, Strand E, Beukelman D, Bell K. Management of motor speech disorders in children and adults. Austin, TX: Pro-Ed, 1999.

[21] Yorkston K, Strand E, Miller R, Hillel A, Smith K. Speech deterioration in Amyotrophic Lateral Sclerosis: implications for the timing of intervention. Journal of Medical Speech-Language Pathology 1993;1(1):35–46.

[22] D. Robin, E. Luschei, inventors. Iowa Oral Performance Instrument. USA Patent 5119831; 1992.