Validation and Feasibility of the Modified Oculobulbar Facial Respiratory Score in Amyotrophic Lateral Sclerosis

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Amyotrophic Lateral Sclerosis (ALS)

- Progressive neurodegenerative disorder affecting the upper and lower motor neurons
- Bulbar and respiratory insufficiency is the leading cause of morbidity and mortality

Rationale

Detecting progressive facial, bulbar, and respiratory weakness allows for optimal patient care

Providing prompt management helps:

- prevent weight loss via diet modification
- reduces risk of choking and aspiration
- decreases risk of respiratory infections
- determines time for gastrostomy placement

Objectives

1) Determine if the Modified Oculobulbar Facial Respiratory score (mOBFRS) can be reliably measured in ALS on a serial basis

2) Correlate the mOBFRS with the ALS Functional Rating Scale (ALSFRS-R) total score and subscore

3) Correlate the mOBFRS with the Bulbar Rating Scale

4) Determine if changes in this score occur in a linear, predictable fashion that can be used as a potential outcome measure in future clinical trials in ALS

mOBFRS

1. Facial muscles	0 (normal)	1 (mildly weak)	2 (severely weak)	3 (severely weak)
Orbicularis oculi				
Frontalis				
Orbicularis oris				
1. Total facial muscle score (out of 6)				
2. Palatal contractility	0 (normal)	1 (mildly weak/ asymmetrical)	2 (non-contractile)	
3. Swallow time	0 (0-7.8 s)	1 (7.9-15 s)	2 (15.1-30 s)	3 (>30 s)
4. Tongue appearance	0 (normal)	1 (lateral thinning)	2 (central furrowing)	3 (triple furrowing)
5. Forced vital capacity	0 (normal)	1 (65-79%)	2 (50-64%)	3 (<50%)
Total mOBFR score (max=17)				

Farrugia ME, Harle HD, Carmichael C, Burns TM. The Oculobulbar Facial Respiratory score is a tool to assess bulbar function in myasthenia gravis patients. *Muscle Nerve* 2011;43:329-34.

Bulbar Rating Scale

Test	Result
a. Orbicularis oculi	☐1 - No movement ☐2 - Unable to close eyes to completely cover iris ☐3 - No resistance to eye closure or incomplete closure (small amount of sclera / no iris visible) ☐4 - Complete eye closure against resistance with no visible iris
b. Orbicularis oris	☐1 - No movement ☐2 - Lip movement, but unable to bring lips together ☐3 - Closes lips, but with no resistance ☐4 - Completely seals lips & holds strongly against resistance (use tongue blade)
c. Jaw opening	☐1 - No movement ☐2 - No resistance tolerated ☐3 - Unable to open ≤ 2 stacked fingers ☐4 - Unable to close
d. Jaw closure	☐1 - No movement ☐2 - Able to close mouth, but no resistance tolerated, where clinician is able to palpate masseter & temporalis ☐3 - Able to open ☐4 - Unable to open
e. Tongue protrusion	☐1 - No movement ☐2 - Minimal protrusion and tongue does not clear mouth ☐3 - Tongue reaches margins of lips ☐4 - Extends beyond lips
f. Tongue deviation	☐1 - No movement ☐2 - Protrudes & slight deviation to the side ☐3 - Tongue reaches corner of mouth ☐4 - Reaches some part of cheek or lateral sulcus
g. Soft palate elevation (observation)	☐1 - No movement ☐2 - Almost imperceptible motion of both the uvula and the arches ☐3 - Uvula moves sluggishly and may deviate to one side or another ☐4 - Uvula moves briskly and elevates while remaining in the midline
h. Posterior pharyngeal wall constriction (tongue blade and cotton swab)	☐1 - No motion ☐2 - Trace of motion ☐3 - Decreased movement or sluggish motion of the pharyngeal wall ☐4 - Brisk contraction of posterior pharyngeal wall
Total Score:	

Bulbar Rating Scale:

- Validated in Kennedy's disease

ALSFRS-R:

- Validated in ALS
- 3/12 questions (subscore)
  - Swallow
  - Speech
  - Saliva

Bulbar Scale: Fernández-Rhodes LE, Kokkinis AD, White MJ, et al. Efficacy and safety of dutasteride in patients with spinal and bulbar muscular atrophy: a randomised placebo-controlled trial. Lancet Neurol 2011;10:140-7.

ALSFRS-R: Cedarbaum JM, Stambler N, Malta E, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. BDNF ALS Study Group (Phase III). J Neurol Sci 1999;169:13-21.

Methods

- Target Enrollment: 125 subjects
- Subjects assessed at Baseline, Month 3, and Month 6 (during routine clinic visit)
- Assessments:
  - mOBFRS performed by licensed speech language pathologist
  - ALSFRS-R performed by physical therapist
  - Bulbar rating scale performed by physician

Inclusion Criteria:

- Age 18 years or older
- Diagnosis of ALS

Exclusion Criteria:

- Unable or unwilling to provide informed consent
- NPO
- Diagnosis of PLS

Feasibility

Current Enrollment	
Total Subjects Enrolled	120
Completed Visit 1	120
Completed Visit 2	91
Completed Visit 3	59

Enrollment began July 2016

- The mOBFRS is quick and **easy** to complete during clinic (approximately **5 minutes**)
- 50/59 completed the mOBFRS, ALSFRS-R, and bulbar rating scale at all three visits

Results

Internal consistency of mOBFRS at each visit (Baseline, Month 3 and Month 6)

	Cronbach's Alpha Coefficient	95% Confidence Interval
Baseline	0.88	(0.83-0.92)
Visit 2	0.87	(0.82-0.92)
Visit 3	0.85	(0.80-0.91)

- A **greater than 0.8** Cronbach's alpha is considered good internal consistency.

Results

Changes of mOBFRS compared to the Bulbar Rating Scale

	Coefficient	Std.Error	Df	P Value
(Intercept)	32.73	0.55	93	<0.0001
mOBFRS	-0.59	0.06	93	<0.0001

Linear mixed effect (LME) model

- The mOBFRS score is significantly associated with the bulbar rating scale along all three visits ($P < 0.0001$)
- One point **increase** in mOBFRS correlates with a 0.59 point **decrease** of bulbar rating scale

Results

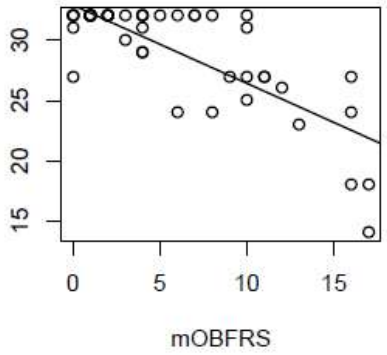
Correlation of the mOBFRS with the bulbar rating scale, subscore of ALSFRS-R and total score of ALSFRS-R

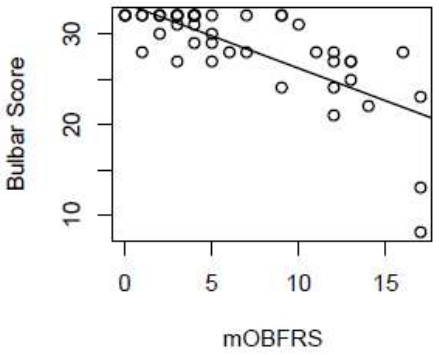
Time	Bulbar Rating		ALSFRS-R Subscore		ALSFRS-R	
	C	P Value	C	P Value	C	P Value
Baseline	-0.78	< 0.0001	-0.81	< 0.0001	-0.66	< 0.0001
Visit 2	-0.74	< 0.0001	-0.83	< 0.0001	-0.67	< 0.0001
Visit 3	-0.73	< 0.0001	-0.76	< 0.0001	-0.69	< 0.0001

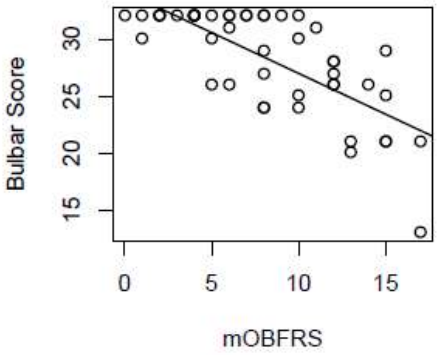
Pearson's correlation and Bonferroni adjustment

- The mOBFRS score is negatively **correlated** with all three scores at all three visits
- The correlation is strongest between mOBFRS and ALSFRS-R subscore

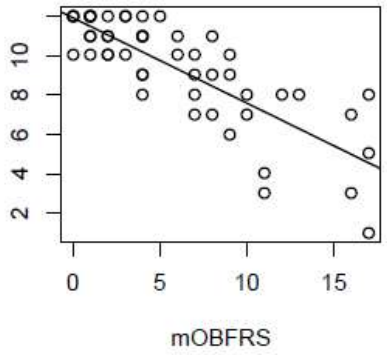
Bulbar rating scale

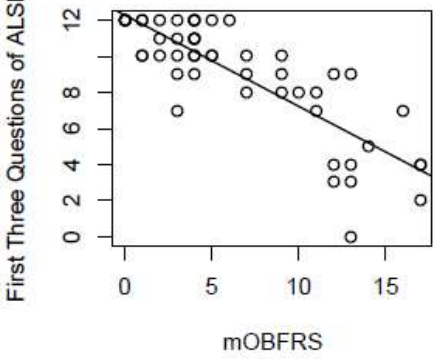


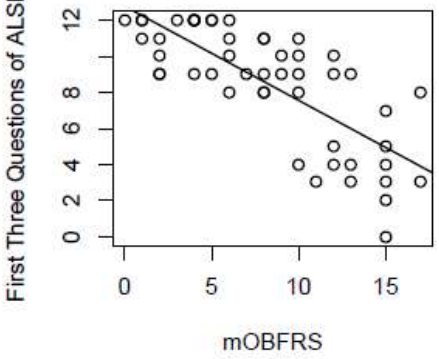




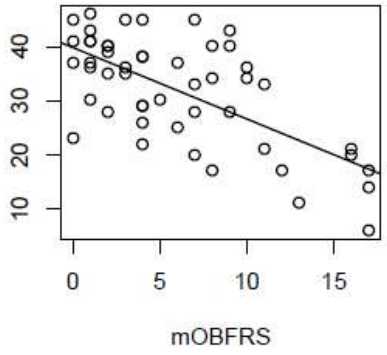
ALSFRS-R subscore

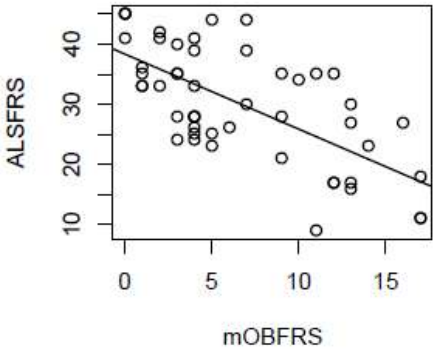


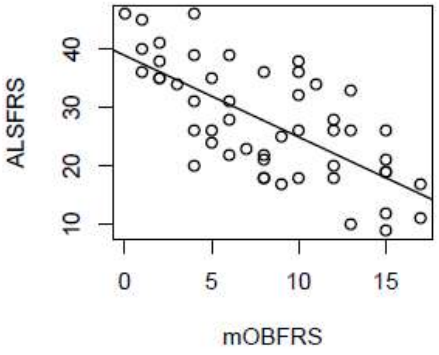




ALSFRS-R total score







Results

Change in mOBFRS over time

Score	Time	Coefficient	Std.Error	Df	P Value
mOBFRS	(Intercept)	5.79	0.72	92	< 0.0001
	Baseline	(Reference)			
	Visit 2	0.87	0.35	92	0.0158
	Visit 3	2.43	0.49	92	< 0.0001
Bulbar Rating Scale	(Intercept)	29.17	0.67	92	< 0.0001
	Baseline	(Reference)			
	Visit 2	-0.53	0.48	92	0.2729
	Visit 3	-0.89	0.47	92	0.0621

Linear mixed model

- The mOBFRS score is more sensitive to change when tracking disease progression

Results

Correlation between mOBFRS swallow time and ALSFRS-R swallow ability at each visit

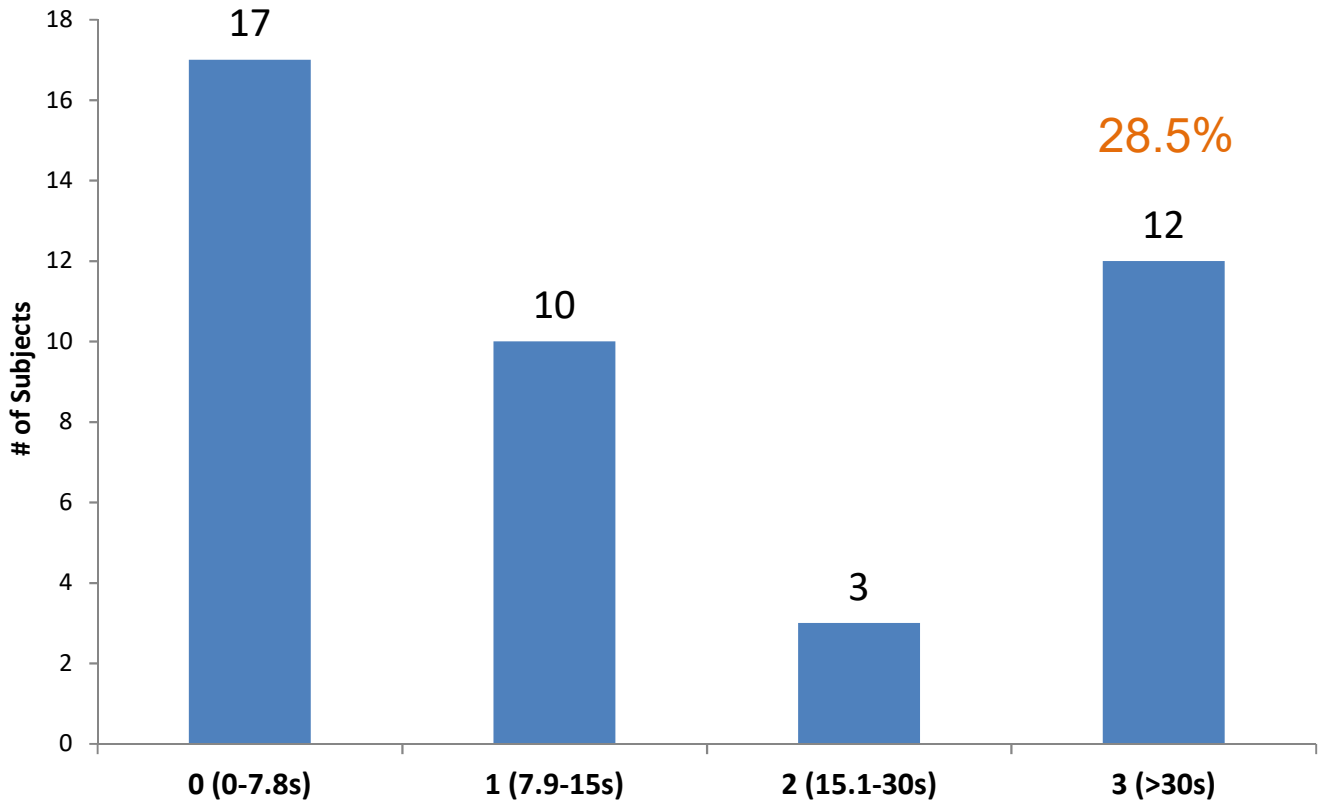
Time	Swallow Ability	
	C	P Value
Baseline	-0.61	< 0.0001
Visit 2	-0.58	0.0003
Visit 3	-0.60	0.0001

Pearson's correlation and Bonferroni adjustment

- The swallow ability question in ALSFRS-R is significantly **correlated** with the mOBFRS swallow time test

Results

Swallow time in patients reporting no or minimal difficulty swallowing on ALSFRS-R (42/50)



Conclusions

- The mOBFRS is **feasible** to conduct in a clinic setting
- Results are **reliable**
- The mOBFRS significantly **correlates** with ALSFRS-R subscore and total ALSFRS-R
- The mOBFRS may detect swallowing dysfunction **earlier** than self reporting

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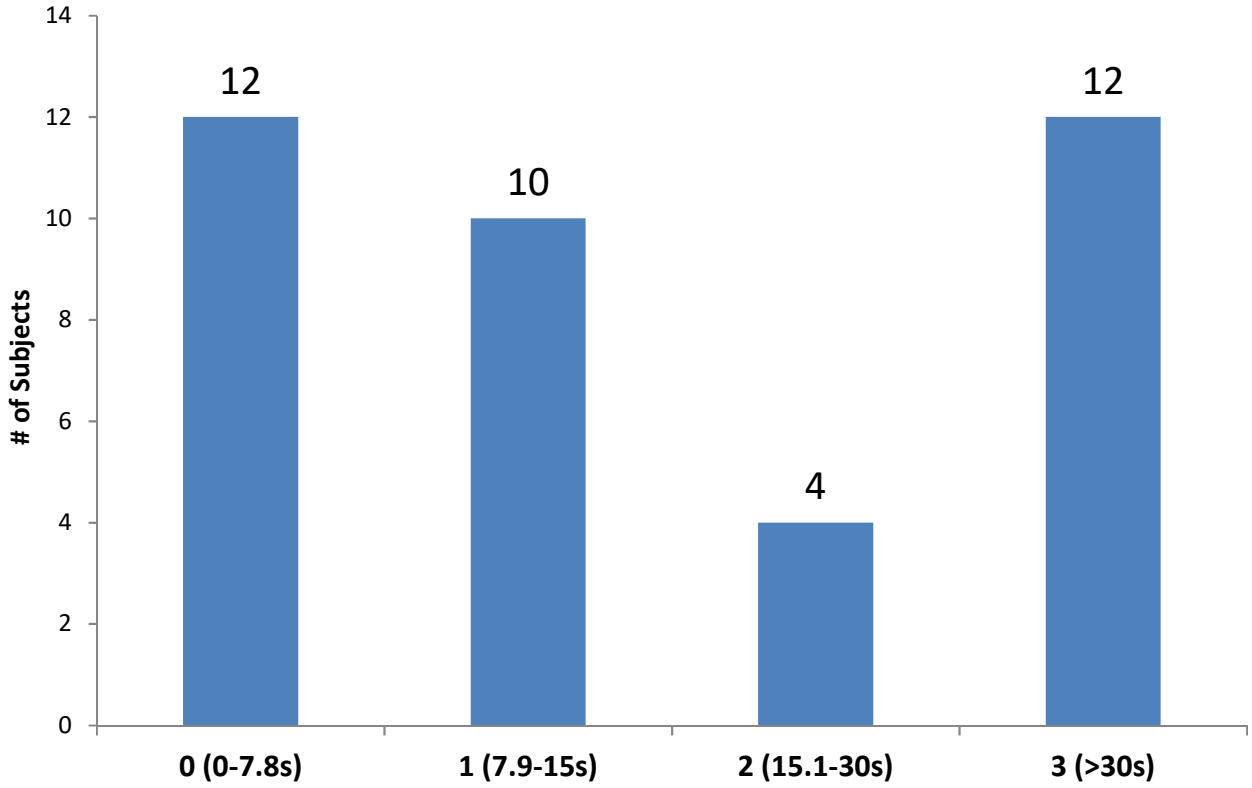
Visit 2 (38/50)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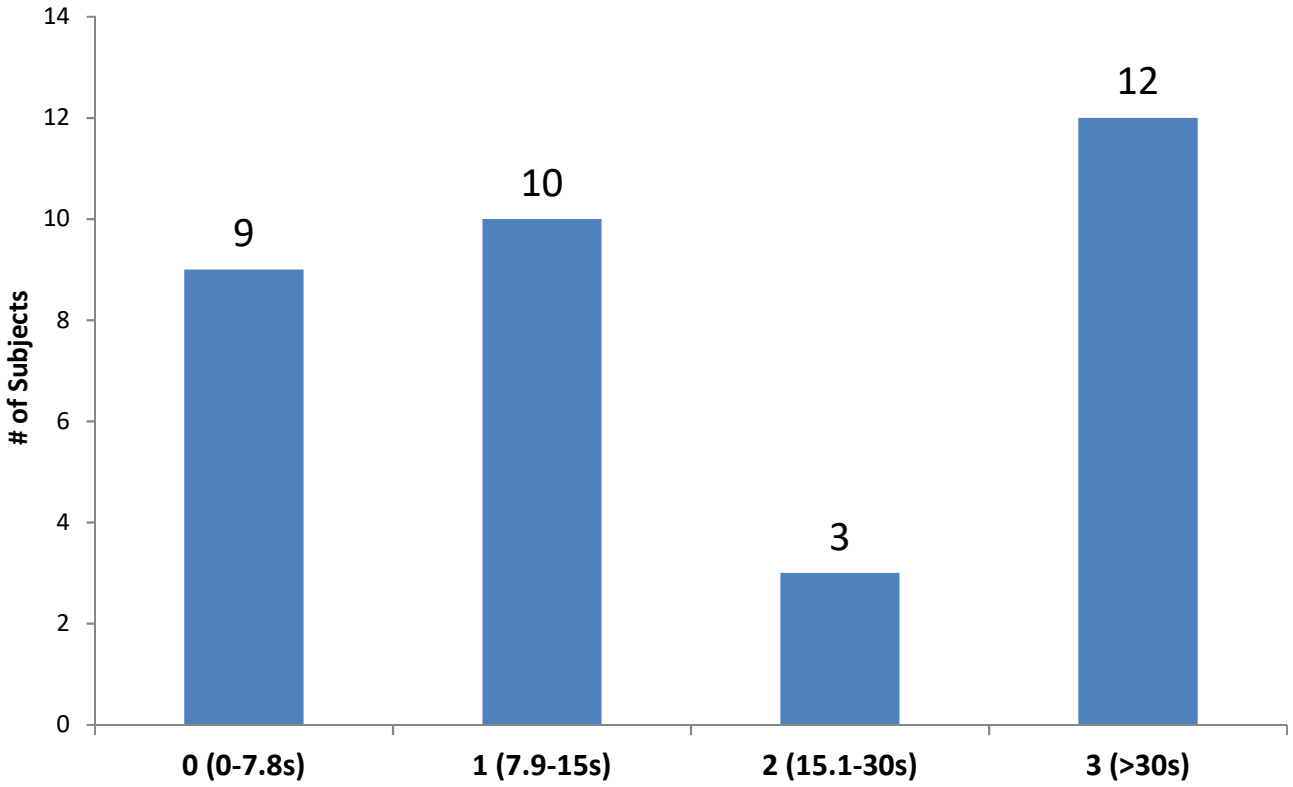
Visit 3 (34/50)