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Correlation between Cognitive Aspects and Dysphagia in Patients with Amyotrophic Lateral Sclerosis: Preliminary Report

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Abstract

Introduction: Cognitive impairment has been identified in 30% - 50% of the population with Amyotrophic Lateral Sclerosis (ALS). Among these patients, dysphagia is not only a very common symptom but also one of the main bulbar symptoms. **Objective**: To correlate cognitive function and dysphagia in patients with ALS. **Methods**: a cross-sectional study. Criteria for inclusion were an ALS diagnosis and the signing of the consent form. Criteria for exclusion were patients who had undergone speech therapy, patients within sufficient oral language skills to participate in cognitive tests, patients receiving enteral feeding and patients who withdrew from the study before completing all the stages. Evaluations of cognition and dysphagia were performed. **Results**: The initial sample consisted of 86 participants, 69 of which fell under exclusion criteria. Seventeen patients were evaluated, with a mean age of 49.8 (±11.3) and a mean education period of 7.1 (±2.8) years. Disease evolution was analyzed in months, with a median of 24 (P25 = 10; P75 = 72) months. In this sample, 70.6% of patients were male ($p = 0.019$). Among the tests performed, those of executive functions were correlated with dysphagia: FAB ($p = 0.019$) and Trail Making Test A ($p = 0.006$). **Conclusion**: This pilot study suggests a correlation between executive functions and dysphagia.

Keywords

Cognition, Dysphagia, Amyotrophic Lateral Sclerosis

1. Introduction

Amyotrophic lateral sclerosis (ALS) belongs to the group of motor neuron dis-

eases, characterized by the progressive degeneration of upper motor neurons (UMNs) and lower motor neurons (LMNs), in association with bulbar and pyramidal signs [1] [2] [3]. The involvement of these neurons results in several symptoms such as respiratory difficulties and dysphagia, as well as physical and cognitive deficits [4] [5] [6].

One of the most severe symptoms faced by patients with neurodegenerative diseases, especially those with ALS, is oropharyngeal dysphagia [6] [7]. Dysphagia is a swallowing disorder that modifies the process of transporting food safely and efficiently from mouth to pharynx to esophagus [8] [9]. Dysphagia can lead to aspiration, malnutrition, dehydration and pneumonia, all of which have a significant impact on the quality of life of patients [10] [11] [12].

Swallowing involves muscular issues as well as cognitive aspects. It is known that the anticipatory and preparatory stages of swallowing are voluntary and may be influenced by cognitive issues which, in turn, may limit self-regulation, perception and the control of risk factors, in addition to the development of compensatory strategies. Thus, in disorders such as Alzheimer's disease (AD), Parkinson's disease (PD), where cognitive functions become altered, complications related to eating and swallowing can arise [9] [10]. Although no studies specific to ALS have been found so far, this issue has already been well described in literature regarding other neurological diseases [13] [14] [15].

Although physical handicaps are most noticeable in ALS, cognitive deficits are also important. Cognitive changes can occur in 35% - 50% of ALS patients, which consequently lead to a spectrum of functional and behavioral deficiencies that directly influence a patient's planning and decision-making capacity. In more recent literature, ALS is recognized as a multisystemic disease that may be associated with varying degrees of cognitive and behavioral dysfunction [3] [16] [17] [18].

Although, cognition is a recently point of discussion in ALS forums, studies have shown that this clinical population may present alterations in cognitive aspects, especially executive function (EFs) alterations [19] [20] [21]. Moreover, studies have shown that individuals with ALS present cognitive impairment, regardless of the type of neuropsychological assessment performed [22] [23] [24] [25]. Understanding cognitive impairment in ALS could provide more information about the pathogenesis of neurodegeneration and inform patient care [3] [26] [27] [28].

Early screening for cognitive deficits in ALS patients may help to better direct healthcare strategies that these individuals may need during disease progression [21] [29]. It is known that, with the advancement of the disease, some phenotypes show a greater decline.

The purpose of this study is to correlate cognitive impairment and dysphagia in patients affected by ASL.

2. Material and Methods

2.1. Study Design and Sample Recruitment

This was a cross-sectional, observational and descriptive study. The sample con-

sisted of individuals attended at a reference hospital in the city of Porto Alegre, Brazil. The research project was analyzed and approved by the Research Ethics Committee of the institution under number 150037.

The inclusion criteria were: patients with a medical diagnosis of ALS, according to the El Escorial [30] revised diagnostic criteria for definite, probable and probably laboratory-supported ALS, along with the signing of the Informed Consent form. The exclusion criteria were: patients who had previously had speech therapy for dysphagia, patients with oral language difficulties which made it impossible to perform cognitive tests, patients receiving enteral feeding and patients who dropped out before completing all the steps of the study.

Initially, a search was done to identify individuals with ALS diagnosis. In **Figure 1** we present the initial sample and the final n meeting the inclusion/exclusion criteria.

2.2. Procedures

Data collection occurred between March and October 2016. The collection was carried out in individual meetings lasting 90 minutes each. At the time of initial collection, medical and sociodemographic data were obtained. Four steps were performed: anamnesis, cognitive evaluation, questionnaires (mood and fragility) and a clinical evaluation of patient dysphagia.

To evaluate the cognitive aspects, the following instruments were used: Mini-Mental State Examination (MMSE) [31], Verbal Fluency Semantics (VFS) [32], the Categorical Verbal Fluency-Animals (VF-animal) [33], Montreal Cognitive Assessment (MoCA) [34], Frontal Assessment Battery (FAB) [35] and Trail Making Test version A and B [36]. The classification of normality was established by age and years of education, according to each cognitive test. The validated and translated versions for Brazilian Portuguese were used.

To evaluate mood we used the Beck Depression Inventory (BDI) [37] and to evaluate fragility we used the Edmonton Fragility Scale [38]. To assess patient self-perception regarding dysphagia, the Eating Assessment Tool (EAT-10) —developed by Belafsky *et al*. (2008) [39] and validated in Brazil by Gonçalves *et*

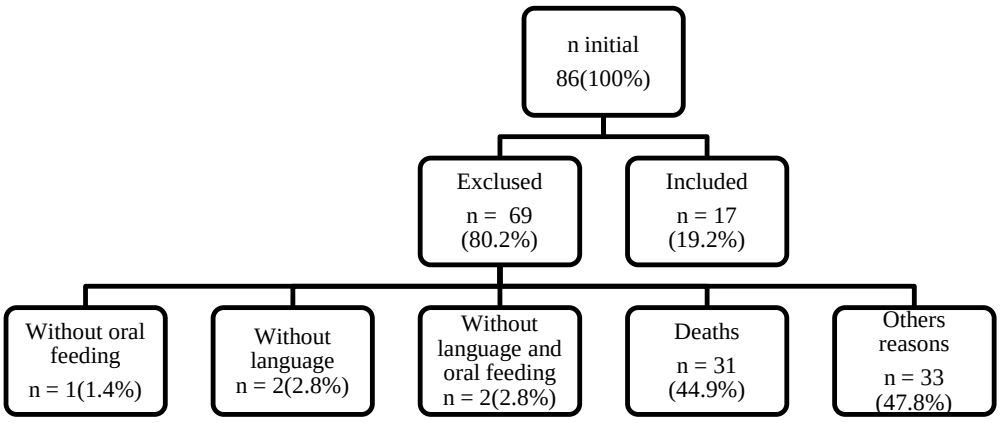

Figure 1. Sample data.

al. (2013) [40]—was used. This test exhibited a sensitivity of 69.70% and a specificity of 72.00%, parameters defined as the limit of separation between pass and fail in the feeding triage, with good accuracy. Patients who scored above three points were considered at risk for dysphagia [40].

Dysphagia was evaluated through clinical evaluation, using the Northwestern Dysphagia Patient Check Sheet—NDPCS, which was developed by Logemann *et al*. (1999) and validated in Brazilian Portuguese by Magalhaes (2013). This assessment was carried out with three consistencies: solid (a wafer), puree (a 50 g cup of yogurt) and thin liquid (a glass of 200 ml of water). All evaluated individuals received the same type of food in the same quantity. After, each patient was classified as having or not having dysphagia, according to the signs and symptoms presented during the process. The signs and symptoms analyzed were based on those described in literature [41] [42] [43] totalizing 21 signs and symptoms which were scored as present or absent. All three types of food were offered freely without interference from the evaluator at the time of feeding.

After the evaluations, the Functional Oral Intake Scale (FOIS), developed by Crary *et al*. (2005), was applied. This instrument is valid and reliable and has a coefficient of reliability among evaluators of 0.98 - 0.99, with mean Kappa coefficient values between 0.86 and 0.91 and adequate consensual validity (agreement of Kendall 0.90) as well as validity criteria (based on The Mann Assessment of Swallowing Ability test) [44]. The translated and validated version in Brazilian Portuguese was used [45].

2.3. Statistical Analysis

Quantitative variables were described by mean and standard deviation or median and interquartile range. Qualitative variables were described by absolute and relative frequencies. The t-student test was applied to compare the qualitative variables. In the case of asymmetry, the Mann-Whitney test was used. The Pearson or Spearman correlation tests were used to evaluate the association between continuous and ordinal variables respectively. The significance level adopted was 5% ($p < 0.05$) and the analyses were performed in the SPSS program version 21.0.

3. Results

Seventeen patients were included in this sample, with a mean age of 49.8 (±11.3) and a mean education period of 7.1 (±2.8) years. Overall disease time was analyzed in months, with a median of 24 (P25 = 10, P75 = 72) months. In this sample, 70.6% of patients were male.

Table 1 shows the performance and classification of normal and altered individuals in cognitive assessments and questionaires.

Table 2 presents results of the clinical evaluation of dysphagia. Regarding self-perception, only 4 participants (23.4%) scored the cutoff point for risk of dysphagia, whereas the result of the clinical evaluation showed a higher incidence of dysphagia (n = 8; 47.1%). FOIS scores ranged from 5 (oral feeding with

Table 1. Data of cognitive evaluation and questionaires.

Variables	n = 17
MMSE – mean ± SD	24.9 ± 3.6
MMSE classification – n (%)	
Changed	10 (58.8)
Normal	7 (41.2)
VF-animal – mean ± SD	13.7 ± 4.3
VF-animal classification – n(%)	
Changed	2 (11.8)
Normal	15 (88.2)
VFS – mean ± SD	21.1 ± 10.0
VFS classification – n(%)	
Changed	16 (94.1)
Normal	1 (5.9)
MoCA – mean ± SD	20.4 ± 5.3
MOCA classification – n(%)	
Changed	15 (88.2)
Normal	2 (11.8)
FAB – mean ± SD	9.9 ± 4.2
FAB classification – n(%)	
Changed	7 (41.2)
Normal	10 (58.8)
Trail Making Test A – MD (P25 – P75)	128 (103 - 186)
Trail Making Test A Classification – n(%)	
Changed	17 (100)
Normal	0 (0.0)
Trail Making Test B – MD (P25 – P75)	275 (132 - 301)
Trail Making Test B Classification – n(%)	
Changed	17 (100)
Normal	0 (0.0)
BDI– md (P25 – P75)	9 (4 - 14)
BDI classification – n(%)	
Changed	4 (23.5)
Normal	13 (76.5)
Fragility – FAB	6.3 ± 2.7
Fragility classification n(%)	
Changed	11 (64.7)
Normal	6 (35.3)

MMSE: Mini Mental State Examination; VFS: Verbal Fluency Semantics; VF-animal: Verbal Fluency categoric-Animals; MoCA: Montreal Cognitive Assessment; FAB: Frontal Assessment Battery; BDI: Beck Depression Inventory; FRAIL: Edmonton Fragility Scale; mean ± SD.

various consistencies, but with special preparation or compensatory restrictions) to 7 (oral feeding without restrictions).

Table 3 shows the correlations between cognitive aspects and dysphagia. Among the tests performed, these Executive Functions (EFs) tests were correlated with dysphagia: FAB (p = 0.019) and Trail Making Test A (p = 0.006). BDI was also significant when associated with dysphagia (p = 0.015).

BDI also correlated with EAT-10 (rs = 0.596, p = 0.012) and FOIS (rs = −0.610, p = 0.009). Fragility was associated with FOIS (rs = −0.592; p = 0.012).

Schooling correlated with the MMSE (p = 0.021 − r = 0.553), VF-animal (p = 0.036 − r = 0.512) and MoCA (p = 0.031 − r = 0.523). Disease duration presented correlation only in the Trail Making test A (p = 0.029 − r = 0.529). Age was not

Table 2. Self-perception data and clinical evaluation of dysphagia and FOIS.

Vaiables	n = 17
EAT-10 – md (P25 – P75)	0 (0 - 5)
EAT-10 classification – n(%)	
Changed	4 (23.5)
Normal Swallowing clinical assessment – n(%)	13 (76.5)
Changed	8 (47.1)
Normal	9 (52.9)
FOIS – n(%)	
5	6 (35.3)
6	3 (17.6)
7	8 (47.1)

EAT-10—Eating Assessment Tool; FOIS—Functional Oral Intake Scale.

Table 3. Association between cognitive data and clinical evaluation of dysphagia.

Variables	With dysphagia	Without dysphagia	p
MMSE – mean ± SD	24.8 ± 2.3	25.0 ± 4.5	0.890[a]
VF-animal – mean ± SD	12.1 ± 3.6	15.1 ± 4.6	0.157[a]
VFS – mean ± SD	21.5 ± 10.5	20.7 ± 10.3	0.871[a]
MoCA – mean ± SD	19.5 ± 5.2	21.2 ± 5.5	0.521[a]
FAB – mean ± SD	7.5 ± 4.2	12.1 ± 2.9	0.019[a]
Trail Making Test A – MD (P25 – P75)	500** (220 - 500**)	110 (85.5 - 160)	0.006[b]
Trail Making Test B – MD (P25 – P75)	500** (301* - 500**)	275 (132 - 500**)	0.093[b]
BDI – md (P25 – P75)	13 (9 - 23)	4 (4 - 8)	0.015[b]
FRAIL – mean ± SD	7.63 ± 2.9	5.11 ± 1.97	0.053[a]

MMSE: Mini Mental State Examination; VFS: Verbal Fluency Semantics; VF-animal: Verbal Fluency categoric-Animals; MoCA: Montreal Cognitive Assessment; FAB: Frontal Assessment Battery; BDI: Beck Depression Inventory; FRAIL: Edmonton Fragility Scale; *Represents the patients who took more than 5 minutes to perform the test ** represents the patients who were unable to perform the test a—Student's test b—Mann-Whitney test; mean ± SD.

significantly associated with cognitive and swallowing data ($p > 0.10$).

4. Discussion

According to the results, oropharyngeal dysphagia was present in 47.1% of the patients in this sample; however, regarding self-perception of dysphagia, only 23.5% of the subjects reported feeding difficulties.As we have seen in the literature, dysphagia is widely discussed in ALS forums, as it is one of the most prevalent symptoms of the disease, and it is even one of the initial bulbar symptoms [10] [46] [47] [48] [49] [50].

However, in our study, we were able to show that executive functions and dysphagia demonstrated a significant correlation, confirming the initial hypothesis of our study with this sample. It is already known that swallowing is also a planning process and therefore an action commanded by the brain. Executive functions (EFs) are always required once action planning needs to take place or when a sequence of appropriate responses needs to be defined or organized. In this way, EFs assist in the selection of the most efficient strategies in order to solve immediate, medium-term and long-term problems [51] [52].

Depressive symptoms are quite common in ALS. They may appear in the first year of diagnosis and persist during the course of the disease, often making clinical management difficult [53] [54]. Psychosocial factors frequently play a significant role in the evolution of the disease and, besides issues related to quality of life (QOL) and food, patients with depression are at higher risk of dying than non-depressives [55] [56]. In a cohort study of 81 patients with ALS [7], the degree of dysphagia was verified along with overall disease progression, both with reference to swallow-related QOL. It was observed that swallow-related QOL was moderately reduced in these patients and profoundly impacted on ALS aspirators as well as on individuals in the advanced stages of the disease. These findings corroborate our observation that depressive symptoms correlated with dysphagia in our study sample.

Unlike other variables, total disease time had little impact and correlated only with the Trail Making Test A; a finding which led us to question if motor aspects could have influenced patient performance in this test. It is necessary, therefore, for us to further discuss whether the cognitive evaluation of these patients was a sound test.

The heterogeneity of ALS presents a significant challenge for an interdisciplinary team because the disease has a progressive course and creates a demand for adequate care in order to deal with the progression of the disease and the necessary, constant changes in intervention. What is more, the fragility or incapacity of these patients could be a useful parameter in decision making, regarding treatment and intervention. In our sample, fragility was associated with the FOIS scale, showing that the greater the functional disability of these individuals, the more food modification they resort to. This is due to the inability or the decreased strength of the oropharyngeal musculature, by cause of general muscular

degeneration [4].

Study Limitations

Because of the small sample, it is reasonable to suppose that a larger number of subjects could confer more reliability to the results. Number of participants alone, however, does not make it impossible to generalize data. As such, developing longitudinal studies is imperative to verify the influence of overall disease time on cognitive performance and swallowing.

5. Conclusion

In conclusion, this pilot study suggests a correlation between executive functions and dysphagia. Our findings serve to underline the importance of early dysphagia intervention in ALS patients whose altered executive functions are detected by neuropsychological tests. Further investigation correlation between mood, dysphagia and neuropsychological features is focus for future research.

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