# Relationship Between Cognitive-Behavioral Impairment and Clinical and Functional Parameters in ALS and Reliability of the Edinburgh Cognitive and Behavioural ALS Screen to Assess ALS: Preliminary Findings

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**Background:** Although it is widely recognized that a high percentage of individuals with amyotrophic lateral sclerosis (ALS) have cognitive and behavioral impairment, the associated clinical and functional parameters remain unknown. ALS is typically assessed via screening tests, such as the Edinburgh Cognitive and Behavioural ALS Screen (ECAS).

**Objective:** To investigate the relationship between cognitive-behavioral impairment and other clinical and functional parameters and to compare the assessment results from a set of standardized neuropsychological tests with those from the ECAS.

**Methods:** Forty individuals with ALS participated in the study. We assessed attention, memory and learning ability, and executive function using a set of standardized neuropsychological tests and the ECAS. Sociodemographic variables, time since onset of symptoms, time since diagnosis, and functional respiratory values were recorded.

**Results:** No relationship was found between time since onset of symptoms and time since definitive diagnosis and either attention ($P = 0.206$, 0.314, respectively), memory and learning ability ($P = 0.618$, 0.692), or executive function ($P = 0.844$, 0.583). The set of standardized neuropsychological tests identified an impairment in executive function in 29% of the participants, whereas the ECAS identified it in 89%.

**Conclusions:** We found no relationship between cognitive-behavioral impairment and time since onset of symptoms nor time since ALS diagnosis. Because the ECAS does not correctly reflect the executive function of individuals with ALS, function-specific neuropsychological tests are preferred. Test selection must take into account individuals' physical characteristics and their consequent ability to respond gesturally or orally.

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**Key Words:** frontotemporal dementia, cognitive impairment, behavioral impairment, amyotrophic lateral sclerosis

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**ALS** = amyotrophic lateral sclerosis. **BMI** = body mass index. **ECAS** = Edinburgh Cognitive and Behavioural ALS Screen. **FrSBe** = Frontal System Behavior Scale. **WAIS–III** = Wechsler Adult Intelligence Scale, Third Edition. **WMS–III** = Wechsler Memory Scale, Third Edition.

Increasing evidence suggests that individuals with amyotrophic lateral sclerosis (ALS) have cognitive and behavioral impairment (Burke et al, 2017) and that dementia may follow (Osborne et al, 2014). Approximately 50% of individuals with ALS present symptoms of frontotemporal syndrome (Goldstein and Abrahams, 2013; Lillo et al, 2012; Phukan et al, 2007; Strong, 2008; Strong et al, 2009), and between 10% and 12% meet the diagnostic criteria for frontotemporal dementia (Beeldman et al, 2016; Elamin et al, 2013). Although progress is being made with regard to which neuropsychological areas are affected in these circumstances, and the effects of mutations of the *C9orf72* gene (Byrne et al, 2012), the pathogenesis of frontotemporal syndrome and its associated factors are still unknown (Burke et al, 2017; Goldstein and Abrahams, 2013; Lillo et al, 2012; Osborne et al, 2014; Phukan et al, 2007; Strong, 2008).

Frontotemporal dementia affects individuals' working memory and executive function, and it may cause impairments to language and social behaviors (Sanchez Cubillo et al, 2012). Because these problems directly affect an individual's perception of his or her illness, they may considerably alter that individual's ability to make complex decisions regarding treatment (Grossman et al, 2007). This impairment of executive function, together with other traits that are characteristic of frontotemporal dementia (Strong, 2008; Strong et al, 2009), is found in up to 50% of patients with ALS and is associated with lower survival—a consequence of either a refusal to accept measures to support life or inadequate compliance with such measures

(Elamin et al, 2011; Hu et al, 2013). Moreover, caregivers of ALS individuals with cognitive and behavioral impairment also present greater perceived burdens and levels of depression as well as a lower perceived quality of life (Chiò et al, 2010).

There are few available data regarding the relationship between cognitive-behavioral impairment and other clinical or functional parameters. Although some authors have reported a relationship between bulbar onset ALS and the possible appearance of frontotemporal dementia (Brooks et al, 2000; Lomen-Hoerth et al, 2003; Neary et al, 2012), other authors have been unable to confirm this relationship (Burke et al, 2017). Similarly, although it is generally thought that the likelihood of the appearance of cognitive impairments increases as the disease progresses, this supposition is not currently supported by hard data (Ahmed et al, 2016; Xu et al, 2017), despite the importance of this issue for the decision-making process that usually takes place when respiratory problems begin.

It is, therefore, essential to determine the real extent of cognitive and behavioral impairment in individuals with ALS in order to be able to establish new decision-making protocols regarding treatment. When it is not possible to undertake an extensive neuropsychological assessment, evaluation of individuals' cognitive state, and their consequent ability to make decisions, has frequently been based on the results of screening tests (Connolly et al, 2015). These screening tests, however, do not take into account individual patients' possible motor and oral limitations, which may compromise their ability to adequately perform the tests, thereby rendering the test results unreliable (Abrahams et al, 2000). Moreover, screening tests typically assess only one cognitive function and may not adequately account for certain cognitive and behavioral changes that can occur in such populations (Woolley et al, 2010).

The two main objectives of this study were to determine the relationship between cognitive-behavioral impairment and functional and clinical parameters in individuals with ALS, and to establish whether the screening test used most often with these individuals, the Edinburgh Cognitive and Behavioural ALS Screen (ECAS; Abrahams and Bak, 2013), is as reliable as an extensive neuropsychological assessment. On the basis of our clinical experience, we hypothesized that because screening tests do not take into account the typical motor and oral limitations of patients with ALS, such tests would not reliably assess the patients' cognitive and behavioral functions.

## METHODS

### Participants

All individuals with a diagnosis of probable or definitive ALS (Brooks et al, 2000) who were managed at our respiratory care unit and were clinically stable, regardless of the extent of the progression of the disease, were eligible to participate in the study. The study protocol was approved by the ethics committee of the University Hospital of Valencia and took place in our respiratory care unit from June 2016 to June 2017. Exclusion criteria were previous pulmonary disease, dementia, and any other serious mental or neurologic illness.

A total of 53 consecutive patients were asked to participate in the study. Eight declined and five were excluded on the basis of the exclusion criteria (one patient presented a mental disorder and four had a previous neurologic disease). Therefore, a final number of 40 patients agreed to participate and provided informed consent. Table 1 presents the sociodemographic and clinical data for all participants and is broken down into those participants with some degree of cognitive or behavioral impairment and those without such impairment.

### Demographics and Clinical Measurements

Demographic and clinical variables measured included sex, age, body mass index (BMI), type of disease onset (spinal or bulbar), time from onset of symptoms, and time from definitive diagnosis. Neurologic function was evaluated using the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (Cedarbaum et al, 1999), and bulbar dysfunction was assessed using the Norris Scale bulbar subscore (Lacomblez et al, 1990), which ranges from 39 (normal state) to 0 (total dysfunction).

Functional respiratory tests were performed under medically stable conditions. A spirometry was performed using a pneumotachograph spirometer (MS 2000, C. Schatzman) in accordance with European Respiratory Society guidelines and suggested values (Brooks et al, 2000). Maximum inspiratory pressure (Black and Hyatt, 1969) and maximum expiratory pressure were measured using the Electrometer 78.905A (Hewlett-Packard) in accordance with the Black and Hyatt (1969) technique. For those individuals with severe bulbar-facial weakness, respiratory function tests were performed using an oronasal King Mask (King Systems) in order to avoid air leaks from the mouthpiece. Sniff nasal inspiratory pressure (Lofaso et al, 2006) was measured, and peak cough flow, maximum insufflation capacity, and manually and mechanically assisted peak cough flow (Sancho et al, 2007) were recorded via the pneumotachograph spirometer.

### Neuropsychological Assessment

A neuropsychological assessment is a part of the care protocol that is implemented by the multidisciplinary team of our respiratory care unit. To carry out our study, we offered all of our patients the opportunity to undergo this assessment during one of their outpatient appointments at the unit. The patients who agreed were given a neuropsychological assessment lasting approximately 2 hours. Patients with language-related limitations who could not respond orally answered by writing or by pointing to letters on an alphabet board. Patients who had limited or no movement of their upper limbs used augmentative communication methods to complete the assessment.

The extensive neuropsychological assessment consisted of the following set of tests that assessed each participant's attention, memory and learning ability, and executive function:

**TABLE 1.** Participants' Sociodemographic and Clinical Data

| Variable | All Participants (N = 40)* | Participants Without Cognitive-Behavioral Impairment (n = 12) | Participants With Cognitive-Behavioral Impairment (n = 24) | *P* |
|---|---|---|---|---|
| Sex (men/women) | 22/18 | 4/8 | 12/12 | 0.343 |
| Age (years) | 64.53 ± 11.56 | 62.92 ± 6.31 | 63.63 ± 12.61 | 0.824 |
| Body mass index | 26.77 ± 4.71 | 23.20 ± 1.47 | 28.29 ± 4.90 | 0.006 |
| Type of disease onset (spinal/bulbar) | 27/13 | 9/3 | 17/7 | 0.792 |
| Time from onset of symptoms (months) | 65.63 ± 54.77 | 60.59 ± 51.03 | 68.07 ± 60.44 | 0.748 |
| Time from definitive diagnosis (months) | 56.38 ± 55.94 | 66.22 ± 64.17 | 52.18 ± 55.37 | 0.501 |
| ALSFRS-R | 25.22 ± 11.35 | 20.60 ± 12.32 | 24.66 ± 10.39 | 0.348 |
| NBS | 24.83 ± 11.73 | 24.90 ± 10.40 | 25.29 ± 11.70 | 0.927 |
| FVC (liters) | 1.66 ± 1.09 | 1.90 ± 1.34 | 1.58 ± 0.98 | 0.477 |
| %FVC (%) | 53.61 ± 29.03 | 57.33 ± 36.13 | 52.35 ± 24.46 | 0.666 |
| sFVC (liters) | 1.49 ± 1.10 | 1.71 ± 1.26 | 1.33 ± 1.06 | 0.475 |
| $PI_{max}$ (cm $H_2O$) | −34.00 ± 26.44 | −38.62 ± 30.81 | −36.80 ± 23.52 | 0.866 |
| $PE_{max}$ (cm $H_2O$) | 25.22 ± 11.35 | 62.62 ± 44.51 | 61.90 ± 37.90 | 0.966 |
| SNIP (cm $H_2O$) | −34.00 ± 26.44 | −38.25 ± 28.43 | −31.90 ± 26.36 | 0.578 |
| PCF (liters per second) | 3.62 ± 2.41 | 4.37 ± 2.84 | 3.45 ± 2.24 | 0.355 |
| MIC (liters) | 1.92 ± 1.00 | 2.17 ± 1.08 | 1.86 ± 1.00 | 0.471 |
| $PCF_{MIC}$ (liters per second) | 3.89 ± 2.36 | 4.79 ± 2.73 | 3.65 ± 2.23 | 0.269 |
| $PCF_{MI-E}$ (liters per second) | 3.59 ± 1.54 | 3.80 ± 1.72 | 3.54 ± 1.57 | 0.693 |

Data are shown as M ± SD unless otherwise indicated.

*Four participants were unable to undergo the tests directly because of their inability to respond to the questionnaires using augmentative communication methods.

**ALS** = amyotrophic lateral sclerosis. **ALSFRS-R** = Revised Amyotrophic Lateral Sclerosis Functional Rating Scale. **FVC** = forced vital capacity. **%FVC** = predicted FVC. **MIC** = maximal insufflation capacity. **MI-E** = mechanical insufflation—exsufflation. **NBS** = Norris Scale bulbar subscore. **NIV** = noninvasive ventilation. **VE** = minute ventilation. **PCF** = peak cough flow. **$PCF_{MIC}$** = manually assisted PCF. **$PCF_{MI-E}$** = mechanically assisted PCF. **$PE_{max}$** = maximum expiratory pressure. **$PI_{max}$** = maximum inspiratory pressure. **sFVC** = supine forced vital capacity. **SNIP** = sniff nasal inspiratory pressure.

- **Attention:** Forward Digit Span subtest of the Spanish version of the Wechsler Adult Intelligence Scale, Third Edition (WAIS–III; Wechsler, 1999); Forward Spatial Span subtest of the Spanish version of the Wechsler Memory Scale, Third Edition (WMS–III; Wechsler, 2004); and Color Trails Test, Part I (D'Elia et al, 1996).
- **Memory and learning ability:** Spanish version of the Complutense Verbal Learning Test (Benedet and Alexandre, 1998); Spanish version of the Hopkins Verbal Learning Test (Bilbao et al, 2007); Backward Digit Span subtest of the Spanish version of the WAIS–III; Backward Spatial Span subtest of the Spanish version of the WMS–III; and Color Trails Test, Part II.
- **Executive function:** Spanish version of the Wisconsin Card Sorting Test (De la Cruz, 1997), Spanish version of the Hopkins Verbal Learning Test, Controlled Oral Word Association Test (Spreen and Strauss, 1998), Matrix Reasoning subtest of the Spanish version of the WAIS–III, and Brixton Test (Burgess and Shallice, 1997).
- **Behavioral impairment:** Spanish version of the Dysexecutive Questionnaire (Pedrero et al, 2009) and Frontal System Behavior Scale (FrSBe; Grace and Malloy, 2001).

We used the Spanish version of the ECAS (Mora et al, 2017) as a screening test to assess patients whose physical limitations, poor tolerance of cognitive effort, or fatigue prevented their taking the extensive neuropsychological assessment. Patients who were able to respond appropriately underwent both assessment processes (the extensive neuropsychological assessment and the ECAS). For those patients whose cognitive performance could not be assessed by either assessment process, we asked each patient's family member or caregiver to complete the FrSBe to provide data regarding the patient's behavioral impairments related to frontotemporal disorder.

Diagnosis of frontotemporal dementia was undertaken by means of consensus clinical criteria established by Neary et al (2012).

## Statistical Analysis

Binary and categorical variables were summarized using frequency counts and percentages. Continuous normally distributed variables were expressed as M ± SD. Categorical data were analyzed using $\chi^2$ tests. Both an ANOVA for multiple measures and multiple regression analyses were used to examine the relationships between neuropsychological variables and clinical variables. For the group of patients who were able to undergo both assessment processes, agreement between the extensive neuropsychological assessment and the ECAS was explored using the kappa statistic.

Univariate and multivariate logistic regression analyses were used to determine those variables that were independently associated with neuropsychological impairment; only those variables that exhibited a significant association in the univariate analysis were included in the multivariate model. Statistical significance was set at $P \leq 0.05$.

# RESULTS

At the time of the neuropsychological assessment, 16 (40%) participants were using noninvasive ventilation at home (time from initiation to assessment = 34.09 ± 32.98 months, with a mean daily use of 11.87 ± 6.42 hours), 18 (45%) were using mechanical insufflation-exsufflation (time from initiation to assessment = 31.38 ± 32.73 months), 12 (30%) were using percutaneous endoscopic gastrostomy (time from insertion to assessment = 15.93 ± 15.77 months), and five (12.5%) had a tracheostomy (time from tracheotomy = 3.37 ± 6.09).

Of the total number of participants assessed (40), four were unable to undergo the tests directly because of their inability to respond to the questionnaires using augmentative communication methods. Therefore, these four participants were assessed by means of the caregivers' responses to the FrSBe. Of the 36 remaining participants, 12 underwent both the extensive neuropsychological assessment and the ECAS, 18 underwent the extensive neuropsychological assessment only, and six underwent only the ECAS owing either to limitations in their ability to respond or to fatigue. Taking into account all of the tests, 24 participants (~67%) presented an impairment in at least one of the areas assessed (cognitive or behavioral).

Using the extensive neuropsychological assessment, clinically important impairments were found in 40.7% of the participants in attentional capacity, 42.3% in memory and learning ability, and 29.0% in executive function (data not shown, but available upon request). Overall, the extensive neuropsychological assessment identified some type of impairment in 64% of the study participants. Using the ECAS, an impairment was found in 89% of the participants. Table 2 shows the mean results for each test.

**TABLE 2.** Mean Values of *t* Scores on the Neuropsychological Tests

| Function Assessed | Neuropsychological Test | M ± SD |
|---|---|---|
| Attention | Forward Digit Span, Max. Series (WAIS–III) | 49.89 ± 8.21 |
| | Forward Spatial Span (WMS–III) | 50.48 ± 10.67 |
| | Color Trails Test, Part I | 43.00 ± 9.24 |
| Memory and Learning Ability | Complutense Verbal Learning Test | |
| | Total learning | 42.85 ± 9.93 |
| | Short-delay Free Recall | 46.19 ± 10.97 |
| | Short-delay Cued Recall | 45.20 ± 12.73 |
| | Long-delay Free Recall | 44.65 ± 10.50 |
| | Long-delay Cued Recall | 44.37 ± 13.26 |
| | Hopkins Verbal Learning Test | |
| | Free Recall–Verbal | 46.33 ± 11.57 |
| | Free Recall–Spatial | 44.28 ± 15.55 |
| | Backward Digit Span, Max. Series (WAIS–III) | 53.69 ± 12.30 |
| | Backward Spatial Span (WMS–III) | 55.87 ± 8.93 |
| | Color Trails Test, Part II | 37.37 ± 12.12 |
| Executive Function | Wisconsin Card Sorting Test | |
| | Perseverative Errors | 50.10 ± 8.84 |
| | Hopkins Verbal Learning Test | 45.38 ± 12.98 |
| | Controlled Oral Word Association Test | |
| | FAS | 40.99 ± 10.44 |
| | Animals | 43.87 ± 12.23 |
| | Matrix Reasoning (WAIS–III) | 53.81 ± 9.84 |
| | Brixton Test | 50.04 ± 15.11 |
| Behavioral Impairment | Dysexecutive Questionnaire | |
| | Frontal System Behavior Scale | |
| | Post Total | 63.60 ± 11.27 |
| | Post Apathy | 72.31 ± 15.26 |
| | Post Executive Function | 56.77 ± 10.89 |
| | Post Disinhibition | 55.20 ± 13.23 |
| Cognitive Screening | ECAS Language | 23.32 ± 30.54 |
| | ECAS Fluency | 23.25 ± 34.51 |
| | ECAS Executive | 27.77 ± 15.64 |
| | ECAS Memory | 35.44 ± 17.61 |
| | ECAS Visuospatial | 43.30 ± 22.07 |
| | ECAS Specific | 20.27 ± 25.71 |
| | ECAS Non-Specific | 34.93 ± 18.83 |
| | ECAS Total | 21.16 ± 26.08 |

**ECAS** = Edinburgh Cognitive and Behavioral ALS Screen. **FAS** = Words that begin with the letters F, A, and S. **WAIS** = Wechsler Adult Intelligence Scale. **WMS** = Wechsler Memory Scale.

## Relationship Between the Clinical and Neuropsychological Variables

With regard to both time since onset of symptoms and time since definitive diagnosis, no relationship was found between these two measures and attentional capacity ($P = 0.206$ and 0.314, respectively), nor with memory and learning ability ($P = 0.618$ and 0.692, respectively), nor with greater impairment to executive functions ($P = 0.844$ and 0.583, respectively). However, from the point of view of the participants' family members (as per the FrSBe), those participants whose disease had progressed further did show

**TABLE 3.** Relationship Between the Degree of Cognitive-Behavioral Impairment and Time Since Onset of Symptoms and Time Since Definitive Diagnosis

| Neuropsychological Variable | Degree of impairment (n) | Time Since Onset of Symptoms (months) | | Time Since Definitive Diagnosis (months) | |
|---|---|---|---|---|---|
| | | M ± SD | *P* | M ± SD | *P* |
| Attention | No disturbance (16) | 60.18 ± 44.51 | 0.206 | 55.69 ± 56.15 | 0.314 |
| | Slight (10) | 101.69 ± 81.32 | | 84.99 ± 69.74 | |
| | Moderate (1) | 5.90 | | 2.83 | |
| | Severe (0) | | | | |
| Memory and Learning Ability | No disturbance (15) | 71.36 ± 69.44 | 0.618 | 68.60 ± 71.47 | 0.692 |
| | Slight (5) | 44.21 ± 17.10 | | 44.32 ± 39.32 | |
| | Moderate (5) | 84.70 ± 54.86 | | 59.35 ± 39.07 | |
| | Severe (1) | 5.90 | | 2.83 | |
| Executive Function | No disturbance (22) | 72.55 ± 68.16 | 0.844 | 68.04 ± 65.94 | 0.583 |
| | Slight (5) | 81.48 ± 53.38 | | 68.89 ± 57.21 | |
| | Moderate (4) | 56.54 ± 55.66 | | 33.45 ± 30.97 | |
| | Severe (0) | | | | |
| Behavioral Impairment | No disturbance (14) | 58.35 ± 43.53 | 0.047 | 39.71 ± 39.69 | 0.043 |
| | Slight (17) | 86.83 ± 72.92 | | 76.80 ± 64.91 | |
| | Moderate (0) | | | | |
| | Severe (0) | | | | |

**TABLE 4.** Demographic and Pulmonary Function Data, Using Univariate Logistic Regression Analysis

| | Odds Ratio | 95% CI | *P* |
|---|---|---|---|
| Sex | 2.00 | 0.47–8.46 | 0.346 |
| Age | 1.01 | 0.94–1.07 | 0.851 |
| Body mass index | 2.50 | 1.13–5.49 | 0.022* |
| Type of disease onset | 0.81 | 0.16–3.91 | 0.793 |
| Time from onset of symptoms | 1.00 | 0.98–1.01 | 0.739 |
| Time from definitive diagnosis | 0.99 | 0.98–1.00 | 0.491 |
| ALSFRS-R | 0.96 | 0.90–1.03 | 0.339 |
| NBS | 1.00 | 0.94–1.07 | 0.924 |
| FVC | 0.76 | 0.37–1.56 | 0.464 |
| %FVC | 0.99 | 0.32–1.66 | 0.653 |
| sFVC | 0.73 | 0.32–1.66 | 0.455 |
| $PI_{max}$ | 1.00 | 0.97–1.03 | 0.860 |
| $PE_{max}$ | 1.00 | 0.97–1.02 | 0.964 |
| SNIP | 1.00 | 0.97–1.04 | 0.563 |
| PCF | 0.85 | 0.61–1.18 | 0.340 |
| MIC | 0.73 | 0.32–0.66 | 0.450 |
| $PCF_{MIC}$ | 0.81 | 0.57–1.16 | 0.265 |
| $PCF_{MI-E}$ | 0.89 | 0.54–1.49 | 0.680 |

*Significant at $P \leq 0.05$.

**ALS** = amyotrophic lateral sclerosis. **ALSFRS-R** = Revised Amyotrophic Lateral Sclerosis Functional Rating Scale. **CI** = confidence interval. **FVC** = forced vital capacity. **%FVC** = predicted FVC. **MIC** = maximal insufflation capacity. **MI-E** = mechanical insufflation—exsufflation. **NBS** = Norris scale bulbar subscore. **PCF** = peak cough flow. **$PCF_{MIC}$** = manually assisted PCF. **$PCF_{MI-E}$** = mechanically assisted PCF. **$PE_{max}$** = maximum expiratory pressure. **$PI_{max}$** = maximum inspiratory pressure. **sFVC** = supine forced vital capacity. **SNIP** = sniff inspiratory pressure.

greater behavioral impairment ($P = 0.047$ and 0.043, respectively; see Table 3).

With regard to the location of disease onset, participants with bulbar onset did not present poorer attentional capacity ($P = 0.094$) nor poorer memory and learning ability ($P = 0.068$) than the participants with spinal onset. However, the participants with bulbar onset did present greater impairments in executive functions ($P = 0.018$). No differences were found between the different onset locations and behavioral impairment ($P = 0.218$).

As for relationships with the clinical variables, statistical differences were found only in BMI between those participants without any impairment and those participants who presented some impairment (Table 1). In the univariate logistic regression analysis, the variable that most accurately predicted neuropsychological impairment was BMI (Table 4). The results of the univariate logistic regression analysis, performed in order to identify predictors of neuropsychological impairment, are shown in Table 4.

## Extensive Neuropsychological Assessment Versus the ECAS

The results from the extensive neuropsychological assessment and the ECAS were inconsistent: The extensive neuropsychological assessment identified 64% of the participants as having some cognitive-behavioral impairment, whereas the ECAS identified 89% of the participants as having some cognitive-behavioral impairment ($\kappa = -0.013$). However, a high degree of consistency was found between those neuropsychological tests focusing specifically on cognitive performance with regard to memory and the memory dimension of the ECAS ($\kappa = 0.750$).

When compared with the results of the extensive neuropsychological assessment, the ECAS and the FrSBe overestimated cognitive-behavioral impairment with regard to executive function. The kappa statistic used to evaluate the correlation between the different tests indicated no consistency between the neuropsychological assessment tests specifically concerning executive function and the executive function dimension of the ECAS ($\kappa = -0.013$) or the executive function dimension of the FrSBe ($\kappa = -0.066$). The extensive assessment identified 29% of the participants as having a deficit in executive function; the ECAS identified 89% as having a deficit.

## DISCUSSION

According to our preliminary findings, there was no relationship between cognitive-behavioral impairment and time since onset of symptoms, nor between cognitive-behavioral impairment and time since diagnosis. Also, the ECAS did not correctly reflect the executive function of individuals with ALS.

Over the course of the disease, individuals with ALS must make decisions about life support, and an accurate cognitive assessment is essential to provide health professionals with reliable and objective information regarding these individuals' ability to make reasoned decisions. Executive functions are crucial to decision-making processes because they include selective attention and working memory (Baddeley and Hitch, 1997), cognitive flexibility and concept formation (Karnath and Wallesch, 1992), abstract reasoning (Duncan et al, 1995), planning and strategy creation (Shallice and Burgess, 1991), and the setting of goals (Anderson, 2001). In short, the executive functions are those functions that drive the complex mental activities needed to plan, organize, guide, assess, modify, and regulate the behavior required to achieve a set objective and make decisions (Barkley, 1997).

In our study, ~67% of the participants presented a cognitive-behavioral impairment of some kind. Admittedly, there is a well-established consensus in the literature that a high percentage of individuals with ALS present cognitive impairment (Burke et al, 2017; Byrne et al, 2012; Goldstein and Abrahams, 2013; Hu et al, 2013; Osborne et al, 2014; Phukan et al, 2007; Strong, 2008; Strong et al, 2009). Still, perhaps because of the heterogeneity of study samples and the use of different forms of assessment, reports vary widely regarding the actual percentage of individuals with cognitive impairment of some kind (Beeldman et al, 2016). Those studies in which an extensive psychological assessment took place, and which took into account the abilities of each individual, reported results similar to ours, with approximately 50% of individuals presenting some cognitive and/or behavioral impairment (Ringholz et al, 2005; Strong 2008; Strong et al, 2009).

One of the objectives of our study was to determine the relationship between cognitive-behavioral impairment and clinical and functional parameters. We found BMI to be the only functional parameter showing a correlation with cognitive impairment. This is consistent with the findings of previous studies, such as Ahmed et al (2016), which found that patients with cognitive impairment exhibited changes in food preference, with caloric intake and BMI increasing as cognitive/behavioral changes took place. Concerning disease duration, our results showed no relationship between time since onset of symptoms and the onset of cognitive deterioration. This finding, with some patients having cognitive impairment at presentation and others remaining cognitively normal throughout, is similar to that of previous studies (Xu et al, 2017) and is consistent with ALS being heterogeneous in nature. Participants with bulbar onset, however, did present great impairments in executive functions, which is consistent with the results of other studies reporting a relationship between bulbar onset and the subsequent appearance of frontotemporal dementia (Lomen-Hoerth et al, 2003; Neary et al, 2012).

In order to carry out an extensive neuropsychological assessment of the type described here, the individual characteristics of each individual must be duly considered because the progressive muscular weakness that the disease causes means that these individuals may be unable to respond appropriately during neuropsychological tests that take response time into account and/or require a motor or oral response. For this reason, most studies assessing cognitive impairment in individuals with ALS have focused on individuals in the initial stages of the disease (Wilson et al, 1996), when they are not yet suffering significant levels of motor impairments.

A second objective of our study was to establish whether the ECAS screening test is as reliable as an extensive neuropsychological assessment that has been adapted to each patient's ability to respond. To this end, each participant was assessed by two methods (when possible). Our data showed that individuals performed similarly on both types of assessment (extensive neuropsychological assessment and ECAS) with regard to memory and learning ability, but the ECAS showed higher levels of impaired executive functioning. In fact, the extensive assessment identified 29% of the participants as having a deficit in executive function, whereas the ECAS identified 89% as having a deficit.

The ECAS is widely used, and has been recommended for use, with individuals with ALS (Abrahams et al, 2014, De Icaza Valenzuela et al, 2018; Lomen-Hoerth et al, 2003). It requires individuals to have suitable ability for motor and oral responses, but an individual with motor and/or oral limitations will take longer to respond, and any deficit will, therefore, be overestimated. In contrast, an extensive neuropsychological assessment enables the cognitive functions and behavior of each individual to be quantitatively and qualitatively evaluated, and the individual's performance can be compared with that of others with similar sociodemographic characteristics, such as age or level of education; likewise, it is possible to compare an individual's performance over time (Lezak et al, 2012). The tests used for the neuropsychological assessment are valid and sufficiently reliable, and they are able to show each individual's real abilities. This sets the extensive neuropsychological assessment apart from the ECAS, as the latter may give unreliable results for individuals whose level of education is either very low or very high. The neuropsychological tests also focus specifically on one type of cognitive

function, enabling the characterization of performance in individual areas. Screening tests, by contrast, are generally only able to offer overall scores: They provide little specific information about any of the by-definition different functions, which is a deficiency that is especially acute in the case of executive function (Lezak et al, 2012).

We therefore agree with the view put forward in some other studies (Pinto-Grau et al, 2017; Poletti et al, 2018) that, although the ECAS is a valid screening tool for individuals with ALS, and the overall scores that it generates do provide information about general cognitive function, the subscale for executive function cannot be reliably interpreted and suffers from important ceiling and floor effects. Moreover, with regard to interpretation of the ECAS results, the screening test takes into account neither premorbid levels of function nor any literacy difficulties the individual may have (Abrahams et al, 2014). In short, although the ECAS does perform well in screening individuals for attention and memory and learning ability, an extensive neuropsychological assessment is clearly preferable to evaluate each individual ALS patient's cognitive state across a range of areas and to examine any possible behavioral changes. However, we recognize that not all ALS medical teams are able to call on a neuropsychologist, and the use of screening tests may then be necessary, despite their limitations, in order to obtain information about an individual's cognitive profile.

One of the limitations of this study was the number of study participants. A larger sample would provide more reliable results, enabling more generalizable conclusions to be made. Moreover, this was a cross-sectional study; a longitudinal study could provide useful information regarding changes to cognitive-behavioral impairment over time.

In summary, our study found no relationship between cognitive-behavioral impairment and time since onset of symptoms nor time since definitive diagnosis. In addition, although screening tests are widely used to assess cognitive performance in individuals with ALS, they have been shown to evaluate executive function inaccurately. Given the importance of the decision-making process that ALS entails, neuropsychological tests that can be adapted to the true physical ability of each individual with ALS are required.

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