Behavioral and Cognitive Dysfunction in Amyotrophic Lateral Sclerosis

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INTRODUCTION

About 49% of amyotrophic lateral sclerosis (ALS) patients exhibit at least mild cognitive dysfunction, and 15% meet criteria for frontotemporal dementia (FTD). Other evidence supporting the association between ALS and FTD includes pathologic, imaging, and genetics investigations.

In FTD, frontal-lobe mediated behavioral dysfunction is commonly found. This type of dysfunction, in the form of apathetic behavior, has been suggested in ALS. However, the extent to which there is behavioral dysfunction in ALS and its relationship to cognitive impairment requires further elucidation.

SUBJECTS

- Recruited from the Baylor College of Medicine MDA/ALS Outpatient Clinic
- Diagnosis of probable/definite ALS (El Escorial criteria)
- A majority of subjects were right handed (91.6%), Caucasian (78.7%), and male (64.6%)

Table 1. Participant Demographics (N=225)

	Mean (SD)
Age	57.65 (13.98)
Education	14.05 (3.05)
FSIQ	100.67 (16.34)
VIQ	99.88 (13.12)
PIQ	101.71 (17.41)

METHODS

- Behavioral Status
- Frontal Systems Behavior Scale (FrSBe)
- Family members rated patients on behavioral change from before- to after-onset of ALS
  - Measure behavioral dysfunction (Total Score) by combining subscores for Apathy, Disinhibition and Executive Dysfunction
  - Elevated scores on the FrSBe indicated increased behavioral digressions
  - T-score ≥ 65 shows clinical behavioral impairment

Cognitive Status

- Comprehensive neuropsychological testing
- Cluster analysis using Block Design, Logical Memory II, RAVLT-Delay, VSAT-time and errors, Stroop color-word, Trails B-time, FAS and Animal Fluency found cognitive subgroups

RESULTS

Figure 1. Behavioral Impairment (N=225)

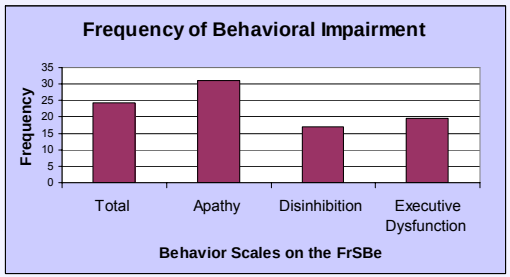


Figure 2. Cognitive Subgroups (N=141)

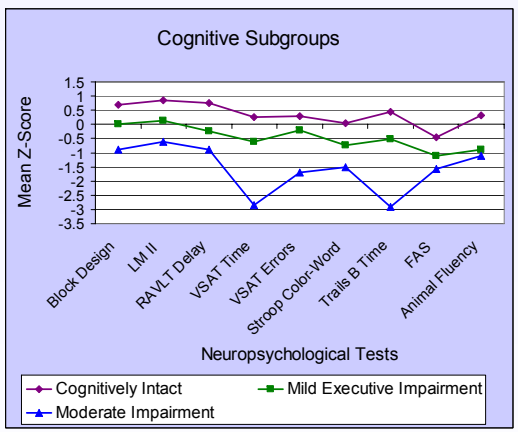
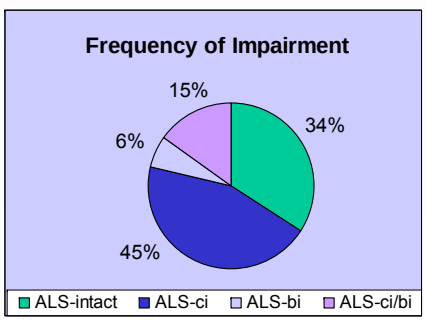


Figure 3. Frequency of Impairment. ALS-intact = intact cognition and behavior. ALS-ci = cognitive impairment. ALS-bi = behavioral impairment. ALS-ci/bi = cognitive and behavioral impairment (N=141)



FURTHER RESULTS

- All measures of frontal-lobe mediated behavior were scored significantly more poorly after onset of ALS (N=39)
  - Total Score, $p < 0.001$; Apathy subscore $p < 0.001$; Disinhibition subscore, $p = 0.02$; Executive Dysfunction subscore, $p = 0.002$)
- Behavioral impairment was not significantly different between bulbar and limb-onset patients
- Cognitive impairment was not significantly different between bulbar and limb-onset patients
- Patients with behavioral impairment were significantly older ($F(224) = 14.0$, $p < 0.001$)
  - Intact Behavior (N = 170), Mean Age = 55.8 ± 13.9
  - Impaired Behavior (N = 55), Mean Age = 63.6 ± 12.4
- Patients with cognitive impairment had no significant difference in age
- Animals (category fluency neuropsychological test) was the only measure able to predict behavioral performance (follow-up regression analyses after correlations found) on the FrSBe
  - $t[140] = -2.11$, $p = 0.04$ for the Total Score
  - $t[140] = -3.13$, $p < 0.001$ for the Apathy Score
  - $t[140] = -2.35$, $p = 0.02$ for the Executive Dysfunction Subscore

CONCLUSIONS

- Behavioral impairment was found in a quarter of ALS patients
  - Apathetic behavior was the most frequent; however, disinhibition and executive dysfunction were also common.
- Cluster analysis revealed 3 cognitive groups: Cognitively Intact, Mild Executive Impairment, and Moderate Impairment suggesting cognitive impairment exists on a continuum
- Frequency of behavioral and cognitive impairment was not affected by site of onset
  - However, dysarthria and weak upper extremity function were not controlled for
  - Further studies should assess this question
- Age did not impact frequency of cognitive impairment
- Age was significantly older in patients with behavioral impairment vs those without behavioral impairment
- Poor performance on Animals predicts poor behavioral performance