FTD-like Cognitive and Behavioral Changes in ALS

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INTRODUCTION

Recent research in ALS has uncovered a variety of structural, pathological, and neuropsychological abnormalities extending beyond motor neurons, which suggest comorbid Frontotemporal Dementia (FTD) (1). Cortical and subcortical frontotemporal changes, have been described in the frontal lobe with MRI, SPECT, PET, and fMRI(2-6) suggesting that extramotor structural abnormalities are common in ALS(6). Pathological studies describe similar frontal and temporal lobe degeneration in ALS and FTD (1,7). Genetic studies have linked ALS and FTD through uncovering mutations in several genes that produce both disorders (8-12).

Cognitive impairment is found in 40-60% of ALS patients(13-16). Most commonly, this impairment is related to frontal lobe mediated executive dysfunction. Fifteen percent of patients exhibit frank dementia, which has features of the FTD type(13). Clinical observation suggests that patients with ALS may also exhibit behavioral changes similar to those seen in FTD patients including apathy, disinhibition and/or executive dysfunction(17). However, the frontal behavioral changes that may be associated with ALS have not been well described. Any changes in behavior and cognition could be very important for ALS caregivers as both may increase their burden(18).

In this study, we applied the FrSBe to a large cohort of ALS patients to glean further insight into potential behavioral changes. Moreover, we performed detailed neuropsychological evaluations to ascertain the relationship between cognitive and behavioral changes in ALS patients.

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%) and Caucasian (78.7%), and male (64.6%)

Table 1 *Subject Demographics (N=225)*

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

METHODS

- Comprehensive neuropsychological testing
- Family members rated patients on behavioral change from before- to after-illness using the Frontal Systems Behavior Scale (FrSBe)
- On the FrSBe, a Total Score is formed through results on three subscales:
  Apathy, Executive Dysfunction, and Disinhibition
- When rating behavior on the FrSBe, increased normalized T-scores indicate increased behavioral impairments
- T-score (Total Score) ≥ 65 indicates clinically impaired behavior

RESULTS

Table 2 *Overall, a quarter of ALS patients were found to exhibit behavioral impairment as shown by clinically impaired behavior on the FrSBe Total Scale (n=225)*

FrSBe Scale	% Elevated (T ≥ 65)
Total	24.4
Apathy	31.1
Disinhibition	16.9
Exec Dysfxn	19.6

Table 3 *Behavioral Change from Before to After Onset-of-Illness (n = 39). The greatest behavioral changes, as shown by elevated T-scores, were noted in Apathy.*

FrSBe Scale	Mean T-Score ± SD	*p*
Total (Before)	50.57 ± 13.19	< 0.01
Total (After)	57.62 ± 16.66	
Apathy (Before)	48.21 ± 11.69	< 0.01
Apathy (After)	60.03 ± 17.49	
Disinhibition (Before)	51.10 ± 15.02	< 0.05
Disinhibition (After)	53.62 ± 15.96	
Executive Dysfxn (Before)	52.54 ± 11.43	< 0.01
Executive Dysfxn (After)	56.28 ± 14.28	

Table 4 *Comparison of FrSBe raw behavioral scores for the overall cohort (n = 225), the impaired behavior ALS group (n = 55), and a group of FTD patients(29, reprinted with permission) (n = 13). While similar patterns of impairment were found in both diseases, the severity of impairment was found to be increased in FTD versus ALS.*

	ALS M ± SD	Impaired Behavior ALS M ± SD	FTD* M ± SD	*p*
Age	57.65 ± 13.98	63.61 ± 12.43	69.9 ± 8.8	< 0.01
Education	14.5 ± 3.05	14.00 ± 3.03	12.5 ± 2.6	NS
FrSBe Raw Score				
Total	82.18 ± 23.22	113.58 ± 15.36	140.9 ± 27.0	< 0.01
Apathy	27.24 ± 9.41	37.89 ± 8.42	48.6 ± 7.9	< 0.01
Disinhibition	23.12 ± 6.93	30.35 ± 7.86	34.5 ± 11.0	< 0.01
Executive Dysfxn	31.78 ± 10.53	45.13 ± 7.48	57.8 ± 13.5	< 0.01

Table 5 *Behaviorally impaired and intact subjects (n=141) were compared with regard to cognitive status.*

	n	Intact Cognition	Mild Cognitive Dysfxn	Moderate Impairment
Impaired Total Behavior	30	30.0%	43.3%	26.7%
Impaired Apathetic Behavior	37	27.0%	43.2%	29.7%
Impaired Exec Fxn Behavior	22	22.7%	54.5%	22.7%
Impaired Disinhibited Behavior	24	37.5%	37.5%	25.0%
Intact Total Behavior	111	43.2%	42.3%	14.4%
Intact Apathetic Behavior	104	45.2%	42.3%	12.5%
Intact Exec Fxn Behavior	119	43.7%	40.3%	16.0%
Intact Disinhibited Behavior	117	41.0%	43.6%	15.4%

Table 6 *The percentage of subjects with behavioral impairment for each cognitive group (n=141). Patients with impaired cognition had greater rates of behavioral impairment.*

		Behavioral Group (% Impaired)			
	n	Total	Apathy	Exec Dysfxn	Disinhibition
Intact Cognition	57	15.8%	17.5%	8.8%	15.8%
Mild Cognitive Dysfunction	60	21.7%	26.7%	20.0%	15.0%
Moderate Cognitive Impairment	24	33.3%	45.8%	20.8%	25.0%

CONCLUSIONS

- Behavioral impairment was found to be frequent, occurring in a quarter of patients
- The most prevalent type of behavioral dysfunction was found to be apathetic behavior
- Significant changes in apathetic behavior, disinhibition, and executive dysfunction occurred with disease presentation
- ALS was found to have similar but less severe behavioral problems to FTD
- Behaviorally intact patients may have cognitive problems, and cognitively intact patients may have behavioral problems

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