Cognitive-behavioural longitudinal assessment in ALS

Cognitive-behavioural longitudinal assessment in ALS: the Italian Edinburgh Cognitive and Behavioural ALS Screen (ECAS)

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Abstract

Objective: The study presents data on the longitudinal administration of the Italian Edinburgh Cognitive and Behavioural ALS Screen (ECAS). We investigated cognitive-behavioural performance in a group of ALS patients over time and the feasibility of repeating the ECAS longitudinally compared to standard neuropsychological tests. Finally, correlations between clinical/genetic and cognitive/behavioural data were considered.

Methods: 168 ALS patients were tested at baseline (T_0). Among these, 48 patients performed the ECAS after 6 months (T_1), 18 patients performed it at T_2 (12 months) and 5 patients were assessed after 24 months (T_3). Participants were also administered two cognitive test (FAB; MoCA) and psychological questionnaires (BDI; STAI/Y). The FBI was carried out with caregivers.

Results: No cognitive deterioration was found across follow-ups. In contrast, although scores did not change between T_0 and T_1, scores improved significantly for ECAS Total/ALS Non-specific and Memory domains when the ECAS was repeated on three occasions (T_0, T_1, T_2). Apathy/Inertia was the most common behavioural symptom, but no worsening of behavioural scores was detected over time. After 12–24 months, patients were still able to perform the ECAS in total, in contrast to FAB and MoCA, which were only partially administrable.

Conclusions: The significant improvement of some ECAS scores over time supports the presence of possible practice effects, particularly in the memory domain, highlighting the need to accommodate for these in longitudinal assessments, through healthy controls groups or alternate versions. This work represents the first Italian ECAS follow-up study and confirms ECAS feasibility in patients with increasing physical disability.

Keywords: *ECAS*; *longitudinal assessment*; *Amyotrophic Lateral Sclerosis (ALS)*; *cognition*; *behavioural change*; *practice effect*

Introduction

Cognitive-behavioural changes in patients with amyotrophic lateral sclerosis (ALS) are now fully recognized as integral elements of the disease, along a spectrum of frontotemporal dysfunctions (1, 2). In recent years, several cognitive screening tools have been developed for ALS (3-8); however, they are not designed to detect a heterogeneous cognitive involvement (9-11), nor to compensate for patients' physical disability (6, 12, 13). In order to overcome such limitations, Abrahams et al. (14) developed a rapid cognitive-behavioural screening tool (Edinburgh Cognitive and Behavioural ALS Screen – ECAS), specifically designed to accommodate for verbal/motor disability. The ECAS has been translated (15, 16, 17) and validated against gold standard neuropsychological measures (15, 16, 18-20), showing high sensitivity and specificity (15, 18).

Although the existence of cognitive-behavioural involvement in ALS is now well-established, its longitudinal evolution has been less investigated. Previous follow-up studies revealed conflicting results (21-29); however, due to the lack of verbal-motor adaptations, it is not possible to determine whether any observed deterioration was caused by increasing physical disability affecting performance or by cognitive decline. Similarly, few longitudinal studies are available on behavioural changes along the disease course (30-32). To date, only one study has focused on longitudinal assessment using the ECAS, specifically investigating a possible learning effect on ECAS repeated measurements (33); however, no data were provided about the relationship between cognitive and clinical aspects, including affective or genetic issues. Moreover, the longitudinal validity of the ECAS Behaviour Interview, also with respect to other standard tools, was not considered. The possible progression of cognitive-behavioural alterations over time represents a crucial issue, since such changes are a negative prognostic factor in ALS (34), associated with shorter survival and faster functional decline (24, 35, 36). This study aimed 1) to investigate cognitive-behavioural change in ALS

patients longitudinally; 2) to compare the feasibility of undertaking an ECAS over time against standard neuropsychological assessment tools; 3) to analyse the relationship between cognitive, behavioural and psychological aspects and clinical/genetic features.

Material and methods

Participants and procedure

168 ALS patients, who fulfilled the revised El Escorial criteria for possible, probable, probable laboratory-supported or definite ALS (37), were recruited at the Department of Neurology, IRCCS Istituto Auxologico Italiano between May 2013 and February 2017. Patients in terminal stage of disease or with major comorbid medical, neurological, psychiatric or cardio-vascular diseases were excluded. Disease status was evaluated using the ALS Functional Rating Scale-Revised - ALSFRS-R (38). Patients were also screened for mutations in *C9orf72*, *SOD1*, *TARDBP* and *FUS* genes according to standard protocols (39, 40). A subset of patients (N=107) was previously included in the Italian ECAS validation study (15).

All patients were invited to take part in a longitudinal study from baseline (T_0), with follow-up at 6 (T_1), 12 (T_2) and 24 (T_3) months when possible given the clinical conditions. Of the 168 patients who performed the ECAS protocol at T_0, 48 patients performed it at T_1, while 18 patients performed it also at T_2. Finally, 5 patients were tested at T_3; however, due to the small proportion of patients who managed to complete this 24-months follow-up, such data were not considered, due to their poor reliability. Further details are reported in Figure 1. Given the rate of attrition, the longitudinal comparison was conducted in the 48 patients who performed the ECAS at T_0 and T_1 and in the 18 patients who performed all the three assessment at T_0, T_1 and T_2.

The study protocol was reviewed and approved by the Ethics Committee of our Institution (N° of approval: 2013_06_25) and all eligible subjects received both verbal and written information about the study. All participants signed an informed consent, according to the Declaration of Helsinki.

Cognitive and Psychological Assessment

The Italian version of the ECAS was administered (15), assessing different cognitive domains, including ALS-Specific and ALS Non-specific tasks. When possible, the mode of testing (spoken or written) was maintained for the longitudinal screens. Moreover, caregivers longitudinally performed the ECAS Behaviour Interview (see Poletti et al. (15) for further details about the procedure adopted); both the number of behavioural symptoms (ECAS Behaviour Interview-Symptoms) and the global score obtained (ECAS Behaviour Interview-Total score) were recorded.

The study protocol also included two widely used screening tools, i.e. the Frontal Assessment Battery (FAB) (41) and the Montreal Cognitive Assessment (MoCA) (42), that were administered at T_0 and at any follow-up, when possible, and the Frontal Behavioural Inventory (FBI), assessing behavioural alterations (43). To explore the relationship between ECAS performance and psychological factors, participants completed the Beck Depression Inventory (BDI) (44) and the State-Trait Anxiety Inventory-Y (STAI-Y) (45), for depressive and anxiety evaluation, respectively.

Statistical analyses

To compare the scores between the longitudinal follow-ups, ANOVA for repeated measures were used followed by a posteriori contrasts when applicable. Otherwise the comparison was performed using Friedman's test followed by Wilcoxon signed rank test with continuity

correction; for discrete variables McNemar test was applied. Benjamini and Hochberg False Discovery Rate was used as correction for multiple testing. Finally, Pearson's correlation coefficient was used to assess the degree of association between measures. An α level of 0.05 was considered for all hypothesis tests. All data analyses were performed using SAS 9.2 software (SAS Institute, Cary, NC, USA).

Results

Patients' demographic characteristics and reasons for attrition are depicted in Figure 1. Performance of 168 patients at T_0, 48 patients at T_1 and 18 patients at T_2 are summarized in Supplementary Table 1.

Nine out of 168 patients (5%) had to use the written version at T_0 due to severe dysarthria and five out of the 48 patients who completed the T_1 evaluation (10%) had to switch to the written version at 6-months follow-up. The proportion of ALS patients for which it was necessary to change to the written version did not increase at 12- and 24-months follow-ups. The cognitive-behavioural performance in the ECAS of patients within the local geographical region who dropped out was analysed (see Supplementary Table 2 for details); results revealed that 38% of them presented with behavioural alterations and met the new revised criteria for ALS with behavioural impairment (ALSbi) (46) basing on ECAS performance at their last evaluation, while 32% could be classified for ALS with cognitive impairment (ALSci) and 13% as ALS with combined cognitive and behavioural impairment (ALScbi).

Longitudinal ECAS in ALS patients

No statistically significant difference was found between any ECAS score from T_0 to T_1 in the 48 patients who performed the ECAS after 6 months from baseline [Table 1 near here].

When considering the subgroup who performed all the three assessments at T_0, T_1 and T_2 (N=18), results from ANOVA demonstrated a significant increase in ECAS Total and ALS Non-specific scores among the three follow-ups; in particular, post-hoc analysis revealed a significant increase from T_0 to T_2 (ECAS Total: p=0.058; ALS Non-specific: p=0.004), as well as from T_1 to T_2 (ECAS Total: p=0.027; ALS Non-specific: p=0.011). Moreover, the score obtained at the Memory subdomain globally increased among the three assessments, in particular between T_0 and T_1 (p=0.039) and between T_0 and T_2 (p=0.012), with patients showing a significantly higher score at the Immediate Recall task globally among the three follow-ups and particularly between T_1 and T_2 (p=0.029) [Table 2 near here].

Of 168 patients, 37% met criteria for ALSci (46) at T_0 and 31% of 48 patients were classified as ALSci at T_1. No patients met criteria for ALS-FTD at any follow-up. When considering the 18 patients who performed all the three assessments,6 (33%) met criteria for ALSci at T_0, 5 (28%) were classified as ALSci at T_1 and 6 (33%) at T_2. No significant difference was detected over time in the percentage of patients classified as ALSci.

Behavioural changes

At baseline and at T_1, the majority of patients showed no relevant behavioural impairment or dysfunction detected across only one behavioural domain at the ECAS Behaviour Interview. Between 40-50% of patients showed evidence of behavioural changes meeting criteria for ALSbi at T_0 (41%) and T_1 (50%), while 33% of patients was classified as ALSbi at T_2. Moreover, 12% of ALS patients was classified as ALScbi at T_0, 21% at T_1 and 22% at T_2. Apathy/Inertia was the most represented symptom (34% at T_0, 42% at T_1, 33% at T_2), followed by Loss of Sympathy/Empathy at T_0 and T_1, while at T_2 Loss of Sympathy/Empathy, Behavioural Disinhibition and Change in Eating Behaviour were equally recorded as the most frequent dysfunctions (11%) after Apathy/Inertia. Data about the

distribution of behavioural dysfunctions at the ECAS Behaviour Interview across each follow-up are reported in Figure 2. Five patients at T_0 (3%), three at T_1 (6%) and none at T_2 had psychotic features; in all cases the only reported symptom was suspiciousness.

When considering the subgroup who completed all the three assessments, no significant increase in behavioural symptoms was detected neither at the ECAS Behaviour Interview-Symptoms (p=0.716), nor at the global score obtained at the ECAS Behaviour Interview-Total Score (p=0.065).

Strong correlations were found between both the number of symptoms and the total score at the ECAS Behaviour Interview and FBI-A, FBI-B and FBI Total score at any follow-up [Table 3 near here].

In the 48 patients who performed the ECAS twice (i.e. after 6 months from baseline), a significant increase of FBI Total Score and FBI-A was detected between T_0 and T_1 (FBI Total: p=0.036; FBI-A: p=0.056). Concerning the subgroup that completed all the three assessments, a significant increase of FBI Total Score could be globally detected (p=0.038); in particular, higher scores were found at T_2 with respect to T_0, but which did not reach statistical significance (p=0.075).

Focusing on the relationship between behavioural alterations in the ECAS Behaviour Interview and cognitive performance, the ECAS Behaviour Interview-Symptoms negatively correlated with ECAS Total, ALS-Specific and ALS Non-Specific scores only at T_2 (see Table 4). On the contrary, no correlations were found between the ECAS Behavioural Interview-Total Score and the ECAS subscores nor at T_0, T_1 or T_2. With concern to the FBI, no significant correlations were found at T_0 and T_1 between FBI-A, FBI-B and FBI Total score and any ECAS cognitive subscore, while at T_2 significant negative correlations of FBI-A and FBI Total scores were found with the ECAS Total, ALS-Specific and ALS Non-specific scores [Table 4 near here].

Longitudinal FAB and MoCA assessment in ALS patients

All patients were able to complete the ECAS without any difficulties at T_1. Even after 12–24 months, the ECAS was still feasible as indicated by completion of the full test by all of the patients bar one who performed these assessments. In contrast, the FAB was administrable only in 71% of patients at T_1 and in 67% of patients at T_2. With the MoCA, only 69% of patients could perform it at T_1 and 72% of patients completed it at T_2. Patients showed neither a significant deterioration nor improvement in the FAB and MoCA scores at T_1 and T_2, when considering the patients' subgroup who completed all the three assessments.

Clinical and affective status

No significant correlations were found between ECAS scores and disease duration or ALSFRS-R scores at any follow-up. Similarly, no correlations were found between disease duration and the number of behavioural symptoms or the ECAS Behaviour Interview-Total score at the carer interview.

With concern to psychological aspects, of the 154 patients who completed the BDI at T_0, 100 (65%) showed scores indicative of clinically significant depression, ranging from mild-to-moderate (66%), moderate-to-severe (26%) and severe (8%). At T_1, 33 out of 47 patients (70%) showed some degree of depression, while at T_2 11 out of 17 patients (65%) showed depressive symptoms. In the subgroup that completed all the three follow-ups, no significant differences were found between T_0, T_1 and T_2. Patients did not show clinically relevant state and trait anxiety levels neither at T_0, nor at T_1 and T_2; moreover, no significant differences concerning anxiety emerged across the serial follow-ups, when considering the patients' subgroup who completed all the three assessments.

Relationship to genetic profile

At T_0 three (19%) of the 16 patients presenting with *C9orf72* repeat expansions performed abnormally on the ECAS Total, ALS-Specific and ALS Non-specific functions scores, while two (12.5%) were impaired at the ECAS Total and ALS-Specific functions scores. The remaining eleven patients (69%) showed normal cognitive performances. Six of 16 *C9orf72* patients (37,5%) who performed the study at T_0 and one of the two patients who performed it at T_2 met criteria for ALSbi, while none of the five *C9orf72* patients who performed the ECAS at T_1 showed cognitive impairment. Moreover, six of 16 patients at T_0, two of 5 at T_1 and one of two at T_2 were classified as ALSbi, while three patients at T_0 and one at T_2 met criteria for ALScbi. None of the *C9orf72* patients showed psychotic abnormalities at any follow-up.

Discussion

Longitudinal neuropsychological studies of ALS are plagued by difficulties in assessing patients with progressive physical disability. The lack of use of cognitive tools accommodating for verbal-motor disability is one of the reason for the sparse and often conflicting data. Our work represents the first Italian longitudinal study assessing both cognitive and behavioural performance in ALS patients through the use of a multi-dimensional screening test able to compensate for verbal-motor disability. All patients bar one were able to complete the whole ECAS. In contrast, the FAB was not administrable in about 30% of patients at 6 and 12 months; comparable data were also obtained for the MoCA. Such findings are to be explained by the presence of subtasks involving motor and verbal skills and not accommodating for physical disability, thus confirming previous literature data (15, 33, 47).

Longitudinal cognitive changes

The Italian ALS population showed no significant changes in ECAS scores from baseline to 6-months follow-up. After 12 months, our patients' subgroup who performed all the three evaluations achieved a significant improvement in some scores (ECAS Total, ALS Non-specific and Memory subdomain), thus presenting a possible practice effect. In contrast, Burkhard et al. (33) did not find any practice effect in an ALS cohort, although this was found in healthy controls. Such conflicting results could be attributed to our larger sample size, rather than to other factors such as age, education or disease duration. Our results seem to support a well-known phenomenon in neuropsychological assessment underlining the presence of potential practice effects or initial unfamiliarity with test situation when patients are assessed repeatedly (48, 49); such an issue has been poorly investigated in ALS and few results are available (28). Recently, in order to overcome this issue, alternate forms of the ECAS have been developed (ECAS B and C) (50, 51). Repeated serial administration of the ECAS original version over a short time period produced improved scores for ALS-Specific, ALS Non-specific and ECAS Total scores, whereas such effects were not found when ECAS alternate versions were administered serially. The current study demonstrates that these practice effects can last over longer months, particularly in relation to the memory domain.

Longitudinal behavioural changes

No increase was observed in the number of behavioural symptoms detected at the ECAS Behaviour Interview, nor at the ECAS Behaviour Interview-Total Score within 12 months. In line with recent literature, Apathy/Inertia and Loss of Sympathy/Empathy were the more frequently observed changes (52, 53); furthermore, at 12 months also Behaviour Disinhibition and Change in Eating Behaviour became prominent in our cohort. Our data are partially in contrast with previous results indicating a slight progression of behavioural alterations at the

ECAS over time (33). However, when considering the FBI scores, an increment of behavioural dysfunction was longitudinally found, thus confirming the possible progression of behavioural features in ALS. Such contrasting data about the longitudinal changes detected at ECAS Behaviour Interview and FBI, as well as the relationship with cognitive performance at the ECAS, could be explained by the fact that, unlike the FBI, the ECAS Behaviour Interview has been designed to diagnose ALSbi and/or ALS-FTD and scores the presence/absence of a behavioural dysfunction, not measuring its severity. Behavioural dysfunction also emerged as a prominent feature characterising our dropped-out patients, thus highlighting the need to consider these symptoms in ALS patients' clinical management.

The lack of significant correlations of disease duration and ALSFRS-R with ECAS cognitive/behavioural performance is in line with previous literature data (54, 55).

Depressive symptoms are prevalent in ALS; however, worsening depression was not observed in our sample during follow-ups, as previously recorded (56, 57). In contrast, no clinically relevant anxiety levels were found at serial investigations, in accordance to previous results (58-60).

Longitudinal cognitive-behavioural performance and genetic profile

Despite recent literature having confirmed the high prevalence of cognitive-behavioural impairment in patients with *C9orf72* repeat expansions (39, 30, 61), only a small proportion of our mutated ALS patients showed such alterations. However, our data could possibly be explained by the small number of mutation carriers who completed the follow-up evaluations in our sample cohort.

More generally, the high drop-out rate of patients during the serial follow-up and the resulting small sample size, also with regard to genetic data, represent a limitation of our study,

together with a bias towards slow progressors and long survivors, thus suggesting the need to enlarge these cohorts in future analyses.

Conclusion

In summary, our results support the use of the ECAS also in moderate and advanced stages of the disease, in order to assess cognitive-behavioural progression in ALS. Our ALS Italian population showed no significant cognitive deterioration at ECAS performance between serial evaluations; on the contrary, we detected a significant improvement between baseline and 12-months assessment at some ECAS scores. No increase of behavioural changes over time was recorded at the ECAS Behaviour Interview even if such changes were detected when measured by FBI, thus suggesting a possible progression of behavioural features in ALS. Moreover, behaviour impairment emerged as a prominent issue characterising our drop-outs, further underlining its critical role in clinical management of ALS patients. Despite the above mentioned limitations, the present work represents the first Italian follow-up study performed with the new gold standard for cognitive/behavioural screen in ALS. Accommodating for verbal-motor components represents a crucial issue for ALS longitudinal assessment. The implementation of Italian ECAS alternate forms represents a future challenge, in order to minimize the presence of possible unfamiliarity/practice effect bias and will help to better describe ALS patients' phenotypes along the course of the disease.

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Disclosure of interest

The authors report no conflict of interest.

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Supplementary material available online

Supplementary Tables 1-2

Tables and Figure Captions

Table 1. Longitudinal performance on the ECAS subdomains and Total score, FAB and MoCA of the 48 ALS patients who completed the ECAS at T0 and T1. Data are expressed as means (standard deviations).

Table 2. Longitudinal performance on the ECAS subdomains and Total score, of the ALS patients subgroup (n=18) who completed the three assessments. Data are expressed as means (standard deviations).

Table 3. Correlations between ECAS Carer Interview (number of symptoms and total score) and FBI at T_0, T_1 and T_2.

Table 4. Correlations between ECAS Carer Interview (number of symptoms and total score) and FBI and cognitive performance at the ECAS at T_0, T_1 and T_2.

Figure 1. Flowchart and basic demographic characteristics of the ALS cohort

Figure 2. Distribution of behavioural changes in ALS patients across each follow-up

Supplementary Table 1. Mean performance of ALS patients at T_0, T_1 and T_2 on the ECAS subdomains and Total score, FAB and MoCA. Number of patients cognitively and/or behaviourally impaired are also reported

Supplementary Table 2. Number of dropped out patients who were classified as cognitively and/or behaviourally impaired at the last evaluation performed

Tables

Table 1. Longitudinal performance on the ECAS subdomains and Total score, FAB and MoCA of the 48 ALS patients who completed the ECAS at T_0 and T_1. Data are expressed as means (standard deviations).

	Baseline (T_0) N=48	6 months (T_1) N = 48	*t-test p-value*
Executive functions	34.25 (6.25)	34.29 (7.60)	*0.952*
Language functions	23.54 (3.68)	24.02 (3.36)	*0.143*
Fluency	17.13 (4.95)	16.92 (5.47)	*0.711*
Memory functions	14.60 (4.60)	15.42 (4.50)	*0.059*
Visuospatial functions	11.38 (0.89)	11.40 (1.30)	*0.921*
ALS-Specific Functions	74.92 (11.79)	75.23 (13.12)	*0.753*
ALS Non-specific Functions	25.98 (4.75)	26.81 (5.04)	*0.053*
ECAS Total Score	100.90 (15.11)	102.04 (17.07)	*0.286*
FAB	15.93 (1.51)	16.13 (1.45)	*0.589*
MoCA	24.35 (3.09)	24.15 (3.55)	*>0.999*

Bold numbers indicate statistical significance with $p < 0.05$. FAB: Frontal Assessment Battery; MoCA: Montreal Cognitive Assessment.

Table 2. Longitudinal performance on the ECAS subdomains and Total score, of the ALS patients subgroup (n=18) who completed the three assessments. Data are expressed as means (standard deviations).

	Baseline (T_0) N=18	6 months (T_1) N=18	12 months (T_2) N=18	*ANOVA p-value*

Executive functions	36.17 (5.35)	34.61 (8.98)	37.83 (4.55)	*0.230*
Language functions	23.78 (3.84)	23.72 (3.44)	24.33 (3.50)	*0.505*
Fluency	17.67 (5.46)	17.89 (5.29)	17.00 (5.58)	*0.423*
Memory functions	13.72 (5.07)	14.39 (5.50)*	16.39 (4.68)*	***0.011***
Visuospatial functions	11.28 (0.89)	11.17 (1.72)	11.50 (0.86)	*0.289*
ALS-Specific Functions	77.83 (12.24)	76.06 (14.55)	79.17 (11.43)	*0.125*
ALS Non-specific Functions	25.00 (5.18)	25.56 (6.32)	27.89 (4.71)*,§	***0.003***
ECAS Total Score	102.83 (16.42)	101.61 (20.12)	107.06 (15.76)*,§	***0.023***

Bold numbers indicate statistical significance with $p < 0.05$. * $p<0.05$ vs T_0; § $p<0.05$ vs T_1

Table 3. Correlations between ECAS Carer Interview (number of symptoms and total score) and FBI at T_0, T_1 and T_2.

		T_0			T_1			T_2		
		FBI-A	FBI-B	FBI-TOT	FBI-A	FBI-B	FBI-TOT	FBI-A	FBI-B	FBI-TOT
ECAS Behaviour Interview – Symptoms	r	0.68	0.52	0.71	0.71	0.74	0.81	0.74	0.78	0.85
	p-value	***<0.001***	***<0.001***	***<0.001***	***<0.001***	***<0.001***	***<0.001***	***0.002***	***<0.001***	***<0.001***
ECAS Behaviour Interview – Total Score	r	0.68	0.60	0.75	0.72	0.76	0.82	0.69	0.89	0.87
	p-value	***<0.001***	***<0.001***	***<0.001***	***<0.001***	***<0.001***	***<0.001***	***0.004***	***<0.001***	***<0.001***

Bold numbers indicate statistical significance with $p < 0.05$. FBI: Frontal Behaviour Inventory.

Table 4. Correlations between ECAS Carer Interview (number of symptoms and total score) and FBI and cognitive performance at the ECAS at T_0, T_1 and T_2.

		T_0					T_1					T_2				
		ECAS Behav Interview-Symptom	ECAS Behav Interview-Tot	FBI-A	FBI-B	FBI-Tot	ECAS Behav Interview-Symptom	ECAS Behav Interview-Tot	FBI-A	FBI-B	FBI-Tot	ECAS Behav Interview-Symptom	ECAS Behav Interview-Tot	FBI-A	FBI-B	FBI-Tot
ALS-Specific Functions	r	-0.09	-0.08	-0.11	-0.09	-0.12	-0.16	-0.16	-0.29	-0.12	-0.27	-0.57	-0.49	-0.72	-0.35	-0.63
	p-value	0.277	0.324	0.193	0.274	0.159	0.287	0.274	0.051	0.431	0.072	***0.026***	0.065	***0.002***	0.204	***0.011***
ALS Non-specific Functions	r	-0.11	-0.09	-0.06	-0.06	-0.07	-0.15	-0.18	-0.24	-0.17	-0.24	-0.54	-0.50	-0.61	-0.43	-0.60
	p-value	0.178	0.274	0.477	0.479	0.414	0.317	0.222	0.112	0.260	0.101	***0.036***	0.057	***0.016***	0.105	***0.018***
ECAS Total Score	r	-0.10	-0.09	-0.10	-0.09	-0.11	-0.17	-0.18	-0.29	-0.14	-0.28	-0.58	-0.51	-0.71	-0.38	-0.64
	p-value	0.217	0.278	0.214	0.284	0.176	0.263	0.228	0.047	0.347	0.060	***0.024***	0.055	***0.003***	0.158	***0.009***

Bold numbers indicate statistical significance with $p < 0.05$. ECAS Behav Interview – Symptom: ECAS Behaviour Interview – number of symptoms; ECAS Behav Interview – Tot: ECAS Behaviour Interview – Total Score; FBI: Frontal Behaviour Inventory.