

### Supplementary Material 1- Neuropsychological Tests Employed and Explored Cognitive Domains

Test	Cognitive Domain
Edinburgh Cognitive and Behavioural ALS screen (ECAS) <sup>1</sup>	Language, Verbal Fluency, Executive Functions, Memory, Visuospatial Abilities
Letter Fluency test (FAS) <sup>2</sup>	
Category Fluency test (CAT) <sup>3</sup>	
Trail Making Test B-A (TMT B-A) <sup>4</sup>	Executive Functions
Frontal Assessment Battery (FAB) <sup>5</sup>	
Nelson's modified version of Wisconsin Card Sorting Test (WCST) <sup>6</sup>	
Rey Auditory Verbal Learning Test Immediate Recall and Delayed Recall <sup>2</sup>	Verbal Memory
Babcock Story Recall Test Immediate and Delayed Recall <sup>7</sup>	
Boston Naming Test <sup>8</sup>	Language
Rey-Osterrieth Complex Figure test Differed recall <sup>7</sup>	Visuo-spatial memory
Rey-Osterrieth Complex Figure Test Immediate Recall <sup>7</sup>	Visuo-constructive abilities
Clock Drawing Test <sup>9</sup>	
Digit Span Forward and Backward <sup>10</sup>	Attention and working memory
Trial Making Test A <sup>11</sup>	
Trial Making Test B <sup>11</sup>	Cognitive flexibility
Raven's Colored Progressive Matrices <sup>2</sup>	Non-verbal (fluid) intelligence
Ekman 60-Faces test (EK-60F) <sup>12</sup>	Facial Emotion Recognition
Reading the Mind in the Eyes Test (RMET-36) <sup>13</sup>	Affective Theory of Mind
Story-Based Empathy Task (SET) <sup>14</sup>	Affective and Cognitive Theory of Mind

## References

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### Supplementary Material 2. Comparison of Social Cognition deficits in ALS Patients and Controls

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- 1- Poletti B, Solca F, Carelli L, Madotto F, Lafronza A, Faini A, Monti A, Zago S, Calini D, Tiloca C, Doretti A, Verde F, Ratti A, Ticozzi N, Abrahams S, Silani V. The validation of the Italian Edinburgh Cognitive and Behavioural ALS Screen (ECAS). *Amyotroph Lateral Scler Frontotemporal Degener.* 2016 Oct-Nov;17(7-8):489-498. doi: 10.1080/21678421.2016.1183679.
- 2- Carlesimo GA, Caltagirone C, Gainotti G. The Mental Deterioration Battery: normative data, diagnostic reliability and qualitative analyses of cognitive impairment. The Group for the Standardization of the Mental Deterioration Battery. *Eur Neurol.* 1996;36(6):378-84. doi: 10.1159/000117297. PMID: 8954307.
- 3- Novelli G, Papagno C, Capitani E, Laiacona M, et al. (1986). Tre test clinici di ricerca e produzione lessicale. Taratura su soggetti normali [Three clinical tests to research and rate the lexical performance of normal subjects]. *Archivio di Psicologia, Neurologia e Psichiatria*, 47(4), 477–506.
- 4- Giovagnoli AR, Del Pesce M, Mascheroni S, Simoncelli M, Laiacona M, Capitani E. Trail making test: normative values from 287 normal adult controls. *Ital J Neurol Sci.* 1996 Aug;17(4):305-9. doi: 10.1007/BF01997792. PMID: 8915764.
- 5- Apollonio I, Leone M, Isella V, Piamarta F, Consoli T, Villa ML, Forapani E, Russo A, Nichelli P, The Frontal Assessment Battery (FAB): normative values in an Italian population sample, *Neurol Sci* (2005) 26:108–116 DOI 10.1007/s10072-005-0443-4.
- 6- Laiacona M, Inzaghi MG, De Tanti A, Capitani E. Wisconsin card sorting test: a new global score, with Italian norms, and its relationship with the Weigl sorting test. *Neurol Sci.* 2000 Oct;21(5):279-91. doi: 10.1007/s100720070065. PMID: 11286040.
- 7- Carlesimo G.A., Buccione I., Fadda L., Graceffa A., Mauri M., Lorusso S., Bevilacqua G., Caltagirone C. (2002). *Standardizzazione di due test di memoria per uso clinico. Breve racconto e figura di Rey.* *Nuovo Rivista di Neurologia*, 12(1):1-13.
- 8- Vestito L, Mori L, Trompetto C, Tomatis M, Alessandria G, DeCarli F, Cocito L & Bandini F (2023) The 15-item version of the Boston Naming Test in Italian: normative data for adults, *Aphasiology*, 37:1, 83-98, DOI: 10.1080/02687038.2021.1988506.
- 9- Caffarra P, Gardini S, Zonato F, Concarì L, Dieci F, Copelli S, Freedman M, Stracciari A, Venneri A. Italian norms for the Freedman version of the Clock Drawing Test. *J Clin Exp Neuropsychol.* 2011 Nov;33(9):982-8. doi: 10.1080/13803395.2011.589373. Epub 2011 Aug 1. PMID: 22082081.
- 10- Monaco M, Costa A, Caltagirone C, Carlesimo GA. Forward and backward span for verbal and visuo-spatial data: standardization and normative data from an Italian adult population. *Neurol Sci.* 2013 May;34(5):749-54. doi: 10.1007/s10072-012-1130-x. Epub 2012 Jun 12. Erratum in: *Neurol Sci.* 2015 Feb;36(2):345-7. PMID: 22689311.
- 11- Giovagnoli AR, Del Pesce M, Mascheroni S, Simoncelli M, Laiacona M, Capitani E. Trail making test: normative values from 287 normal adult controls. *Ital J Neurol Sci.* 1996 Aug;17(4):305-9. doi: 10.1007/BF01997792. PMID: 8915764.
- 12- Dodich A, Cerami C, Canessa N, Crespi C, Marcone A, Arpone M, Realmuto S, Cappa SF. Emotion recognition from facial expressions: a normative study of the Ekman 60-Faces Test in the Italian population. *Neurol Sci.* 2014 Jul;35(7):1015-21. doi: 10.1007/s10072-014-1631-x. Epub 2014 Jan 19. PMID: 24442557.
- 13- Serafin M, Surian L. Il Test degli Occhi: uno strumento per valutare la "teoria della mente". *Giornale Italiano Psicologia.* 2004;4(4):839- 862. doi:10.1007/s10072-014-1631-x 20.
- 14- Dodich A, Cerami C, Canessa N, et al. A novel task assessing intention and emotion attribution: Italian standardization and normative data of the story-based empathy task. *Neurol Sci.* 2015;36(10):1907- 1912. doi:10.1007/s10072-015-2281-3.

SC subdomain	SC test (min- max score)	Corrected scores, mean (SD)			Prevalence of SC deficit	
		Patients	Controls	p values	Patients (n=50)	Controls (n=2)
Facial Emotion Recognition	EK-60F (0-60)	46.15 (6.78)	54.28 (6.77)	<b>&lt; 0.001</b>	10 (8.2%)	0 (0.0%)
	Happiness (0-10)	9.32 (1.16)	9.51 (0.71)	0.325	4 (3.3%)	0 (0.0%)
	Surprise (0-10)	8.54 (1.97)	9.07 (0.93)	0.097	7 (5.7%)	0 (0.0%)
	Disgust (0-10)	6.92 (2.05)	7.49 (2.06)	0.130	6 (4.9%)	0 (0.0%)
	Anger (0-10)	6.99 (2.05)	7.61 (1.63)	0.088	10 (8.2%)	0 (0.0%)
	Fear (0-10)	3.79 (2.62)	5.98 (2.20)	<b>&lt; 0.001</b>	23 (19.0%)	2 (3.5%)
	Sadness (0-10)	6.69 (2.46)	8.44 (1.94)	<b>&lt; 0.001</b>	11 (9.0%)	0 (0.0%)
Theory of Mind	RMET-36 (0-100) <sup>∞</sup>	57.11 (25.65)	80.32 (19.29)	<b>&lt; 0.001</b>	4 (3.3%)	0 (0.0%)
	SET-GS (0-6)	12.96 (3.58)	16.46 (1.40)	<b>&lt; 0.001</b>	16 (13.2%)	0 (0.0%)
	SET-IA (0-6)	4.57 (1.30)	5.65 (0.59)	<b>&lt; 0.001</b>	12 (9.9%)	0 (0.0%)
	SET-EA (0-6)	4.29 (1.40)	5.62 (0.659)	<b>&lt; 0.001</b>	14 (11.5%)	0 (0.0%)

**ALS:** Amyotrophic Lateral Sclerosis; **EK-60 F:** Ekman-60 Faces Test; **RMET-36:** Reading the Mind in the Eyes Test; **SET-GS:** Story-Based Empathy Task-Global Score; **SET-IA:** Story-Based Empathy Task-Intention Attribution; **SET-CI:** Story-Based Empathy Task-Causal Inference, **SET-EA:** Story-Based Empathy Task-Emotion Attribution; **SET-EA:** Story-Based Empathy Task-Emotion Attribution. <sup>∞</sup>: RMET-36 scores are reported as percentiles.

**p values were obtained with Mann-Whitney U test with Bonferroni correction for multiple comparison, significant p was set at: 0.004 (0.05/12). Significant p-values are reported in bold.**

**Supplementary Material 3. Relationship between Social Cognition and Executive Functions According to Cognitive Profile:  
Multiple Linear Regression Analysis results.**

	ALS-CN (n= 65)					ALSci-bi-cbi-FTD (n= 56)				
	EK-60F	RMET-36	SET-GS	SET-IA	SET-EA	EK-60F	RMET-36	SET-GS	SET-IA	SET-EA
<b>Adjusted R<sup>2</sup></b>	0.011	0.097	0.051	0.109	0.141	0.184	0.304	0.263	0.07	0.283
<b>p value</b>	0.518	0.111	0.217	0.946	0.046	0.059	0.007	0.016	0.259	0.011
	<b>p values</b>									
<b>Sex (M/F)</b>	0.06	0,42	0,38	0,84	0,97	0,77	0,83	0,77	0,48	0,83
<b>Age (years)</b>	0.81	0,03	0,53	0,81	0,76	0,47	0,19	0,11	0,28	0,09
<b>Education (years)</b>	0.70	0,20	0,03	0,06	0,01	0,98	0,23	0,54	0,72	0,87
<b>Pathogenic variants (Y/N)</b>	0.62	0,24	0,56	0,73	0,59	0,24	0,20	0,04	0,08	0,01
<b>Onset site (s/b)</b>	0.91	0,21	0,45	0,44	0,41	0,88	0,43	0,60	0,52	0,45
<b>HADS-Anxiety</b>	0.04	0,77	0,98	0,68	0,30	0,20	0,07	0,49	0,33	0,27
<b>HADS-Depression</b>	0.14	0,56	0,90	0,56	0,08	0,74	0,69	0,31	0,10	0,26
<b>FAS</b>	0.41	0,33	0,71	0,57	0,34	0,35	0,02	0,38	0,86	0,15
<b>CAT</b>	0.40	0,14	0,02	0,21	0,35	0,36	0,26	0,53	0,39	0,47
<b>FAB</b>	0.44	0,045	0,51	0,91	0,75	0,01	0,49	0,40	0,62	0,39
<b>TMT B-A</b>	0.11	0,30	0,22	0,37	0,66	0,80	0,03	0,44	0,28	0,41
<b>WCST</b>	0.89	0,15	0,25	0,39	0,08	0,84	0,98	0,03	0,33	0,04

MLR: Multiple Linear Regression; M: male; F: female; s: spinal; b: bulbar; Y: yes; N: no; EF: Executive Functions; EK-60F: Ekman-60 Faces Test, RMET-36: Reading the Mind in the Eyes Test, SET-IA: Story-Based Empathy Task-Global Score; FAS: Letter Fluency Test; CAT: Category Fluency Test; TMT B-A: Trail Making Test B-A; FAB: Frontal Assessment Battery, WCST: Wisconsin Card Sorting

**Supplementary Material 4. Relationship between Social Cognition and Behavioural Changes- Multiple Linear Regression Analysis**

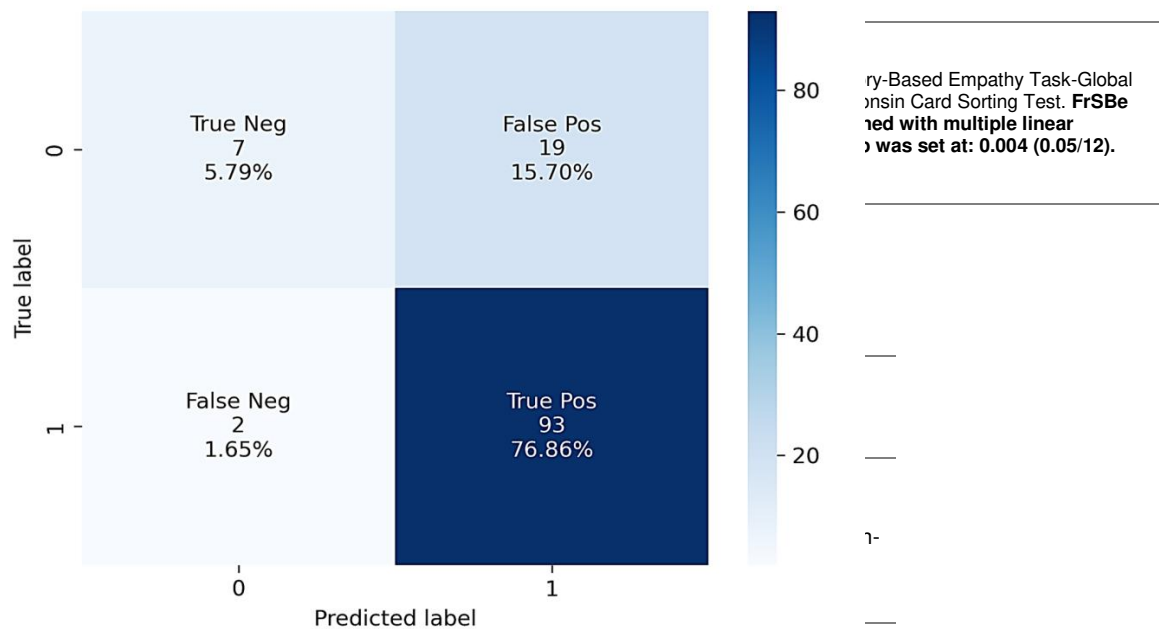
Test. R<sup>2</sup> adj were obtained with multiple linear regression analysis. p values were obtained with Mann-Whitney U test with Bonferroni correction for multiple comparison, significant p was set at: **0.004 (0.05/12)**. Significant p-values are reported in bold.

		Apathy "after" score	Disinhibition "after" score	FRSB "after" total score
		R <sup>2</sup> adj 0.050; p 0.133	R <sup>2</sup> adj 0.007; p 0.05	R <sup>2</sup> adj 0.019; p 0.30
		<b>p values</b>		
<b>Clinical features</b>	<b>Sex (M/F)</b>	0,24	0,66	0,36
	<b>Age (years)</b>	0,53	0,25	0,86
	<b>Education (years)</b>	0,36	0,04	0,51
	<b>Pathogenic variants (Y/N)</b>	0,80	0,06	0,42
	<b>Onset site (s/b)</b>	0,54	0,06	0,08
<b>Emotional disorders</b>	<b>HADS-Anxiety</b>	0,29	0,26	0,73

	<b>HADS-Depression</b>	0,85	0,44	0,66
<b>Social Cognition</b>	<b>RMET-36</b>	0,86	0,55	0,96
	<b>EK-60F</b>	0,35	0,89	0,61
	<b>SET-EA</b>	0,26	0,15	0,69
	<b>SET-GS</b>	0,37	0,16	0,80

**Supplementary Material 5. Relationship between Social Cognition and Executive Functions: Random Forest Analysis results.**

M: male; F: female; s: spinal; b: bulbar; Y Score; FAS: Letter Fluency Test; CAT: C; "after" scores refers to behaviour change regression analysis. p values were obtained. Significant p-values are reported in bold.



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was set at: 0.004 (0.05/12).

**Supplementary Material 6- Se**

<b>EF tests</b>	<b>EF deficit- YES</b>	<b>21 [TP]</b>	<b>12 [FN]</b>
FAB- TMT B-A- WCST- EK-60F- RMET-36- SET-GS	<b>EF deficit- NO</b>	<b>5 [FP]</b>	<b>83 [TN]</b>

Precision is calculated as True Neg/(True Neg + False Neg), resulting in 7/(7+2)= 0.78 (78%).

Recall is calculated as True Neg/( True Neg + False Pos), resulting in 7/(7+19)= 0.27 (27%).

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**Specificity:  $83/(83+5)= 94.31\%$  - Sensitivity:  $21/(21+12)= 63.63\%$**

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EF, Executive Functions; ECAS, Edinburgh Cognitive and Behavioural ALS screen; FAB, Frontal Assessment Battery; TMT B-A, Trail Making Test B-A; WCST, Wisconsin Card Sorting Test; EK-60F, Ekman-60 Faces Test; RMET-36, Reading the Mind in the Eyes Test; SET-GS, Story-Based Empathy Task-Global Score; TP, True Positive; FN, False Negative; FP, False Positive; TN, True Negative.

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**Supplementary Material 7- Sensitivity and Specificity of ECAS in detecting Fluency deficit**  
**Supplementary Material 8- Sensitivity and Specificity of ECAS in detecting Social Cognition deficit**

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**ECAS Fluency subscores**

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**ECAS SC Subscore**

Fluency 'S' score, Fluency 'T' score

		ECAS SC Subscore	
		Fluency 'S' score	Fluency 'T' score
		SC deficit- YES	SC deficit- NO
		Fluency deficit- YES	Fluency deficit- NO
<b>SC tests</b>	<b>Fluency tests</b>	<b>Fluency deficit- YES</b>	<b>Fluency deficit- NO</b>
EK-60F, FMET-36, SET-GS, PAS-CAT		10 [FP]	3 [FN]
		22 [FP]	89 [TN]
<b>Sensitivity</b>		$\frac{10}{10+3} = 76.9\%$	
<b>Specificity</b>		$\frac{89}{89+22} = 80.1\%$	
<b>Positive Predictive Value</b>		$\frac{10}{10+22} = 31.0\%$	
<b>Negative Predictive Value</b>		$\frac{3}{3+89} = 3.3\%$	
<b>Accuracy</b>		$\frac{10+89}{10+3+22+89} = 83.2\%$	

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ECAS, Edinburgh Cognitive and Behavioural Assessment; FMET-36, Frontal Modified Trail Making Test; SET-GS, Semantic Error Test; PAS-CAT, Category Fluency Test; EK-60F, Category Fluency Test; FN, False Negative; FP, False Positive; TN, True Negative.

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Mind in the Eyes Test; SET-GS, Story-Based Empathy Task-Global Score; TP, True Positive; FN, False Negative; FP, False Positive; TN, True Negative.

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**Supplementary Material 9. Relationship between Social Cognition and Executive Functions according to ECAS scale:  
Multiple Linear Regression Analysis Results**

		ECAS Executive Subscore:
		Social Cognition
		R <sup>2</sup> adj 0.256
		<b>p &lt; 0.001</b>
Demographic and clinical features	Sex (M/F)	0.807
	Age (years)	0.865
	Education (years)	0.948
	Pathogenic variants (Y/N)	0.312
	Onset site (s/b)	0.238
	Fluency 'S' score	0.178
ECAS	Fluency 'T' score	0.563
Executive Functions subscores	Executive subscore: backward/reverse digit span	0.041
	Executive subscore: alternation	0.032
	Executive subscore: sentence completion	0.038

M: male; F: female; s: spinal; b: bulbar; Y: yes; N: no; EF: Executive Functions; EK-60F: Ekman-60 Faces Test, RMET-36: Reading the Mind in the Eyes Test, SET-IA: Story-Based Empathy Task-Global Score; FAS: Letter Fluency Test; CAT: Category Fluency Test; TMT B-A: Trail Making Test B-A; FAB: Frontal Assessment Battery, WCST: Wisconsin Card Sorting Test. R2 adj were obtained with multiple linear regression analysis. **p values were obtained with Multiple Regression Analysis with Bonferroni correction for multiple comparison, significant p was set at: 0.005 (0.05/10). Significant p-values are reported in bold.**