

6. Boulanger M, Béjot Y, Rothwell PM, Touzé E. Long-term risk of myocardial infarction compared to recurrent stroke after transient ischemic attack and ischemic stroke: Systematic review and meta-analysis. *J Am Heart Assoc.* 2018;7:e007267.
  7. Ridker PM, Everett BM, Thuren T, MacFadyen JG, Chang WH, Balantyne C, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med.* 2017;377:1119–31.
  8. Li J, Pan Y, Xu J, Li S, Wang M, Quan K, et al. Residual inflammatory risk predicts poor prognosis in acute ischemic stroke or transient ischemic attack patients. *Stroke.* 2021;52:2827–36.
  9. Masson W, Lobo M, Molinero G, Masson G, Lavalle-Cobo A. Role of colchicine in stroke prevention: An updated meta-analysis. *J Stroke Cerebrovasc Dis.* 2020;29:104756.
  10. Varghese B, Feldman DI, Chew C, Valilis E, Blumenthal RS, Sharma G, Calkins H. Inflammation, atrial fibrillation, and the potential role for colchicine therapy. *Heart Rhythm O2.* 2021;2:298–303.
  11. Yilmaz E, Akay KH. The efficacy of colchicine on carotid intima-media thickness: A prospective comparative study. *J Stroke Cerebrovasc Dis.* 2021;30:105580.
  12. Okawa H, Yamawaki-Ogata A, Narita Y, Munakata H, Hashizume R, Usui A. P3112 The oral administration of colchicine prevents the progression of aortic aneurysm. *Eur Heart J.* 2019;40, <http://dx.doi.org/10.1093/eurheartj/ehz745.0187>.
  13. Kelly P, Weimar C, Lemmens R, Murphy S, Purroy F, Arsovska A, et al. Colchicine for prevention of vascular inflammation in Non-CardioEmbolic stroke (CONVINCE) - Study protocol for a randomised controlled trial. *Eur Stroke J.* 2021;6:222–8, <http://dx.doi.org/10.1177/2396987320972566>.
  14. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J.* 2021;42:3227–337.
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## Impact of age and education on performance in the Spanish-language version of the Edinburgh Cognitive and Behavioural ALS Screen in a cohort of patients with amyotrophic lateral sclerosis



## Influencia de la edad y la escolaridad sobre el rendimiento de la versión española del Edinburgh Cognitive and Behavioural ALS Screen en una cohorte de pacientes con esclerosis lateral amiotrófica

### Introduction

In recent years, growing evidence has been reported on the presence of non-motor symptoms in amyotrophic lateral sclerosis (ALS), such as those affecting cognition. Between 30% and 50% of patients with ALS may present cognitive disorders<sup>1,2</sup>, and approximately 15% meet diagnostic criteria for frontotemporal dementia<sup>3</sup>. These patients' cognitive profile is characterised by deficits in executive function (especially in fluency), language, social cognition, and verbal memory<sup>1</sup>. The Edinburgh Cognitive and Behavioural ALS Screen (ECAS)<sup>4</sup> is a screening tool designed to assess behavioural alterations and cognitive performance in multiple domains in patients with ALS. The ECAS has been validated in a Spanish population and cut-off scores have been established<sup>5</sup>; however, age- and education-adjusted cut-off scores are yet to be published. Sociodemographic variables should be considered due to their impact on ECAS scores.

This study aims to analyse the association between these sociodemographic factors and ECAS scores in a cohort of patients with ALS.

### Methods

We collected clinical and sociodemographic data and ECAS scores from a cohort of patients with ALS (probable/definite ALS according to the El Escorial criteria) from our centre. We gathered total ECAS scores, ALS-specific ECAS scores (including the cognitive domains of language, fluency, and executive functions), ALS-nonspecific ECAS scores (including memory and visuospatial functions), and individual ECAS domain scores. We calculated the Spearman correlation coefficient to analyse the association between education level and ECAS scores, and the Mann-Whitney U test and effect sizes (Hedges' *g*) were used to compare groups in terms of age (< 65 vs ≥ 65 years, based on the established age limit of onset of neurodegenerative diseases) and education (< 10 vs ≥ 10 years of schooling).

### Results

Our sample included 23 patients (60.9% men; mean age, 63.9 ± 11.46 years; mean years of schooling, 10.2 ± 4.48); 20 (86.96%) had spinal-onset ALS and 3 (13.04%) had bulbar-onset ALS. Age and education level were significantly correlated with total ECAS score (Spearman  $\rho = -0.593$ ;  $P = .003$  and  $\rho = 0.691$ ;  $P < .001$ , respectively) (Fig. 1), ALS-specific ECAS score ( $\rho = -0.610$ ;  $P = .002$  and  $\rho = 0.681$ ;  $P < .001$ , respectively), and ALS-nonspecific ECAS score ( $\rho = -0.436$ ;  $P = .037$  and  $\rho = 0.519$ ;  $P = .011$ , respectively), as well as with individual ECAS domain scores (age:  $\rho = -0.521$  to  $-0.608$ ;  $P \leq .05$ ; education level:  $\rho = 0.428$  to  $0.674$ ;  $P \leq .05$ ). Table 1 compares ECAS scores between age and education groups, providing effect sizes. We found significant differences ( $P \leq .05$ ) in ECAS scores between patients younger than and older than 65 years (except for ALS-nonspecific ECAS scores:  $P = .201$ ) and between patients with less than or more than 10 years of schooling (except for ECAS fluency score:  $P = .092$ ). The effect size was moderate for differences between age groups in ALS-nonspecific ECAS score and ECAS visuospatial score ( $g = 0.61$  and  $g = 0.56$ , respectively) and for differences between education groups for ALS-

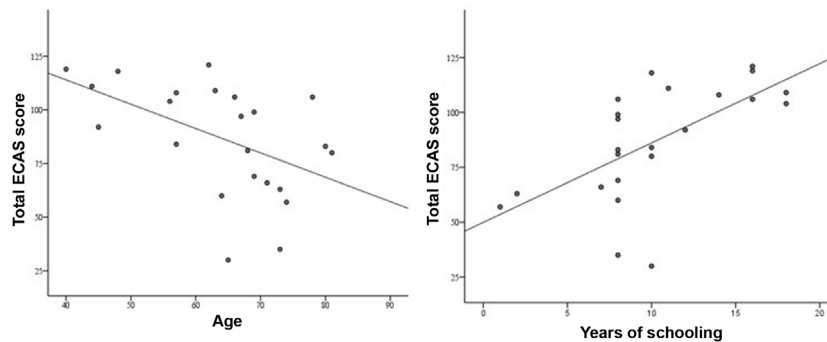


Figure 1 Correlation between total ECAS score and age (left) and level of education (right).

Table 1 ECAS scores by age and education group.

	Total ECAS	ALS-specific ECAS	ALS-nonspecific ECAS	ECAS Language	ECAS Fluency	ECAS Executive	ECAS Memory	ECAS Visuospatial
<b>Age</b>								
< 65 years (n = 9)	108 (88–118.5)	84 (61.5–88.5)	28 (22.5–31.5)	25.5 (20–26.5)	20 (14–20)	39 (25–41)	19 (15.5–19.5)	12 (11–12)
≥ 65 years (n = 14)	80.5 (61.5–100.7)	57.5 (38.5–74)	24.5 (16–29.2)	20.5 (15–24)	10 (8–16)	26 (11.7–32.7)	14.5 (11–18)	10 (9–11.2)
<i>P</i> <sup>a</sup>	.016*	.007*	.210	.009*	.011*	.046	.039*	.039*
<i>g</i>	1.05	1.16	0.61	1.24	0.92	1.02	0.93	0.56
<b>Schooling</b>								
< 10 years (n = 11)	69 (60–97)	50 (39–67)	23 (20–27)	20 (15–24)	10 (10–16)	20 (10–29)	14 (11–17)	10 (9–11)
≥ 10 years (n = 12)	107 (86–116.2)	80 (58.7–87.5)	29.5 (25–32)	25.5 (20.7–26)	17 (9.5–20)	39 (27.2–41.7)	19 (15.2–20)	12 (11–12)
<i>P</i> <sup>a</sup>	.007*	.011*	.027*	.023*	.091	.019*	.006*	.007*
<i>g</i>	1.04	1.02	0.65	0.94	0.65	1.07	1.21	1.04

Data are expressed as medians (p25–p75).

ECAS: Edinburgh Cognitive and Behavioural ALS Screen; ALS: amyotrophic lateral sclerosis; *g*: Hedges’ *g*.

<sup>a</sup> Mann-Whitney U test.

\* Statistical significance was set at  $P \leq .05$ .

nonspecific ECAS score and ECAS fluency score ( $g = 0.65$ ). We found a large size effect in the remaining comparisons. No correlation was observed between Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) scores and ECAS scores in the total sample, nor did we find differences in ALSFRS-R scores between age groups.

### Discussion

Age and education level were found to have an impact on ECAS scores. Overall, patients with higher education levels scored better, while older patients performed worse. The effect size of the difference between age and education groups was large for most cognitive scores. Non-significant differences may be due to the small size of the groups; however, most differences did show statistical significance. These results were not correlated with ALSFRS-R scores, which were similar in both age groups, suggesting that age does not have an impact on disease progression.

The main limitation of our study is its small sample size, which limits the possibility of drawing general conclusions. However, our results are in line with those of studies reporting an association between age and education in the English and Swiss-German ver-

sions of the ECAS in control populations,<sup>6,7</sup> which provides age- and education-adjusted cut-off scores.

### Conclusions

Age and education level were found to have an impact on cognitive performance in our sample. Our results underscore the need to analyse these sociodemographic variables in a control population to obtain more sensitive age- and education-adjusted cut-off scores for the Spanish version of the ECAS, with the aim to improve the detection of cognitive impairment in ALS patients.

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## References

1. Beeldman E, Raaphorst J, Klein Twennaar M, de Visser M, Schmand BA, de Haan RJ. The cognitive profile of ALS: A systematic review and meta-analysis update. *J Neurol Neurosurg Psychiatry*. 2016;87:611–9.
2. Gillingham SM, Yunusova Y, Ganda A, et al. Assessing cognitive functioning in ALS: A focus on frontal lobe processes. *Amyotroph Lateral Scler Frontotemporal Degener*. 2017;18:182–92.
3. Ringholz GM, Appel SH, Bradshaw M, Cooke NA, Mosnik DM, Schulz PE. Prevalence and patterns of cognitive impairment in sporadic ALS. *Neurology*. 2005;65:586–90.
4. Abrahams S, Newton J, Niven E, Foley J, Bak TH. Screening for cognition and behaviour changes in ALS. *Amyotroph Lat Scler Frontotemp Degener*. 2014;15:9–14.
5. Mora JS, Salas T, Fernández MC, et al. Spanish adaptation of the edinburgh cognitive and behavioral amyotrophic lateral sclerosis screen (ECAS). *Amyotroph Lateral Scler Frontotemporal Degener*. 2018;19:74–9.
6. Pinto-Grau M, Burke T, Lonergan K, et al. Screening for cognitive dysfunction in ALS: Validation of the Edinburgh Cognitive and Behavioural ALS Screen (ECAS) using age and education adjusted normative data. *Amyotroph Lateral Scler Frontotemporal Degener*. 2017;18:99–106.
7. Loose M, Burkhardt C, Aho-Özhan H, et al. Age and education-matched cut-off scores for the revised German/Swiss-German version of ECAS. *Amyotroph Lateral Scler Frontotemporal Degener*. 2016;17:374–6.

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