# Edinburgh Cognitive and Behavioural ALS Screen (ECAS) in myotonic dystrophies: a valuable screening tool for cognitive impairment

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## Introduction and aim:

Cognitive impairment is a clinical hallmark of myotonic dystrophies (DM), affecting executive functions, visuo-spatial abilities, and social cognition in both DM1 and DM2, and it significantly impacts quality of life and disease outcome. The Edinburgh Cognitive and Behavioural ALS Screen (ECAS) is a brief, easy to perform, multidomain cognitive assessment, developed for ALS (amyotrophic lateral sclerosis) patients[1], that doesn't require motor skills. It has already been tested in DM2 patients, demonstrating effectiveness in detecting cognitive impairment[2]. Circulating neurofilament light chain (NfL) levels have been recognized as a sensitive prognostic and monitoring biomarker of neuroaxonal damage in various central nervous system disorders, and recent evidence supports their role also in myotonic dystrophies, particularly in type 1[3]. This study aimed to evaluate the validity of the ECAS in identifying cognitive abnormalities in DM patients and their relationship with plasma NfL levels.

## Methods:

We enrolled a cohort of patients with a molecular diagnosis of Myotonic Dystrophy, type 1 and 2, consecutively referring to the Neuromuscular Unit of Policlinico Tor Vergata, Rome. Participants underwent to clinical evaluation, including the 6-Minute Walking Test (6MWT), and neuropsychological examination using ECAS, a cognitive assessment battery designed to detect impairments in five cognitive domains: language, memory, verbal fluency, executive functions, and visuospatial abilities.
A subset of patients, following the collection of informed consent, underwent blood sampling for the assessment of NfL levels, using the Fujirebio Lumipulse® assay, which were then compared to age-matched reference values.

Table1

| | TOT | DM1 | DM2 |
|---|---|---|---|
| N° | 58 | 46 | 12 |
| Male | 26 (45%) | 22 | 4 |
| Female | 32 (55%) | 24 | 8 |
| Age | 45 (±14) | 45 | 53 |
| Education (yrs) | 12 (±3) | | |
| <14 yrs | 50 | 38 | 12 |
| ≥14 yrs | 8 | 8 | 0 |
| ECAS total score | 91.1 (±24.4) | 92 (±23) | 87.8 (±30.2) |
| ECAS < cut-off | 31/58 (53%) | 26/46 (56.5%) | 5/12 (41.6%) |
| NfL > cut-off (n° tot) | 21 (44) | 17 (34) | 4 (10) |
| NfL pg/ml | 19.5 (±17.4) | 16.3 (±10) | 30.39 (±30) |
| 6MWT (m) | 420 (±99) | 425 (±92) | 403 (±114) |
| Infantile-onset (1–10 y) | | 6 (13%) | |
| Juvenile-onset (11–20 y) | | 11 (24%) | |
| Adult-onset (21–40 y) | | 19 (41%) | |
| Late-onset (>40 y) | | 10 (21%) | |
| E1 | | 14 (30%) | |
| E2 | | 29 (63.4%) | |
| E3 | | 3 (6.5%) | |

Figure 1

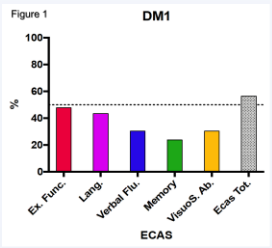



Figure 2

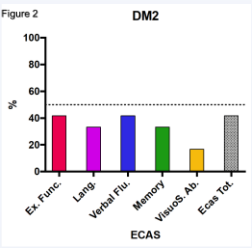



Figure 3

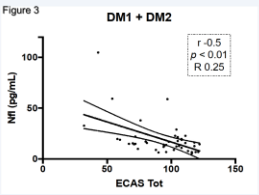
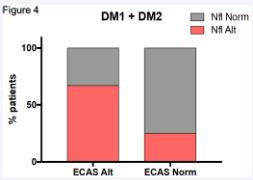



Figure 4




## Discussion and conclusions:

ECAS appears to be a promising tool for screening cognitive impairments in myotonic dystrophies. It is a simple, rapidly administered, and universally accessible test that can be considered a first-level screening tool for identifying patients who may require more detailed neuropsychological assessment.

## Results:

The study involved forty-six DM1 (47.8% male) and twelve DM2 patients (16.6% male). ***Table 1***.
A **pathological** total score at **ECAS** was observed **in 56.5%** of **DM1** patients and **41.6% of DM2**.
Executive functions and language were the most affected cognitive domains in the DM1 group, while executive functions and verbal fluency were the most affected cognitive domains in the DM2 group. ***Figure 1-2***
No significant differences in ECAS total scores were found between DM1 and DM2 patients.
At least one altered domain was observed in 65% of DM1 patients and 58% of DM2 patients.
**NfL levels above** the age-adjusted normative cutoff were found **in 50% of DM1 and in 40% of DM2 patients**.
In the combined DM1 and DM2 groups, **NfL levels** showed a statistically significant **inverse correlation with the ECAS total score (r = –0.5, *p* < 0.01), *Figure 3*, and a direct correlation with the number of impaired ECAS domains (r = 0.38, p < 0.05).**
Stratifying patients based on pathological vs normal plasma NfL levels revealed a statistically significant difference in cognitive performance. **Patients with elevated NfL levels scored lower on cognitive testing**, suggesting the test's ability to detect underlying neurodegeneration (Fisher's exact test, *p* = 0.007), ***Figure 4.*** The ECAS score showed good sensitivity (76%) and negative predictive value (75%), with moderate specificity (65%) and positive predictive value (67%), supporting its potential role as a screening tool for neurodegeneration in myotonic dystrophies.

**References:**
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2) Theodosiou, T, et al. Executive dysfunction, social cognition impairment, and gray matter pathology in myotonic dystrophy type 2: A pilot study. *Cognitive and Behavioral Neurology, 35*(3), 204–211. https://doi.org/10.1097/WNN.0000000000000314
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