MBNI Approach in ALS: Identifying Mild Behavioral and Neurocognitive Impairment provides key Prognostic Insights

Valentina Virginia Iuzzolino1, Myriam Spisto1,2, Gianmaria Senerchia1, Lucia Aruta1, Gabriella Santangelo2, Luigi Trojano2, Raffaele Dubbioso1

1.Department of Neurosciences, Reproductive Sciences and Odontostomatology, University Federico II of Naples, Naples, Italy.
2.Department of Psychology, University of Campania Luigi Vanvitelli, Naples

Introduction

Amyotrophic lateral sclerosis (ALS) is a multisystem neurodegenerative disease encompassing cognitive and behavioral impairments. The Revised Diagnostic Criteria for ALS-frontotemporal spectrum disorder (ALS-FTDS), while widely adopted, may overlook subtle impairments, limiting their prognostic value.

This study aimed to apply the Mild Behavioral and Neurocognitive Impairment (MBNI) approach, adapted from other neurodegenerative diseases, to ALS patients and assessed its prognostic utility for survival and disease progression.

Methods:

A prospective cohort of 201 ALS patients was evaluated between January 2018 and July 2024. Participants underwent comprehensive cognitive and behavioral assessments. The MBNI approach identified patients with mild cognitive impairment (MCI), mild behavioral impairment (MBI), or combined mild cognitive-behavioral impairment (MCBI). Prognostic value was analyzed using Kaplan-Meier survival curves, Cox proportional hazards models, and logistic regression for disease progression, adjusting for clinical covariates.

Results

MBNI was identified in 67% of patients previously classified as cognitively normal by the Revised Diagnostic Criteria for ALS-FTDS (figure 1). At a median follow-up of 15 months, these patients had shorter tracheostomy-free survival compared to those with normal cognition (Figure 2). Mild cognitive impairment and frontotemporal dementia independently predicted poor outcomes. Logistic regression showed mild cognitive-behavioral impairment and frontotemporal dementia were associated with rapid disease progression (Figure 3).

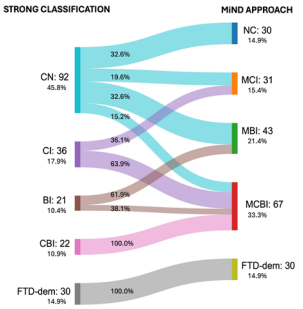

Figure 1

Figure 1. Distribution of ALS patients across cognitive and behavioral impairment categories, comparing the Strong classification with the MBNI approach.

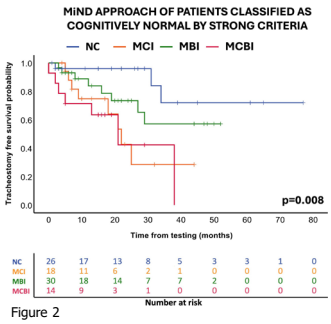

Figure 2

Figure 2. Survival analysis by Kaplan-Meier curves reveals that a subgroup analysis of patients classified as CN under the Strong criteria indicates that those with MCI and MCBI exhibit a poorer prognosis compared to NC individuals.

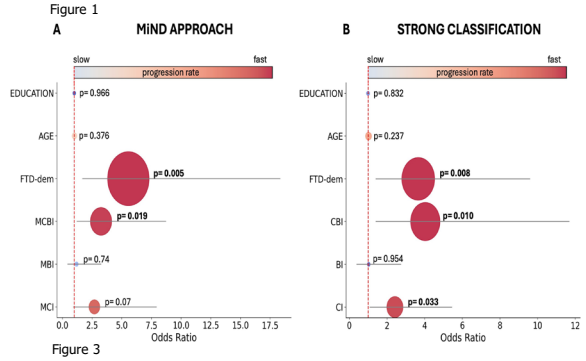

Figure 3

Figure 3. Binary logistic regression for disease progression rate. The plots display the odds ratio (OR) for each variable on the horizontal axis, based on cognitive classification: MBNI on the left (A) and Strong on the right (B). Values greater than 1 indicate a higher likelihood of disease progression, while values less than 1 suggest a lower likelihood. Each bubble represents a variable, with the size of the bubble reflecting its statistical significance (larger bubbles indicate smaller p-values). The colour of the bubble corresponds to the rate of progression: red shades indicate fast progression, while blue shades represent slow progression. The horizontal bars extending from each bubble show the 95% confidence intervals.

Discussion and Conclusions

The MBNI approach enhances detection of mild cognitive and behavioral impairments in ALS, providing prognostic insights and improving stratification over ALS-FTDS criteria. This supports personalized care and clinical trial design for early disease stages.