

Exploring the role of Interleukin-18 and neuroinflammation in Amyotrophic Lateral Sclerosis

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Background and objectives

Amyotrophic Lateral Sclerosis (ALS) is a heterogeneous and fatal neurodegenerative disorder, urgently requiring reliable biomarkers for diagnosis, prognosis, and therapeutic monitoring. This study investigates the role of Interleukin-18 (IL-18), a pro-inflammatory cytokine implicated in neuroinflammation, as a potential biomarker in ALS.

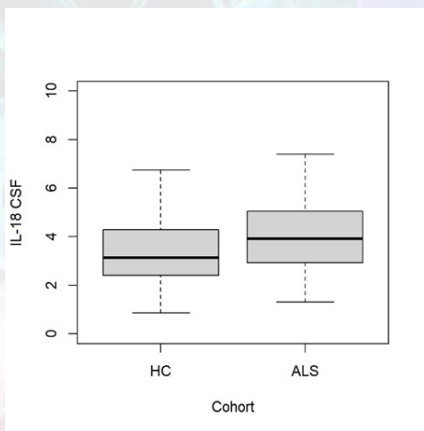
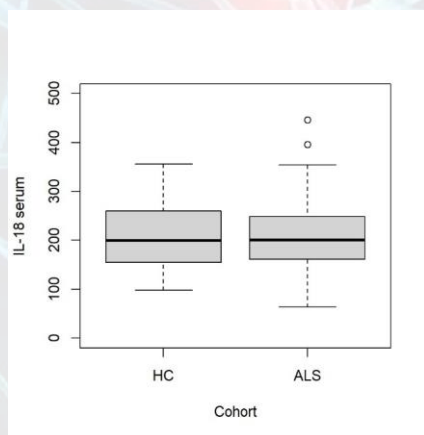
The present study aims to:

1. Evaluate IL-18 levels in serum and cerebrospinal fluid (CSF) of ALS patients versus healthy controls;
2. Examine associations with clinical and genetic features in ALS subgroups.

Methods

- Mixed retrospective and prospective cohort design, including 49 ALS patients and 24 matched healthy controls.
- IL-18 concentrations measured in serum and CSF via Ella Simple Plex automated ELISA technology.
- Clinical data from the Emilia-Romagna ALS Registry included phenotype classification, ALSFRS-R, disease staging (King's and MiToS), respiratory function, cognitive status, and genetic profiles.

Results



IL-18 levels did not significantly differ between ALS patients and controls in either serum or CSF.

Conclusions

IL-18 appears insufficiently sensitive or specific to reflect ALS heterogeneity in a clinically actionable way and it does not emerge as a reliable standalone diagnostic biomarker in ALS.

In partial contrast to literature, our study points toward a potential protective role of this cytokine. Specific associations exist with respiratory function, IV and ALS-FTD, hinting at a role in certain subtypes. Continued integration of clinical phenotyping, genomics, and biomarker research is essential for unlocking personalized approaches to ALS.

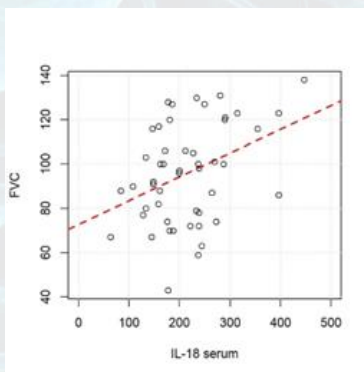
Potential protective role of IL-18

ALS-FTD patients showed significantly lower CSF IL-18 levels compared to those without cognitive involvement (2.81 ± 1.33 pg/mL vs. 4.17 ± 1.44 pg/mL, $p = 0.034$).

IL-18 values in serum and survival

Variable	Hazard ratio (HR)	95% CI	p-value
NIV	0.995	0.991 1.000	0.062
PEG	0.997	0.991 1.002	0.218
IV	0.993	0.986 1.000	0.041
Death or IV	0.993	0.988 0.998	0.004

With each 10-unit increase in serum IL-18 value, the risk of tracheostomy or death is reduced by 7%.



Each one-unit increase in serum IL-18 was associated with an average increase of 0.108 in FVC (95% CI: 0.032 to 0.183, $p = 0.007$).