Investigating Neuroinflammation in Frontotemporal Dementia: The Emerging Role of Galectin-3

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BACKGROUND

Frontotemporal dementia (FTD) encompasses a spectrum of neurodegenerative disorders characterized by progressive atrophy of the frontal and temporal lobes. It represents the second most common cause of early-onset dementia after Alzheimer's disease. Increasing evidence implicates neuroinflammation as a key contributor to FTD pathophysiology (1).

Among the molecular mediators involved, Galectin-3 (Gal-3), a galactoside-binding lectin predominantly expressed by activated microglia, has emerged as a modulator of neuroinflammatory pathways. A recent study reported elevated cerebrospinal fluid (CSF) Gal-3 levels in patients with FTD, supporting its potential role in disease mechanisms (2). Interestingly, Gal-3 has been implicated in synaptic dysfunction, neuronal injury, and glial reactivity, and may represent a novel biomarker for inflammatory activity in neurodegenerative diseases (3).

This study aims to evaluate CSF Galectin-3 levels in FTD subtypes and healthy controls, and to investigate its relationship with established biomarkers of neurodegeneration.

METHODS

- ✓ We analyzed CSF samples from 52 participants recruited at our Dementia Center, University of Torino:
- 24 patients with behavioral variant FTD (bvFTD), 6 with semantic variant Primary Progressive Aphasia (svPPA), 4 with non-fluent/agrammatic variant PPA (nfvPPA), diagnosed according to current clinical criteria; ;
- 18 cognitively healthy controls.
- ✓ Galectin-3 concentrations were measured using a commercially available ELISA kit.
- ✓ CSF biomarkers of neurodegeneration Aβ42, Aβ42/40, total tau (t-Tau), phosphorylated tau at threonine 181 (p-Tau181), and neurofilament light chain (NfL) were measured using the Lumipulse platform (Fujirebio, Ghent, Belgium).

RESULTS

- ✓ Mean Galectin-3 levels were significantly higher in the overall FTD group (465.1± 227.3 pg/mL) compared to controls (261.4± 115.5 pg/mL; p< 0.001) (Fig. 1).
- ✓ When analyzing the clinical subtypes, bvFTD patients showed the highest levels (503.4± 256.8 pg/mL vs controls, p= 0.001). Gal-3 was also increased in the PPA subgroup (p= 0.003).
- ✓ Furthermore, a positive correlation was found between Gal-3 and p-Tau181 in the PPA subgroup (r= +0.39, p= 0.023).
- ✓ No correlation was found between Gal-3 and Aβ42, Aβ42/40, t-Tau, NfL.

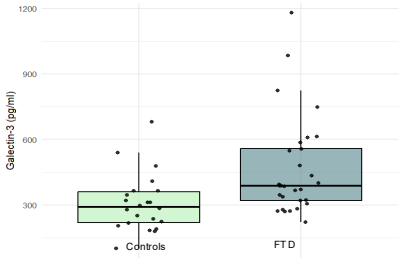

Fig. 1. Boxplots illustrate differences in CSF Gal-3 levels between FTD patients and controls.

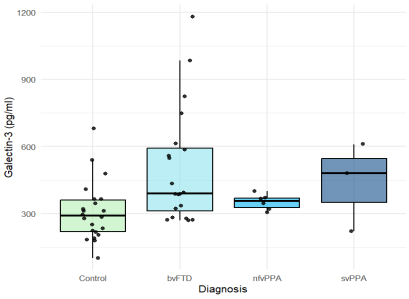

Fig. 2. Boxplots illustrate differences in CSF Gal-3 levels among clinical subgroups and controls.

CONCLUSION

We observed significantly elevated Gal-3 levels in patients with bvFTD and PPA variants, suggesting a shared neuroinflammatory mechanism across FTD clinical phenotypes. Interestingly, the correlation between Gal-3 and p-Tau181 might reflect a potential interaction between tau pathology and microglial activation.

In conclusion, our data support Galectin-3 as a biomarker of neuroinflammation in Frontotemporal dementia. Further studies are warranted to validate these findings.

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