

Sex Differences in FNDC5/Irisin-BDNF Levels and Correlations with Cognition and Alzheimer's Biomarkers

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1 Background & Rationale

- Women are disproportionately affected by Alzheimer's disease (AD) by mechanisms not fully understood.
- Physical exercise reduces AD risk partially by the upregulation of the peptide hormone FNDC5/irisin, which modulates inflammation and enhances Brain-Derived Neurotrophic Factor (BDNF) expression in the brain.

Main question: Do biological sex and menopause modulate this axis in the aging human brain?

Objective: Here, we compared cerebrospinal fluid (CSF) FNDC5/irisin and BDNF levels in aging post-menopausal women and men, and correlated them with cognitive outcomes and systemic inflammatory biomarkers.

2 Study's Design and Participants' Characteristics

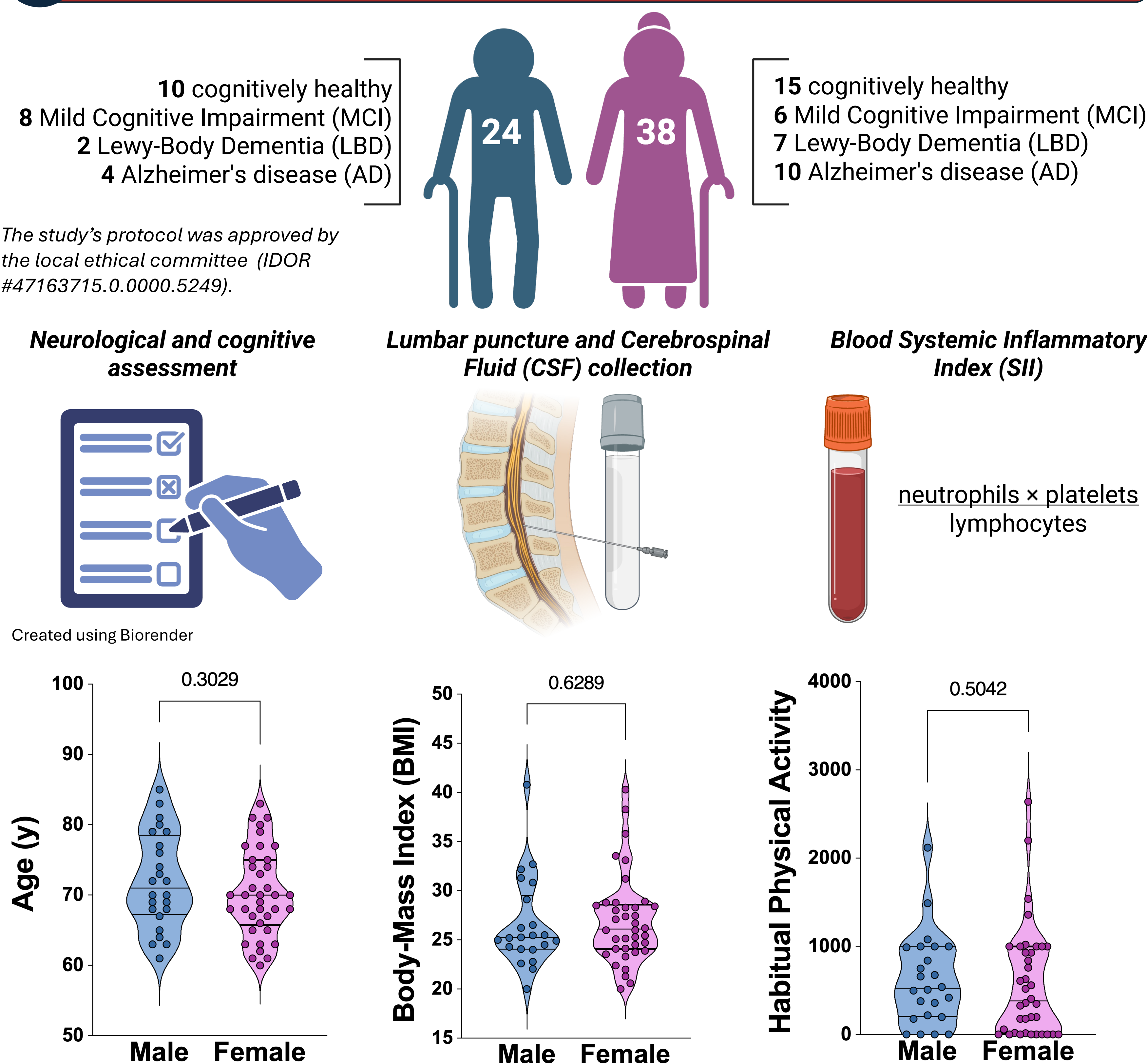


Fig. 1. Barros-Aragão et al., data not published. Groups were compared using t-test.

3 Results

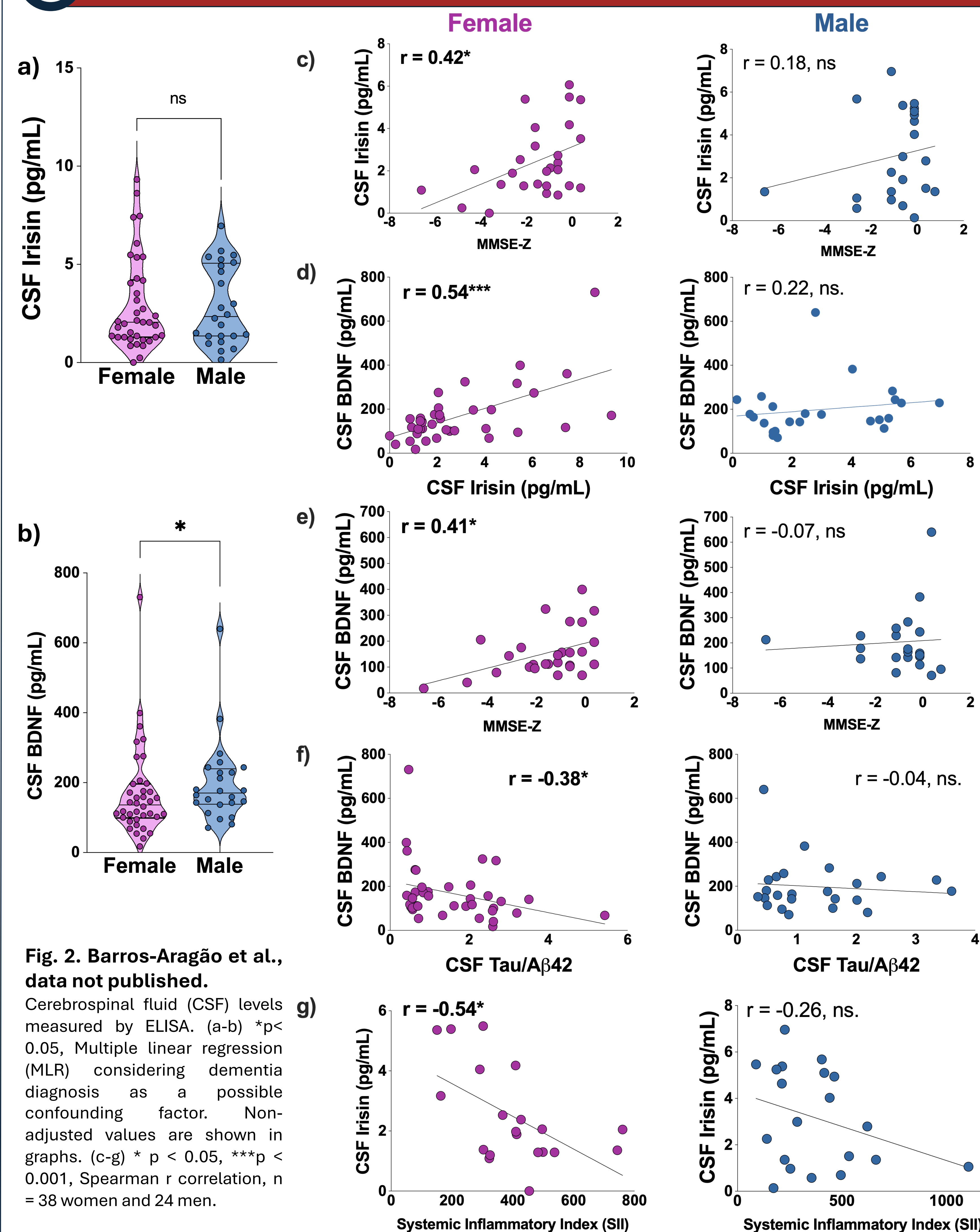


Fig. 2. Barros-Aragão et al., data not published.

Cerebrospinal fluid (CSF) levels measured by ELISA. (a-b) * $p < 0.05$, Multiple linear regression (MLR) considering dementia diagnosis as a possible confounding factor. Non-adjusted values are shown in graphs. (c-g) * $p < 0.05$, *** $p < 0.001$, Spearman r correlation, $n = 38$ women and 24 men.

CONCLUSIONS. Our data indicate sex differences in the central nervous system FNDC5/irisin-BDNF pathway, independent of cognitive status. FNDC5/Irisin-BDNF signaling links cognition, AD neuropathological changes (ADNPC), and systemic inflammation only in post-menopausal women. These sex differences could impact AD risk and exercise-based preventive strategies.