Association of Mild Behavioural Impairment with peripheral inflammatory biomarkers in individuals with Mild Cognitive Impairment (MCI)

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What We Already Know

Inflammatory processes have emerged as playing a **significant role** in the progression of **neurodegenerative diseases**, particularly Alzheimer's disease (AD) [1]. Neuroinflammation is characterized by the **recruitment of peripheral immune cells** and activation of resident immunocompetent cells such as microglia and astrocytes, which triggers signalling cascades that produce inflammatory mediators [2,3]. As such, **elevated levels of inflammatory biomarkers** have been observed in cerebrospinal fluid and plasma of **AD patients [4].**

Our Study incorporates the **framework of Mild Behavioural Impairment (MBI),** a validated neurobehavioral syndrome which **captures late-life emergent and persistent neuropsychiatric symptoms (NPS)** over transient symptoms to identify a high-risk group for incident cognitive decline and dementia [5]. We aim to utilize the MBI framework to bridge the knowledge gap concerning the relationship between behavioural changes and peripheral inflammation in older adults.

Our Research Aim

Investigate the link between plasma inflammatory biomarkers and MBI to enhance our understanding of the biological underpinnings of MBI.

Research Question

Do individuals with MBI have higher levels of plasma inflammatory biomarkers in comparison to individuals who do not have MBI?

How We Did It

ADNI Alzheimer's Disease Neuroimaging Initiative

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MCI participants with completed NPI-Q, and inflammatory biomarker data

↓

390 total participants with MCI

MBI +: 30.7% Females | Mean Age: 74.5 years | Mean Education : 15.6 years

MBI -: 61.2% Females | Mean Age: 75.0 years | Mean Education : 15.6 years

Measures

MBI Status
Operationalized using the NPI-Q and the two-thirds visit approach [6]

Inflammatory Biomarkers
Obtained using analyte multiplex immunoassay panel at baseline and 1-year

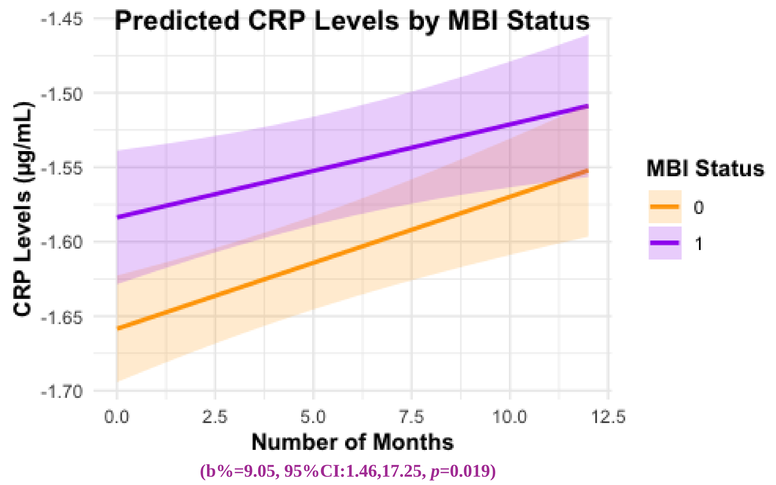
Statistical Model

Predictor: MBI Status → **Outcome: Plasma inflammatory biomarker levels:**
- C-reactive protein (CRP)
- Interleukin-3 (IL-3)
- Interleukin-8 (IL-8)
- Tumor necrosis factor alpha (TNF-α)

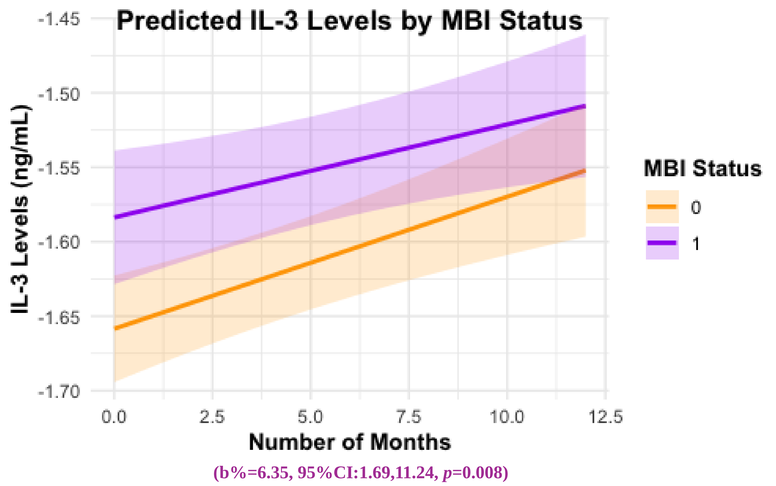
Moderator: Time (BI/M12)

All models were adjusted for age, sex, education, MMSE, APOE4, BMI, and systolic blood pressure.

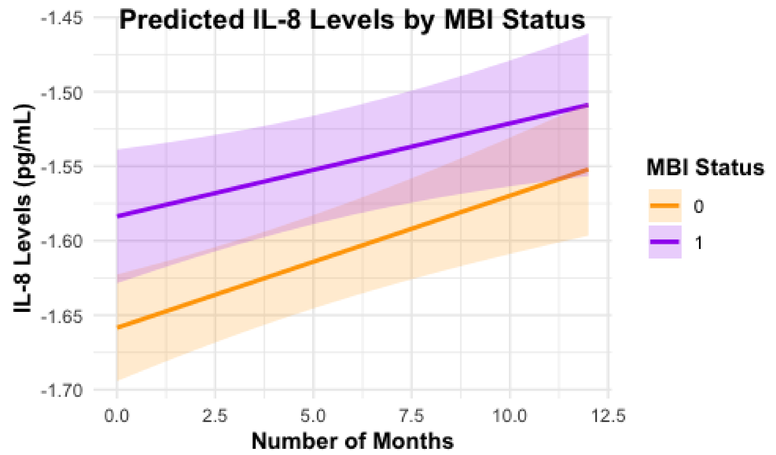
What We Found



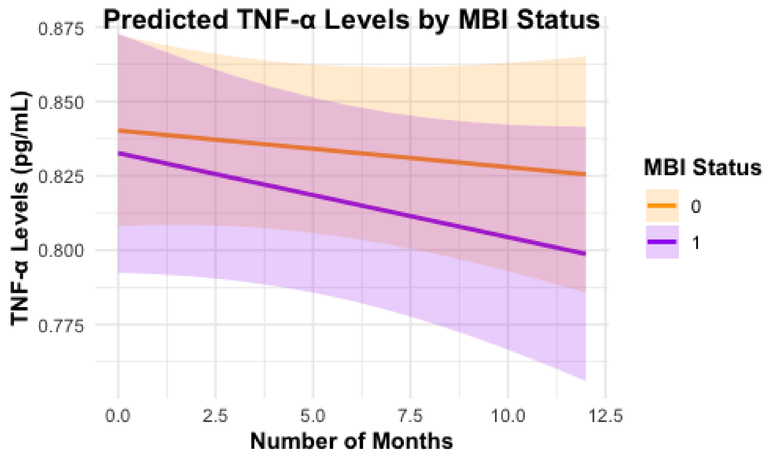
(b%=9.05, 95%CI:1.46,17.25, *p*=0.019)



(b%=6.35, 95%CI:1.69,11.24, *p*=0.008)



(b%=3.16, 95%CI:-0.10,6.55, *p*=0.06)



(b%=-1.55, 95%CI:-5.45,2.50, *p*=0.45

Figure 1. The relationship between MBI status and plasma levels of inflammatory markers measured at baseline and at the 1-year follow-up
Abbreviations: MBI, mild behavioural impairment; CRP, C-reactive protein; IL-3, interleukin-3; IL-8, interleukin-8; TNF-α, tumor necrosis factor-alpha.

Why It Matters

- **Association between MBI and inflammation:** Significant link between MBI and elevated peripheral inflammation helps in understanding MBI as a potential early marker for dementia.
- **Clinical tool for early risk identification:** MBI can be used to identify individuals at high risk for early dementia.
- **Insights into inflammation:** Reveals the impact of inflammation on early stages of neurodegenerative diseases like Alzheimer's.

The Future

- **Targeted therapeutic intervention**
- **Integration with other biomarkers**: Provides for a comprehensive assessment aiming to improve detection and intervention
- **Mechanistic research:** Investigate the biological mechanisms linking MBI to systemic inflammation and neurodegeneration
- **Longitudinal studies across the AD continuum**: Including cognitively normal individuals

Hotchkiss Brain Institute · University of Calgary · Alberta Health Services

Provincial Seniors Health and Continuing Care program Undergraduate Summer Studentship

Scan for references: