

Brain morphometry correlates of GFAP and NFL in Parkinson's Disease

Introduction

Complementary information from blood-based biomarkers on neurodegenerative and neuroinflammatory diseases:

- **Glial Fibrillary Proteic Acid (GFAP):** astrocytic destruction and gliosis in acute phase
- **Neurofilament Light Chain (NFL):** neuronal and axonal damage

Both systemic and brain-specific. Inflammation and neurodegeneration are implicated in Parkinson's Disease (PD), with the current hypotheses suggesting the ascension of inflammation-triggered synuclein from the gut or from the deep brain [1,2].

Dataset

56 PD patients aged between 65 and 80 years old:

- **sex** (22 males, 34 females)
- **cognitive status** (21 PD with no cognitive impairment PD-CU and 35 PD with cognitive impairment PD-CI)

Data: II-level neuropsychological assessment
magnetic resonance imaging acquisition: T1-weighted and FLAIR T2-weighted MRI on a 3 Tesla Philips scanner, 1mm isotropic voxels

Methods

- Subcortical parcellation + surface-based morphometry using FreeSurfer to extract the **gray matter volumes** of each parcel.
- Schaefer 400-region parcellation with homeotopic Yeo 2018 labels: cortex divided into 400 regions subdivided into 17 resting state networks pertaining to 7 functions
- Volumes normalized to estimated total intracranial volume
- **Principal Component Analysis** to extract orthogonal sources of variability
- **ANCOVA** model to find associations between principal component expression and one biomarker among plasma **GFAP [ng/L], NFL [ng/L] or their ratio GFAP/NFL**
- Control for covariates: age, sex, years of education, creatinine

Results

- **No significant associations with NFL [ng/L] or GFAP [ng/L].**
- **One Significant association for the GFAP/NFL ratio** ($p < 0.05$, Bonferroni corrected)
- The indicated component shows a heterogeneous pattern of positive and negative associations
- Once the component map is z-scored, hubs of maximal variance are:
- **Positive:** 3rd Ventricle, CSF, Left choroid plexus, left Temporal Language, left Temporo-Occipital Ventral Attention, right PreFrontal Control, right Frontal Ventral Attention, right SomatoMotor
- **Negative:** left & right Ventral diencephalon, left Frontal Control, left Frontal Ventral Attention, left & right PreFrontal Default, right PreFrontal Control, right PreFrontal Dorsal Attention

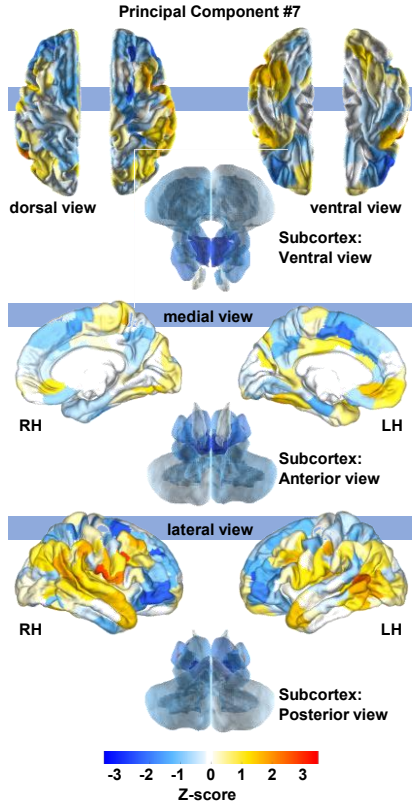
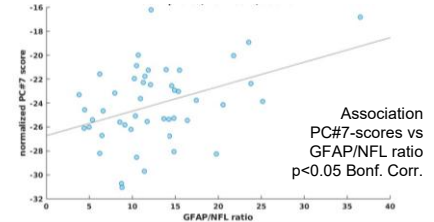
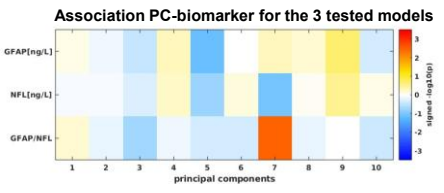
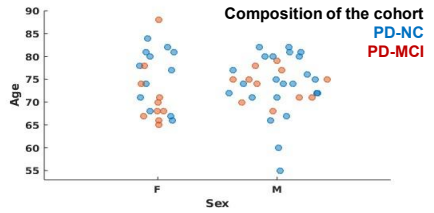
Discussion

Creatinine improves significance -> possibly cleaning out contributes from renal dysfunction in biomarkers levels.
 One PC related to GFAP/NFL:

- large symmetry
- increasing GFAP/NFL associated with **atrophy in bilateral ventral diencephalon, in lateral frontal pole, and in prefrontal cortices pertaining to the default mode and dorsal attention networks.**
- Positive effects on volume for **ventricular size, for prefrontal regions of the executive control networks, superior temporal regions and occipital-temporal cortical regions of the ventral-attention network.**
- **The GFAP/NFL ratio has been hypothesized to be useful in partially controlling for nuisance patient factors** [3].
- The score can be used as an indicator for a brain-specific component in systemic blood-based biomarkers.
- This Parkinson-specific fingertip of biomarkers on brain morphometry is suggested to express detrimental and compensatory mechanisms that are specific to the progression of PD patients showing high levels of inflammation and/or low levels of neuronal damage.

Bibliography

- [1] Wang X., et al., "Peripheral GFAP and NfL as early biomarkers for dementia: longitudinal insights from the UK Biobank", BMC Med, 2024,
- [2] Adams B., et al., "Parkinson's Disease: A Systemic Inflammatory Disease Accompanied by Bacterial Inflammagens", Front Aging Neurosci, 2019
- [3] Sheth U., et al., "Comprehensive cross-sectional and longitudinal comparisons of plasma glial fibrillary acidic protein and neurofilament light across FTD spectrum disorders", Molecular Neurodegeneration, 2025



TASK 3.2 - Identifying accurate diagnostic biomarkers for age-related neurodegenerative diseases, multimorbidity, frailty and disability



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