

Glial Fibrillary Acidic Protein (GFAP)-based Phenotyping Reveals Early Cognitive and Pathological Profiles in Cognitively Unimpaired South East Asian Adults

Angelica Krestianto¹, Pricilia Tanoto¹, Kiirtaara Aravindhan¹, Nagaendran Kandiah^{1, 2, 3 *}

¹ Dementia Research Centre (Singapore), Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; ² Neuroscience and Mental Health Programme, Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; ³ National Healthcare Group, Singapore; *Corresponding author: nagaendran_kandiah@ntu.edu.sg

INTRODUCTION

- Neuroinflammation (NI) is increasingly recognised as an early pathophysiological change in dementia, preceding objective cognitive decline
- Cognitively unimpaired (CU) individuals may already exhibit these alterations, although changes remain underexplored
- This study examined differences in cognitive performance and plasma biomarkers between CU individuals with predominant neuroinflammation phenotype (CU-NI) and those without (CU non-NI) in a Southeast Asian cohort

METHODS

- A cross-sectional study of 457 community-dwelling, CU participants from the BIOCIS cohort¹
- Neuropsychological battery assessed global cognition and cognitive domains of executive function, processing speed, visuospatial, episodic memory, and language
- Plasma blood biomarkers were analysed using Single Molecule Array (SiMOA)
- Participants were stratified into 2 groups based on tertiles of GFAP (Tertile 1 = 153 CU non-NI, Tertile 2 and 3 = 304 CU-NI)
- Analysis of Covariance (ANCOVA) was performed to examine group differences, adjusting for age and education years

DISCUSSION

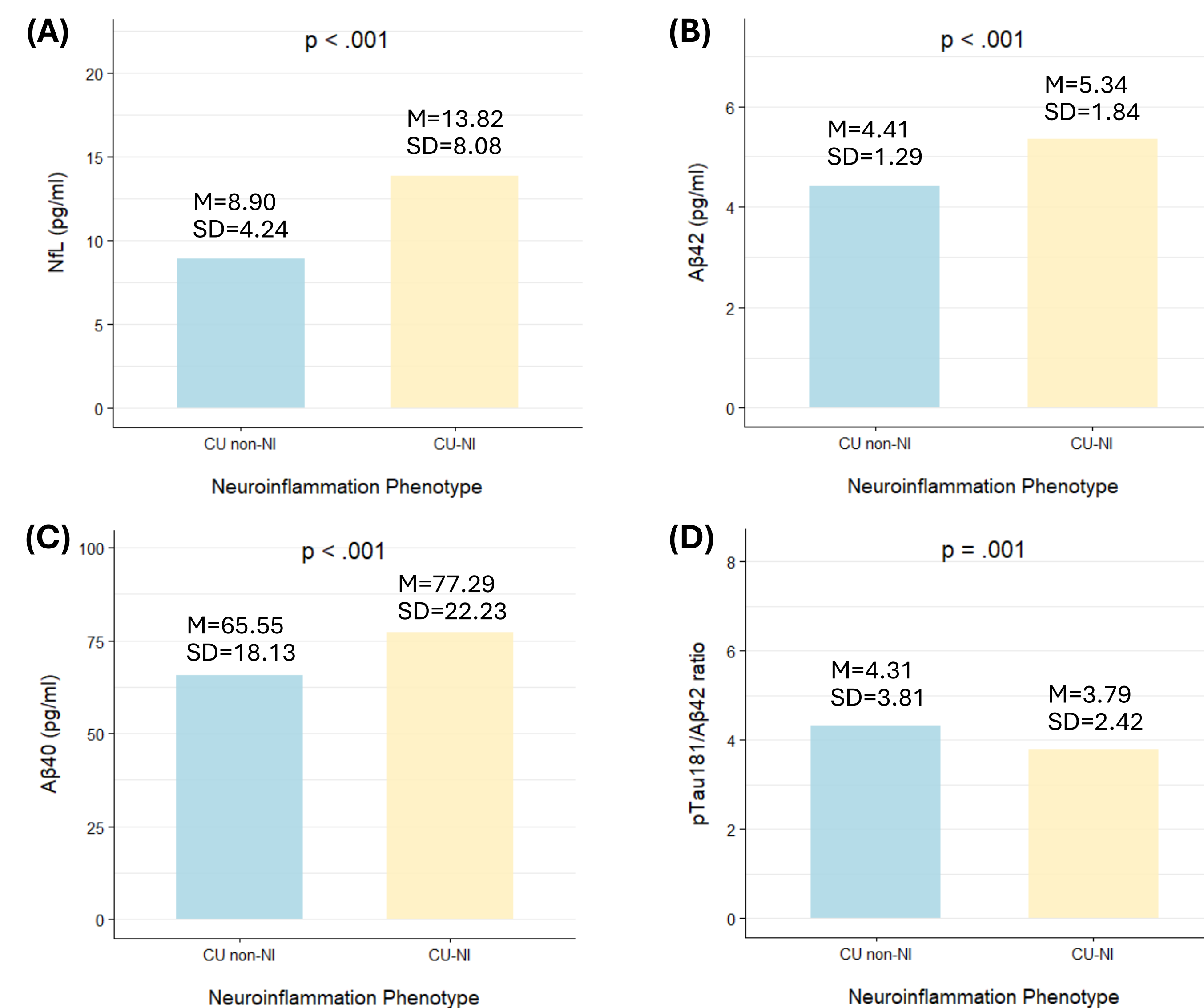
- Participants characteristics were shown in Table 1
- CU-NI participants were significantly older (59.19 ± 7.80 vs 52.36 ± 7.03) and had fewer education years (15.19 ± 3.13 vs 16.09 ± 2.87) than CU non-NI (all $p < .001$)
- CU-NI participants significantly demonstrated poorer global cognition, executive function, processing speed, visuospatial ability, and trends of poorer episodic memory (Figure 1)
- CU-NI participants also exhibited higher NfL, A β 42, and A β 40 levels, whereas lower in pTau181/A β 42 ratios (Figure 2), which is consistent with current literature²
- Characterisation by neuroinflammatory phenotype may help detect cognitive decline and inform pathological profiles of CU individuals who are at-risk
- Future longitudinal studies may provide deeper insights into neuroinflammatory pathologies and help guide targeted interventions in preventing cognitive decline

Table 1. Participant Characteristics

Characteristic	Overall N = 457
Age ^a	56.91 $\pm$ 8.20
Education years ^a	15.49 $\pm$ 3.07
Gender (Female) ^b	289 (63%)
GFAP ^a	67.74 $\pm$ 21.94
Tertile 1 (n = 153) ^c	22.7–56.2
Tertile 2 (n = 152) ^c	56.3–75.8
Tertile 3 (n = 152) ^c	75.9–158.0
Cognitive performance	
MoCA ^a	26.78 $\pm$ 2.23
VCAT ^a	27.69 $\pm$ 2.09
Executive function ^a	0.08 $\pm$ 0.74
Processing speed ^a	0.09 $\pm$ 0.86
Visuospatial ^a	0.19 $\pm$ 0.65
Episodic memory ^a	0.15 $\pm$ 0.59
Language ^a	0.17 $\pm$ 0.94
Blood biomarkers	
APOE ϵ 4 ^b	87 (19%)
NfL ^a	12.18 $\pm$ 7.41
A β 42 ^a	5.03 $\pm$ 1.73
A β 40 ^a	73.38 $\pm$ 21.65
A β 42/40 ^a	0.07 $\pm$ 0.02
pTau181 ^a	17.30 $\pm$ 8.67
pTau181/A β 42 ^a	3.97 $\pm$ 2.97

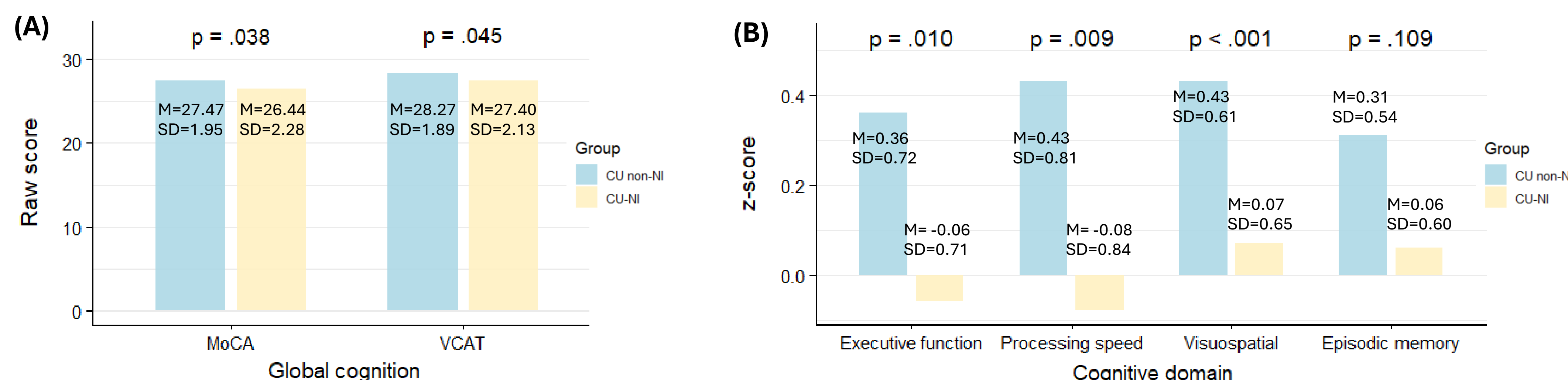
Note. ^a = Mean $\pm$ SD; ^b = Frequency (%); ^c range for 33.3rd or 66.7th percentile cutoff for GFAP.

Figure 2. Blood Biomarker Profiles by Neuroinflammatory Phenotype



Note. Group differences between CU-NI and CU non-NI are shown for (A) neurofilament light chain, (B) amyloid-beta 42, (C) amyloid-beta 40, and (D) phosphorylated tau181/amyloid-beta 42.

Figure 1. Cognitive Performance by Neuroinflammatory Phenotype



Note. Group differences between CU-NI and CU non-NI are shown for (A) global cognition (MoCA and VCAT) and (B) specific cognitive domains.

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ABBREVIATIONS

GFAP = Glial Fibrillary Acidic Protein; MoCA = Montreal Cognitive Assessment; VCAT = Visual Cognitive Assessment Test; APOE ϵ 4 = Apolipoprotein E epsilon 4; NfL = neurofilament light chain; A β 42 = amyloid-beta 42; A β 40 = amyloid-beta 40; A β 42/40 = amyloid-beta 42/40; pTau181 = phosphorylated tau 181; pTau181/A β 42 = phosphorylated tau 181/amyloid-beta 42.

Angelica Krestianto
BPsychSc (Hons)



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