The Impact of Amyloid Plaques on Hippocampal Asymmetry and Cognitive Function in Thai Older Adults

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Background

- Although amyloid PET is considered the gold standard for early detection of Alzheimer's disease (AD), its use in Thailand is limited by high cost and restricted availability.
- MRI-based hippocampal asymmetry has been suggested as a surrogate biomarker, but its clinical significance remains unclear, particularly in non-Western populations.

Objective

- This study aimed to investigate the associations between hippocampal asymmetry, amyloid burden, and cognitive function, and to evaluate whether hippocampal asymmetry mediates the relationship between amyloid burden and cognition in older Thai adults.

Methods

- Retrospective, cross-sectional study of 93 Thai older adults (mean age 69.5 ± 6.4 years; 38.7% normal cognition, 50.5% mild cognitive impairment, 10.8% AD).
- Amyloid-β burden was measured using 18F-Florbetaben PET (Centiloid scale). High-resolution T1-weighted MRI was processed with the Winterburn protocol for automated segmentation of hippocampal subfields (CA1, CA2-3, CA4-dentate gyrus, SR-SL-SM, subiculum)
- Asymmetry indices were calculated for whole hippocampus and subfields.
- Cognitive function was assessed with a standardized neuropsychological battery: Memory (CERAD word list learning, delayed recall, recognition), Executive: CERAD verbal fluency, MoCA letter fluency, abstraction), Attention (MoCA digit span forward/backward, vigilance, MMSE serial 7s), Language (CERAD Boston naming), Visuospatial (CERAD constructional praxis)
- Statistical analyses were performed in STATA 18.5, using multiple linear regression and bootstrapped mediation models, adjusting for demographics, depression, and vascular risk; significance set at $p < 0.05$.

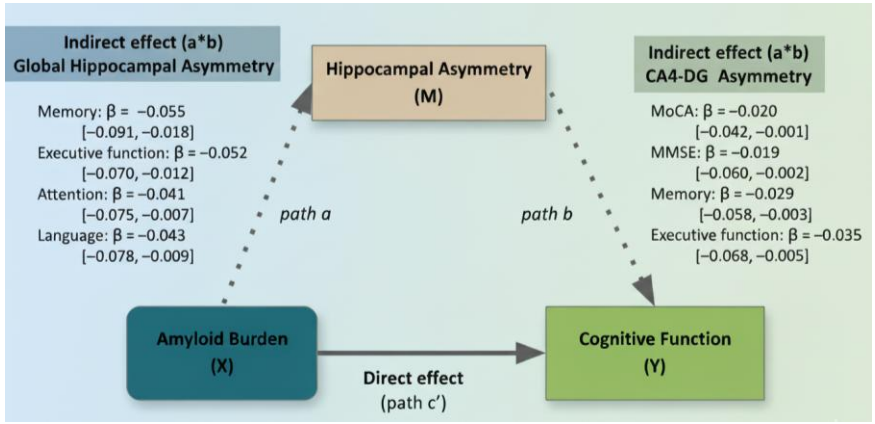

Figure 1: Hippocampal Asymmetry as a Mediator of Amyloid-Related Cognitive Decline

Results

- Higher global amyloid burden was significantly associated with poorer performance across multiple cognitive domains, with larger effect sizes observed for memory (β=–0.152, p<0.001) and executive function (β=–0.085, p<0.001)
- Global hippocampal asymmetry was not directly associated with cognitive scores, asymmetry of the CA4-dentate gyrus (CA4-DG) subfield was significantly linked to lower executive function (β=5.01, p=0.009) and memory (β=0.29, p=0.035).
- Mediation analysis revealed that the effect of amyloid burden on memory and executive function was significantly mediated by global hippocampal asymmetry (Fig.1) and more specific for CA4-DG asymmetry.

Conclusion

- Hippocampal subfield asymmetry, particularly of the CA4-DG region, serves as a sensitive structural mediator of amyloid-related cognitive decline in Thai older adults.
- These findings highlight the potential of refined, subfield-level MRI analysis as an accessible and biologically relevant biomarker for early AD detection and risk stratification, especially in resource-limited settings where PET imaging is not widely available.

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