

Depressive Symptoms And Accelerated Brain Ageing Interact To Reduce Cognitive Performance in Older Adults

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BACKGROUND

- Sub-clinical depression and the co-occurrence of depression with dementia have been shown to increase the risk of and accelerate cognitive decline in elderly.
- The involvement of other contributory factors in this relationship, however, remains poorly understood.
- One such potential factor is age-related neurodegeneration.

OBJECTIVE

- We investigate the interplay of depressive symptoms and abnormal brain ageing on cognitive function.

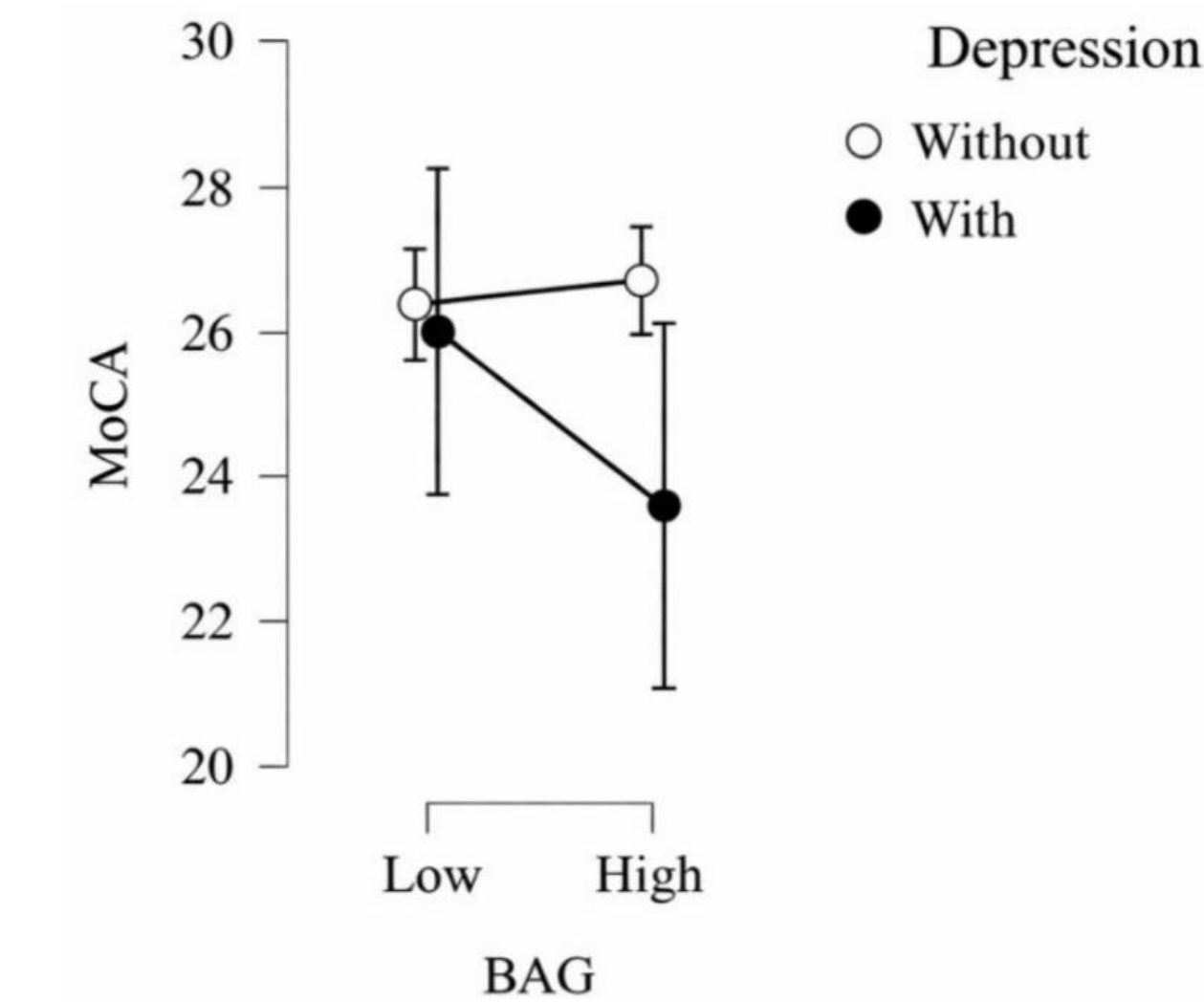
METHODS

- This cross-sectional study recruited 138 participants [23 healthy controls, 111 amnesic mild cognitive impairment and Alzheimer's Disease dementia, 4 vascular cognitive impairment/vascular dementia] from National Neuroscience Institute, Singapore between 2023 and 2025.
- Mood, anxiety and stress levels were obtained using the Depression Anxiety and Stress Scale - 21 Items.
- Abnormal brain ageing was measured using brain age gap (BAG), the difference between brain age, as derived from T1-weighted magnetic resonance imaging via a machine learning model, and chronological age.
- Global cognitive function was measured using the Montreal Cognitive Assessment.
- Neuropsychological assessment across cognitive domains was tested using the Repeatable Battery for the Assessment of Neuropsychological Status, Colour Trails Test and Boston Naming Test.

RESULTS

- Two-way Analysis of Covariance (ANCOVA) was performed to test the effects of depressive symptoms and BAG on MoCA, adjusting for covariates - age and education.
- The interaction effect (Depression × BAG) was significant, $F(1,132) = 4.23, p = 0.042$.
- The adjusted mean difference of MoCA between low and high BAG groups was 2.72-points for participants with depression, and 0 for those without.
- The simple effect of BAG within the depression group was significant, $F(1,132) = 5.36, p = 0.022$.
- Exploratory analyses examined the relationship between BAG and individual forms of psychological distress (depression, anxiety and stress) and cognitive function (overall cognition and across cognitive domains).
- Two-way ANCOVA showed no significant interaction effects in the models tested ($p > 0.05$).

Fig 1. The Relationship between BAG and Cognitive Function Varied by Depression



CONCLUSION

- Individuals with depressive symptoms and higher BAG showed poorer global cognitive function.
- Our findings provide further evidence that early screening for depressive symptoms should be implemented broadly in memory clinics to identify individuals who may be more susceptible to cognitive decline.
- Prevention programs should include mood-based interventions specifically targeting patients with signs of depression and increased neurodegeneration to improve brain health and cognitive outcomes.