

Chain Mediation of Nutrition and Cognition an *ApoEε4*'s Link to Neuropsychiatric Symptoms in Alzheimer's Disease



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This study provides novel evidence that MNA and MMSE scores act as chain mediators between APOE ε4 and three specific NPS (hallucinations, apathy, and aberrant motor activity) in aMCI/AD patients, underscoring the synergistic effects of nutrition and cognition on NPS development and highlighting targeted nutrition as a potential intervention to counteract APOE ε4-related NPS risk.

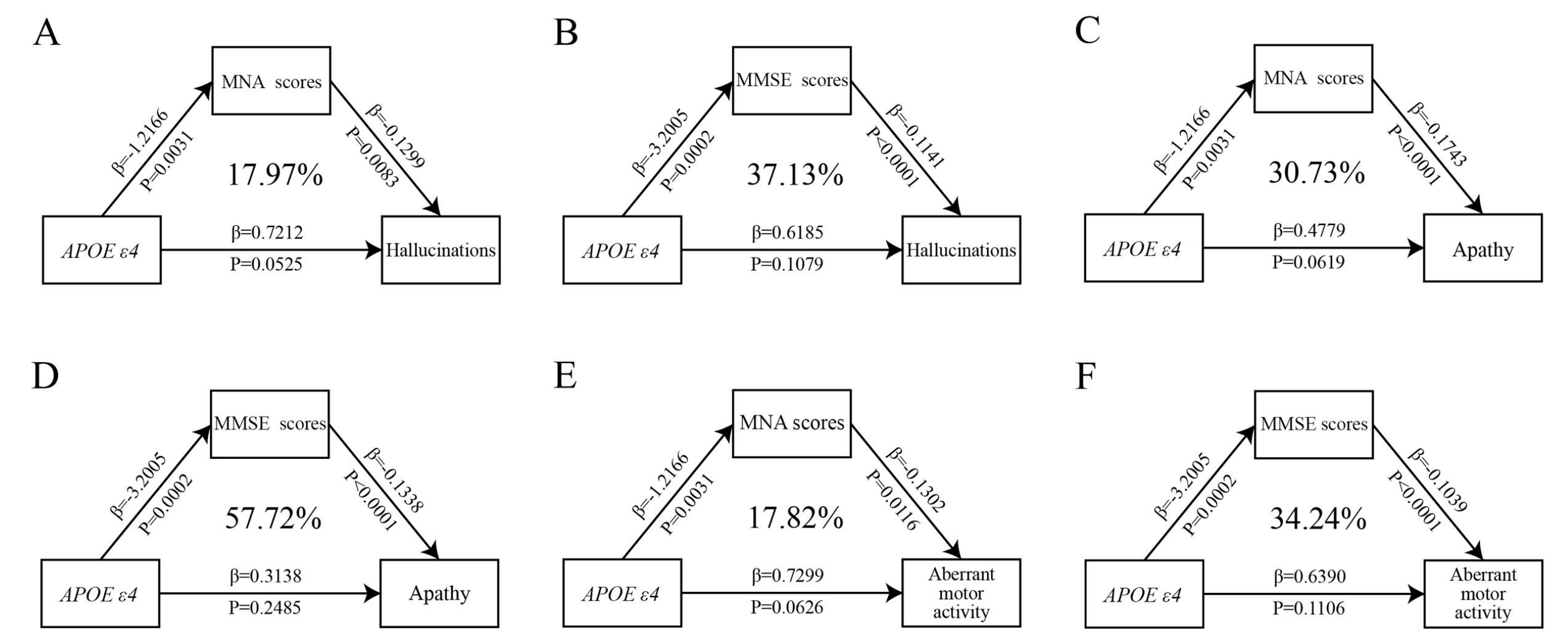
INTRODUCTION

Apolipoprotein E (*APOE*) is the most recognized risk gene for cognitive decline and clinical progression of late onset Alzheimer’s disease (AD); nonetheless, its association with neuropsychiatric symptoms (NPSs) remains inconclusive. This study aimed to investigate the association of *APOEε4* with NPSs and explore nutritional status and cognition as joint mediators of this association.

METHODS

Patients with amnesic mild cognitive impairment (aMCI) or AD were recruited from the CIBL study between June 2021 and October 2022. NPSs were assessed using the Neuropsychiatric Inventory, while global cognition and nutritional status were evaluated using the MMSE and Mini-Nutritional Assessment (MNA), respectively. Simple mediation and multiple chain mediation models were developed to examine the mediating effects of the MNA and MMSE scores on the relationship between *APOEε4* and specific NPS.

RESULTS



Chain-mediating effect of MNA and MMSE scores on the association of <i>APOE ε4</i> with three specific NPSs				
Pathway		Effect	SE	95% CI
Hallucinations				
Direct effect		<i>APOE ε4</i> →Hallucinations	0.5252	0.3974
Total indirect effect			0.2237	0.1158
Indirect effect		<i>APOE ε4</i> →MNA→Hallucinations	0.0228	0.0611
		<i>APOE ε4</i> →MMSE→Hallucinations	0.1497	0.0959
		<i>APOE ε4</i> →MNA→MMSE→Hallucinations	0.0512	0.0321
Apathy				
Direct effect		<i>APOE ε4</i> →Apathy	0.2619	0.2843
Total indirect effect			0.3973	0.1613
Indirect effect		<i>APOE ε4</i> →MNA→Apathy	0.0986	0.0699
		<i>APOE ε4</i> →MMSE→Apathy	0.2226	0.1197
		<i>APOE ε4</i> →MNA→MMSE→Apathy	0.0761	0.0447
Aberrant motor activity				
Direct effect		<i>APOE ε4</i> →Aberrant motor activity	0.5670	0.4065
Total indirect effect			0.2341	0.1288
Indirect effect		<i>APOE ε4</i> →MNA→Aberrant motor activity	0.0353	0.0621
		<i>APOE ε4</i> →MMSE→Aberrant motor activity	0.1491	0.0990
		<i>APOE ε4</i> →MNA→MMSE→Aberrant motor activity	0.0496	0.0357

CONCLUSIONS

Nutritional status and cognition jointly mediate the association between *APOEε4* and neuropsychiatric symptoms in patients with aMCI or AD.

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