Association of the plasma levels of short chain fatty acids with amyloidosis, tau pathology and neurodegeneration in patients with Alzheimer's Disease

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Introduction

Short chain fatty acids (SCFAs) are gut microbial metabolites found altered in Alzheimer's disease (AD) animal models and in the saliva of AD patients. Data on SCFAs in the plasma of AD patients and their association with disease pathology are scarce.

The aims of the present study were to compare the SCFAs plasma level in patients with cognitive impairment due to AD (CI-AD), not due to AD (CI-NAD) and cognitively unimpaired subjects (CU) and assess their association with the hallmarks of AD and its diagnosis.

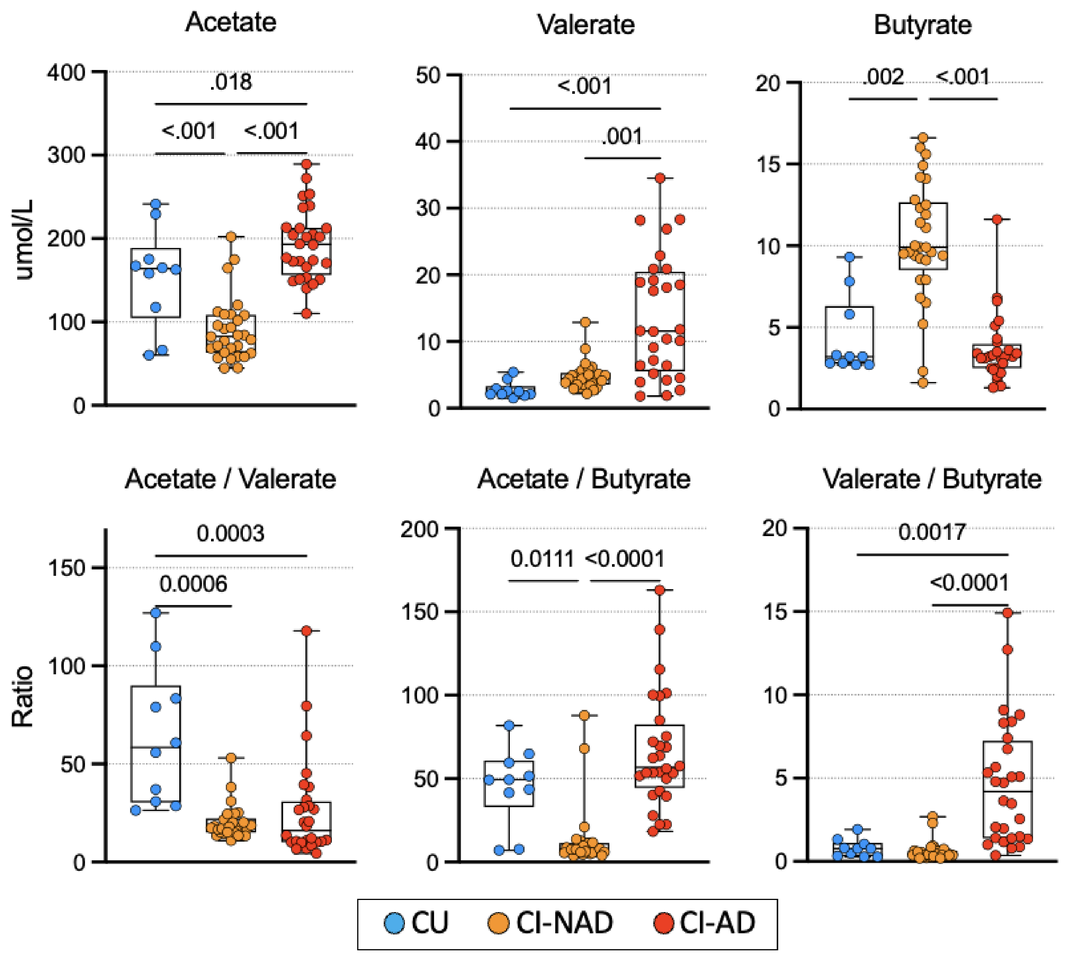
Methods

A cohort of 84 subjects comprising 28 CI-AD, 29 CI-NAD, and 10 CU were enrolled from the IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli in Italy.

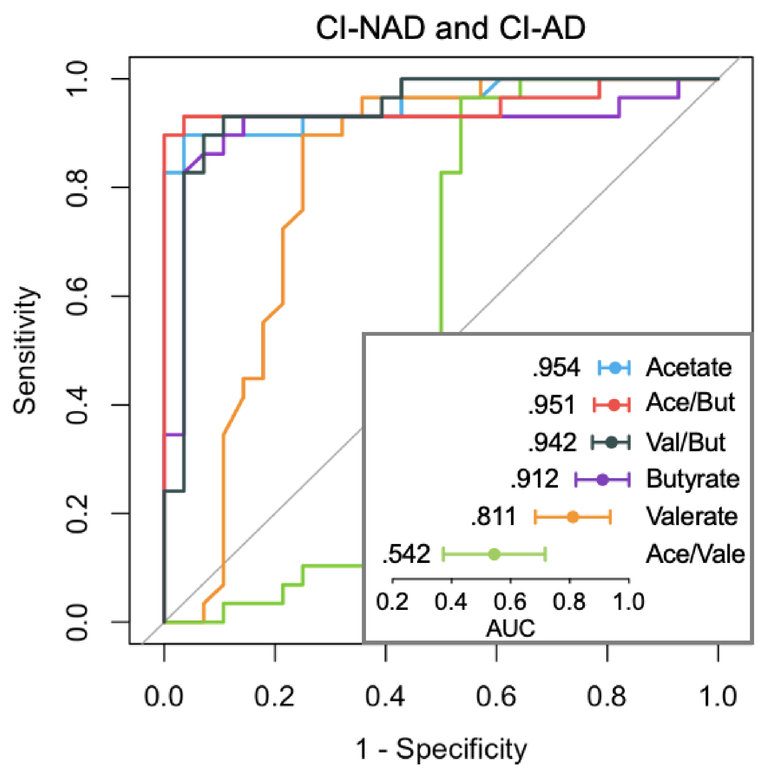
Plasma levels of SCFAs were measured by GC-FID gas-chromatography and included acetate, propionate, valerate and butyrate. AD markers included amyloid PET, plasma phosphorylated tau (pTau-181), Neurofilament light chain (NfL), plasma glial fibrillary acidic protein (GFAP). Global cognitive performance was measured using MMSE and ADAScog.

Results

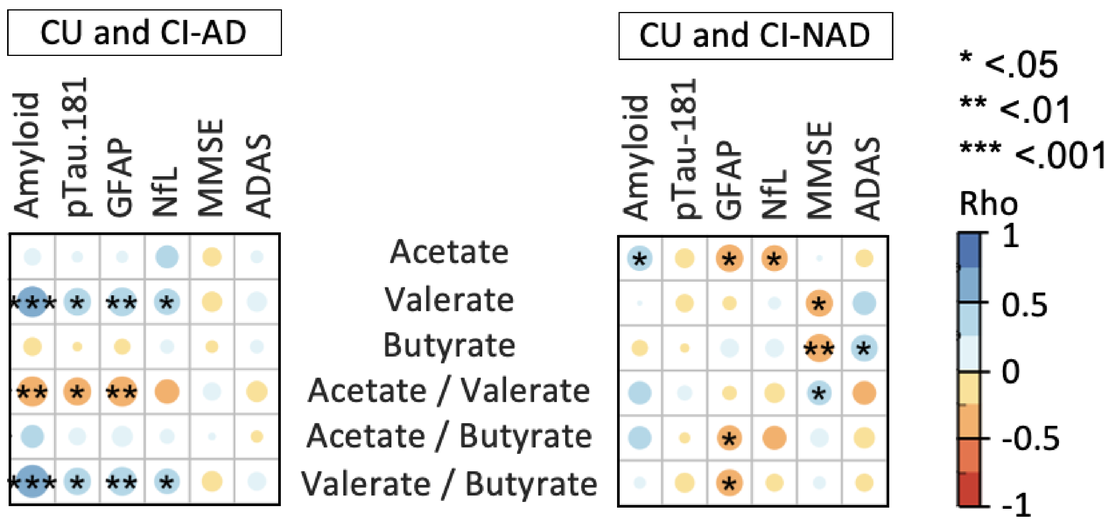
CI-AD were characterized by elevated acetate, valerate, valerate/butyrate and acetate/valerate ratios and CI-NAD by reduced acetate, acetate/butyrate ratio and increased butyrate



In the distinction between CI-AD and CI-NAD, acetate showed better accuracy than the other SCFAs and the best plasma AD biomarker, GFAP



Valerate, valerate/acetate and valerate/butyrate ratios were positively associated with amyloid and tau pathology as well as neurodegeneration but not cognitive impairment in CU and CI-AD



Conclusion

These results support the hypothesis that gut bacteria may modulate AD pathology via circulating molecules such as the SCFAs. Their use for diagnosis and as treatment target deserve further studies.

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