

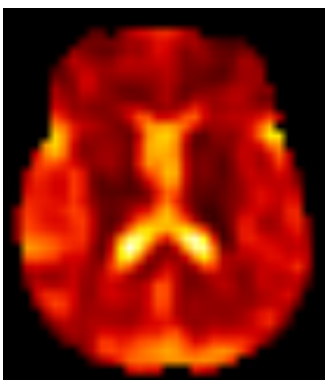
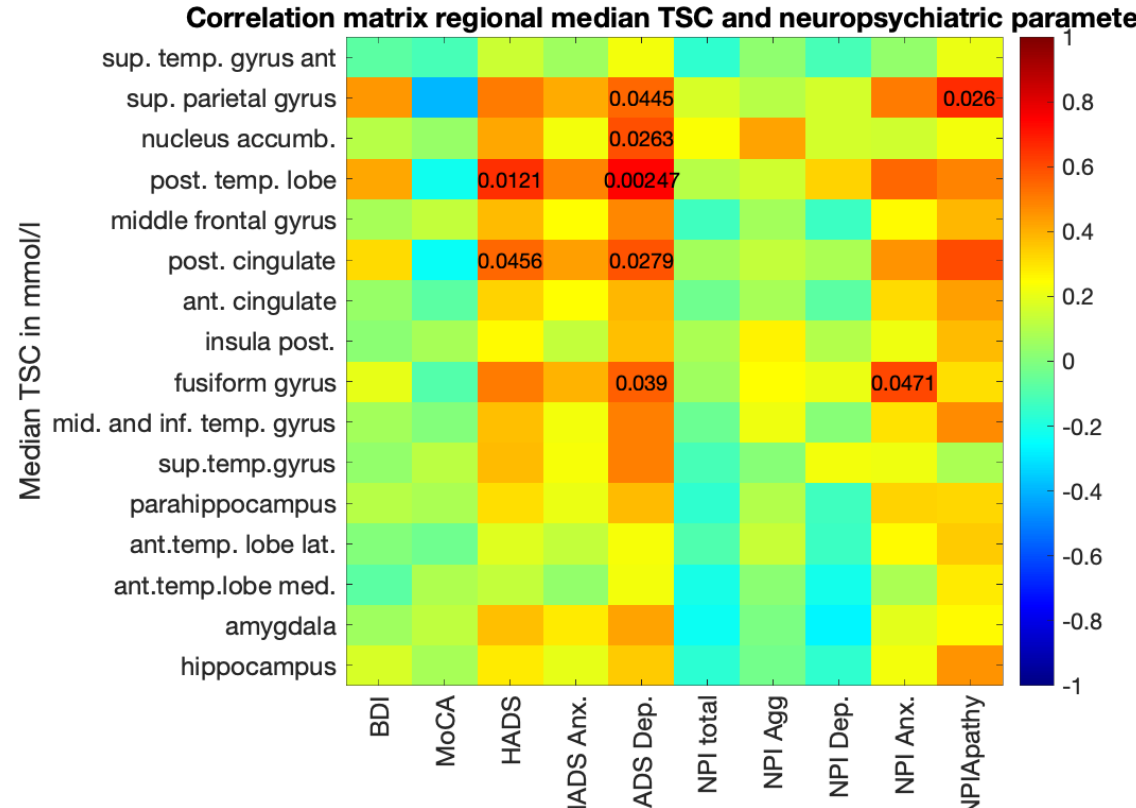
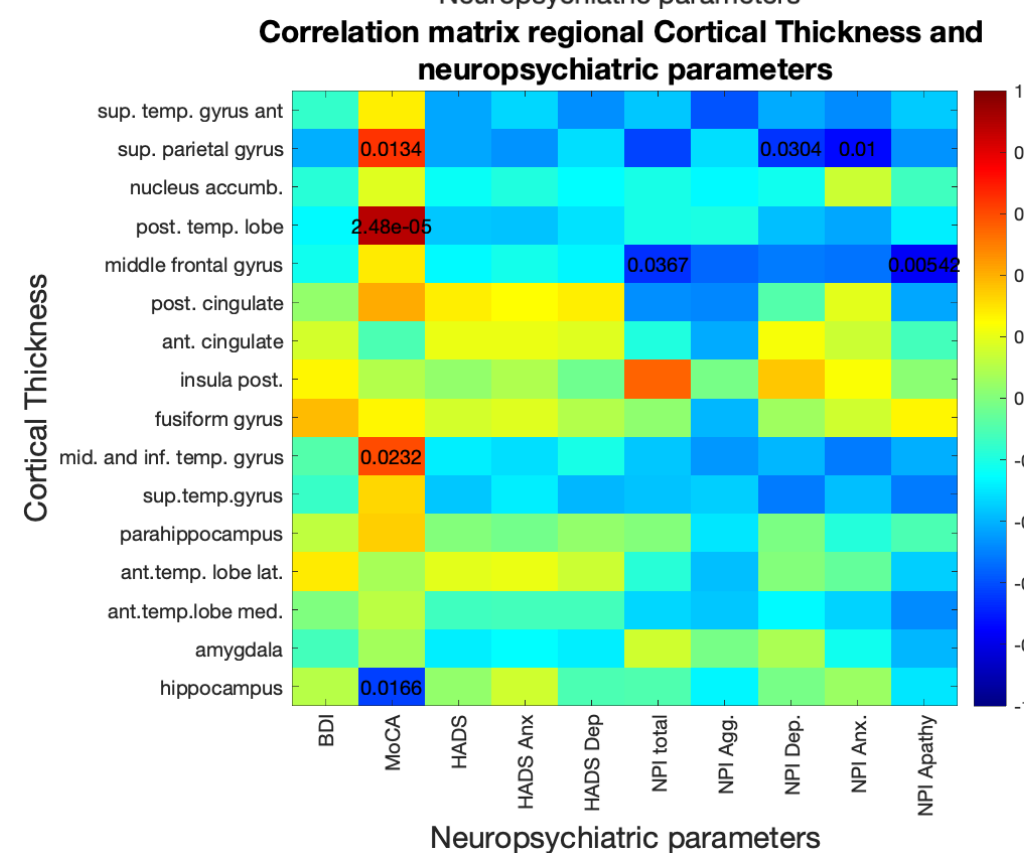
Differentiating Late-Life Depression from Alzheimer’s Disease Using Metabolic Brain Imaging

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Due to its clinical and preventive relevance, investigation of the pathophysiological changes in mild cognitive impairment (MCI) due to late-life depression (LLD) in comparison with Alzheimer's disease is highly relevant. We show that amyloid- and tau-negative patients with MCI due to LLD still show metabolic alterations in substructures of the temporal lobe and cingulate cortex, supporting a link between LLD and neuro-degeneration beyond Alzheimer’s pathology.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS
Late-life depression (LLD) is a relevant risk factor for dementia but also represents a prodromal symptom. Mild cognitive impairment (MCI) can occur in both depression and early Alzheimer’s disease (AD), complicating clinical differentiation. Prior MRI point to an association between depression and energy deficiency, reduced metabolism, and altered neurotransmission. Characterizing distinct cerebral and metabolic changes in MCI due to AD versus depression may improve understanding of underlying pathophysiological mechanisms and support prevention strategies.	Three participant groups including (1) MCI due to AD according to NIA-AA criteria with a cerebrospinal fluid (CSF)-constellation matching the AD-continuum¹; (2) MCI due to depression with no neurodegeneration in CSF; and (3) cognitively unimpaired control subjects are included. Study participants are examined via a multimodal MRI protocol including structural and metabolic 3T-MRI sequences with sodium brain imaging (²³Na-MRI)². 115 subjects participated so far.  23Na-MRI	55 patients with AD (mean age 66.9 ± 8 years; MoCA 18.4±6; BDI-II 7.1±6.2), 26 patients with depression-related MCI (62.6±6.7 years; MoCA 22.4±3.7; BDI 17.1 ± 12.3), and 34 controls (60.4±5.5 years; MoCA 27.3±1.9; BDI 4.1±3.9) were included. Preliminary neuroimaging analyses indicate increased tissue sodium concentration (TSC) in AD compared to controls. Depression-related MCI showed increased normalized TSC in the parahippocampus, anterior and posterior cingulate, and insula compared to controls. Structural differences were more limited, with reduced superior parietal volume and temporal gyrus cortical thickness. Preliminary correlation analyses in AD (<i>n</i>=14) suggest more pronounced associative patterns between neuropsychiatric measures and TSC compared with classical volumetric measures and cortical thickness. Correlation matrix regional median TSC and neuropsychiatric parameters  Median TSC in mmol/l Correlation matrix regional Cortical Thickness and neuropsychiatric parameters  Cortical Thickness	Our findings point to possible region-specific metabolic alterations in depression-related MCI, particularly in temporal lobe subregions and the cingulate cortex. Detecting these changes may support diagnostic differentiation and contribute to understanding pathways linking LLD to neurodegeneration for future.
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REFERENCES 1) Jack et al., Alzheimer's & Dementia, 2018 2) Haeger et al., 2022, Neuroimage Clinical			