

Twenty cognitively healthy elderly persons were used as controls (age 72 ± 8 , MMSE 29 ± 1). Patients were followed for 4 years and assessed yearly with a comprehensive neuropsychological and behavioural battery and 16 converted to AD (cMCI, age 73 ± 5 , MMSE 26 ± 2) while 30 remained stable (sMCI, age 67 ± 8 , MMSE 28 ± 2). A voxel-based statistical mesh modeling technique (cortical pattern matching) and a related region-of-interest analysis based on Brodmann areas (BAs) were used to map gray matter volume changes between groups and over time. **Results:** At baseline (T0), cMCI patients had 10-30% lower cortical gray matter volume than healthy controls in regions known to be affected by AD pathology (entorhinal, temporoparietal, posterior cingulate, and orbitofrontal cortex, $p < .0001$). sMCI patients had on average 10-20% volume deficits confined to the posterior cingulate and orbitofrontal cortex ($p < .008$). Patients with cMCI were losing 10-15% more gray matter than sMCI during the time interval between T0 and T1 scans, in the posterior cingulate/retrosplenial and frontal, medial temporal and temporal polar cortices ($p < .024$), with the olfactory network being more involved. **Conclusions:** Structural gray matter changes in amnesic MCI patients who develop AD in the short term map to cortical areas pertaining to memory networks known to be affected in the earliest stages of the pathology.

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THE RELATIONSHIP OF WHITE MATTER HYPERINTENSITIES TO DEPRESSION AND APATHY IN MILD COGNITIVE IMPAIRMENT

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Background: Depressive symptoms have been associated with changes in specific neuroimaging measures, including white matter hyperintensities (WMHs), in community dwelling older adults. In individuals with dementia, both apathy and depression have been associated with various changes, including atrophy in the dorsolateral prefrontal cortex (DLPFC) and hippocampus, hypoperfusion in the anterior cingulate, and frontal and right parietal WMHs. The aim of the current study was to investigate the relationship between WMHs and apathy and depression in Mild Cognitive Impairment (MCI). **Methods:** Participants in the current study were 419 community-dwelling individuals enrolled in the Sydney Memory and Ageing Study who had MRI scans and were able to be classified as either having no cognitive impairment (60%) or MCI. Apathy was measured with 7 questions derived from an informant-based interview, and validated with factor analysis and correlational analysis. Depression was measured with the 15-item Geriatric Depression Scale (GDS). WMH proportions were defined as the volume of WMHs on T2 FLAIR divided by the volume of the region of interest. **Results:** In the whole sample, higher right parietal WMH proportions were associated with higher depression scores after controlling for age, sex, and education. This relationship was not found to be significant in the separate MCI or cognitively unimpaired groups however. Unexpectedly, higher frontal WMH proportions were associated with lower apathy scores after controlling for age, sex, and education. This negative relationship also held within the MCI group, but not within the cognitively unimpaired group. After adding GDS in as a control variable, these findings remained, thus indicating that these do not simply reflect relationships of WMHs with depression. This was further supported by a low correlation between GDS and apathy scores. **Conclusions:** The distinct findings for apathy and depression suggest different mechanisms underlying each. These results for MCI differ from previous findings in dementia, indicating a distinction between the two disorders in terms of the relationship between white matter pathology and these psychological factors.

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USE OF AN ALZHEIMER'S DISEASE-RELATED HYPOMETABOLIC CONVERGENCE INDEX TO PREDICT PROGRESSION FROM MILD COGNITIVE IMPAIRMENT TO ALZHEIMER'S DEMENTIA

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Background: Using fluorodeoxyglucose positron emission positron emission tomography (FDG PET) data from the Alzheimer's Disease Neuroimaging Initiative (ADNI), we introduce the concept of an AD-related "hypometabolic convergence index (HCI)," a single voxel-based index which, in comparison with data from normal control (NCs), reflects the extent to which the pattern and magnitude of hypometabolism in an individual subject converges with the pattern and magnitude of hypometabolism in probable AD patients. After using a cross-validation procedure to identify the threshold for each biomarker, cognitive, or clinical measurement to distinguish between MCI converters and non-converters, we characterize and compare the ability of abnormal HCIs, other magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) measurements, memory scores and clinical ratings in predicting 18-month progression from mild cognitive impairment (MCI) to Alzheimer's dementia. **Methods:** The Cox proportional hazards model was used to characterize and compare the prediction ability of "abnormal" HCIs, hippocampal volumes, CSF $A\beta_{1-42}$, t-tau, p-tau_{181p} levels and ratios, auditory verbal learning test total and long-term memory (LTM) scores, and three different clinical ratings to predict time-to-progress to Alzheimer's dementia. **Results:** Abnormally high HCI's and small hippocampal volumes were associated with the highest odds of 18-month progression from MCI to Alzheimer's dementia (OR = 7.38 and 6.35, respectively), more likely to progress to AD than those who were normal. ORs for the other biomarker, cognitive and clinical measurements were between 1.33 and 4.94. MCI patients with both an abnormally high HCI and abnormally small hippocampal volume had an even higher odds ratio of clinical progression (OR = 36.72), and each of these measurements were correlated with cognitive and clinical measurements of disease severity in the overall group of probable AD, MCI and NC subjects. **Conclusions:** While additional studies are needed, the HCI offers promise in automatically characterizing the AD-related pattern of hypometabolism in FDG PET images in a single measurement, predicting progression from MCI to Alzheimer's dementia alone or in combination with hippocampal volume measurements, and providing an indicator of disease severity in different clinical and research settings. Among other things, it raises the possibility of generating Alzheimer's disease-related convergence indices using imaging modalities and voxel-based data analysis algorithms.