

## Visualizing stages of cortical atrophy in progressive MCI from the ADNI cohort

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**Learning objectives:** To investigate the cortical pattern of atrophy at different stages in patients with mild cognitive impairment (MCI), which progress to clinically definite Alzheimer's disease.

**Topic area:** Neuroimaging – Early detection and tracking

**Keywords:** ADNI, Alzheimer's disease, MCI, MRI, cortical thickness, prediction

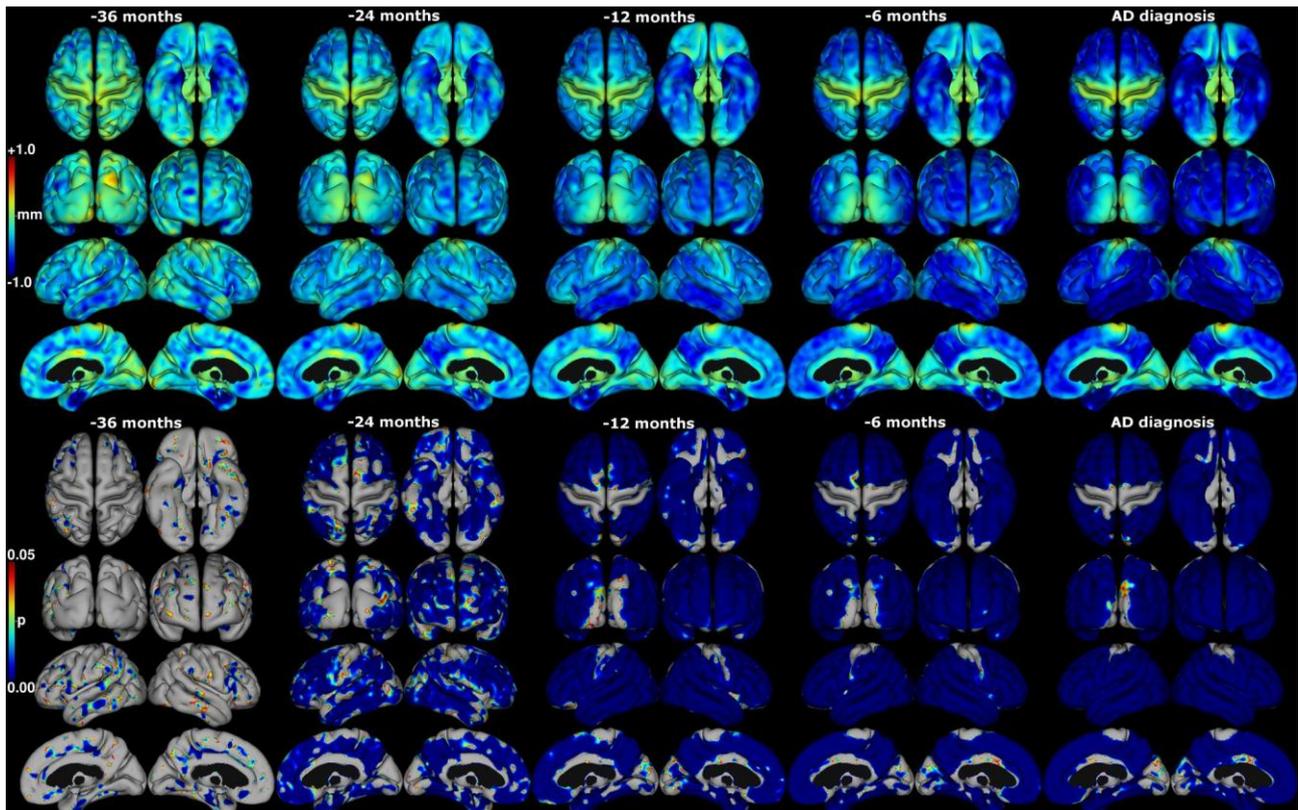
**Background:** Amnesic mild cognitive impairment (MCI) is considered a condition where patients are at risk of developing clinically definite Alzheimer's disease (AD) with an annual conversion rate of approximately 15%[1]. AD is characterized by progressive brain atrophy with major impact on the cerebral cortex and medial temporal lobe structures such as hippocampus. Understanding the structural pattern of cortical atrophy at different stages of MCI, before AD can be diagnosed, may help in patient monitoring and prognosis. We used data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) to calculate and visualize the cortical atrophy at different stages in patients who eventually converted to clinically definite AD.

**Methods:** We selected patients with a diagnosis of MCI from the ADNI database who converted to AD during the follow-up period. T1-weighted MRI scans were collected at time of conversion (n=140) and at intervals prior to the date of conversion: 6 months (n=121), 12 months (n=128), 24 months (n=62) and 36 months (n=29). As control group we collected all baseline scans of healthy controls (HC) (n=226). Images were denoised[2], bias field corrected[3], linearly co-registered[4], skull-stripped[5], and cortical thickness were measured using FACE[6] and mapped to an average cortical surface. Statistical maps of differences in cortical thickness between groups of MCI patients and HC were constructed and corrected for multiple comparisons.

**Results:** Three years prior to clinically definite AD, the MCI patients show signs of atrophy in the parahippocampal gyrus, the cingulate gyrus and temporal lobes (figure). At two years before conversion, atrophy has spread to large parts of the temporal and frontal lobes, much of the cingulate gyrus and parts of the orbitofrontal region. Twelve months before conversion, atrophy is present over all the cortex except

the occipital lobe and the sensory-motor areas. Six months later and at conversion this pattern persists, but with more severe atrophy.

**Conclusions:** Focal atrophy can be observed in patients with MCI three years before they are diagnosed with clinically definite AD. The atrophy accelerates during the MCI stage and affects the entire cortex except the occipital and sensory-motor cortex at the time of diagnosis - not unlike the progressive patterns of amyloid deposition described by Braak[7]. These patterns may be used to assess the disease progression in patients with MCI.



Cortical thickness statistics of MCI patients compared to healthy controls at intervals before AD diagnosis and at time of diagnosis. Top row: differences in mean cortical thickness. Bottom row: statistical maps of differences in cortical thickness. FDR corrected p-maps.

#### References:

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