

## **In vivo neuropathology of cortical changes in incipient Alzheimer's disease**

Annapaola Prestia, PsyD <sup>(1)</sup>, Paul E. Rasser, MSc <sup>(2)(3)</sup>, Matteo Bonetti, MD <sup>(4)</sup>, Paul M. Thompson, PhD <sup>(5)</sup>, and Giovanni B. Frisoni, MD <sup>(1)(6)</sup>

<sup>(1)</sup> Laboratory of Epidemiology Neuroimaging and Telemedicine, IRCCS Centro San Giovanni di Dio FBF, The National Centre for Research and Care of Alzheimer's and Mental Diseases, Brescia, Italy

<sup>(2)</sup> Schizophrenia Research Institute, Sydney, Australia

<sup>(3)</sup> Priority Centre for Brain & Mental Health Research and School of Design, Communication & I.T., University of Newcastle, Newcastle, Australia

<sup>(4)</sup> Service of Neuroradiology, Istituto Clinico Città di Brescia, Brescia, Italy

<sup>(5)</sup> Laboratory of Neuro Imaging, UCLA School of Medicine, Los Angeles, USA

<sup>(6)</sup> Psychogeriatric Ward, IRCCS Centro San Giovanni di Dio FBF, The National Centre for Research and Care of Alzheimer's and Mental Diseases, Brescia, Italy

**Corresponding Author:** Giovanni B. Frisoni, IRCCS Fatebenefratelli, via Pilastroni 1, 25125

Brescia, Italy - Telephone +39 030 3501361, email [gfrisoni@fatebenefratelli.it](mailto:gfrisoni@fatebenefratelli.it)

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## **Abstract**

**Background:** Patients with mild cognitive impairment (MCI) have memory deficits without functional impact on activities of daily living and have a 10-fold greater risk of developing Alzheimer's dementia (AD) in the following 5 years. Neurodegenerative changes in patients with AD at the dementia stage have been well characterized using structural magnetic resonance imaging (MRI) but earlier changes are still relatively poorly understood. Here we aimed to map the cortical changes in MCI patients, a subgroup of whom later developed AD.

**Methods:** Structural T1-weighted high-resolution MR scans were acquired at baseline (T0) and after  $1.4 \pm 0.3$  (SD) years (T1) from 46 elderly patients with amnesic MCI (age  $69 \pm 8$  years, MMSE  $27 \pm 2$ ). Twenty cognitively healthy elderly persons were used as controls (age  $72 \pm 8$ , MMSE  $29 \pm 1$ ). Patients were followed for 4 years and assessed yearly with a comprehensive neuropsychological and behavioural battery and 16 converted to AD (cMCI, age  $73 \pm 5$ , MMSE  $26 \pm 2$ ) while 30 remained stable (sMCI, age  $67 \pm 8$ , MMSE  $28 \pm 2$ ). 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.

**Conclusion:** 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.

**Key words:** Mild Cognitive Impairment, Alzheimer disease, early diagnosis, neuroimaging, Brodmann areas;

**Topic area:** Diagnosis, neuroimaging, and clinical course of Alzheimer's disease and related disorders