

## STRUCTURAL MRI - THE CONTINUUM FROM NORMAL AGING TO ALZHEIMER'S DISEASE

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Structural MRI changes that are seen in normal aging and Alzheimer disease (AD) include atrophy, white matter hyperintensities, iron accumulation, microbleeds and invisible changes. Similar findings occur with Alzheimer's disease and for all lesion type a continuum exists between the normal and the disease status. Automated measurement methods allow to determine loss of brain volume over time, and importantly either visual or automated measurement of atrophy of the medial temporal lobe has become a supportive feature in the diagnosis of prodromal AD. White matter abnormalities are almost ubiquitous in the brains of elderly people and patients with Alzheimer's disease. Microbleeds are less common, but they appear to be related to white matter changes and both types of lesions are considered to represent the radiological correlate of small vessel disease. White matter lesions and microbleeds predict cognitive decline in normal aging and evidence emerges that the same is true in Alzheimer dementia. The importance of white matter hyperintensities in the aging brain depends on the type of abnormalities. Coalescent lesions have a malignant course, while punctuate changes in the deep white matter and most periventricular lesions are benign. Studies examining the regional distribu-

tion of white matter lesions and microbleeds in Alzheimer disease suggest a heterogeneous etiology of lesions with posterior involvement being suggestive of amyloid angiopathy and frontal location suggesting arteriolosclerosis. Different location may be linked to different clinical outcome, but even more importantly in the context of anti-amyloid treatment strategies different risk for adverse events such as vasogenic edema or bleeding. The natural course of small vessel disease related brain changes, particularly of cerebral microbleeds in normal aging and Alzheimer's disease is widely unknown, but represents a crucial issue when using these abnormalities in clinical trials to determine adverse or beneficial treatment response. Iron accumulates with age in a region-specific manner and most interestingly ultra-high field magnets allow to delineate iron in plaques. This method has thus been suggested to represent a way of non-invasive in vivo study of cortical amyloid plaque detection. Microstructural tissue changes in normal appearing brain tissue as seen with diffusion tensor and magnetisation transfer imaging play an important role in cognitive decline during normal aging, the contribution of such tissue alterations in AD are less well explored.