

ALZHEIMER'S DISEASE

Alzheimer's disease

Prof Roberto Cappai

The University of Melbourne - Department of Pathology

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Alzheimer's disease (AD) is the most common form of dementia and is characterized by progressive memory loss, confusion, and cognitive deficits. In 2011, an estimated 269,000 Australians are currently living with dementia and without a significant medical breakthrough soon, it is anticipated that this will rise to about 981,000 by 2050 [1]. The major pathological hallmarks of AD are significant loss of neurons and the nerve terminals (synapses) as well as the deposition of protein aggregates typified by the extracellular amyloid beta containing plaques and the intracellular neurofibrillary tau containing tangles. Definitive diagnosis involves post mortem examination of brain pathology, in combination with the clinical assessment.

The etiology of AD remains unresolved. About 5-10% of cases are due to dominantly inherited familial AD (FAD). Three genes have been identified to cause FAD: amyloid precursor protein, Presenilin 1 and Presenilin 2. Point mutations, deletions or gene copy number variation will lead to dominantly inherited forms that typically have an earlier age of onset. The majority of AD is deemed to be sporadic with a late onset and the exact cause(s) are unknown. Aging is a clear risk factor with a marked increase in the number of cases as people age beyond 70. There is doubling in incidence for every 5 years from 70 onwards. Approximately 20-25% of people in the 85 plus age group are affected by AD. ApoE4 allele remains the strongest genetic risk factor for AD, where carriers of the apoE4 allele have a significantly greater likelihood to develop AD than E3 and E2 carrier. It is important to note that in themselves, neither aging nor apoE4 status will necessarily lead to AD; they just increase the likelihood of developing the disease. Despite extensive genome wide studies other major risks factors have not been identified. Nor have major environmental or lifestyle factors. To shed further light on this important issue, large longitudinal studies are underway to study the development of dementia in normal and cognitively impaired cohorts to identify genetic, lifestyle and biomarkers that could allow us to detect and treat, much earlier, individuals who are at risk from developing the disease.

A significant advancement in the earlier diagnosis of disease has been the development of imaging techniques based on positron emission tomography (PET) to detect amyloid in living subjects. This has the potential to identify and quantitate brain amyloid beta plaque burden via a non-invasive technique. The quantification of amyloid plaque loads by PET could play an important role in the treatment and management of AD by permitting early and more accurate diagnosis of subjects. Importantly, recent advancements have been made in creating PET ligands that can detect tau deposits. This would allow the assessment of tau pathology in AD subjects, and allow the differentiation of AD from other dementias that have a stronger tau component. As the field tries to develop drugs that target either amyloid beta and/or tau, these PET imaging techniques will be important for monitoring the effectiveness and specificity of the drugs.