ALZHEIMER'S DISEASE

The early detection of Alzheimer's disease

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Alzheimer's disease is a neurodegenerative disorder characterised by a slow decline in cognition, particularly memory and executive functions, as well as changes in mood and personality. As the disease progresses and cognitive function worsens, the performance of even the most routine tasks of daily living become impossible. As a result, Alzheimer's patients are highly dependent on specialised care, placing significant emotional strain on both patients and caregivers. Although individuals as young as 30 years of age can be affected by the disease, the vast majority of cases occur in older individuals. Considering the rate at which the global population is ageing, it is predicted that the incidence of those affected will increase markedly over the next few decades, making Alzheimer's disease one of the most pressing health issues of this century. Despite considerable research over recent years aimed at developing therapies for Alzheimer's disease, there are currently no effective treatment strategies for arresting disease progression.

A large reason for the limited success of current treatments relates to the stage of disease progression at which a diagnosis can be made. The diagnosis of Alzheimer's disease relies heavily upon clinical assessments of cognitive function, requiring deficits in memory and other cognitive domains to be so severe that activities of daily living are compromised. Clinical symptoms manifest relatively late during disease progression, and it is likely that considerable damage will have already occurred prior to a clinical diagnosis being made. Therefore, being able to diagnose patients at the earliest, preclinical stages of the disease is crucial for allowing therapeutic intervention the best chance of arresting disease progression.

A key feature of the Alzheimer's disease brain is the deposition of misfolded proteins, namely ß-amyloid (Aß), forming extracellular neuritic plaques, and tau filaments, forming intracellular neurofibrillary tangles. These plaques and tangles are thought to be the primary factors initiating neuronal dysfunction and cortical thinning, which in turn produce deficits in cognitive ability. There has been much recent interest in the diagnostic application of biomarkers that indicate the incidence of these pathological changes. In particular, over the course of the past decade there has been a growth in the use of neuroimaging techniques in Alzheimer's disease patients. Initially used as standard diagnostic practice to exclude other potentially treatable causes of dementia symptoms, neuroimaging has now been implemented (in research settings, at least) to detect brain changes specific to Alzheimer's disease aetiology. For instance, structural neuroimaging techniques such as computerised tomography (CT) and magnetic resonance imaging (MRI) can be used to detect cortical thinning and volume loss in those brain regions most affected by plaques and tangles in Alzheimer's patients. Similarly, functional neuroimaging techniques such as positron emission tomography (PET) and single-photon emission computerised tomography (SPECT) can be used to detect metabolic changes in these same brain regions, providing an indirect

measure of neuronal dysfunction. PET imaging may also be used to visualise plaque and tangle formation in Alzheimer's patients using radiotracers that bind fibrillar forms of Aß and tau, respectively. In particular, PET imaging of Aß plaques may provide an early marker of Alzheimer's disease pathology before structural and/or functional brain changes manifest.

Neuroimaging biomarkers have become an important factor in Alzheimer's disease research, not only by advancing our understanding of the underlying brain processes but also by providing a means to assess the effectiveness of new drug treatments. However, their diagnostic application in the clinic has yet to gain routine use. This has been due to several factors, including a lack of standardised testing protocols, as well as limitations with widespread applicability in various community settings due to their high cost and reliance on specialist equipment. Additionally, many individuals who show signs of Alzheimer's disease, as assessed using these neuroimaging biomarkers, may never develop symptoms.

The ability to detect Alzheimer's disease-related brain changes in individuals prior to the development of cognitive impairment is key to more effective early intervention. Although neuroimaging biomarkers have shown great promise, more research will be required to develop low-cost and highly standardised testing protocols capable of accurately detecting those cognitively intact individuals at increased risk for developing the disease. Should these requirements be met, it is not unlikely that these biomarkers will be considered alongside clinical assessment as standard practice in the early diagnosis of Alzheimer's disease.