Alzheimer’s disease (AD) is the most common form of dementia and currently affects over 27 million people worldwide (Qiu, De Ronchi et al. 2007; Access Economics 2009). The earliest notable symptom of AD is a decline in episodic and working (short-term) memory (Backman and Small 1998), usually accompanied by behavioural changes. The progression of AD is associated with a gradual decline in long-term memory (Backman, Jones et al. 2005), and in later stages of the disease, a complete loss of self care and communication skills occurs, which eventually results in the need for long term and constant care (McKhann, Drachman et al. 1984). Patients with AD generally survive 7-10 years after diagnosis (Brookmeyer, Corrada et al. 2002).

The world’s population is growing older due to improved healthcare and nutrition. Consequently, AD prevalence will exponentially increase in the coming decades (Anderson and Hussey 2000), resulting in a worldwide epidemic requiring billions of dollars of government funding for the care and treatment of individuals with this disease. In Australia, projections indicate that approximately one million individuals will be suffering from dementia-related illnesses by 2050, with AD accounting for approximately 70% of these cases. This rise in AD cases will have a devastating financial impact, with projected increases in the yearly cost of care climbing from $11.1 billion in 2010 to an estimated $59.6 billion in 2050 (Access Economics 2009). Currently, no cure for AD exists, thus it is essential that effective preventative approaches to delay onset are developed thereby reducing incidence and prevalence of this devastating disease.

Both micro and macroscopic changes are evident in the brain of AD patients, with regions associated with learning and memory particularly affected. AD pathology is characterised by the presence of extracellular amyloid plaques and intracellular neurofibrillary tangles (Goedert 1993; Masters and Beyreuther 1995). Beta-amyloid (Aβ), the toxic protein cleaved from amyloid precursor protein, forms the basis of the amyloid plaques, and can also accumulate around blood vessels, resulting in a condition known as cerebral amyloid angiopathy (CAA; Revesz, Holton et al. 2002).

There is much debate as to whether these hallmarks are causative or result from other pathophysiological processes. Multiple factors have been implicated in the aetiology and pathogenesis of AD. These factors include genetic defects, energy metabolism deficits, inflammation, abnormal amyloid precursor protein processing, deficiency of neurotrophic factors, glutamate excitotoxicity and free-radical induced neuronal degeneration. It is unlikely that any of these factors are isolated, and far more likely that a ‘complex web’ of dysfunctional biochemistry is established, resulting in characteristic AD pathology.
Regardless of aetiology, the net result is the same, with cumulative pathology causing failure of information transfer at the synapses, which triggers synaptic decline, leading to death of neurons. This neuronal death results in loss of brain volume, which begins in the hippocampus, a brain structure vital to learning and memory.

Advances in imaging techniques have enabled visualisation and quantification of amyloid burden within living brain. We now know that brain amyloid deposition commences well before detectable cognitive change, and approximately 15-20 years before clinical diagnosis of AD (Villemagne, et al. 2013). This time course of Aβ deposition thereby provides a potential window of opportunity to change disease trajectory. Thus, attention has turned to identifying lifestyle factors that may influence disease course.

Leading a healthy lifestyle, including regular physical activity, good diet, and remaining mentally active, appears to be protective, however the contribution of one critical lifestyle element, namely sleep, remains poorly understood. Poor sleep appears to act as a risk factor both for developing AD and for increased disease severity. AD animal model data suggests a link between poor sleep and increased amyloid deposition in the brain (Kang et al. 2009). Furthermore, a recent study of community-dwelling older adults at one time-point described an association between self-reported shorter sleep duration, and poorer sleep quality and greater brain amyloid burden (Spira et al. 2013).

With AD incidence expected to quadruple by mid-century, there is an urgent need for an effective treatment; however, development of preventative strategies is also critical. How sleep quality correlates with cognitive decline, AD pathology and risk is not yet fully understood and understanding this relationship will likely contribute to the evolution of preventive public health strategies to delay AD onset.

References


