

Alzheimer's disease

SLEEP AND ALZHEIMER'S DISEASE

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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 with 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). A fatal disease, patients with AD generally survive 7-10 years after diagnosis (Brookmeyer, Corrada et al. 2002). Globally, the prevalence of AD is expected to soar as westernised countries experience marked increases in aging of their populations (Anderson and Hussey 2000), along with an increase in life expectancies. For these reasons, the prevalence of AD in Australia, and associated costs of caring for individuals afflicted with this disease, are projected to quadruple by 2050 (Access Economics 2009). To date, there is no treatment for AD; thus it is necessary to find modifiable factors that may alter the incidence and prevalence of this disease. In addition, there is a genetic risk factor for AD, named the apolipoprotein E4 allele. Nevertheless, neither poor lifestyle nor carriage of the E4 allele indicates imminent development of AD. Thus, further investigations into the causal pathways of AD are required.

Neuropathological changes and neuronal loss, particularly in regions most commonly associated with learning and memory, are evident in the brains of individuals with AD. More specifically, AD pathology is characterised by the presence of amyloid plaques and neurofibrillary tangles (Goedert 1993; Masters and Beyreuther 1995). The toxic protein that forms the basis of the senile amyloid plaques, beta-amyloid (A β), can also accumulate around blood vessels, resulting in a condition known as cerebral amyloid angiopathy (CAA; Revesz, Holton et al. 2002). In addition, oxidative stress within the brain has been a defining characteristic of AD neuropathology (Martins, Harper et al. 1986). In Alzheimer's disease, this cumulative pathology causes the information transfer at the synapses to fail, which then causes synapses to decline, which leads to the death of neurons. This death of neurons leads to atrophy of the brain, particularly beginning in the hippocampus, a brain structure vital to learning and memory.

The exact causes of AD are yet to be elucidated; however, there is common agreement among experts that the cause is likely multifactorial, including genetic, environmental, and lifestyle factors. Leading a healthy lifestyle, including regular physical activity, good diet, and staying mentally active, appears to be protective, but a critical element not fully understood relates to

sleep. Kang et al. (2009) has demonstrated that sleep has a direct link with the levels of A β produced and secreted into the interstitial fluid (ISF) within the brain. During periods of wakefulness the level of soluble A β produced increases, while at sleep the levels decrease. Sleep deprivation has also been shown both in mice and humans to contribute to increased production of A β , while the infusion of an Orexin antagonists (used to induce sleep) reduced the accumulation.

With AD incidence rates expected quadruple by mid-century, there is an urgent need for an effective AD treatment, yet each piece to the puzzle that may prevent AD is also critical. While sleep disturbances are common in the aged, they are equally problematic across many aged groups.

How reported sleep quality correlates with AD blood biomarkers and key genetic markers, such as APOE 4 is not yet understood. While it is known that each person's genetic predisposition is individual it may be critical for some compared to others to control sleep patterns to lower their risk of AD. Understanding the relationship of sleep and AD is therefore an important step in then further clarifying the role of prescribing sedatives to induce sleep.

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