

Review of: "Association of sleep duration in middle and old age with incidence of dementia"

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A large 25-year follow-up of the Whitehall II cohort study of men and women found that short sleep duration (≤ 6 h) in midlife was associated with a higher risk of new-onset dementia later in life. The association was independent of several sociodemographic and lifestyle factors, cardiometabolic and mental diseases (1). No strong evidence was found for an association between long sleep duration and dementia risk. Although an observational study cannot prove causation, as plausible mechanisms explaining the link with short sleep duration, the authors discuss several effects of sleep on brain health, including neuroinflammation and impaired clearance of amyloid-beta from brain via the glymphatic system (1). Earlier studies have suggested that both short and long sleeping pattern contributes to dementia risk. However, investigations have often had several flaws diminishing their reliability. Because cognitive disorders may have a long incubation period, follow-up times have been too short to reliably exclude reverse causation. With its long follow-up this bias was unlikely in the Whitehall study. Also several potential confounding factors were adjusted for in this study. One important point is distinguishing the etiology of dementia. Is short sleep a risk factor for "pure", neurodegenerative Alzheimer disease (with amyloid accumulation) or for vascular or mixed disorder (2), where, for example, sleep apnea with its cardiovascular sequelae, and metabolic syndrome may be contributing. The present authors aimed to control this by stratifying their cohort by cardiovascular disease.

Sleep and lack of it is currently a topic which highly attracts lay people and news media. Stressful life and modern 24/7 culture easily disturbs sleeping and is associated with various symptoms and problems – more or less really due to lack of sleep. Although too little sleep is often seen a villain leading to problems, actually distinguishing which comes first is difficult – the classic chicken-egg question. It is certain that sleep is a necessity for psychological and somatic health (3,4). The fatal effects of sleep deprivation in experimental animals and lack of sleep predisposing to delirium in humans prove the importance of sleep for health and wellbeing. Modern neuroscience is also recognizing new, plausible mechanisms for health effects (3). Sleep is a period of necessary rest for the brain and body, glymphatic system works during sleep and cleans the brain, including dispelling amyloid and tau protein – key factors in the development of Alzheimer disease. So, sleep is absolutely necessary for you, but how much is enough, that is one question. Is > 6 h needed for everyone? Furthermore, what are the root causes for short duration of sleep. Some people may be short sleepers genetically without

ill effects on health, and many notorious persons have been reported to sleep only a few hours per night and still been super performers like Finnish pediatrician Arvo Ylppö (1887-1992) who held the title of archiater (the most respected physician in Finland, lifelong status for only person at a time) for forty years. He is reported to have slept only 4 hours and still lived without cognitive or other serious problems up to 105 years.

Besides genetics, also prenatal conditions may contribute. In a study of 8-year old children lower birth weight and shorter length at birth were associated with lower sleep efficiency (5). Furthermore, children of mothers, who had consumed alcohol during pregnancy, had increased risk of having short sleep and low sleep efficiency.

Moreover, in the same children short (≤ 7.7 h) vs. average sleep duration (7.8-9.3 h) was associated with higher cortisol awakening response and higher diurnal cortisol levels across the entire day (6). Thus, short sleep may signal altered neuroendocrine functioning and offer insight into the pathways linking shortage of sleep with poor health, eg. metabolic syndrome, later in life. Because metabolic syndrome predisposes for cardiovascular disease, it could be a mediating link explaining cumulative evidence that sleep quality (both duration and fragmentation) is associated with adverse cardiovascular events (7). Metabolic syndrome is also a risk factor for dementia (8), but the association between dementia and short sleep remained, although attenuated, in the Whitehall cohort study after adjusting for cardiometabolic factors (1). In the end, the gold standard of proving cause and effect is a randomized controlled trial (RCT). It is obviously challenging to organize this type of study for sleep. There is an RCT of one-night sleep deprivation leading to increased amyloid levels (9), but what is the relevance with shorter -- not deprived -- sleep duration? And what would the trial intervention to prolong sleep duration? Sleep hygiene counselling? Sleep drugs? Remembering the problems with intervention studies aimed to change lifestyle, I think that in the end we are left with observational evidence (there are no RCTs about smoking cessation!). For this regard the careful and extensive study from the Whitehall II cohort study is an important contribution to literature.

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