UR MEDICINE

GER-E-NEWS

URMC Division of Geriatrics & Aging June 2022

Sleep and Aging

Mark Shehata, MD, MBA

Why Sleep Matters

Sleep is crucial to a number of physiologic functions including memory formation, cell and DNA repair, regulation of the metabolism, supporting the immune system, and clearance of wastes via the "glymphatic system"- a series of extra-cellular channels which clear waste from the brain at night, including beta amyloid involved in the pathology of Alzheimer's disease. Poor quality and quantity of sleep have been implicated in a number of pathologies including diabetes and the metabolic syndrome, cardiovascular disease, obesity, stroke, depression, impaired immune response, and dementia.

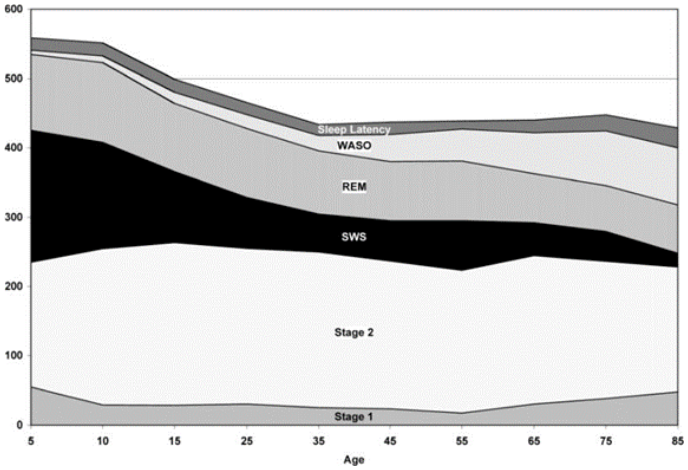
Anecdotally, Margaret Thatcher and Ronald Reagan had more in common than their conservative politics - both are widely reported to have slept only 2-4 hours nightly and both shared a diagnosis of dementia, likely in part due to their sleep habits.

Regulation of Sleep

The body has two systems of signaling the need for sleep. The first is the circadian clock- also known as Process C. Process C, regulated by the super-chiasmatic nucleus (SCN) follows a 24-hour rhythm with a peak in sleepiness at night and a smaller peak in the early afternoon. Peaks are signaled by melatonin release from the pineal gland and are influenced by factors including, but not limited to, light exposure, body temperature, eating patterns, exercise, and stress. The homeostatic process, also known as Process S is the second system in which sleep inducing substances, most significantly adenosine, gradually accumulate in the brain over the course of the day, building a "sleep pressure" until they can be cleared during sleep overnight. Adenosine receptors are blocked by caffeine to promote wakefulness, but the adenosine itself remains— accounting for the crash felt after caffeine is metabolized and the receptors again become available.

Sleep Architecture and Aging

Sleep includes rapid eye movement (REM) and non-REM phases, with three NREM stages preceding REM in a repeating approximately 90-minute cycle. The majority of physiologic functions of sleep occur during NREM sleep stages. While REM is less characterized, it is when the brain is most active and thought to play a roll in creativity and emotional wellbeing. Changes observed with aging, visualized below, include a shorter total sleep time, increase in sleep latency (time to fall asleep), decreased sleep efficiency (more nighttime awakenings), advanced sleep phase (earlier awakenings and bedtime), decrease in time spent in slow wave (stage 3) and REM sleep, and decreased effectiveness of Process S. Changes can be modest in healthy aging or profound in those with a high chronic disease burden. Furthermore, a vicious cycle can be seen: inadequate sleep across the lifespan leads to accelerated aging of the brain and thus further sleep impairment later in life.



Non-Pharmacologic Sleep Hygiene Measures
Avoid nicotine use
Avoid alcohol before bed
Exercise regularly
Manage stress
Reduce evening blue light exposure
Reduce noise at night
Go to sleep and wake up at consistent times
Avoid meals within 2 hours of bed
Refrain from electronic use in bed
Avoid caffeine in the afternoon
Seek sunlight exposure on waking

Medication Management

Medication choices for sleep in older adults differ from those often employed earlier in life. Particularly, antihistamines and benzodiazepines should be avoided. The older adult is much more prone to side effects, dependence, and the deleterious effects on sleep architecture of these medications. Melatonin, on the other hand, has limited efficacy in younger adults outside of shifts in time zones and work schedules, but becomes more efficacious as we age due to an age-related decrease in natural melatonin secretion from the pineal gland. Starting doses of 1-3 mg are recommended. Additional choices for chronic insomnia include the anti-depressants mirtazapine and trazadone. 15mg mirtazapine nightly is most effect for insomnia in most, with higher doses often having a paradoxical stimulating effect. Dosing for trazadone for insomnia usually ranges from 25-100mg nightly, lower than those historically used for depression.

References

1. Zielinski MR, McKenna JT, McCarley RW. Functions and Mechanisms of Sleep. AIMS Neurosci. 2016;3(1):67-104. doi:10.3934/Neuroscience.2016.1.67
2. Li J, Vitiello MV, Gooneratne NS. Sleep in Normal Aging. Sleep Med Clin. 2018;13(1):1-11. doi:10.1016/j.jsmc.2017.09.001
3. Lie JD, Tu KN, Shen DD, Wong BM. Pharmacological Treatment of Insomnia. P T. 2015;40(11):759-771.
4. Deboer T. Sleep homeostasis and the circadian clock: Do the circadian pacemaker and the sleep homeostat influence each other's functioning? Neurobiol Sleep Circadian Rhythms. 2018 Mar 1;5:68-77. doi: 10.1016/j.nbscr.2018.02.003. PMID: 31236513; PMCID: PMC6584681.