Sleep in Older Adults and Women during Menstrual Cycles and Menopause

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Objectives

- Understand normal changes in sleep that occur as people age
- Discuss how sex hormones could affect sleep and memory
- Understand how sleep and memory change during menopause



Sleep Physiology

- NREM Sleep
 - 75% of total sleep time
 - Stages 1-4
 - Physiological state of hypoarousal
 - Slow HR (5-10 beats slower), low BP, reduced muscle tone



Sleep Physiology

- NREM Stages
 - Stage 1 (5%): Theta waves
 - Stage 2 (45%): K-complexes and Sleep spindles
 - Stage 3 and 4 (25%): Delta waves and slow oscillation "deep sleep"



Sleep Physiology

• REM

- 25% of total sleep time
- Called "Paradoxical Sleep"
- EEG similar to awake state
- Almost total paralysis of skeletal muscles



Sleep Architecture

- Progression of sleep across the night is called sleep architecture and is displayed on a sleep histogram
- NREM sleep
 - Stage 3 and 4 generally observed during the first half of the sleep period
- REM sleep
 - Occurs most frequently during the last 1/3 of the sleep period



- Advanced sleep timing
 - Loss of neurons in the suprachiasmatic nucleus with advanced age may account for the age-related circadian phase shift





- Shorter overall sleep duration
- Increased sleep fragmentation
- More fragile sleep (i.e. more easily awoken)

Thorpe, L. (2010) Sleep and Circadian Rhythm Disorders in the Elderly

- Longer sleep-onset latency
- Increased time spent awake throughout the night (WASO: Wake Time After Sleep Onset)
- Sleep quality and efficiency is 70-80% of younger subjects.



- Light sleep (Stages 1 and 2) increases with age = More awakenings
- Slow Wave sleep (Stages 3 and 4) decreases from ~25% down to 3% of total sleep time (the most dramatic change)
 - Decreased homeostatic drive –more extracellular adenosine, but widespread loss of <u>adenosine A1</u> receptors
 - Loss of melatonin
- The depth of <u>slow-wave</u> sleep, as measured by the arousal threshold to auditory stimulation, also decreases with age.
 - In the otherwise healthy older person, slow-wave **sleep** may be completely absent, particularly in males.
- Shorter and fewer NREM-REM sleep cycles

Sleep in the Old Vs. Young



• REM sleep impairments only emerge as adults progress into their 70s and or as a symptom of degenerative dementias



- Increased frequency of daytime naps
- Excessive daytime sleepiness
 - 1 in 4 older adults report experiencing daytime sleepiness severe enough to impair daytime plans on a regular basis



Sleep, aging and memory

• Impairment in spindles significantly predicts poor hippocampal functioning, which leads worse learning ability



Sleep, aging and memory

• The degree of impaired SWA across older adults predicts worse overnight memory consolidation, resulting in greater next-day forgetting



Sex difference

- Within sex: older men have less SWS than younger men; no difference for women.
- Between sex: men over 70 had less slow wave sleep compared with age-matched women.
- Divergence starts at 30s
- Women suffer subjective complaints of poor sleep



Sex differences in cognition

- Females perform better on verbal tasks (e.g., verbal fluency)
- Males perform better on spatial tasks (e.g., spatial ability)



Sex hormones and memory across lifespan



Sex hormone



Menstrual cycle and sleep

- Sleep latency and sleep efficiency remain stable across the menstrual cycle in young women
- Small decrease in REM during luteal phase
- Percentage of SWS and SWA in NREM sleep, averaged across the night do not change in young women
- The most dramatic change in sleep in association with the menstrual cycle is sleep spindles

Menstrual cycle and sleep





- Women perform better on verbal tasks during high estrogen/progesterone
- Women perform better on spatial tasks during the low-hormone phase

OVULATION

9 10 11 12 13

LUTEAL PHASE

FOLLICULAR PHASE

HORMONE LEVEL

LH FSH ESTROGEN PROGESTERONE

• Estrogen levels correlated positively with verbal fluency and negatively with scores on a test of spatial ability in young, cycling women

• Genzel et al. 2012



• Genzel et al. 2012



• Genzel et al. 2021



• Sattari et al., 2017



• Memory performance (Sattari et al., 2017)



- Correlation between EEG features and memory (Sattari et al., 2017)
- Specifically, sleep-dependent improvement correlated with slow oscillations when women were outside their menses, while spindle activity correlated with improvement during menses.

The menopausal transition

- The menopausal transition: the years leading up to menopause, or final menstrual period (occurs at a median age of 51.4 years)
 - changes in menstrual cycle lengths (early transition),
 - progressing to increased variability in cycle lengths and skipping cycles (late transition), and finally, menopause.

Hormone changes in MT

- Decline in estrogen and progesterone
- Amplified hormonal fluctuation within a cycle



- More likely to report sleep difficulties, with sleep difficulties due to frequent awakenings the most common problem
- Luteal phase was characterized by more awakenings and arousals and less N3 sleep percentage during MT women but not young (de Zambotti et al. 2015).
- The luteal phase was associated with increased spindle activity

Sleep during MT

- Sudden feeling of warmth, usually most intense over the face, neck, and chest, and profuse sweating
- Strongly associated with disturbed sleep architecture and quality and are also linked with poor memory function (Baker et al., 2017)



Memory during MT

- Complaints of memory difficulties (self-report)
- Studies about memory performance have been inconsistent (labtested)
- Women in the menopausal transition who report memory problems do perform lower on memory tests (Maki 2015).
 - Associated with estrogen

Beyond menopause



- Alzheimer's disease disproportionately affects women in both prevalence and severity
- Women with Alzheimer's show worse subjective and objective memory impairment compared to men (Chapman et al., 2011).
- Need more research on sleep, memory and sex hormones.