Understanding Alzheimer's Disease and Its Connection with Sleep Disorders

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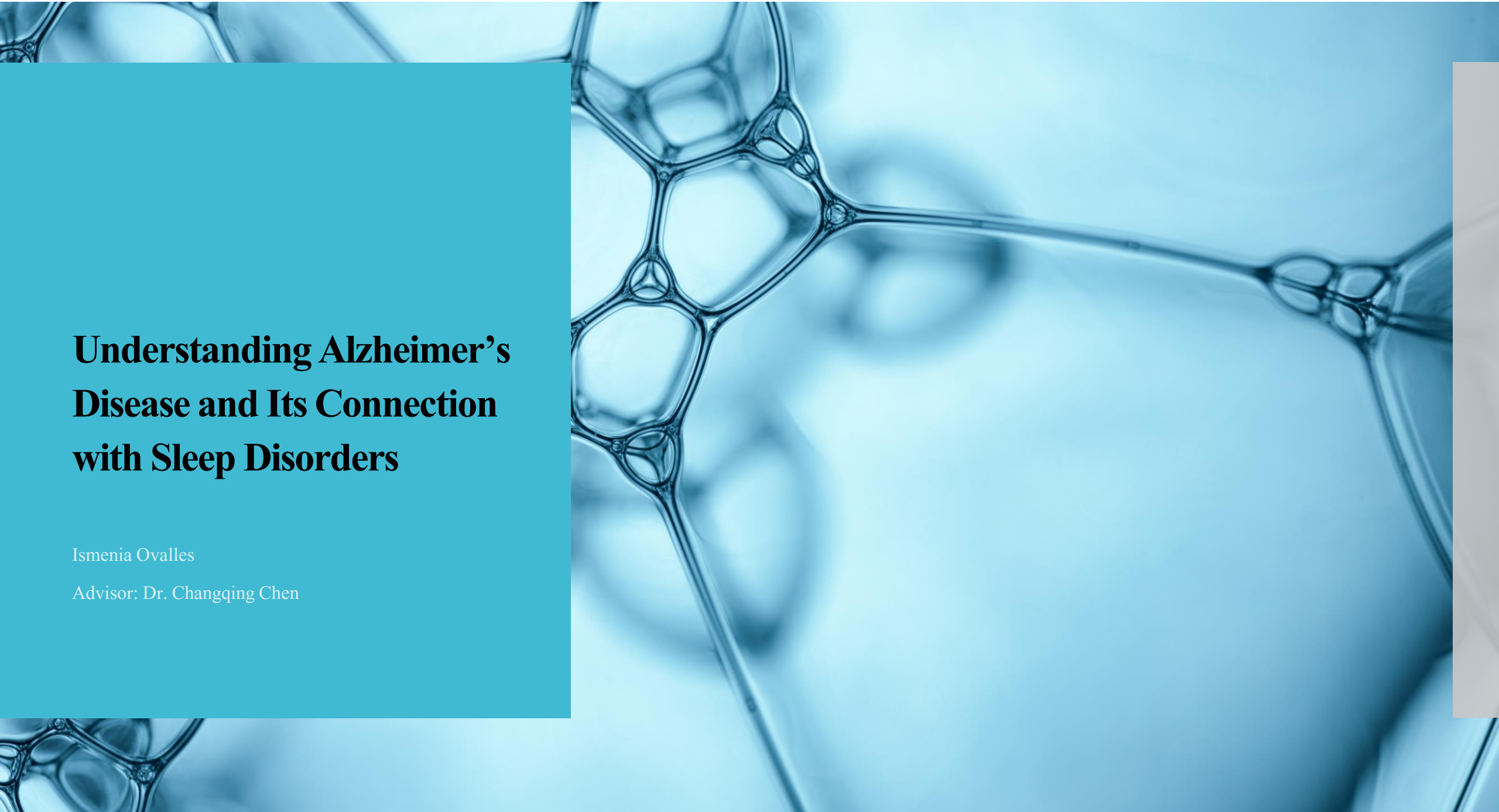

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Alzheimer’s 101

Alzheimer’s Disease (AD)

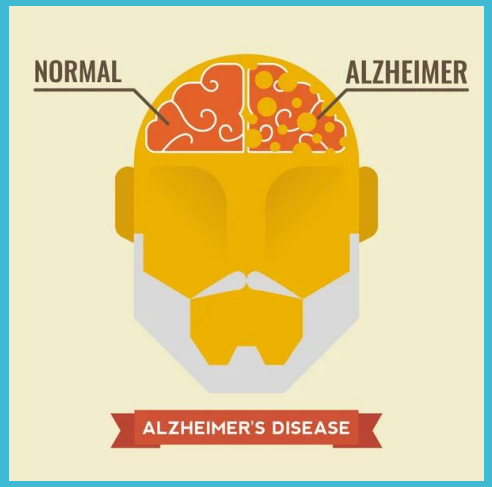
Most common form of Dementia among people from 65 years and older.

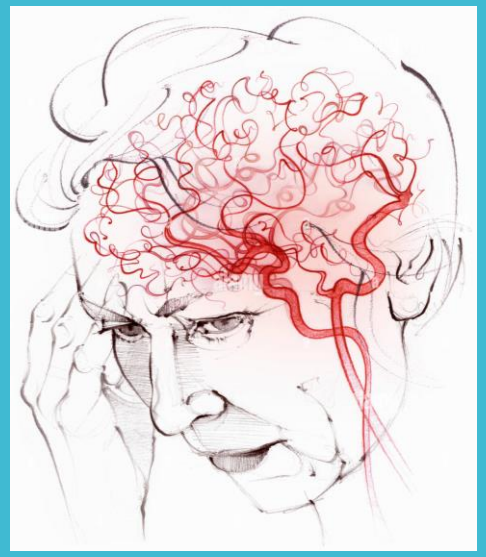
Dementia

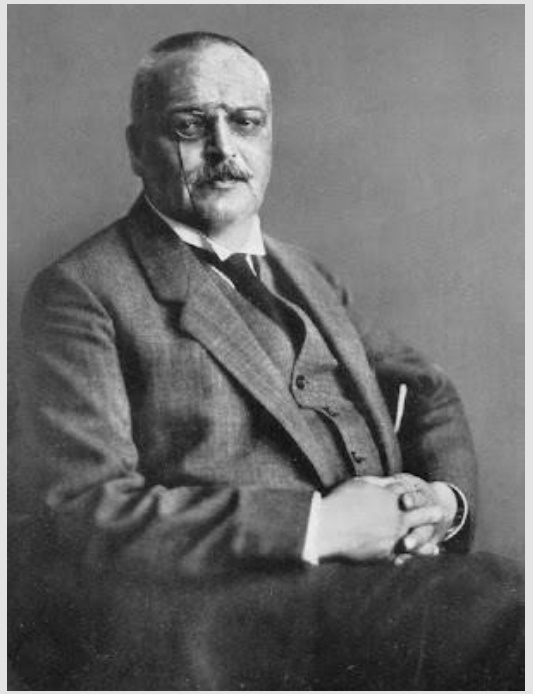
Brain disorder that seriously affects a person's ability to carry out daily activities.

Mild cognitive impairment (MCI)

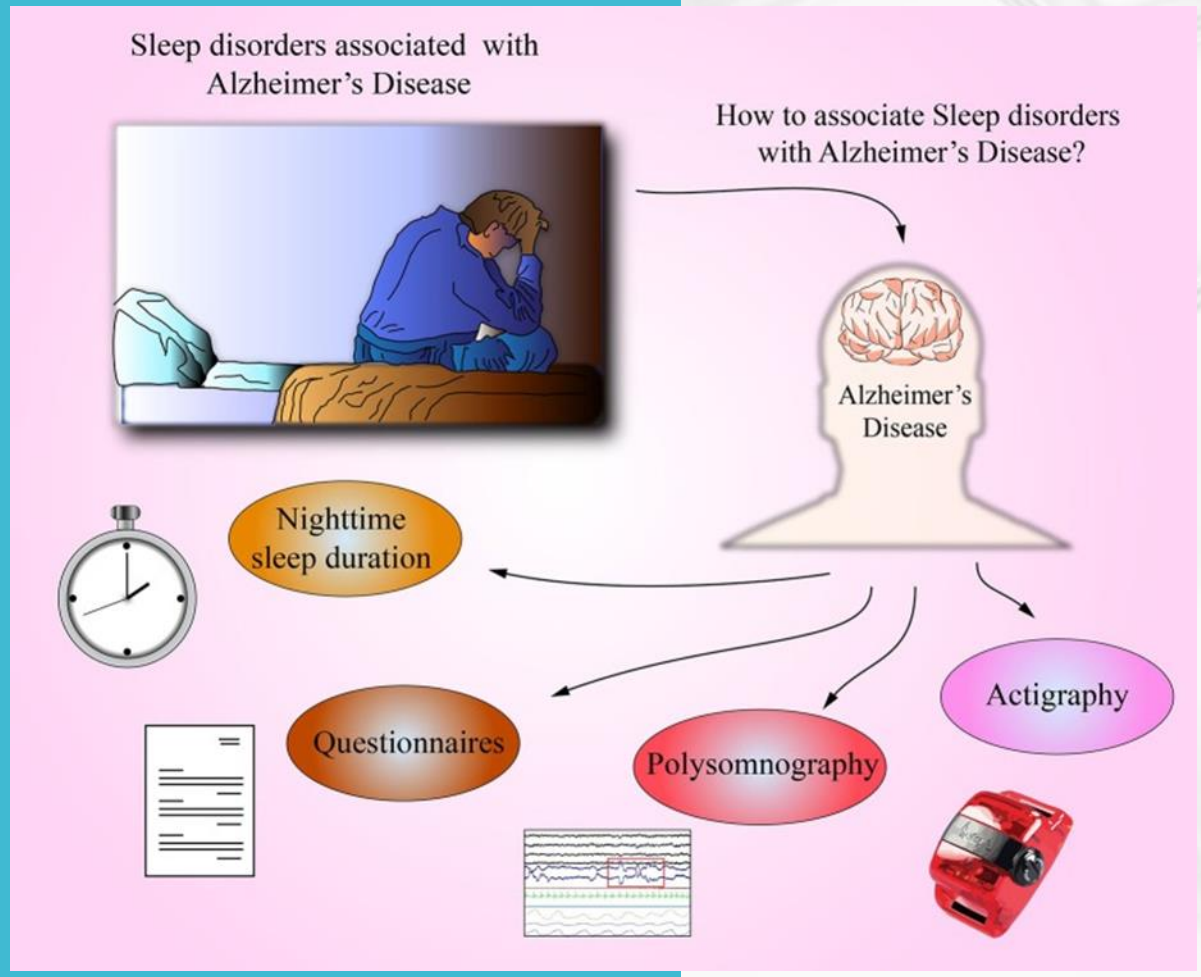
Causes more memory problems than normal for people of the same age. Fewer than 1 in 5 Americans are familiar with mild cognitive impairment (MCI), which can be an early stage of Alzheimer’s. About 1/3 of people with MCI develop dementia within 5 years of diagnosis.







Alois Alzheimer



Reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5990625/

Night-time sleep duration and AD

Based on results obtained in empirical study conducted among healthy men in middle age, it has been hypothesized that $A\beta_{42}$ increases with chronic sleep deprivation.

Treatments:

- Normal healthy men (40–60 years) without cognitive impairments. 13 were not allowed to fall asleep at night, while the other 13 were permitted to unlimitedly long sleep.

Measurements:

- Concentration of $A\beta_{42}$ in cerebrospinal fluid.

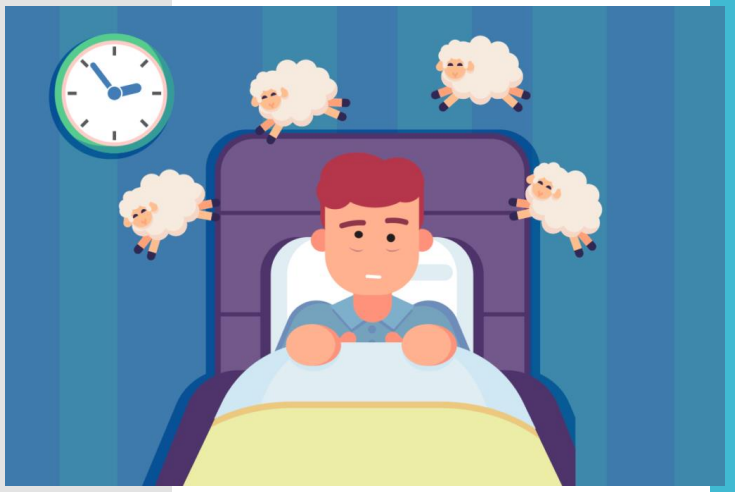
Results: People who slept at night showed a 6% decrease of $A\beta_{42}$ level. People that didn't sleep showed increased levels of $A\beta_{42}$ in CSF after sleep deprivation.

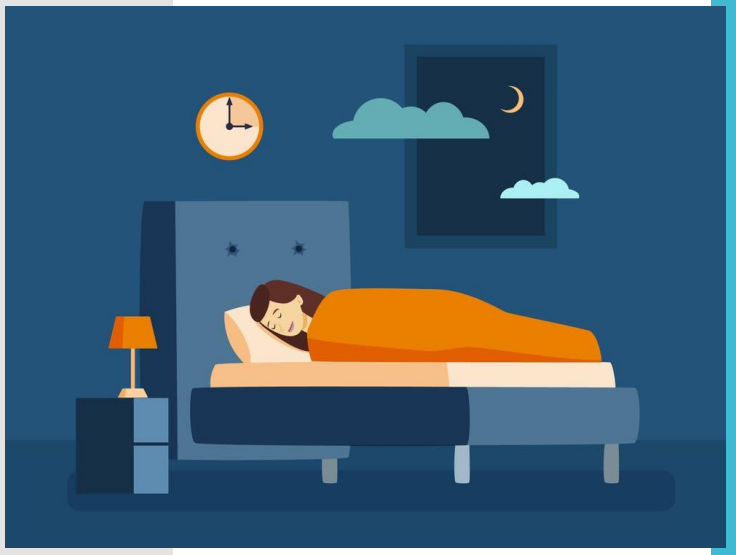
Diagnostics of sleep disorders based on questionnaires in AD patients

In patients with AD, the diagnostics of sleep disorders based on specific questionnaires are difficult due to cognitive impairment affecting reliability of self-report measures of sleep.

A study comparing results of sleep questionnaires, with the results of actigraphy in 55 patients with AD and 26 controls revealed limited value in early and moderate AD stage.

Results: sleep disorders occurred in 24.5% of patients with mild to moderate form of AD.





Polysomnography (PSG) in the diagnostics of sleep disorders in AD patients

PSG is a sleep study that monitors several parameters to diagnose sleep disorders. In the patients with AD, PSG usually shows prolonged sleep latency, i.e., time taken to fall asleep.

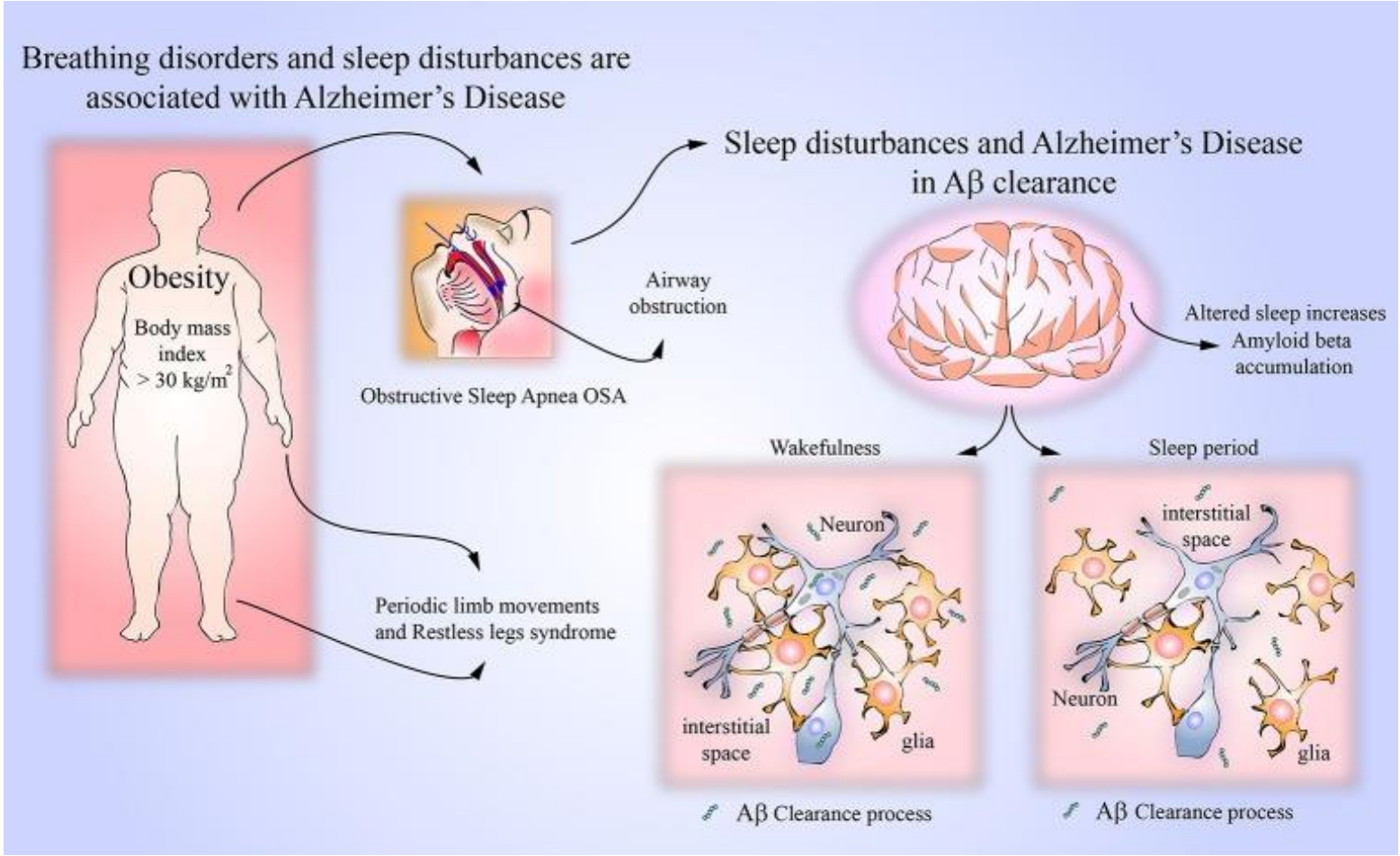
Increased number of awakenings and lengthened time of wakefulness after sleep onset causes reduced sleep efficiency. Abnormalities in the PSG recordings were also noted in patients with preclinical AD. In patients with amnestic MCI, abnormalities in the sleep structure were also observed.

Actigraphy to examine sleep disorders in patients with AD

Study based on actigraphy conducted in 737 men and women at the average age of 81.6 has shown that after an average 3.3 years, risk of symptoms of AD was 1.5 times higher in subjects with high sleep fragmentation as compared to subjects with slight sleep fragmentation.

Sleep studies based on actigraphy were conducted in 142 persons without cognitive disorders at the age of ≥ 45 years. The results of the study have confirmed that the most important sleep disorder in AD is sleep fragmentation, causing worsening of the sleep quality.

Breathing disorders during sleep in AD patients



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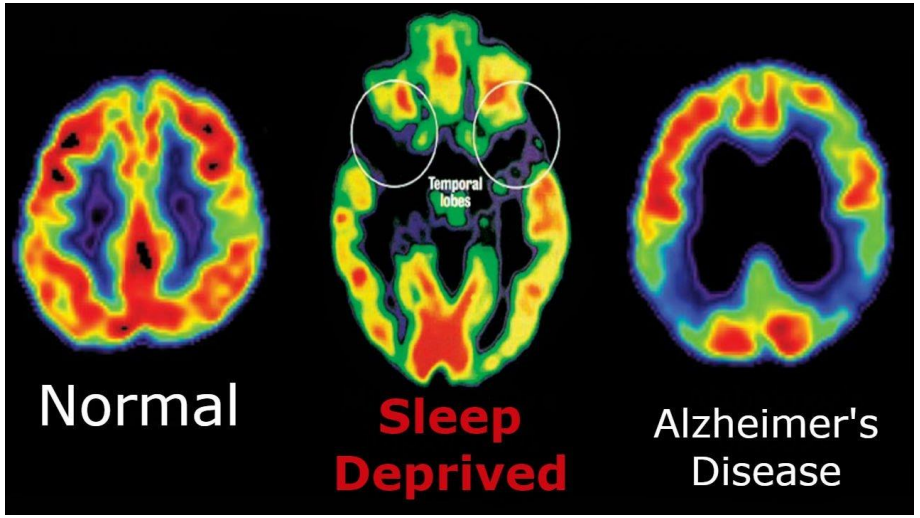
Sleep and brain glymphatic system in AD

- The system of structures and processes that allows soluble waste substances to pass from the cerebrospinal fluid into the surrounding tissue fluid for removal, mediated by glial astrocytes and operating mainly during sleep.
- It seems that sleep may influence glymphatic system function. During natural sleep, there is a marked increase of the brain's interstitial space as compared with wakefulness, possibly resulting from the shrinkage of astroglia cells. Altered sleep quality might contribute to the onset and progression of the AD both through impaired glymphatic clearance and disturbances in the Aβ production in case of disordered slow wave sleep.



Conclusions

- Clinical observations indicate the possible relationship between abnormalities of sleep and AD.
- The following observations allow to conclude that disordered sleep may contribute to the development of AD pathology:
  - Changes in sleep structure
  - Worse sleep quality in both preclinical and symptomatic AD
  - Correlation of cognitive impairments with sleep structure abnormalities
  - Changes in CSF Aß concentrations induced by sleep apneas and correlating with severity of sleep disordered breathing
  - The influence of physiological sleep on clearance of Aβ through the glymphatic system
  - Possible influence of impaired glymphatic system on Aβ level
  - Observations with the use of the newest technical equipment reflecting impairment of the glymphatic system in AD patients

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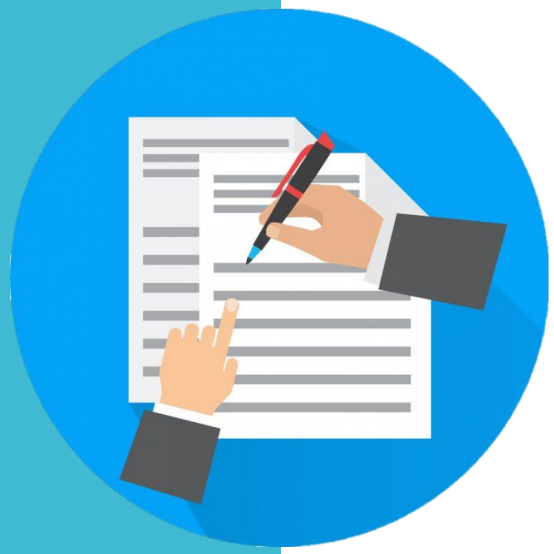

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