Journal of Pharmaceutical Research International

32(40): 49-53, 2020; Article no.JPRI.63360
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

The Prospect of Treating Alzheimer Disease through Sleep

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

Article Information

DOI: 10.9734/JPRI/2020/v32i4031032
Editor(s):
(1) Dr. Mohamed Fathy, Assiut University, Egypt.
(2) Dr. Syed A. A. Rizvi, Nova Southeastern University, USA.
Reviewers:
(1) Said Moselhy, Ain shams University, Egypt.
(2) Soheir, N. Abd El-Rahman, Agricultural Research Centre, Food Technology Research Institute, Egypt.
(3) Egorova Margarita Vladimirovna, Siberian State Medical University, Russia.
(4) Vinicius Oliveira de Andrade, CAISM-Franco da Rocha, Brazil.
Complete Peer review History: http://www.sdiarticle4.com/review-history/63360

Mini-review Article

Received 17 October 2020
Accepted 22 December 2020
Published 11 January 2021

ABSTRACT

Alzheimer's disease is caused by the deposition of amyloid and Tau proteins. These two proteins are present in normal brain cells, but in Alzheimer's disease, they accumulate in large quantities, affecting how brain cells function normally. The result is that brain cells can't communicate properly, leading to memory loss. The current treatment for Alzheimer's disease is mostly controlled by drugs. The three main drugs are Donepezil, Rivastigmine, and Galantamine, Reminyl. However, it has limited side effects and usually manifests as gastrointestinal distress. One of the functions of sleep is to accelerate the removal of amyloid in the brain, which can effectively improve the accumulation of amyloid and Tau proteins.

Keywords: AD; amyloid & tau proteins; sleep deprivation; sleep disorders; sleep-rhythm.

1. INTRODUCTION

Alzheimer's disease can be divided into prophase, early phase, middle phase and late phase, depending on the severity of the disease. Amyloid and Tau protein deposits are higher in females than in males, with an average incidence of about 6% worldwide. Other clinical symptoms include memory impairment, decreased ability to care for themselves, and personality changes.

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Amyloid and tau proteins that accumulate in brain cells are thought to be the cause of Alzheimer's disease, so inhibiting amyloid and tau is thought to slow the development of the disease.

2. CURRENT STATUS OF TREATMENT FOR ALZHEIMER

2.1 Drug Treatment

At present, several drugs have been developed for early AD, which can help temporarily improve cognitive ability. However, because the difficulty of Alzheimer's disease has not been completely solved, three main drugs have been proved. Donepezil, Rivastigmine, Exelon, Galantamine and Reminyl. All three types of drugs help improve memory, but side effects limit the development of the drug. Another prescription drug, Memantine hydrochloride (Namenda), which is commonly used in combination with the aforementioned drug, also helps to delay the progress of AD. Doctors can also prescribe drugs to help reduce anxiety, anxiety and unpredictable behavior, as well as improve sleep patterns and treat depression [1]. These drugs do not work for everyone, and their effects are limited to early and middle AD. Of course, the side effects are limited, usually manifested by gastrointestinal distress.

2.2 Cognitive Training

In addition to drug therapy, there is cognitive training therapy, which is non-drug therapy. Cognitive training focuses on instructional practice, a series of exercises designed to demonstrate specific cognitive functions such as memory, attention, and problem solving. But A study by Dr. Bahar-fuchs A, Clare L, Woods B found that cognitive training did not produce any significant effect. Trial reports indicate that the effectiveness of interventions for some subjects may not fully meet existing standardized outcome measures [2].

3. TREAT ALZHEIMER'S DISEASE BY IMPROVING SLEEP AND RHYTHM

3.1 Bad Sleep Qualities on AD Patients'

Typical disturbances in the neurophysiological sleep structure during AD include deep sleep and abnormal sleep deprivation. Among the sleep disorders that occur in patients with AD, the most common disorders are sleep-disordered breathing and restless leg syndrome. Sleep disturbances may affect the diurnal fluctuations of amyloid beta in the interstitial fluid and cerebrovascular fluid associated with the glial system of the brain and the production of amyloid beta. Sleep disorders can lead to cognitive decline and pathologic development of AD [3]. Many older people have sleep problems, but people with dementia often have more trouble falling asleep. Sleep disorders can affect up to 25 percent of people with mild to moderate dementia and up to 50 percent of people with severe dementia [4]. As dementia progresses, sleep disturbances become more severe. The chart below shows that the age groups most at risk for Alzheimer's disease are older adults. Sleep problems in the elderly themselves are worse than in middle age, and are even worse after Alzheimer's disease.

3.2 Sleeping Affects AD Mechanisms

One of the functions of sleep is to accelerate the removal of amyloid in the brain, which can effectively improve the accumulation of amyloid and Tau proteins. APOE4 is the strongest genetic risk factor for late-onset Alzheimer's disease, according to research in the journal Nature. Compared with other ApoE subtypes, ApoE4 increased pathological changes of brain amyloid - hydroxytryptamine. It shares the same pathogenic mechanism as amyloid and Tau proteins. An increase in protein in the brain. By generation of P301S transgenic mice in human ApoE knockdown (KI) or Apolipoprotein E knockdown (KO) background, here, we showed that the level of P301S/E4 mice was significantly higher than somatodendritic in brain and redistributed 3 months of age to a greater extent compared to P301S/E2, P301S/E3, P301S/EKO recent mice. At 9 months of age, P301 mice with different ApoE genotypes showed different patterns of phosphorylated Tau protein (P-Tau) staining. P301S/E4 mice showed more brain atrophy and neuroinflammation than P301S/E2 and P301S/E3 mice, while P301S/EKO mice were largely unaffected by these changes. In vitro, microglia expressing E4 showed higher innate immune reactivity after LPS treatment. Compared with the co-culture of neuron /E2 and neuron /E3, the co-culture of neurons expressing P301S Tau and mixed glial cells expressing E4 could significantly increase the secretion level of tumor necrosis factor-a (TNF-A) and significantly reduce the viability of neurons. Neurons co-cultured with EKO glial cells had the highest

survival rate at the lowest level of TNF- cell secretion [5]. Structure and Pathology of Tau Protein in Alzheimer Disease are shown in the diagram below. For AD and related tau pathology, the manifestation is slow progressive neurodegeneration, which is mainly related to the accumulation of tau proteins in the cell, leading to so-called neurofibrillary bundles. (NFTs) [6].

3.3 Sleep Reduces Production of Amyloid Beta

Sleep removes amyloid and reduces the accumulation of amyloid and Tau proteins. Thus, reducing the incidence of Alzheimer's disease. Sleep disruption increases soluble amyloid beta, according to the study, which "tested this response in humans with continuous cerebrospinal fluid (CSF) sampled through an induced lumbar spine catheter when participants were sleep-deprived, treated with sodium hydroxide, or allowed normal sleep". All participants were injected with 13C6-leucine to measure amyloid - hemodynamics. We found that sleep deprivation increased nocturnal levels of amyloid-36, amyloid-34, and amyloid 34-42 by 25 to 30 percent compared to the sleep control group" [7]. From this experiment, sleep deprivation, sleep disruption can lead to an increase in amyloid.

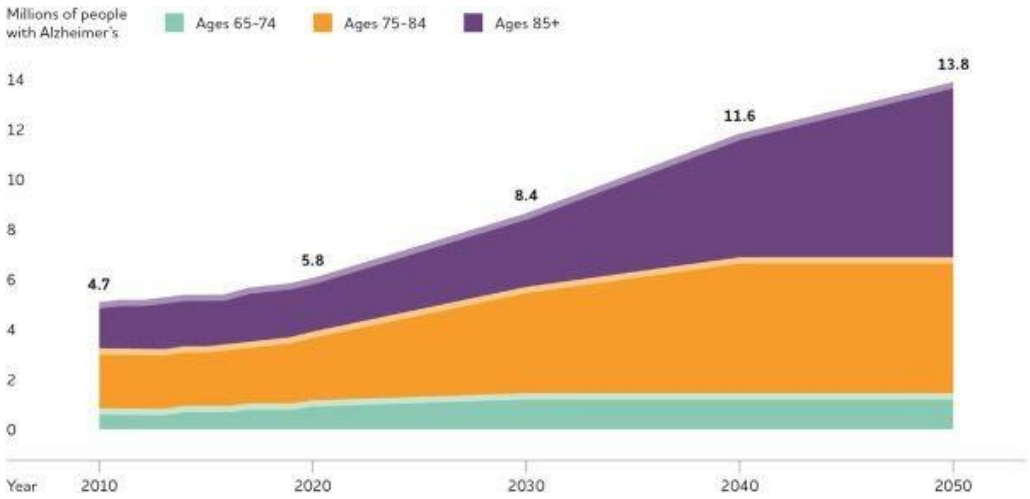

Fig. 1. "2019 Alzheimer's disease facts and figures" by Alzheimer's association [4]

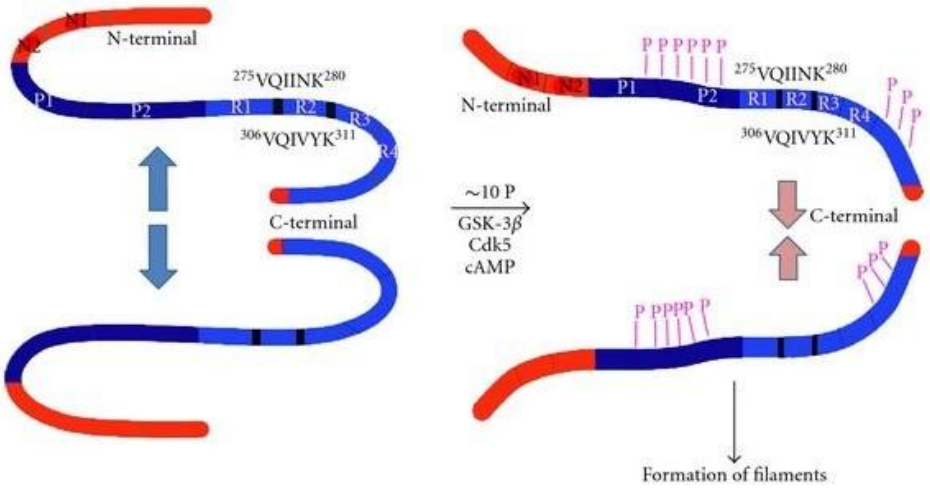

Fig. 2. "Tau protein: Function and pathology" by Michala Kolarova [6]

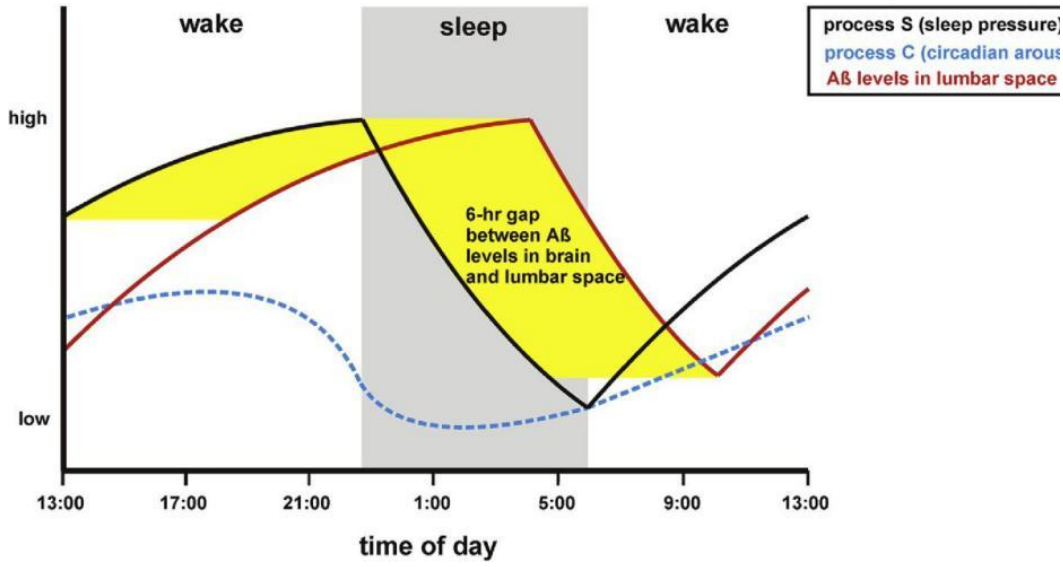

Fig. 3. "Candidate mechanisms for the association between sleep-wake disruption and Alzheimer's disease" by J. Cedernaes, R. Osorio [9]

4. SIDE EFFECTS OF SLEEPING TREATMENT

4.1 Existing Issues

4.1.1 Insomnia

Many people with Alzheimer's wake up more often during the night and stay awake longer. Brain wave studies have shown that sleep is reduced.

4.1.2 Sleep too long

Time disorder. Easy to make the brain mental disorders, consciousness is not awake.

4.2 Medication Stabilizes Sleep

There is a difference between the side effects of using drugs to stabilize sleep and treating Alzheimer's directly with drugs. The drug used to stabilize sleep has a circadian rhythm, with suppressed secretion during the day and active secretion at night. Unlike the drug Namenda mentioned above, it has a drowsy effect. But serious side effects can include blood clots, psychosis and heart failure. Sleep medications can be "Benzodiazepines", such as lorazepam, oxazepam and temazepam "Sleeping pills" such as zolpidem, zaleplon and chloral hydrate "Atypical" antipsychotics such as risperidone, olanzapine and quetiapine [8].

The authors show a temporal relationship between steady-state sleep stress and cerebrospinal fluid amyloid concentration. Sleep preference is thought to be regulated by two interacting mechanisms: a circadian process and a homeostatic process. Process C drives arousal, which helps determine the start time of normal sleep, while process S drives sleep stress, which increases with the duration of wakefulness and decreases during slow-wave sleep.

5. CONCLUSION

Alzheimer's disease is caused by the deposition of amyloid and Tau proteins. In Alzheimer's disease, they accumulate in large amounts, affecting the normal functioning of brain cells.

Current treatments for Alzheimer's have limited side effects. But insomnia caused by sleep therapy and chronic sleepiness can also lead to the recurrence of Alzheimer's disease. You need to control your sleep with drugs that have fewer side effects. But Alzheimer's conundrums remain unsolved. Both sleep and drug treatments are available, but more work needs to be done. How to get a regular sleep schedule and use non-drug therapy with fewer side effects is needed for Alzheimer's disease.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/63360