Sleep Deprivation: What is the Connection to Alzheimer's Disease?

Raneem Samman
Lake Forest College
Lake Forest, Illinois 60045

Sleep deprivation is so commonly experienced and observed around the world. It influences and impacts the human brain in multiple distinct ways; some were researched more than others. It also messes up the rhythm of the circadian clock, which controls humans' sleep-wakefulness cycles. A study showed the impact of one night of sleep deprivation on the risk factor of Alzheimer's Disease. Specifically, by studying the accumulation of amyloid beta plaques in the cerebellum.

Beta-amyloid plaques are waste products of the metabolic mechanisms and reactions that occur in the brain (Cheng, 2020). Thus, their accumulation indicates a malfunction in the intracellular proteasomal degradation and autophagy systems in the brain (Nedergaard, 2013), which are the systems responsible for breaking down and getting rid of the toxic molecules in the brain, such as beta-amyloid plaques. The degradation systems are influenced by multiple factors: some are inherited while others are environmental and can be controlled by individual decisions day-to-day (Liu, 2019). The work of Shokri-Kojori et al. (2018) explores the impact of sleep deprivation on human brains and its connection to Alzheimer's Disease. The researchers argue that the scientific literature lacks knowledge and evidence about the impact of sleep deprivation on the accumulation of amyloid-beta in the human brain. In order to explore this argument, the researchers used PET scans to show the impact of acute sleep deprivation on amyloid-beta burden. PET technology allows them to measure amyloid-beta burden (ABB) in the living human brain. Positron emission tomography (PET) has multiple radiotracers which are types of radioactive biochemical substances used for diagnostic purposes. Each PET radiotracer serves a specific purpose. Thus, for this study, the researchers used F florbetaben (FBB) because FBB binds to soluble and insoluble amyloid-beta plaques. Thus, the use of FBB with PET scans allow the scientists to detect amyloid-beta burden (ABB) in the human brain to a great extent and generate the most accurate results. The study consisted of two main goals. Firstly, the researchers aimed to evaluate one-night sleep deprivation's impact on the brain ABB in healthy participants, which were used as the controls for the study, using PET-FBB technology. They would then take the data collected and compare it to the measurements recorded from the same participants after a night of well-rested sleep, which was labeled rested-wakefulness (RW). The researchers referred to the data collected after a well-rested sleep night as the baseline brain ABB. Secondly, the scientists aimed to be able to generate and generalize their findings by looking at sleep history and brain amyloid-beta burden. The scientists focused on looking at the hippocampus, precuneus, and the medial prefrontal cortex because they are the regions of the brain that are mostly affected and altered by Alzheimer's disease. As a starter, in order to compare the data collected through FBB (a night of sleep deprivation vs a night of well-rested sleep), the scientists needed to quantify the FBB measurements. Thus, FBB was quantified as the relative standard uptake value (SUVr) and was used as a marker or indication of amyloid-beta burden. As a result, they were able to conduct a statistical t-test to analyze the data, which showed a significant increase in the amyloid-beta burden in the hippocampal region after one night of sleep deprivation. These observations were not seen after one night of well-rested sleep. In other words, more FBB binding occurred after one night of sleep deprivation in comparison to a night of well-rested sleep. In order to confirm the results and to ensure that there were no confounding variables causing this significant change, the scientists quantified FBB SUVr in a priori hippocampal ROI. ROI, also known as region of interest, is an analysis method that refers to selecting a cluster of voxels or brain region posteriori. Using that method, the results were consistently showing a significant increase in FBB SUVr (thus, amyloid-beta burden) after one night of sleep deprivation. Furthermore, the scientists looked at the number of sleep hours and the total score for sleep quality, which was self-reported using Pittsburgh Sleep Questionnaire Inventory. They found that those factors, sleep hours and the total score for sleep quality, were not associated with the increase of amyloid-beta burden after sleep deprivation. Thus, after supporting and testing their first finding, the researchers were able to explore their second aim. The scientists were looking at the longer-term effects of sleep deprivation and whether their first findings would be consistent when looking at the sleep history of participants and correlating it with the corresponding FBB SUVr measurements. To do so, the researchers tested the association between reported sleep hours, sleep quality, and amyloid-beta burden measured during well-rested sleep and sleep deprivation. They found that there was an inverse correlation between sleep hours and FBB SUVr at RW and a positive correlation under sleep deprivation. In other words, the results supported the hypothesis that there would be an increase in ABB with less SH, especially in the subcortical region of the brain. Furthermore, the scientists looked at different regions of the brain that showed an association between FBB SUVr at well-rested sleep and sleep hours as well as the APOE-based genetic risk for Alzheimer's Disease. APOE stands for apolipoprotein E, which is a gene that plays a major risk factor for Alzheimer's Disease (Kim, 2009). They found that the different observations of low and high FBB SUVr binding at different regions of the brain suggest that there are various brain factors for Alzheimer's Disease influencing each region semi-independently. However, most importantly for the goal of this research, they were able to show that the disruption of deep sleep increases amyloid-beta in the human brain, especially in the thalamus, which is one of the main regions for observing the development of early-onset Alzheimer's. Moreover, another significance to their results is that they reflect the decreased clearance of amyloid-beta in those regions, indicating a role for sleep in the glymphatic system, which is a macroscopic network of vessels for waste clearance in the brain and the overall processing of amyloid-beta clearance in human brains (Jessen, 2015).

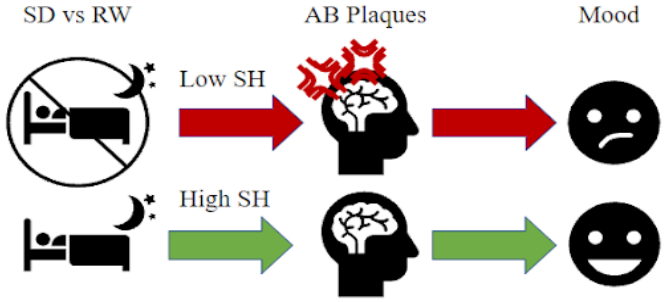

Figure 1: The effects of well-rested sleep and sleep deprivation on the human brain.
Sleep plays a crucial role in the degradation machinery of the brain. Shokri-Kojori et al. (2018) provides evidence that amyloid-beta burden is highly influenced by the sleep a person has. Statistical and screening tests that resulted in consistent PET FBB scans activities across the participants on the rested wakefulness and sleep deprivation tests showed higher FBB SUVr binding on the brain of participants after sleep deprivation in comparison to the scans after a night of well-rested sleep. This indicates a higher accumulation of amyloid-beta in the brain. Moreover, the figure shows that the scientists were able to test for the influence of sleep hours on amyloid-beta burden and found consistent results: the more sleep hours participants got, the less amyloid-beta accumulation detected. Similarly, mood was also negatively influenced by sleep deprivation, as participants were more likely to record negative moods after a night of sleep deprivation in comparison to a night of well-rested sleep (RW).
The research and work of Shokri-Kojori et al. (2018) provided supporting evidence for the role of sleep deprivation on increasing the accumulation of amyloid-beta in the human brain. This work is revolutionary as it is usually done on rodents and not human brains. Thus, we are now able to access data and recordings of the influence of sleep deprivation, sleep hours, and sleep quality on the different regions of the human brain. This is significant because the scientists were not only able to observe and record an increase in ABB after sleep deprivation in the hippocampus and the thalamus, which play a vital role in the development of Alzheimer's Disease, but also because no study was able to directly measure the effect of sleep and the glymphatic function in the human brain's amyloid-beta clearance.
Nonetheless, it is still plausible to argue that the accumulation of

amyloid-beta in the brain is reflecting an increase in the synthesis of amyloid-beta rather than a decrease in the amyloid-beta clearance or the glymphatic system's activity. This is where future studies can dive in and uncover more of the sleep-brain-Alzheimer's dilemma. Besides, the research in this field is of high importance as it is clinically relevant for the diagnosis of Alzheimer's Disease and enhancing both the detection of amyloid-beta accumulation and their degradation.