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Letter to the Editor

Sleep deprivation and plasma biomarkers for Alzheimer's disease

To the Editor

Studies suggest that sleep is important for brain-to-blood clearance of several Alzheimer's disease (AD)-associated proteins, potentially through the glymphatic system [1]. Human data have shown a correlation between total sleep deprivation and an increase of central nervous system (CNS)-derived biomarkers in cerebrospinal fluid (CSF) [2]. Our group recently published data from an experiment where 13 healthy adults were subjected to partial sleep deprivation (PSD) (five consecutive nights with 4 h of sleep) [3]. This intervention did not affect CSF biomarkers associated with AD. We have now performed a follow up analysis of plasma from the same experiment showing unaltered concentrations of amyloid β 40, amyloid β 42, tau and neurofilament light (Table 1).

The interpretation of the current findings is not obvious; as a negative result and a small sample size introduces the risk of a type two error. However, our data suggests that a more "clinically relevant" sleep deprivation protocol does not produce a profound change in CNS protein dynamics, because protein transport from the interstitial space or CSF to plasma does not seem to be affected. Neither CSF nor plasma mirrors the interstitial space fluid chemistry perfectly but has a useable correlation [4].

It is important to emphasize that we have not examined CNS clearance of these AD-related proteins in older adults at increased risk of AD. Our polysomnographic (PSG) data suggest that a young and healthy brain responds to PSD so that the duration of SWS/NREM stage 3 is maintained, which in turn suggest that slow wave sleep (SWS) is the sleep phase during which the glymphatic clearance system is most active. This could protect from build-up of potentially neurotoxic proteins and metabolites during the times of PSD that people so often experience during normal life.

Table 1
Plasma biomarker data.

Baseline (CS) vs PSD		Mean (SD)	*P* Value	Prolonged PSD (N = 4)
Variable	Baseline (CS) (N = 13)	Partial Sleep Deprivation (N = 13)		
Plasma value				
Aβ40, pg/mL	272.4 (28.2)	276.3 (26.2)	0.55	274.8 (37.0)
Aβ42, pg/mL	14.3 (2.2)	14.5 (2.4)	0.70	14.8 (2.1)
Tau, pg/mL	2.8 (1.1)	3.0 (1.3)	0.28	3.0 (0.6)
NfL, pg/mL	6.1 (5.7)	5.5 (4.1)	0.42	7.5 (4.2)

Abbreviations: CS, controlled sleep. PSD, partial sleep deprivation. Aβ, β-amyloid. NFL, neurofilament light.
P-values represent within group (the same subjects exposed to two sleep conditions) differences for the controlled sleep period samples compared with the partial sleep deprivation samples. P-values have not been calculated for the prolonged PSD group because of the small sample size.

The situation could be different in the aging brain with a diminishing SWS potion of normal sleep. In conclusion, further studies are needed to clarify when, or if, sleep becomes a limiting factor for protein clearance from the brain.

Authors' contributions

Zetterberg and Olsson had full access to the data in the study and take full responsibility of the accuracy of data analysis and the integrity of the data.

Study concept and design: Olsson, Ärlig, Hedner, Blennow, Zetterberg.

Obtained funding: Hedner, Blennow, Zetterberg.

Study supervision: Hedner, Blennow, Zetterberg.

Data acquisition, analysis and/or interpretation: Ärlig, Olsson, Hedner, Blennow, Zetterberg.

Statistical analysis: Olsson, Zetterberg.

Drafting of the manuscript: Olsson, Zetterberg.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.12.029.

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