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OREXINS PLAY A DUAL ROLE IN IMMOBILITY EPISODES ON TAIEP RATS A MODEL OF H-ABCCarmen Cortes¹, Karely Espinoza², Carlos De Ovando², Hugo Hernandez³, Valeria Piazza⁴Benemerita Universidad Autónoma de Puebla ¹ Benemérita Universidad Autónoma de Puebla ² Dept. of Chemical, Electronic and Biomedical Engineering, University of Guanajuato ³ Center for Research in Optics, León. Gto. México ⁴

Introduction: Leukodystrophies are a heterogenous group of congenital myelin alterations with more than 30 classified diseases was described until now. Among them there are several mutations in the a and b tubulins the so called tubulinopathies, that affect the central nervous system. The hypomyelination with atrophy of the basal ganglia and cerebellum (H-ABC) is due to a mutation in the tubulin b 4a (TUBB4A) and the taiep rats is the only available model of this human disease with similar magnetic resonance changes and a punctual mutation in the TUBB4A. Taiep rats had immobility episodes (IEs) with a peak between at 9 months of age. Importantly, electroencephalographic recordings shown that IEs had a rapid eye movement (REM) sleep characteristic pattern supporting that are equal to human cataplexy episodes that are key sign of narcolepsy. It is possible to induced IEs when taiep rats are manipulated from the tail or the thorax. Narcolepsy in humans and narcoleptic dogs had a significant decreased in orexin levels in the cerebrospinal fluid (CSF) and a concomitantly decreased of orexin neurons in the lateral hypothalamus.

Methods: We used 21 male rats from taiep at 9 months of age. All rats were kept in standard conditions and were implanted for EEG, EMG and EOG recordings to characterize IEs. We administered orexin A and B agonists and characterized the sleep-wake cycle and frequency of IEs, the peptides were administered by a intracerebroventricular (i.c.v.) injections diluted in artificial CSF. We also measured the number of positive orexin neurons in the lateral hypothalamus through immunohistochemistry.

Results: The i.c.v. administration of [Ala11, D-Leu 15] orexin B agonist significantly decrease the frequency of IEs with 3 and 10 nM doses ($P \leq 0.05$ and $P \leq 0.03$, respectively), without affecting the sleep-wake pattern. However, the i.c.v. administration of Orexin A (17-33) an agonist did not affect the sleep-wake pattern or the frequency of IEs. It is relevant that the number of orexins neurons did not differ between taiep and control Sprague-Dawley (SD) male rats.

Conclusion: Our results showed that IEs had a REM sleep EEG characteristic pattern with cataplexic-like atonia, there are sensible to orexin B agonist, but the number of orexin positive neurons do not differ with respect to SD male rats. In conclusion taiep rats a model of H-ABC is an adequate model of cataplexy-like episodes due to myelin disease.

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IMPACT OF CHRONIC SLEEP DISRUPTION ON GLYMPHATIC FUNCTION, COGNITIVE PERFORMANCE, AND NEUROPATHOLOGY IN THE 5XFAD MOUSE MODELTaylor Pedersen¹, Samantha Keil², Sanjana Agarwal³, Mohammad Badran⁴, David Gozal⁴, Jeffrey Iliff²University of Washington ¹ VISN ²⁰ Mental Illness Research, Education and Clinical Center (MIRECC) ² University of Washington, Department of Psychiatry and Behavioral Sciences ³ Department of Child Health, Child Health Research Institute, The University of Missouri School of Medicine ⁴

Introduction: Recent studies suggest a bidirectional relationship between sleep disruption and Alzheimer's disease, with mid-life sleep disruption associated with the development of Alzheimer's-related amyloid and tau pathology. Yet, the mechanistic link between sleep disruption, particularly over chronic time scales, and the development of Alzheimer's pathology remains unclear.

Methods: In this study, we evaluated the impact chronic sleep disruption has on the onset of cognitive impairment and neuropathologic disease progression using the 5xFAD amyloidosis mouse model. Chronic sleep disruption in male and female C57BL/6 and 5xFAD+ mice was performed in Lafayette sleep fragmentation cages from 10-18 weeks of age. Cognitive impairment was evaluated through behavioral tasks indicative of spatial memory, short-term memory, locomotion, anxiety, and activities of daily living. Upon completion of behavioral experiments, glymphatic function was assessed by measuring the influx of fluorescent cerebrospinal fluid tracers into brain tissue. Aquaporin-4 localization, amyloid plaque deposition, and markers of astroglial and microglial activation were assessed by immunofluorescence.

Results: We observed that chronic sleep disruption impaired cognitive performance and increased neuropathological outcomes in 5xFAD+ and littermate controls. The impact on glymphatic function was assessed in parallel and correlated with neuropathological and behavioral outcomes.

Conclusion: These findings highlight the critical association between dysfunctional sleep and the development of cognitive impairment and neuropathologic disease progression. They indicate that there is a potential interaction between inflammatory expression after chronic sleep disruption and neuropathologic disease progression.

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ELEVATED LEVELS OF EXTRACELLULAR VESICLE CYTOKINES ARE ASSOCIATED WITH POOR SLEEP QUALITY IN WARFIGHTERS WITH CHRONIC MILD TBIVivian Guedes¹, Jackie Gottshall¹, Sara Mithani¹, Jackie Leete², Chen Lai³, Jessica Gill⁴, Kimbra Kenney⁵, Kent Werner¹Uniformed Services University ¹ University of Arizona ² NIH ³ Johns Hopkins University ⁴ Walter Reed National Military Medical Center ⁵

Introduction: Sleep disorders are common in military populations and frequently occur comorbidly with mild traumatic brain injury (mTBI), resulting in substantial health risks. Although inflammation and cytokine elevations have independently been reported both after traumatic brain injury (mTBI) and in association with sleep dysfunction, the impact of these factors on inflammatory processes in a combined context (i.e. post-mTBI sleep dysfunction) has yet to be explored. Extracellular vesicles (EVs) are a particularly promising source of these cytokines; EVs are lipid bilayer-enclosed