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ASSOCIATIONS BETWEEN ALZHEIMER'S DISEASE PATHOLOGY AND THE PSYCHOMOTOR VIGILANCE TASK IN COGNITIVELY UNIMPAIRED ADULTS WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA

David Plante[1], Kieulinh Tran[1], Jesse Cook[1], Erika Hagen[1], Paul Peppard[1], Gwendlyn Kollmorgen[2], Ivonne Suridjan[3], Kaj Blennow[4], Henrik Zetterberg[4], Cynthia Carlsson[1], Sterling Johnson[1], Barbara Bendlin[1]

University of Wisconsin-Madison [1] Roche Diagnostics GmbH [2] Roche Diagnostics International Ltd [3] The Sahlgrenska Academy at University of Gothenburg [4]

Introduction: Daytime sleepiness is a risk factor for Alzheimer's disease (AD) pathology and is associated with more severe cardiometabolic sequalae in persons with obstructive sleep apnea (OSA). However, limited studies have examined objective measures of decreased alertness in the context of AD. Here, we examined performance on the psychomotor vigilance task (PVT) in relation to AD pathology as indexed by AD biomarkers in cerebrospinal fluid (CSF), among individuals with and without OSA.

Methods: Sixty-one cognitively unimpaired adults (39 women), mean age 66.1±7.5 years, enrolled in the Wisconsin Alzheimer's Disease Research Center completed a multifaceted sleep assessment. WatchPAT at-home overnight recordings characterized OSA severity, defined by the apnea-hypopnea index (AHI). Actigraphy determined habitual sleep-wake characteristics. 10-minute PVT measured neurobehavioral alertness. CSF biomarkers were measured using the Roche NeuroToolKit assays (Roche Diagnostics International Ltd, Rotkreuz, Switzerland), an exploratory panel of immunoassays for neurodegeneration. Generalized linear models examined associations between AD biomarkers, AHI, and PVT performance. Primary AD biomarkers of interest were phosphorylated-tau (p-tau) and amyloid-beta (Ab) 42/40 ratio, measured in CSF. The primary PVT variable of interest was the mean response time of the 10% slowest responses, which is associated with daytime sleepiness and default mode network activity. Log transformed PVT and AHI+1 were utilized for analysis. Covariates included age, sex, body mass index, total sleep time, sleep efficiency, APOEe4 status, years of education, AD parental history, biomarker-to-sleep assessment time interval, and Ab42/40 (for p-tau).

Results: No significant relationship of AHI or PVT was observed for Ab42/40. In fully adjusted models, a significant AHI*PVT interaction was observed for p-tau (p=0.0003). Specifically, among individuals with OSA (AHI>5/hour; n=24), slower PVT was associated with increased p-tau (b=13.2, p=0.006), an association that was not significant among those without OSA.

Conclusion: PVT performance may be an objective measure of sleepiness relevant to AD pathology, particularly among individuals with OSA. Replication and expansion of these findings in larger and longitudinal datasets are indicated.

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CIRCADIAN RHYTHMS AMONG YOUTH WITH CRANIOPHARYNGIOMA

Dana Kamara[1], Valerie McLaughlin Crabtree[2], Stephanie Crowley[3], Donna Hancock[1], Joshua Semko[1], Thomas Merchant[1], Belinda Mandrell[1]

St. Jude Children's Research Hospital [1] St. Jude Children's Hospital [2] Rush University Medical Center [3]

Introduction: Craniopharyngioma is an intracranial tumor located in the hypothalamic and pituitary region. Despite high survival rates for youth with craniopharyngioma, quality of life is substantially affected. Morbidity includes high rates of sleep disruption, particularly disorders of hypersomnolence. Circadian rhythms may also be affected due to the proximity of the tumor and subsequent treatment to the hypothalamic-pituitary-adrenal axis, though the role of circadian rhythms has been less studied in this patient population. To evaluate circadian rhythms among youth with craniopharyngioma, dim light melatonin onset (DLMO), an established marker of the circadian system, was estimated.

Methods: Fifty-five patients between the ages of 7 and 20 years participated in this study. Data were collected prior to completion of proton therapy (if indicated). Participants provided hourly saliva samples, in their homes, starting 3 hours prior to habitual bedtime until 1 hour following in dim light conditions (<30 lux). DLMO was calculated based on a threshold of 4 pg/ml. Participants also wore actigraphs to measure sleep patterns. We derived bedtime and waketime from actigraphy and calculated phase angles to bedtime and waketime. DLMO timing and phase angles were compared to published norms for healthy youth ages 9 to 17 years.

Results: DLMO could not be estimated for almost half of the sample (n=25), most often due to a melatonin value above the threshold at the first collection time point. Higher grade of hypothalamic involvement and the presence of diabetes insipidus predicted inability to capture DLMO. Subsample analyses of participants with DLMO (n=30) showed later DLMO timing and shorter phase interval to bedtime than the healthy reference sample.

Conclusion: With standard practice for DLMO estimation, we only obtained estimates for slightly more than half our sample. This may reflect circadian rhythm disturbances or advanced circadian phase. Relative to published norms, those with captured DLMO had later DLMO timing and shorter phase angles to bedtime, indicating sleep at an earlier circadian phase. These findings suggest possible circadian rhythm disruption in pediatric craniopharyngioma. Methodological differences among samples may also contribute to findings. Further examination of circadian rhythm disruption and relations with other sleep disturbances is needed.

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