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**Introduction:** Alzheimer's disease (AD) is a neurodegenerative disorder with no cure that is thought to be triggered by the accumulation of B-amyloid (AB) plaques. Obstructive sleep apnea (OSA) increases risk for developing AD, and has been associated with longitudinal accumulation of AB pathology. However, the mechanisms for the link between OSA and AB burden remains unknown. One candidate mechanism is inflammation, which is increased by OSA and interacts with AB to facilitate AD pathophysiological progression. Here, we test the hypothesis that OSA severity is associated with anti-inflammatory interleukin (IL) cytokines that are also associated with cortical AB burden.str
**Materials and Methods:** Eighteen cognitively unimpaired older adults (Mini Mental State Exam scores≥27; mean age =73.1±5.3; 10 female) enriched for OSA (mean AHI=21.2±22.7) were evaluated with overnight polysomnography (PSG). Plasma samples were collected both prior to sleep and following sleep. OSA severity was quantified using PSG measures of Apnea-Hypopnea Index (AHI), Respiratory Disturbance Index (RDI), and measures of blood oxygen desaturation (number, duration, and frequency of desaturations ≥ 4%, desaturation nadir) stratified by non-rapid eye movement (NREM) and REM sleep stages. Concentrations of inflammatory cytokines were determined with Simoa CorPlex Human Cytokine 10-plex Panel 1 assay (CPX) (interferon gamma (IFNγ), IL-1β, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p70, IL-22, and Tumor Necrosis Factor alpha (TNF-α)). Subjects underwent 18F-florbetapir positron emission tomography (PET) amyloid imaging, and cortical standardized uptake value ratios (SUVR) were collected 50-70 minutes post-injection using a cerebellar gray matter reference to estimate AB burden. Pearson's correlations, Kendall's tau-B, and multiple linear regressions were implemented where appropriate to examine associations between OSA severity, inflammation measures, and cortical amyloid.
**Results:** OSA severity during NREM sleep (log NREM sleep RDI) was significantly correlated with reductions in log IL-5 plasma levels(r=-0.478, p=0.045), and REM sleep AHI (r= -0.677, p=0.002) and RDI (r=-0.692, p=0.001) were significantly associated with reductions in anti-inflammatory IL-10 concentrations. These relationships survived adjustment for sex and age in regression models (e.g., $R^2$=0.488, p=0.0216, with REM sleep RDI as a predictor for IL-10 p=0.006). IL-10 was also significantly associated with PET-measured cortical AB burden (Kendall's tau= -0.414, p= 0.016).
**Conclusions:** These findings support suppression of anti-inflammatory marker IL-10 as a candidate linking OSA to AB pathophysiology, and inflammation as factor linking OSA to AD risk. That decrements in IL-10 were associated with both OSA severity during REM sleep and AB burden suggests that REM sleep-related apnea may be particularly relevant for AD risk. Future studies should utilize OSA treatment to determine if reducing hypoxemia and sleep fragmentation impacts anti-inflammatory cytokines such as IL-10, reduces longitudinal AB accumulation, and delays AD onset.
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## BEHAVIORAL AND LIFESTYLE CORRELATES OF SLEEP IN AN OLDER ADULT POPULATION: RESULTS FROM THE CANADIAN LONGITUDINAL STUDY ON AGING

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**Introduction:** Poor sleep patterns represent an emerging risk factor for mortality and chronic disease outcomes and tend to be associated with behavioral factors such as diet, smoking and physical activity. While these associations are widely acknowledged in the available evidence, it is important to quantify the direction and magnitude of these associations, in order to inform clinical and public health guidelines and improve prediction of health outcomes. The objective of this study was to explore the associations between sleep patterns and a range of behavioral and neighborhood correlates.
**Methods:** We used cross-sectional baseline data from the Canadian Longitudinal Study on Aging (CLSA), a survey of 30,097 community-dwelling adults, aged 45-85 years at baseline. Self-reported sleep measures included sleep duration, sleep dissatisfaction (vs satisfied/neutral), and sleep disturbances (difficulty initiating or maintaining sleep). A range of behavioral and neighborhood factors were explored, including tobacco and alcohol use, physical activity, perceived neighborhood safety, nutrition, condition/repair of living environment, and social media usage. The factors of interest were selected based on a review of the existing literature. Univariate logistic regression analyses were used to estimate odds ratios (ORs) for the associations between each individual behavioral/lifestyle factor and a binary outcome of dissatisfied sleep vs neutral/satisfied sleep. Multiple variable logistic regression was performed with all behavioral factors included. Each model was additionally adjusted for individual level sociodemographic variables including age, sex, BMI, education, household income, marital status, and rural/urban location.
**Results:** In the primary unadjusted models, we observed that daily and former smokers had higher odds of dissatisfied sleep than non-smokers (daily smoker OR: 1.28, 95%CI: 1.15 − 1.42; former smoker OR: 1.10, 95% CI: 1.04 − 1.16). Frequent alcohol drinkers had a lower OR of dissatisfied sleep compared to non-drinkers (OR: 0.87, 95%CI 0.79 − 0.94). Higher nutritional risk scores (AB-SCREEN II) were associated with higher odds of sleep dissatisfaction than persons with low nutritional risk (OR: 1.62, 95%CI: 1.53 − 1.71). Living in an area perceived to be unsafe was associated with higher odds of experiencing sleep dissatisfaction than living in a perceived safe area (OR: 1.12; 95%CI: 1.03 − 1.22). Individuals who experienced no issues with home repair had lower odds of sleep dissatisfaction than those with home repair issues (OR: 0.70, 95%CI: 0.66 − 0.74). The OR for the association between physical activity and sleep dissatisfaction in our sample was statistically significant, but the OR was close to one (OR: 1.0, 95%CI: 0.99 − 1.0). Results from the fully adjusted analysis will be available at the conference presentation.
**Conclusion:** These findings improve our understanding of how different behavioral and neighborhood factors may be correlated with sleep and provide additional insight into the complex associations between various behavioral and lifestyle factors and self-rated sleep satisfaction in a population-based sample of middle-aged and older adults in Canada.

## CHANGES IN SLEEP DISORDERS IN OLDER ADULTS PRODUCED BY THE COVID-19 PANDEMIC

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**Introduction:** The COVID-19 pandemic has rocked our society to its core. Ageing is associated with alterations in circadian activity rhythms, a tendency toward internal desynchronization and decreased sensitivity to phase-resetting signals, including light and those induced by sleep medications. Insomnia is the most common sleep disorder in later life and affects approximately 20-50% of older adults >65 years. The objective of this study is to analyze changes in sleep disorders in older patients affected by the COVID-19 pandemic.
**Materials and Methods:** consecutive noninstitutionalized individuals aged ≥ 65 years of the sleep unit were recruited, 50 patients before a COVID-19 pandemic (BeCOVID) and 50 patients posterior a COVID-19 pandemic (PostCOVID). Clinical history specific for sleep disorders; scores on sleep-questionnaires: Epworth Sleepiness Scale (ESS) ≥ 8 meaning mild, moderate or severe sleepiness; Insomnia Severity Index (ISI) ≥15, indicating moderate or severe clinical insomnia; psychological tests Beck depression inventory (BDI-II), being non-depressed or mild with ≤19 points and moderate or severe with 20-63 points; the state-trait anxiety inventory (STAI) was positive above 50th percentile. Polysomnography parameters were made according to the American Academy of Sleep Medicine (AASM). Diagnosis of sleep disorders was made according to

ICSD3 criteria. Statistical analysis: general descriptive statistics, ANOVA, Wilcoxon signed-rank test and Mann-Whitney were performed using SigmaStat.
**Results:**A total of 44/34% BeCOVID/POSTCOVID women and 56/66% men. Chronic disease 46/88% (hypertension 64/70%; mellitus diabetes 24/22%, dyslipidemia 32/52%; heart disease 10/18%, glaucoma 18/8%), psychiatric disease previous 10/8%. Regarding sleep disorders, a significant increase of chronic insomnia 16/46% (P = <0,001). No significant difference in other sleep disorders, obstructive sleep apnea 88/92%, rest leg syndrome 20/24%, periodic leg movement (PLM) disorders 48/32%, REM sleep behaviors disorders 8/8%, Circadian rhythms disorders 2/4%. When comparing polysomnography significant difference were observed in changes of phases number ( P=0.004), no significant changes in others sleep architecture parameters such as sleep latency, REM sleep latency, efficiency, total sleep time, proportion of sleep stages (N1, N2, N3 y REM), wake after sleep onset, arousals index,PLM index or apnea-hypopnea index (AHI)were observed. Moderate or severe clinical insomnia in 42/54%. Significant increase of anxiety state (P = 0,008) and trait (P = <0,001) and sleepiness (P = 0,008). No significant difference in depression (P = 0,125).
**Conclusion:** The COVID-19 pandemic has brought us relevant changes in sleep disorders in older people, as a rise in chronic insomnia and generalized anxiety disorder.

## CHRONOTYPE ADVANCE AS A PREDICTOR OF SUBSEQUENT COGNITIVE FUNCTION AND BRAIN VOLUME REGRESSION: A 4-YEAR LONGITUDINAL COHORT STUDY

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**Introduction:** Maintaining adequate sleep quantity and quality is vital for many aspects of overall health and neurocognitive function in the elderly. Accumulating evidence suggests that there exists a bidirectional link between circadian rhythm deterioration and neurodegeneration. We aimed to investigate the impact of circadian rhythm disruption on structural and functional brain deteriorations in a late adulthood population.
**Materials and Methods:** We analyzed data from 1874 participants (aged 49–80 years, women 50.3%) in the Korean Genome and Epidemiology Study. Midsleep time on free days corrected for sleep debt on workdays (MSFsc) at baseline was adopted as a marker of chronotype in late adulthood and used to categorize the participants into three groups. "Advancers" were defined as those falling in the bottom third of MSFsc (earlier than 2:15 am), while "delayers" were defined as those falling in the top third (later than 3:30 am). The relationships of chronotype with longitudinal change in cognitive function and gray matter volume (GMV) over four years were investigated.
**Results:** The average MSFsc at baseline was 2:45 am, and the earlier chronotype was linearly associated with lower right entorhinal GMV ($p = 0.001$) in addition to the poor visual memory function test scores ($p < 0.001$). Compared to baseline, follow-up GMVs were all reduced with advancing age regardless of brain lobes. In longitudinal analysis, the earlier chronotype was significantly associated with more faster atrophy in the temporal lobe ($p = 0.018$). Advancers exhibited significantly decreased scores in the digit-symbol coding test and categorical verbal fluency test. Compared to the practice effect in the delayer group, there was no definite change in verbal memory test score in the advancer group.
**Conclusion:** Given the long preclinical period, it is imperative to find a clinically useful indicator for screening high-risk groups in the preclinical stages of neurodegenerative disorders. We suggest that chronotype in midlife measured using a questionnaire can be a practical and valuable indicator for selecting a target group that should be closely monitored for further neurodegenerative disorder development.
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## EFFECTS OF INTERACTION BETWEEN SEX AND APOE GENOTYPE ON SLEEP-STAGE SPECIFIC EXPRESSION OF OBSTRUCTIVE SLEEP APNEA AND SLEEP-DEPENDENT MEMORY

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**Introduction:** Alzheimer's disease (AD) is a world-wide healthcare crisis among older adults resulting in cognitive decline and dementia. It is therefore imperative to understand how AD risk factors interact to impact cognition in healthy older adults at risk for AD. Sex and apolipoprotein E (APOE) genotype are among the most impactful risk factors for developing late onset AD. Sleep disturbance, such as the presence of obstructive sleep apnea (OSA) is also impacted by sex and APOE genotype, and is a risk factor for developing AD. However, it remains unclear how these risk factors interact and how they may disrupt episodic memory, a cognitive ability particularly sensitive to AD. Here, we tested the hypothesis that sex and APOE genotype (ε4 carrier/non-carrier) would interact to impact the expression of OSA events across non-rapid eye movement (NREM) and REM sleep stages and sleep-dependent consolidation of episodic memory.
**Materials and Methods:** Fifty-eight cognitively unimpaired, older adults (mean±SD; 61.4±6.3 years, 38 female, 15 *APOE* ε4 carriers) underwent in-laboratory polysomnography during their habitual time. Participants encoded 88 word-pairs in the evening prior to sleep. Encoding was followed by an immediate recall test, and a delayed recall test occurred in the morning following sleep. Memory consolidation was computed by comparing performance accuracy across testing sessions (post-sleep − pre-sleep memory accuracy). Sleep architecture (TST: total sleep time, time and percent spent in each sleep stage N1, N2, N3 and REM sleep) and OSA severity (apnea-hypopnea index, AHI, measured during REM and NREM sleep stages) were quantified. Univariate ANOVA and post hoc testing was implemented to examine interacting effects of sex and *APOE* genotype on OSA expression and sleep-dependent memory.
**Results:** A significant sex×*APOE* genotype interaction predicted sleep-dependent memory consolidation (p=0.04). Post hoc analysis revealed a trend among *APOE* ε4 carriers, such that sleep-dependent memory consolidation was reduced in men as compared to women (p=0.06). Associations between OSA severity and sleep-dependent memory consolidation also differed by sex and *APOE* genotype. Specifically, among *APOE* ε4 non-carriers, AHI during REM sleep was negatively associated with sleep-dependent memory (r=-0.44, p=0.02) in women but not men (r=0.25, p=0.39). Further, these two correlation coefficients were significantly different (z-score= -1.98, p=.05). Among *APOE* ε4 carriers, REM sleep duration was negatively associated with sleep-dependent memory in men (r=-0.89, p=0.04) but not women (r=-0.51, p=0.16). However, these two correlations coefficients were not significantly different (z-score=-1.05, p=0.29)