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Title

EFFECT OF SEX DIFFERENCES ON INFLAMMATION IN SCHIZOPHRENIA: RELATIONSHIPS WITH SLEEP DISTURBANCES, COGNITIVE FUNCTIONING, AND CARDIOMETABOLIC RISK

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reduced sleep and eating (due to fear of poisoning by neighbors); she otherwise had maintained her ADLs, IADLs, and a busy social calendar with multiple volunteer activities.

Conclusions: The case of Ms. L illustrates a rare presentation of first episode of psychosis at advanced age with relative sparing of cognitive and functional status. This syndrome has been called very-late-onset schizophrenia-like psychosis. The poster will describe the features of this distinct syndrome and advocate for its inclusion in future diagnostic manuals. **This research was funded by:** none

Poster Number: EI - 52 EFFECT OF SEX DIFFERENCES ON INFLAMMATION IN SCHIZOPHRENIA: RELATIONSHIPS WITH SLEEP DISTURBANCES, COGNITIVE FUNCTIONING, AND CARDIOMETABOLIC RISK

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Introduction: Persons with schizophrenia (SZ) have life expectancies that are 15-20 years shorter than the general population, primarily due to cardiovascular-related deaths. In addition to premature mortality, persons with SZ have high rates of disability largely due to cognitive deficits. While cardiometabolic risk as well as cognition are known to be associated with poor sleep and inflammation in the general population, this has not been systematically examined in persons with SZ, although SZ is associated with inflammatory pathology and sleep disturbances that predate the use of antipsychotic medications and accumulation of poor lifestyle habits. Within the general population, women have higher inflammatory marker levels and are more likely to have sleep disturbances and cognitive decline as they age. This study examines the link between sleep, cognition and cardiometabolic risk within persons with SZ, focusing on sex differences.

Methods: The sample included 152 subjects with SZ (DSM-IV-TR criteria) and 141 non-psychiatric comparison (NC) subjects (age range 26 to 65 years; mean 48), with comparable sex and race distribution. We examined sleep (self-reported duration and quality), cardiometabolic risk [Framingham 10-year Risk of cardiovascular disease, high-sensitivity C-reactive protein or hs-CRP, insulin resistance using the Homeostatic Model of Assessment for Insulin Resistance or HOMA-IR], cognition [executive functioning (D-KEFS), overall cognitive functioning (TICS - modified)]; and blood-based inflammatory markers (TNF-a, IL-6, IL-10). In a subset of subjects, we also examined objective measures of sleep (total sleep time (TST), wake after sleep onset (WASO), latency, and efficiency) using wrist-worn actigraphy. The sleep-inflammation-cardiometabolic risk links were examined using Spearman's correlations and general linear models with a backward elimination approach to trim the models. Results: The SZ group reported higher total sleep time and worse sleep quality, worse cardiometabolic risk, and increased levels of inflammatory markers compared to NCs. Within the SZ group, SZ men had higher Framingham Risk, lower hs-CRP and IL-6 levels, as well as better overall cognitive functioning than SZ women (Cohen's d=-0.65, 0.48, 0.38, and -0.33, respectively.) In SZ men, shorter sleep duration and poor sleep quality was associated with higher IL-6 and TNF-a levels and better executive functioning. Within the SZ group, Framingham Risk was associated with sex (as expected), age, IL-6, TNF-a, and overall cognition such that younger women with lower levels of IL-6 and TNF-a as well as better overall cognition had lower Framingham Risk (partial etasquared = 0.19, 0.27, 0.03, 0.04, and 0.02, respectively). The levels of hs-CRP and HOMA-IR were not associated with sex. The levels of hs-CRP was associated with age, IL-6 and overall cognition (partial eta-squared = 0.02, 0.19, and 0.08, respectively). HOMA-IR was associated with age, duration of sleep, sleep quality, IL-6, and overall cognition such that younger persons with longer sleep duration, better sleep quality, lower inflammation and better cognitive functioning had less insulin resistance (partial eta-squared = 0.02, 0.02, 0.05, 0.03, and 0.08, respectively.)

Objective measures of sleep disturbances (TST, WASO) were associated with HOMA-IR, executive functioning, as well as levels of hs-CRP and IL-6.

Conclusions: There are complexities in the associations of different inflammatory biomarkers with clinically meaningful measures of sleep, cardiometabolic health and cognition that reveal sex differences in SZ. Self-reported sleep disturbances and increased inflammation are associated in persons with SZ. Levels of inflammation and sleep disturbances, and their relationships, were sex-dependent in the SZ group, but not the NC group. Longitudinal examination of the sleep-inflammation links, their contribution to clinical outcomes, and the relationship with objective sleep measures and sex-specific factors is warranted. **This research was funded by:** This study was supported, in part, by the National Institutes of Health (grant R01MH094151-01 to DVJ [PI]), by the National Institute of Mental Health T32 Geriatric Mental Health Program (grant MH019934 to DVJ [PI]), by the Stein Institute for Research on Aging at the University of California San Diego, and by the National Institutes of Health, Grant UL1TR001442 of CTSA funding. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.