#32: Objective, but not Subjective, Sleepiness is Associated with Inflammation in Sleep Apnea

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Background

Daytime sleepiness is common in patients with obstructive sleep apnea (OSA), and an important criterion for diagnosis and treatment of OSA. The prevalence of EDS in OSA is 16-22% in epidemiologic samples, and is the most common complaint in clinical samples.

The Multiple Sleep Latency Test (MSLT) is considered the gold standard method for the objective measure of daytime sleepiness, whereas the Epworth Sleepiness Scale (ESS) is the most widely used self-report questionnaire for the assessment of subjective daytime sleepiness in clinical settings. Objective and subjective measures of excessive daytime sleepiness (EDS) are only weakly associated. However, no study has examined whether these two measures differ in terms of underlying mechanisms and/or prognostic value. It has been suggested that pro-inflammatory cytokines, such as interleukin-6 (IL-6), promote sleepiness/fatigue, whereas, cortisol, the end product of the hypothalamic-pituitary-adrenal (HPA) axis, promotes vigilance and hyperarousal. We have previously hypothesized that sleepiness is associated with higher levels of pro-inflammatory cytokines and lower levels of cortisol.

Objective

In the current study, our overall objective was to examine whether the underlying pathophysiologic mechanisms between objective vs. subjective sleepiness differ in a population of patients with OSA. Specifically, we hypothesized that objective, but not subjective, EDS is associated with higher IL-6 levels and lower cortisol levels in patients with OSA.

Methods

We studied 58 OSA patients (mean age 53.73 ± 7.02 years, and 63.8% were male gender) who underwent 8-hour in-lab polysomnography for four consecutive nights. Sleep variables were calculated based on the mean values from nights 2 and 3, so that we controlled for first night effect as well as the sleep-disturbing effect of blood drawing (night 4). A thorough medical assessment, including physical examination, routine laboratory tests and sleep history was completed for each subject. Objective EDS was evaluated using MSLT and subjective EDS was evaluated using on the fourth day. A clinical cut-off point of MSLT values ≤ 8 minutes and ESS scores > 10 were defined as objective and subjective EDS, respectively. 7,8 24-hour serial blood samples were collected every 60 minutes and IL-6 and cortisol levels were assessed on the fourth day and night in the sleep laboratory.

Results

OSA with objective EDS was associated with 1) significantly elevated mean 24-hour (Odds Ratio (OR) =1.56, 95% confidence interval (CI) 1.04-2.34, p=0.03) and daytime (OR =1.79, 95% CI 1.08-2.96, p=0.03) IL-6 levels, and marginally significantly elevated nighttime (OR= 1.26, 95% CI 0.96-1.65, p=0.10) IL-6 levels; and 2) significantly decreased 24-hour (OR= 0.38, 95% CI 0.16- 0.92, p= 0.03) and daytime (OR=0.37, 95% CI 0.16-0.84, p= 0.02) cortisol levels as compared to OSA without objective EDS. In contrast, subjective EDS was not associated either with elevated IL-6 levels or decreased cortisol levels.

Conclusion

Our findings suggest that OSA with objective EDS is the more severe phenotype of the disorder associated with low-grade inflammation, a link to cardiometabolic morbidity and mortality. Objective EDS compared to subjective EDS is a stronger predictor of OSA severity and may be useful in the clinical management of the disorder.

#33: Induction of tolerogenic mediators in uterine immune cells during early pregnancy in dairy heifers

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