430.061 - Sleep Disruptions in Individuals with 16p11.2 Copy Number Variants

Background: Sleep disruptions are significantly more common in individuals with autism, with difficulty falling asleep being the most frequently reported concern. Poor sleep is associated with reduced quality of life measures in affected individuals as well as family members. Interestingly, the disrupted sleep phenotype appears consistent across multiple genetic animal models of autism, including 16p11.2 copy number variations (CNVs). Mouse models of 16p11.2 microdeletion demonstrate decreased sleep efficiency, decreased total sleep time, and decreased REM sleep compared to wild-type litter-mates. Furthermore, this disrupted sleep phenotype appears to be present only in male mice. Despite the importance of sleep in early development, there are currently no published studies on sleep in humans with 16p11.2 CNVs.

Objectives: This is the first study to characterize sleep disruptions in individuals with 16p11.2 deletions and duplications.

Methods: As part of a pilot study, participants from the Simons Variation in Individuals Project (Simons VIP) were recruited at the 2019 16p11.2-CNV family conference in Denver, Colorado. All individuals completed the Pittsburgh Sleep Quality Index (PSQI) questionnaire. The PSQI is a 19-item self-report questionnaire, widely used for sleep assessment across clinical and research settings. It has good internal consistency, test-retest reliability, and diagnostic validity. Institutional Review Board (IRB) approval was received from Columbia University Medical Center, and informed consent was obtained from all participants prior to participation.

Results: Our pilot sample includes 11 individuals, 6 of whom are 16p11.2 duplications carriers (3 females, 3 males) and 5 with 16p11.2 deletions (3 males, 2 females). The duplication group reported a mean sleep latency of 14 minutes, whereas the deletion group reported a clinically significant mean of 55 minutes to fall asleep. This between group finding approached statistical significance, $F(1,9)=3.88$, $p=0.0804$. Consistent with prior mouse models, this finding appears specific to males, with mean sleep latency of 88 minutes (SD=33) for male deletion carriers compared to a mean latency of 5 minutes (SD=0) for female deletion carriers. Duplication with a larger sample size is necessary for adequate statistical power. Further analyses will also examine specific sleep-related concerns and total PSQI scores across groups.

Conclusions: This is the first study to examine sleep disruptions in humans with 16p11.2 copy number variants. Our initial findings support prior animal data and stress the importance of further work in this population. Interpretations are limited due to the small sample size but strongly suggest an effect of male gender on sleep in 16p11.2 microdeletions. It is important to better understand sleep-related genotype-phenotype correlations, given the prevalence of sleep disruptions in developmental disorders and their impact on quality of life. We hope to bolster our pilot findings with larger sample sizes and objective sleep measures going forward.

Authors

H Reed
Columbia University Medical Center

A Jutla
New York State Psychiatric Institute / Columbia University

J Veenstra-VanderWeele
New York State Psychiatric Institute / Columbia University

W Fifer
Columbia University Medical Center