

## **A Genome-wide Association Study of Apnea-Hypopnea Index in Children with Obstructive Breathing**

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Obstructive sleep apnea syndrome (OSAS) is a complex sleep disorder that imposes a large burden on our society in terms of morbidity, quality of life, and healthcare costs. Childhood OSAS is characterized by habitual snoring, disturbed sleep and problems with daytime neurobehavioral functioning. OSAS appears to result from diverse gene-gene interactions and association with environment changes. There have been no published GWAS in children for OSAS. The identification of genetic variants associated with increased risk for OSAS could potentially translate into earlier recognition and treatment with reduced morbidity, and may also serve to identify potential targets for novel therapies. Here we present a genome-wide association study of the Apnea-Hypopnea Index measured in a cohort of children referred to the sleep clinic at the Children's Hospital of Philadelphia for suspected obstructive breathing. Our aim was to identify common genetic variants that increase OSAS severity in children with sleep difficulties. A total of 2,473 children participated in the sleep study. The primary reason for referral was for suspected OSA and they had a Polysomnography (PSG) exam performed. 1,782 children in the sample were given a potential diagnosis of OSA prior to the sleep study. Also, a total of 1201 children were listed as having at least one mental disorder. All participants were genotyped using either the Illumina HumanHap550 or 610 Quad arrays. The association between the natural log of the Apnea-Hypopnea Index (AHI) and SNP was assessed using a linear model in PLINK. Principal components for each individual were calculated using GCTA, and the first 5 PCs were fitted as covariates in the analysis along with age, gender, BMI and total sleep recording time. No SNPs in the study passed the threshold for genome-wide significance ( $p < 5 \times 10^{-8}$ ), either within the ethnic groups separately, or in the meta-analysis of both groups. However, many of the marginally significant SNPs are located in or near genes that have shown evidence of association with related traits such as waist circumference and C-reactive protein, suggesting they may become useful biomarkers as we grow our sample size.

