

# Genomic variants correlated with cognitive behavioral development in the Canadian Healthy Infant Longitudinal Development (CHILD) study

Amirthagowri Ambalavanan<sup>1</sup>, Jihoon Choi<sup>1</sup>, Amel Lamri<sup>2</sup>, Sukhpreet K. Tamana<sup>3</sup>, Sonia S. Anand<sup>3</sup>, Diana L. Lefebvre<sup>2</sup>, Malcolm R. Sears<sup>2</sup>, Meghan B. Azad<sup>4</sup>, Allan B. Becker<sup>4</sup>, Stuart E. Turvey<sup>5</sup>, Theo J. Moraes<sup>6,7</sup>, Padmaja Subbarao<sup>6,7</sup>, Piush J. Mandhane<sup>3</sup>, Qingling Duan<sup>1,8</sup>

<sup>1</sup> Department of Biomedical and Molecular Sciences, Queens University, Kingston, Ontario, Canada

<sup>2</sup> Dept of Medicine, McMaster University, Hamilton, Ontario, Canada

<sup>3</sup> Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada

<sup>4</sup> Department of Pediatrics & Child Health and Community Health Sciences, University of Manitoba, Winnipeg, MB, Canada

<sup>5</sup> Department of Pediatrics, University of British Columbia, Vancouver, British Columbia, Canada

<sup>6</sup> Department of Paediatrics, University of Toronto, Toronto, Ontario, Canada

<sup>7</sup> The Hospital for Sick Children, Toronto, Ontario, Canada

<sup>8</sup> School of Computing, Queen's University, Kingston, Ontario, Canada

Corresponding author: Qingling Duan ([qingling.duan@queensu.ca](mailto:qingling.duan@queensu.ca))

## BACKGROUND

Sleep disordered breathing (SDB), a collective term for chronic conditions including habitual snoring and obstructive sleep apnea, affects up to 10% of children between 2 and 8 years old. Earlier studies have shown that SDB in children is associated with neurobehavioral functions related to executive functioning, behavior development and attention deficit hyperactivity disorder (ADHD) [1]. We hypothesize that preschool SDB may share a common genetic predisposition with neurobehavioral functions during early childhood.

## METHODS

In this study, genomics data were ascertained from the Canadian Healthy Infant Longitudinal Development (CHILD) study using the Illumina HumanCore Exome BeadChip. A total of 2048 Caucasian subjects had available SDB variables derived from parent-reported sleep related breathing disorder subscale (age 5) in addition to cognitive behaviour assessments (i.e. Child Behavior Checklist (CBCL) internalizing and externalizing scores, which are associated with anxiety and aggressive behaviours, respectively). We selected 108 loci for a candidate gene analysis of both SDB and CBCL scores that included variants previously associated with schizophrenia from the psychiatric genomic consortium (PGC) genome wide association study [2]. In addition to main genetic effects, we investigated the potential for genetic interactions with exposures such as exclusive breastfeeding until 3 months.

## RESULTS

Single variant association of CBCL externalizing score identified 14 significant variants located at chromosome 6q12 ( $p < 3.63 \times 10^{-5}$ ). In addition, we identified 2 variants significantly associated with SDB at chromosome 6p22.1 ( $p = 1.8 \times 10^{-5}$ ). Moreover, we identified an interaction effect between genetic variants at chromosome 16q21 and exclusive breastfeeding at 3 months for CBCL externalizing score.

## CONCLUSION

Our study identified that genetic variants associated with schizophrenia in adults may contribute to cognitive behavioural traits and SDB among children during early childhood. These results suggest a common genetic predisposition that can be detected early in childhood and is

modifiable by environmental exposures such as breastfeeding. On-going analyses include genetic risk score analysis and gene-set association tests of rare variants. Furthermore, we will explore gene-environmental interactions using additional exposures such as parental SDB, sleep duration, apnea-hypopnea index, sleep habits, and physical activity.

## **ACKNOWLEDGEMENTS**

Imputation of markers for CHILD subjects was performed by G Pare and colleagues at McMaster University. Genomic analysis was performed with support provided by the Centre for Advanced Computing (CAC) at Queen's University in Kingston, Ontario. The CAC is funded by: The Canada Foundation for Innovation, the Government of Ontario, and Queen's University. The CHILD study was primarily funded by the Allergy, Genes and Environment (AllerGen) Network of Centres of Excellence and the Canadian Institutes of Health Research.

## **REFERENCES**

1. Tamana SK, Smithson L, Lau A, Mariasine J, Young R, Chikuma J, Lefebvre DL, Subbarao P, Becker AB, Turvey SE, Sears MR; CHILD Study Investigators, Pei J, Mandhane PJ **Parent-Reported Symptoms of Sleep-Disordered Breathing Are Associated with Increased Behavioral Problems at 2 Years of Age: The Canadian Healthy Infant Longitudinal Development Birth Cohort Study**, *Sleep*. 2018 Jan 1;41(1).
2. Schizophrenia Working Group of the Psychiatric Genomics Consortium, **Biological insights from 108 schizophrenia-associated genetic loci**, *Nature*. 2014 Jul 24;511(7510):421-7.