

Iodine Modifies the Effect of Fluoride Exposure in Pregnancy on Preschool Boys' Intelligence

Carly V. Goodman¹, Meaghan Hall¹, Rivka Green¹, Jonathan Chevrier², Pierre Ayotte³, E. Angeles Martinez-Mier⁴, Taylor McGuckin¹, John Krzeczowski¹, David Flora¹, Richard Hornung⁵, Bruce Lanphear⁶, & Christine Till¹

¹Department of Psychology, York University; ²Department of Epidemiology, McGill University Faculty of Medicine; ³Département de médecine sociale et préventive, Faculté de médecine, Université Laval; ⁴Indiana University School of Dentistry; ⁵Pediatrics and Environmental Health, Cincinnati Children's Hospital Medical Center (retired); ⁶Faculty of Health Sciences, Simon Fraser University

Introduction

- Animal studies show that the combination of in-utero fluoride exposure and low iodine status has greater negative effects on offspring learning and memory than either alone¹⁻²
- It is unknown, however, whether the combination of iodine deficiency and fluoride exposure during pregnancy is associated with more severe decrements in children's intelligence

Objective

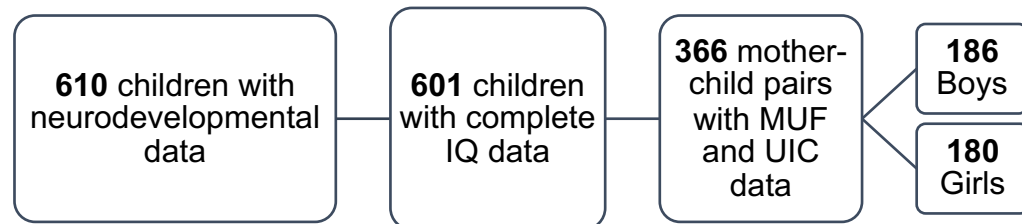
To evaluate whether maternal iodine status modifies the effect of prenatal fluoride exposure on preschool boys' and girls' intelligence in a prospective Canadian cohort

Method

Participants:

N = 366 mother-child dyads in the Canadian multi-site Maternal-Infant Research on Environmental Chemicals (MIREC) Study living in areas with and without water fluoridation

Figure 1. Population Flow Chart



Exposures:

1. Maternal urinary fluoride (MUF) averaged across three trimesters of pregnancy
 2. Maternal urinary iodine concentration (UIC) averaged across trimester 1 and 2
- MUF and UIC adjusted for creatinine

Outcome:

Full-Scale IQ (FSIQ) on the Weschler Preschool and Primary Scale of Intelligence (WPPSI-III)

Method

Table 1. Demographic, Exposure, and Outcome Characteristics

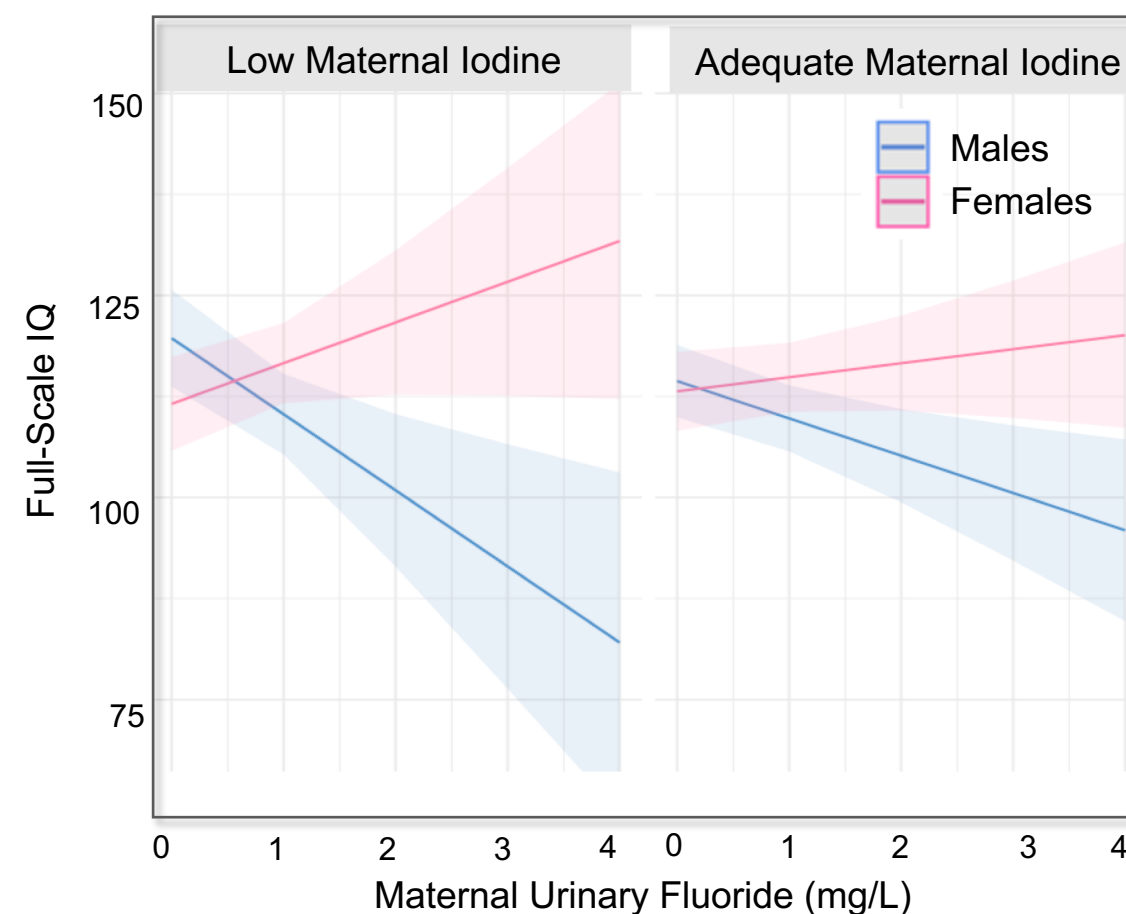
Mothers	
White	334 (91.26%)
≥College Degree	243 (66.39%)
MUF (mg/L)	0.77 ± 0.59
UIC (µg/g)	306 ± 127
Children	
HOME Score	47.23 ± 4.44
FSIQ	107.46 ± 13.75

Analyses:

- Multiple linear regression with a three-way interaction between MUF, UIC, and child sex
- UIC centered around a "low" level and "adequate" level of iodine

Results

Figure 2. Effect of Maternal Urinary Fluoride on Intelligence by Sex and Maternal Iodine Status



Results

- Significant three-way interaction between MUF, UIC, and sex ($p = .019$).
- UIC by MUF interaction was significant for boys ($p = .042$), but not girls ($p = .190$).

Boys:

- Every 1 mg/L increase in MUF predicted a **9.3-point lower** FSIQ score (95% CI: -15.28, -3.23, $p = .003$) for mothers with **low iodine**
- Every 1 mg/L increase in MUF predicted a **4.7-point lower** FSIQ score (95% CI: -7.84, -1.49, $p = .004$) for mothers with **adequate iodine**.

Girls:

- MUF did not predict a significant difference in FSIQ regardless of iodine status (low iodine: $B = 4.93$, 95% CI: -0.61, 10.47, $p = .081$; adequate iodine: $B = 1.77$, 95% CI: -1.53, 5.07 $p = .292$).

Discussion

The effect of prenatal fluoride exposure on boys' FSIQ was exacerbated by low iodine in pregnancy

- Combination of these two risk factors produces cumulative effects on neurodevelopment
- Together, low iodine and high fluoride may induce oxidative stress³
- Boys may be more vulnerable as fetal sex can impact the intrauterine environment⁴
- Highlights the need to further assess the interplay between fluoride and iodine

References

1. Wang J, et al. (2004). Effects of high fluoride and low iodine on biochemical indexes of the brain and learning-memory of offspring rats. *Fluoride* 37(4): 201-208.
2. Hong, J. H., Ge, Y. M., & Ning, H. M. (2005). Effects of High Fluoride and Low Iodine on Learning-Memory and TchE of Brain in Offspring Rats. *China Preventive Medicine*, 6, 489-491.
3. Wang, J. D., Ge, Y. M., Ning, H. M., & Wang, S. L. (2004). Effects of high fluoride and low iodine on oxidative stress and antioxidant defense of the brain in offspring rats. *Fluoride*, 37(4), 264-70.
4. DiPietro, J. A., & Voegtline, K. M. (2017). The gestational foundation of sex differences in development and vulnerability. *Neuroscience*, 342, 4-20.