of human emotion, cognition, behaviour, and social functioning, rather than within distinct diagnostic categories.
Results: Using lead exposure as an example, this presentation will outline a framework for how researchers can use this dimensional approach to develop more specific hypotheses that can reveal how and why neurotoxin exposure increases risk for multiple adverse outcomes and elucidate the mechanisms that may underly these links.
Conclusions: Additionally, given that adverse development within domains of functioning can be detected prior to the onset of full-blown diagnoses, this research could enable us to develop more precise, targeted prevention and risk reduction campaigns. Adopting a dimensional framework will provide a more complete picture of the overall impact of prenatal exposure to neurotoxins – critical for informing public health policy.

Categories: Drug/Toxin-Related Disorders (including Alcohol)
Keyword 1: transdisciplinary research
Keyword 2: neurotoxicity
Keyword 3: brain development
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2 Sex difference of Developmental Neurotoxicants on Intellectual Abilities: A Systematic Review and Meta-Analysis

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Objective: Early life exposures to lead, mercury, polychlorinated biphenyls (PCBs), polybromide diphenyl ethers (PBDEs), organophosphate pesticides (OPPs), and phthalates have been associated with diminished IQ scores in children. Some studies suggest that these neurotoxicants impact boys and girls differently. We conducted a systematic review and meta-analysis to identify and quantify sex differences in IQ deficits from pre- and post-natal exposures to these developmental neurotoxicants.
Participants and Methods: We used PubMed and PsychINFO to screen abstracts of articles published between January 1, 1950 and December 31, 2021 for empirical studies of six neurotoxicants [lead, mercury, PCBs, PBDEs, OPPs, and/or phthalates] that (1) used an individualized biomarker; (2) measured exposure during the prenatal period or within the first six years of life; and (3) provided different effect estimates on children's intellectual abilities by sex. We assessed each study for risk of bias using Navigation Guide (Woodruff & Sutton, 2014). For studies with combinable data, we performed separate random effects meta-analyses for boys and girls with subgroup analyses by neurotoxicant. To homogenize the magnitude of effect observed in each study, we recalculated results to be expressed as the absolute change in intellectual abilities for a relative change of 1.5 times (i.e., 50% increase) in the exposure variable.
Results: Of 3205 studies screened, 53 met inclusion criteria: 34 evaluated prenatal exposure, 11 postnatal exposure, and 8 both pre- and post-natal exposure. We generally rated these studies as "low" to "probably low" risk of bias. Among the studies examining prenatal exposure, 27 reported no significant differences between the sexes, 7 found negative associations in boys, 4 found negative associations in girls, 5 found negative nonsignificant associations in boys and positive nonsignificant associations in girls, and 3 found no clear pattern, where differences by sex depended on the specific phthalate compound or outcome measurement. Among the studies examining postnatal exposure, 14 reported no significant differences between the sexes, 1 found a negative association in boys, 2 found negative associations in girls, and 2 found positive associations for either boys or girls. In our meta-analysis of 16 studies (4 lead, 4 mercury, 2 PBDEs, 2 OPPs, 4 phthalates), we found that prenatal exposure to developmental neurotoxicants was associated with decreased full-scale intelligence in boys (B = -0.26; 95% CI: -0.45, -0.08), but not girls (B = 0.09; 95% CI: -0.14, 0.31). In subgroup analyses by neurotoxicant, prenatal exposure to lead (B = -1.07; 95% CI: -1.63, -0.52), and ΣPBDEs (B = -0.57; 95% CI: -1.14, -0.01) were associated with decreased full-scale intelligence in boys, whereas the girls' effect sizes were consistently near zero.
Conclusions: During fetal development, boys appear to be more vulnerable than girls to IQ

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deficits from neurotoxic exposures, and especially from lead and PBDEs. More research is needed to examine the nuanced sex-specific effects found for postnatal exposures to toxic chemicals.

Reference:
Woodruff, T. J., & Sutton, P. (2014). The navigation guide systematic review methodology: A rigorous and transparent method for translating environmental health science into better health outcomes. Environmental Health Perspectives, 122(10), 1007–1014.
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Categories: Drug/Toxin-Related Disorders (including Alcohol)
Keyword 1: neurotoxicity
Keyword 2: intellectual functioning
Keyword 3: prenatal factors
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3 Fluoride Exposure and Hypothyroidism in Pregnant Women: A Potential Mechanism of Fluoride Neurotoxicity

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Objective: Fluoride exposure has been associated with thyroid dysfunction, but fluoride's impact on thyroid function in pregnancy is unclear, especially during early gestation when the fetus is dependent on maternal thyroid hormone. We examined the potential thyroid-disrupting effects of maternal fluoride exposure in pregnancy and tested whether thyroid disruption in pregnancy mediates the association between maternal fluoride exposure and child intelligence quotient (IQ) among Canadian mother-child dyads living in areas with optimal fluoridation.

Participants and Methods: We measured fluoride concentrations in drinking water and in spot urine samples collected in each trimester from pregnant women enrolled in the Maternal-Infant Research on Environmental Chemicals study. We also measured thyroid hormone (thyroid stimulating hormone [TSH], free thyroxine [FT4], and total thyroxine [TT4]) levels during the first trimester of pregnancy and categorized women as euthyroid (n=1301), subclinical hypothyroid (n=100), or primary hypothyroid (n=28). Those categorized as primary hypothyroid were combined with an additional 79 women who reported clinical diagnoses at time of study enrolment (total n=107). In a sample of 1508 women, we used logistic regression to estimate the association between fluoride exposure and risk of either subclinical or primary hypothyroidism, separately, and linear regression to estimate associations between fluoride exposure and women's thyroid hormone levels (TSH, FT4, TT4). We tested effect modification by child sex and thyroid peroxidase (TPO) antibody status. In a subsample of 439 mother-child pairs, we measured child Full-Scale IQ (FSIQ) at 3-4 years of age using the Wechsler Preschool and Primary Scale of Intelligence. We used linear regression to test associations between maternal hypothyroidism or thyroid hormone levels, and children's FSIQ scores. Finally, mediation analysis in the counterfactual framework was used to estimate the proportion of the effect of maternal fluoride exposure on child FSIQ mediated by maternal hypothyroidism, through evaluation of the natural direct (not through hypothyroidism) and indirect (through hypothyroidism) effects.
Results: Using categorical measures of thyroid status, a 0.5 mg/L increase in water fluoride concentration was associated with a 1.64 (95% confidence interval [CI], 1.04 to 2.58) increased odds of primary hypothyroidism. This association was stronger among women with normal TPO antibody levels (< 5.61 IU/mL) (odds ratio, 2.80; 95% CI, 1.24 to 6.36). In contrast, we did not find a significant association between maternal urinary fluoride and hypothyroidism. For continuous measures of thyroid hormone levels, a 1 mg/L increase in maternal urinary fluoride was associated with a 35% (p=0.01) increase in TSH among women pregnant with a female fetus. In our subsample analyses, children born to women with primary hypothyroidism had lower FSIQ than children of euthyroid women, especially among boys (B, -

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