Some references on EDCs, glucocorticosteroids, and neurodevelopment

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1 EDCs and neurodevelopment

1.1 Bouchard et al. (2010)

- Title: *Attention-Deficit/Hyperactivity Disorder and Urinary Metabolites of Organophosphate Pesticides.*
- Exposures: dialkylphosphate metabolites (biomarkers of organophosphate pesticide exposure).
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: ages 8-15.
- Outcomes: ADHD diagnostic status.
- Timing outcome assessment: ages 8-15.
- Results:
  - Exposure to OP pesticides might contribute to ADHD.
- Sex-specific results: NA.

1.2 Cartier et al. (2016)

- Title: *Organophosphate Insecticide Metabolites in Prenatal and Childhood Urine Samples and Intelligence Scores at 6 Years of Age: Results from the Mother–Child PELAGIE Cohort.*
- Exposures: dialkylphosphate metabolites (biomarkers of organophosphate pesticide exposure).
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: age 6.
- Outcomes: Wechsler Intelligence Scale for Children.
- Timing outcome assessment: age 6.
- Results:
  - No association between total DAP metabolites and WISC scores.
  - WISC working memory score inversely associated with levels of DE metabolites.
- Sex-specific results: NA.

1.3 Furlong et al. (2017)

- Title: *Prenatal exposure to organophosphorus pesticides and childhood neurodevelopmental phenotypes.*
- Exposures: organophosphorus pesticides. Total diethylphosphate and total dimethylphosphate.
- Medium exposure assessment: spot urine samples.

- Timing exposure assessment: prenatal between 25 and 40 weeks of gestation.
- Outcomes: behavior, executive functioning, and IQ.
- Timing outcome assessment: ages 6–9.
- Results:
  - Dimethylphosphate metabolites negatively associated with Internalizing factor scores.
  - Dimethylphosphate metabolites positively associated with Executive Functioning factor scores.
  - Diethylphosphate metabolites negatively associated with Working Memory Index.
- Sex-specific results: no interactions by sex.

1.4 González-Alzaga et al. (2015)

- Title: *Pre- and postnatal exposures to pesticides and neurodevelopmental effects in children living in agricultural communities from South-Eastern Spain.*
- Exposures: dialkylphosphate metabolites (biomarkers of organophosphate pesticide exposure).
- Medium exposure assessment: urine samples.
- Timing exposure assessment: ages 6-11.
- Outcomes: Wechsler Intelligence Scale for Children.
- Timing outcome assessment: ages 6-11.
- Results:
  - DAP levels inversely associated with performance on intelligence quotient and verbal comprehension domain.
- Sex-specific results: stronger associations in males.

1.5 H.-B. Huang et al. (2015)

- Title: *Association of Exposure to Endocrine-Disrupting Chemicals During Adolescence With Attention-Deficit/Hyperactivity Disorder–Related Behaviors.*
- Exposures: seven metabolite of phthalate esters.
- Medium exposure assessment: urine samples.
- Timing exposure assessment: prenatal and at ages 2, 5, 8, and 11.
- Outcomes: Bayley and Wechsler tests for assessing neurocognitive functions and intelligence (IQ).
- Timing outcome assessment: ages 2, 5, 8, and 11.
- Results:
  - Children's phthalate exposure (MEOHP and sum of DEHP metabolites) inversely associated with cognitive development.

- Sex-specific results: NA.

1.6 P.-C. Huang et al. (2017)

- Title: *Intellectual evaluation of children exposed to phthalate-tainted products after the 2011 Taiwan phthalate episode.*
- Exposures: 5 phthalate metabolites.
- Medium exposure assessment: first-morning urine samples.
- Timing exposure assessment: ages 3-12.
- Outcomes: Wechsler tests for assessing the children's intelligence quotient.
- Timing outcome assessment: ages 3-12.
- Results:
  - MEOHP, MnBP, and MiBP inversely associated with verbal intelligence.
- Sex-specific results: NA.

1.7 J. I. Kim et al. (2017)

- Title: *The effects of maternal and children phthalate exposure on the neurocognitive function of 6-year-old children.*
- Exposures: phthalate metabolites.
- Medium exposure assessment: urine samples.
- Timing exposure assessment: age 6
- Outcomes: IQ scores and continuous performance test variables.
- Timing outcome assessment: age 6.
- Results:
  - DEHP metabolites (including MEHHP and MEOHP) inversely associated with intelligence, attention, and response time variability.
- Sex-specific results: NA.

1.8 Li et al. (2018)

- Title: *Relationship between bisphenol A exposure and attention-deficit/ hyperactivity disorder: A case-control study for primary school children in Guangzhou, China.*
- Exposures: bisphenol-A.
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: ages 6-12.
- Outcomes: ADHD.
- Timing outcome assessment: ages 6-12.

- Results:
  - Positive association between BPA levels and odds of ADHD.
- Sex-specific results: stronger associations in males.

1.9 Oh et al. (2023)

- Title: *Early childhood exposure to environmental phenols and parabens, phthalates, organophosphate pesticides, and trace elements in association with attention de cit hyperactivity disorder (ADHD) symptoms in the CHARGE study.*
- Exposures: phenols/parabens, phthalates, OP pesticides, trace elements.
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: ages 2-5.
- Outcomes: ADHD symptoms.
- Timing outcome assessment: ages 2-5.
- Results:
  - Positive associations of MECPP and MEHHP with Hyperactivity subscale scores and hyperactivity/impulsivity subdomain scores.
  - Positive associations of MNBP with hyperactivity/impulsivity subdomain scores.
  - Inverse associations of TCS with Hyperactivity subscale scores.
  - Inverse associations of TCS with inattention subdomain scores.
  - Positive associations of mixture of phthalates with scores of the ABC Hyperactivity subscale and hyperactivity/impulsivity subdomain.
    - Drivers by subdomain, hyperactivity/impulsivity subdomain: MHPP, MEHHP, and MBZP.
  - Positive associations of mixture of phenols/parabens with inattention subdomain score.
    - Drivers by subdomain, inattention subdomain: MEPB, PRPB, and OHMEP.
- Sex-specific results: association of mixture of phthalates with hyperactivity-related subscale and subdomain significant in males only.

1.10 Rodríguez-Carrillo et al. (2019)

- Title: *Bisphenol A and cognitive function in school-age boys: Is BPA predominantly related to behavior?.*
- Exposures: bisphenol-A.
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: ages 9-11.
- Outcomes: comprehensive neuropsychological test battery.
- Timing outcome assessment: ages 9-11.

- Results:
  - No consistent association between BPA levels and cognitive abilities.
  - Possible inverse association between BPA levels and working memory.
- Sex-specific results: assessment only in males.

1.11 Shoaff et al. (2020)

- Title: *Association of Exposure to Endocrine-Disrupting Chemicals During Adolescence With Attention-Deficit/Hyperactivity Disorder–Related Behaviors.*
- Exposures: phthalates, parabens, phenols, and triclocarban.
- Medium exposure assessment: urine samples.
- Timing exposure assessment: age 15.3
- Outcomes: Conners Attention Deficit Scale and the Behavior Assessment System for Children.
- Timing outcome assessment: age 15.3
- Results:
  - Exposure to antiandrogenic phthalates increases the risk of ADHD-related behavior problems.
- Sex-specific results: stronger associations in males.

1.12 Tewar et al. (2016)

- Title: *Association of Bisphenol A exposure and Attention-Deficit/Hyperactivity Disorder in a national sample of U.S. children.*
- Exposures: bisphenol-A.
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: ages 8-15.
- Outcomes: presence of ADHD in the past year.
- Timing outcome assessment: ages 8-15.
- Results:
  - Positive association between BPA levels and ADHD.
- Sex-specific results: stronger associations in males.

1.13 Vilmand et al. (2023)

- Title: *Prenatal and current phthalate exposure and cognitive development in 7-year-old children from the Odense child cohort.*

- Exposures: phthalates metabolites.
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: 7 years.
- Outcomes: IQ (subtests from Wechsler Intelligence Scale for Children).
- Timing outcome assessment: 7 years.
- Results:
  - Inverse associations of MCPP, sum of DnHxPm, sum of DiDPm, and sum of DiNPm with IQ points.
- Sex-specific results: no evidence of effect modification by sex.

1.14 Yu et al. (2016)

- Title: *Increased risk of attention-deficit/hyperactivity disorder associated with exposure to organophosphate pesticide in Taiwanese children.*
- Exposures: dialkylphosphate metabolites (biomarkers of organophosphate pesticide exposure).
- Medium exposure assessment: urine samples.
- Timing exposure assessment: ages 4-15.
- Outcomes: ADHD.
- Timing outcome assessment: ages 4-15.
- Results:
  - Dose–response relationship between urinary concentrations of dimethylphosphate and ADHD.
- Sex-specific results: NA.

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2 EDCs and glucocorticosteroids

2.1 J. H. Kim et al. (2018)

- Title: *Association of phthalate exposures with urinary free cortisol and 8-hydroxy-2'-deoxyguanosine in early childhood.*
- Exposures: four phthalate metabolites.
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: prenatal and at ages 0, 3, 9, 12, 15 months.
- Outcomes: free cortisol.
- Medium outcome assessment: spot urine samples.

- Timing outcome assessment: prenatal and at ages 0, 3, 9, 12, 15 months.
- Results:
  - Positive associations between MEHHP, MEOHP, MiBP, and MnBP, with free cortisol.
- Sex-specific results: no evidence of modification by sex.

2.2 Sears et al. (2023)

- Title: *Evaluating mixtures of urinary phthalate metabolites and serum per-/polyfluoroalkyl substances in relation to adolescent hair cortisol: The HOME Study.*
- Exposures: phthalate metabolites.
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: ages 1-5 and 8.
- Outcomes: cortisol.
- Medium outcome assessment: hair.
- Timing outcome assessment: age 12.
- Results:
  - Positive association between mixture of phthalates metabolites measured in childhood and hair cortisol measured in adolescence. Driven by MEP, MiBP, MBzP.
- Sex-specific results: no evidence of modification by sex.

2.3 Sun et al. (2018)

- Title: *Associations between repeated measures of maternal urinary phthalate metabolites during pregnancy and cord blood glucocorticoids.*
- Exposures: phthalate metabolites.
- Medium exposure assessment: spot urine samples.
- Timing exposure assessment: 14, 24, and 36 weeks of gestation.
- Outcomes: cortisol and cortisone.
- Medium outcome assessment: cord blood.
- Timing outcome assessment: 14, 24, and 36 weeks of gestation.
- Results:
  - Positive association of MEHP 3rd trimester with cortisol.
  - Inverse association of MECPP and MEOHP 3rd trimester with cortisone.
  - Positive association of MBzP 1st trimester with cortisol/cortisone ration.
- Sex-specific results: evidence of modification by sex, but not significant.

- Females: positive associations with glucocorticoids (MEHP and MBzP 1st trimester, and DEHP 3rd trimester).
- Males: inverse associations with glucocorticoids (MECPP, MEHHP, and MEOHP 3rd trimester).

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3 Glucocorticosteroids and neurodevelopment

3.1 Lupien et al. (2009)

- Title: *Effects of stress throughout the lifespan on the brain, behaviour and cognition.*

The HPA axis, which can be activated by stress, is responsible for the production of glucocorticoids. The brain, and its proper functioning, is a potential target, due to the presence of receptors for these hormones. Glucocorticoids are necessary for brain maturation, although their under- or over-production might interfere with its normal development and ultimately lead to long-term impaired functioning.

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