**Supplementary Table 5:** Associations between exposure to ambient air pollutants and cognitive impairment/learning difficulties

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| --- | --- | --- | --- | --- | --- | --- |
| **Author, year** | **Pollutant (s)** | **Exposure window** | **┼Key association** | **Exposure measurement** | **Effect estimates** | **Overall study quality** |
| Fuertes, 2016 (57) | PM2.5 | Childhood | **+** | Long-term (annual average) concentrations of NO2, PM2.5 mass were estimated to each participant's home address at birth, 10 years and 15 years using land-use regression (LUR) models originally derived as part of the “European Study of Cohorts for Air Pollution Effects” | For dyscalculia: Significant associated with PM2.5 (1.29 [1.03, 1.61]). No significant association with NO2 exposures across birth, 10 years and 15 years  For dyslexia: No associations with either NO2 or PM2.5 across birth, 10 years and 15 years addresses | \*\*\* |
| NO2 | Childhood | **-** |
| Kerin, 2018 (19) | NO2 | Gestation through Infancy | **-** | The CALINE4 line-source air quality dispersion model to estimate average concentrations for the specific locations and time periods (trimesters of gestation and first year of life) for each participant. A second approach was to use the regional air quality data for the exposure assignments for PM2.5 and nitrogen dioxide derived from the US Environmental Protection Agency’s Air Quality System data and geocoded to the participants' birth certificate and residential history | Overall prenatal or year 1 exposures of PM2.5 were not significantly associated with any of the scores on cognitive or adaptive scales in children with ASD.  During pregnancy, 11.0% (95% CI: −17.0%, −1.45%) decrease in VABS composite score per 2 SD increase in NO2 (6.82 ppb). NO2 was also associated with decreased performance on the communication (−13.3% [95% CI: −23.7%, −2.71%]) and socialization (−9.60% [95%CI: −18.6%, −0.43%]) | \*\* |
| Gestation | **+** |
| Infancy | **-** |
| PM2.5 | Gestation | **-** |
| Infancy | **-** |
| Kusters, 2022 (94) | NO2 and NOx | Gestation through Childhood | **-** | NO2 and NOx measured at 80 sites and PM 2,5 at 40 sites across Netherlands and Belgium. An annual mean concentration for each pollutant, to obtain mean exposure concentration for each air pollutant during pregnancy and childhood, using weighted air pollutant concentrations based on the time spent at each home address for all participants | Exposure to PM2.5 and NO2, NOx during pregnancy or childhood was not associated with a decline in full-scale IQ (0.77 points (95% CI -2.24; 3.78) per 5 ug/m3 increase in PM2.5) | \*\*\* |
| Gestation | **-** |
| Childhood | **-** |
| PM2.5 | Gestation through Childhood | **-** |
| Gestation | **-** |
| Childhood | **-** |
| Lertxundi, 2019 (72) | NO2 | Gestation | **-** | Weighted average concentration of PM2.5 measured during her whole pregnancy | The adjusted combined co-efficient were negative and not significant for PM2.5 and NO2 for each cognitive functions and motor skills. After stratifying by gender, the associations become more negative for boys, with some of the associations becoming statistically significant (memory and verbal both for PM2.5 and NO2), and global cognition, verbal, numeric and fine motor scale for NO2 | \*\*\* |
| Boys | **+** |
| PM2.5 | Gestation | **-** |
| Boys | **+** |
| Luminati, 2022 (62) | NO2 | Childhood | **-** | Annual mean outdoor NO2 concentrations at the home address of the children were predicted by a land use regression (LUR) model based on NO2 measurements over 2 one-week periods at 80 locations in 2019 | We found no association between yearly NO2 exposure and children's cognitive development (beta -0.05, 95% CI [-0.20; 0.10]) or behavioral problems (beta 0.02, 95% CI [-0.80; 0.12]) | \*\*\* |
| McGuinn, 2022 (29) | PM2.5 | Gestation | **+** | A satellite based model was used to assign PM2.5 exposure averages during pregnancy, each trimester, and the first year of life | For all participants, increase by 1 ug/m3 in PM2.5 exposure and MSEL composite scores for several developmental windows including the first (β: −0.35, 95% CI: −0.65, −0.05) and second (β: −0.27, 95% CI−0.57, −0.02) trimesters, as well as exposures averaged over the entire pregnancy period (β: −0.97, 95% CI: −1.69, −0.25) were significant | \*\*\* |
| 1st trimester | **+** |
| 2nd trimester | **+** |
| Pregnancy | **+** |
| Ni, 2022 (71) | NO2 | Gestation through Infancy | **-** | Biweekly nitrogen dioxide (NO2), PM2.5 predictions from region-specific models were estimated, and averaged the exposure concentrations over each trimester, the whole pregnancy, and the two postnatal windows from childbirth to 2 y old and from 2 to 4 y old obtained | Prenatal and Postnatal exposures to NO2 and PM2.5 is not associated significantly with cognitive decline or low IQ scores | \*\*\* |
| PM2.5 | Gestation through Infancy | **-** |
| Sentis, 2017 | NO2 | Gestation through Childhood | **-** | Using land-use regression models (LUR), regional annual averages of estimated prenatal and postnatal NO2 levels at the participants' residential addresses | Prenatal exposure to NO2 with an impaired standard error (SE) of the hit reaction time (HRT) (increase of 1.12 ms [95% CI; 0.22 - 2.02] per 10 μg/m3 increase in prenatal NO2) and increased omission errors (6% [95% CI; 1.01 to 1.11] per 10 μg/m3 increase in prenatal NO2).  Postnatal exposure to NO2 is similar but borderline significant increase of omission errors (5% [95% CI; =0.99 to 1.11] per 10 μg/m3 increase in postnatal NO2) | \*\*\* |
| Gestation | **-** |
| Childhood | **-** |
| Tokuda, 2023 (64) | PM2.5 | Gestation through Childhood | **-** | Exposure to outdoor PM2.5 during pregnancy and the first five years of life with a machine learning-based spatio temporal model. residential addresses geocoded. Average concentrations of outdoor PM2.5 for each trimester, the entire pregnancy, and 0–1, 1–3, and 3–5 years after childbirth | Outdoor PM2.5 during pregnancy and early childhood was not associated with decreased cognitive performance | \*\*\* |
| Gestation | **-** |
| Infancy | **-** |
| Childhood | **-** |

**┼**: [**+**] Statistically significant, [**-**] Statistically Non – significant