Chronic Early Life Exposure to Carbon Monoxide in Woodsmoke and Children's Neurodevelopment in Rural Guatemala: A Pilot Study

Linda Dix-Cooper
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Global Health & Environment | School of Public Health | University of California, Berkeley

Global Health & Environment
Environmental Health Sciences
50 University Hall
Berkeley, CA 94720-7360
Tel: 510.643.5160
Email: ehs_div@berkeley.edu
Website: http://ehs.sph.berkeley.edu/ghe/

Carbon monoxide is the primary component of woodsmoke with unknown chronic neurodevelopmental toxicity. Chronic in utero exposure to co-pollutants of CO correlates with declines in verbal and non-verbal intelligence during childhood and acute poisoning cases are linked to impairments in motor-related cortical regions. This is the first study to examine the neurodevelopmental and behavioral effects of chronic exposure to CO in woodsmoke during early life. In San Marcos, rural Guatemala, the Randomized Exposure Study of Pollution Indoors and Respiratory Effects (RESPIRE) stove intervention trial measured personal passive 48-hour CO samples among pregnant mothers and their infants from 2002 to 2005. In the current pilot study, we performed follow-up child neurodevelopment and behavioral evaluations at 6 years of age to examine the relationship between children's performance and their pregnant mothers' chronic, elevated exposure to CO from woodsmoke during the third trimester.

The study population is a Mam-speaking (Maya), indigenous group living at relatively high altitude (2500 m) in Western Guatemalan Highlands. From March to June, 2010, 39 follow-up cognitive assessments were performed among 6-year-old children who had formerly participated in the RESPIRE birth cohort. Administered by two trained, local indigena Mam-speaking Guatemalan field workers, a battery of non-verbal cognitive tests was piloted and culturally adapted for these communities. Maternal interviews assessed relevant covariates for children's neurodevelopment including: home environment stimulation, pesticide exposure history, and child use of the temascal (a sauna house used for bathing). We confirmed the feasibility of conducting a cognitive study in a rural Guatemalan context and compared Guatemalan cognitive performance scores to standardized means and cut-off scores for delayed and gifted children. Using multivariate linear regression models, we examined the association between average CO personal passive 48-hour exposure for mothers during the 3rd trimester as well as for infants during the first 9 months of life and child cognitive performance on a battery of neuropsychological tests at age six years.

Mothers' personal passive 48-hour mean CO exposures during the third trimester were 3.83 ppm ± 3.03ppm with a range of 0.6 to 12.5ppm (n=39). During the first 9 months of life, infants had a mean CO measured of 2.20 ± 1.98 and a range of 0.3 to 9.8ppm. After adjustment for child sex, age, vision scores, and socio-economic status, or many other potentially confounding factors,

maternal $\log_{10}$-transformed CO concentrations during the 3rd trimester were inversely associated with children's visuo-spatial integration ($p<0.05$), short ($p<0.05$) and long-term memory recall ($p<0.05$), and fine motor performance ($p<0.01$) on the Bender Gestalt-II's Copy, Immediate Recall, and Delayed Recall Figures drawing tests, as well as the Reitan-Indiana's electric finger tapping test, respectively. Overall, an inverse linear relationship was observed between maternal CO exposure and most neurodevelopment tests at age 6 years, with 4 out of 11 brief cognitive tests showing significant associations (one-tailed; $p<.05$). For every ten-fold increase in maternal CO-ppm, Copy Figures scores decreased 4.2 points (n=39), $\log_{10}$-transformed Immediate Recall scores decreased 0.3 points (n=39) (meaning a 1% change in mother's 3rd trimester CO leads to a 30% decrease in Immediate Recall Scores), Delayed Recall figures scores decreased 4.3 points (n=36), and the average number of finger taps in ten seconds decreased by 6 (n=37). Other variables that accounted for the most variance in the final multiple regression models included home environment stimulation score, examiner, WHO height-for-age percentile and age the infant stopped breastfeeding. Tests for robustness with restricted sample sizes excluding potentially influential scores did not markedly change the results.

These findings suggest that early life exposure to CO in woodsmoke in the rural Guatemalan western highlands may impair 6-year-old children's cognitive performance across a variety of domains including visuo-spatial, short and long term memory, and fine motor skills. Using high quality CO biomarkers of mothers' personal exposure and refined non-verbal cognitive tests, we observed significant inverse associations at chronic elevated CO exposure levels despite the relatively small sample size (n=39). Further data collection may only increase the robustness and significance of these associations between mothers' 3rd trimester CO and cognition in this population. Neurodevelopmental deficits can have long-lasting impacts on children's social and psychological development, predicting future school and work performance. Acute CO poisoning cases show that eliminating CO exposure may reverse the neurologic effects. More research is needed to fully characterize the chronic neurodevelopmental toxicity of carbon monoxide in woodsmoke.