# Prenatal mycoestrogen exposure and infant cognitive and language development

Grace Lee, Carolyn Kinkade, Zorimar Rivera-Núñez, Emily Barrett

Zearalenone (ZEN), a fungal-derived mycotoxin commonly found in cereal grains and processed foods, is linked to adverse effects on female reproduction. As climate change leads to warmer and moisture conditions that promote fungal growth, the study of these mycotoxins has become a priority for the World Health Organization and the United Nations. Recent epidemiological studies suggest that prenatal exposure to mycoestrogens is associated with alterations in gestational weight gain, sex steroid hormones, and infant size. Here we extend this line of research to study prenatal mycoestrogen exposure in relation to cognitive and language scores at 12 months of age in UPSIDE, a medically normal risk U.S. birth cohort. Mycoestrogens (ZEN, AZAL, and total mycoestrogens) were measured in placental samples collected at birth. When the resulting infants were 12 months old, trained study staff administered the Bayley Scales Of Infant and Toddler Development III (n=187). Higher scores on the cognitive and language subscales indicate more advanced development. We fitted multivariable linear regression models examining associations between log-transformed mycoestrogen concentrations and Bayley subscores, both in the full cohort and stratified by child sex. Given percent detection, the models considered total mycoestrogens and ZEN as continuous variables. We also considered AZAL as a binary variable (above vs below limit of detection). In the full cohort, mycoestrogen concentrations tended to show non-significant, positive associations Bayley scores. For example, a log-unit increase in total mycoestrogens was associated with 0.45 unit (95%CI: -1.57, 2.46) higher cognitive scores and 1.40 unit (95%CI: -2.3, 5.1) higher language scores. In sex-stratified analyses, associations tended to be positive in males, but negative in females. For example, a log-unit increase in total mycoestrogens was associated with 2.72 unit (95%CI: -0.39, 5.82) higher cognitive scores in males, but 1.88 unit (95%CI: -4.62, 0.87) lower scores in females. This is the first study to examine prenatal exposure to mycoestrogens in relation to neurodevelopment in humans. Our results suggest potential sex differences that warrant replication in larger samples. Acknowledgements: We thank the UPSIDE staff and participants as well as Dr. Brian Buckley, Dr. Anita Brinker, and Dr. Lauren Aleksunes for their support with mycoestrogen analyses. Funding for the current analysis was provided by the National Institute of Health (Grants F31ES034269, R21ES032047, UH3OD023349, R01HD083369, R01ES029275, T32ES019854, P30ES005022, P30ES001247) and The Wynne Family Center.