

map known neuroclinical deficits among individuals with schizophrenia onto a high-risk, non-clinical sample. A secondary aim of the study is to demonstrate prediction of symptom severity over time measured by a combination of ERPs and clinical symptom scores. METHODS/STUDY POPULATION: Recruited participants are pre-screened for eligibility via telephone interview. This process includes administration of Community Assessment of Psychotic Experiences (CAPE), and the Mini International Neuropsychiatric Interview (MINI). During in-person lab assessment, participants provide written informed consent and complete a battery of ERP tasks, semi-structured clinical interviews, and self-report questionnaires that assess for presence and severity of sub-threshold psychotic-like experiences. Six months following the laboratory visit, participants will be provided a link to online questionnaires that were completed during laboratory visit in order to reassess presence and severity. RESULTS/ANTICIPATED RESULTS: The target number of participants included in this study is 60. We hope to recruit individuals who range in symptom severity as measured by CAPE. It is of interest to determine relationship among known deficits in individuals with schizophrenia and individuals exhibiting sub-clinical symptoms of psychosis. Additionally, we plan to examine ERPs and symptoms together as a "profile" of high risk psychosis, yielding more robust information about this population than any one ERP or symptom measure alone. The within subjects design of this study allows for examination of symptom progression and potential prediction of symptoms based on brain activity. Many studies examine only single ERP components thus limiting the ability to draw broader conclusions regarding general cognitive frameworks among populations. We use a combination of well-validated ERPs (i.e. P300, N400, ERN) with behavioral and symptom data in order to predict variation in symptoms over the course of 6 months. The project aims to take a novel approach at identifying high-risk profiles based on neurophysiological and behavioral data and using this as a basis for predicting symptom severity across time. DISCUSSION/SIGNIFICANCE OF IMPACT: Individuals endorsing psychotic-like experiences are at heightened risk for developing a psychotic disorder in the future, and have been linked with similar social, behavioral, and emotional risk factors similar to those of schizophrenia. Subjective data (e.g. self-report, interview) sheds light on important information regarding observable symptom manifestation; however, neural measures can detect relatively subtle deficits in information processing that precede and predict overt symptom onset, which necessitates other important methodological considerations. Specifically, extant literature has shown that quantifiable indices of cognitive deficits may represent a vulnerability to psychosis in high-risk populations, and can be measured using event-related potentials (ERPs). This study integrates a psychophysiological approach by mapping neural deficits from schizophrenia onto a high-risk sample. Many studies examine only single ERP components thus limiting the ability to draw broader conclusions regarding general cognitive frameworks among populations. We use a combination of well-validated ERPs (i.e. P300, N400, ERN) with behavioral and symptom data in order to predict variation in symptoms over the course of 6 months. The project aims to take a novel approach at identifying high-risk profiles based on neurophysiological and behavioral data and using this as a basis for predicting symptom severity across time. We will parse heterogeneity within a high-risk group in order to create innovative profiles and potentially predict variation in course of symptoms. In other words, a "fingerprint" physiologic aberration may be exhibited within high-risk individuals and can be used as biomarkers to identify those at risk even before onset of observable symptoms.

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### Organophosphate pesticide exposure during pregnancy, gestational weight gain and long-term postpartum weight retention

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OBJECTIVES/SPECIFIC AIMS: Little is known about potentially obesogenic endocrine-disruptors' effects on excessive gestational weight gain (GWG) and postpartum weight retention (PPWR), which increase risk of adverse pregnancy and postnatal outcomes. We explored associations between prenatal organophosphate (OP) pesticide exposure and increased weight both during and after pregnancy. METHODS/STUDY POPULATION: Three dimethyl (DM) and three diethyl (DE) OP metabolites were measured in spot urine samples collected at <18, 18-25, and >25 gestational weeks among 688 participants in the Generation R Study. Metabolite levels were expressed as molar concentration/gram creatinine and log10-transformed. GWG and PPWR were calculated as the difference between weight at each prenatal/postnatal visit or maximum gestational weight and pre-pregnancy weight. In covariate-adjusted regression models we assessed associations of metabolite concentrations at each prenatal visit and, where appropriate, averaged across pregnancy with early-to-mid pregnancy, mid-to-late pregnancy, late pregnancy-to-maximum, and total GWG; insufficient and excessive GWG according to Institute of Medicine guidelines; and long-term PPWR at 6 and 10 years postpartum. Based on OP pesticides' lipophilicity and association with hypomethylation, we investigated interactions with pre-pregnancy body mass index, periconceptional folic acid supplementation, and breastfeeding duration. RESULTS/ANTICIPATED RESULTS: A 10-fold increase in late pregnancy DE metabolite concentration was associated with 1.34 kg [95% confidence interval: 0.55, 2.12] higher late pregnancy-to-maximum GWG. A 10-fold increase in mean DE metabolite concentration across pregnancy was associated with 2.41 kg [0.62, 4.20] lower PPWR at 6 years. Stratified analysis suggested that the prenatal finding was driven by women with pre-pregnancy BMI  $\geq 25$  kg/m<sup>2</sup>, while the postnatal finding was driven by women with pre-pregnancy BMI <25 kg/m<sup>2</sup> and with inadequate folic acid supplementation. We found no associations between OP pesticide metabolites and insufficient or excessive weight gain and no interaction with breastfeeding. DISCUSSION/SIGNIFICANCE OF IMPACT: In this longitudinal analysis, we observed a positive association of OP pesticide metabolites with GWG in late pregnancy among overweight/obese women, potentially reflecting inhibition of OP pesticide detoxification by oxidative stress. Postnatally, under/normal weight women with higher OP pesticide metabolites had lower PPWR, possibly due to better metabolic function and a more healthful diet. These results suggest that there may be a critical period during the late phase of pregnancy when OP pesticide exposure may increase GWG, and this association may be amplified in overweight/obese women. Areas for future research include examination of how the interaction between OP pesticides and polymorphisms of the paraoxonase (PON1) gene, which detoxifies OP pesticides, affect GWG/PPWR; exploration of the interplay among maternal pre-pregnancy BMI, oxidative stress, and PON1 levels; and characterization of the variability of OP pesticides exposure across pregnancy using more frequent repeated urine samples.