tool for assessing motor pathways in infants with early brain injury, highlighting its potential for clinical translation in neurodevelopmental disorders, and offering a pathway to improved care.

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Characterizing clinical predictors of metabolic syndrome associated with second-generation antipsychotics in pediatric populations

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OBJECTIVES/GOALS: Second-generation antipsychotics (SGA) are used to treat mental disorders in youth but are linked metabolic syndrome (MetS). Most data on prescribing practices and risk factors are from short-term studies (6–12 months). We aim to characterize prescribing and identify clinical and genetic predictors of MetS using electronic health records (EHR). METHODS/STUDY POPULATION: EHR data were extracted from Cincinnati Children's Hospital Medical Center (CCHMC) for patients aged ≤21 years prescribed SGAs from 7/1/2009 and 7/1/2024, identifying prescribing prevalence. Next steps are to create an SGA-MetS case–control dataset 8 weeks after an SGA prescription. A case will be defined by meeting 3 of 5 criteria: 1) BMI ≥95th percentile for age/sex; 2) fasting glucose ≥100 mg/dL or use of anti-diabetics; 3) triglycerides ≥110 mg/dL; 4) HDL-C ≤40 mg/dL; 5) systolic/diastolic BP ≥90th percentile for age/sex or use of antihypertensives. The prevalence of SGA-MetS will be calculated by dividing SGA-MetS cases by total SGA users. Logistic regression will identify clinical predictors of MetS, and we will evaluate the association of polygenic risk scores (PRS) of BMI and type 2 diabetes with SGA-MetS risk. RESULTS/ANTICIPATED RESULTS: Our preliminary analysis identified 30,076 patients who were prescribed SGAs (mean age 12 years, SD = 4; 58.8% female; n = 17685). Most self-identified as non-Hispanic (95%, n = 28,595) and of White race (76%; n = 22,935), with 18.5% self-identifying as Black or African American (n = 5,579). The most commonly prescribed SGAs were risperidone (n = 12,382, 41.1%), aripiprazole (n = 9,847, 32.7%), and quetiapine (n = 5,263, 17.5%), with much lower prescribing rates of other SGA known of their low risk of MetS (e.g., ziprasidone 5.5%, lurasidone 1.4%, paliperidone (n = 316, 1.1%), or others cariprazine (n = 72), asenapine (n = 43), brexipiprazole (n = 39), iloperidone (n = 24), and clozapine (n = 20). DISCUSSION/SIGNIFICANCE OF IMPACT: Our analyses found that risperidone, quetiapine, and aripiprazole were the most prescribed SGA, with risperidone/quetiapine linked to a higher risk of MetS. We will present ongoing work identifying risk factors for SGA-MetS and examining the association with PRS. Our work has the potential to identify high-risk patients for personalized treatment.

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DNA targeting autoantibody for brain tumor therapy*

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OBJECTIVES/GOALS: Nucleoside transport by ENT2 facilitates transit of the lupus anti-DNA autoantibody Deoxymab into cells and across the blood–brain barrier into brain tumors. This work examines the Deoxymab-nucleoside interactions that contribute to membrane crossing and apply them in brain tumor therapeutics. METHODS/STUDY POPULATION: Deoxymab interactions with individual nucleosides, nucleobases, and pentose sugars are examined by surface plasma resonance (SPR) and cell penetration assays in a panel of cell lines including glioblastoma, breast cancer, and normal breast epithelial cells. Deoxymab-conjugated gold nanoparticles are generated and tested for binding to normal human astrocytes and glioma cells, and the impact of supplemental nucleosides on this binding is determined. Deoxymab-gold nanoparticles are tested for brain tumor localization by systemic and local administration in mice bearing orthotopic glioblastoma brain tumors and enhancement of laser interstitial thermal therapy (LITT) examined. RESULTS/ANTICIPATED RESULTS: Individual nucleosides significantly increase the efficiency of cell penetration by Deoxymab in all cell lines tested. In contrast, component nucleobases and pentose sugars significantly suppress the uptake of the autoantibody into cells. Deoxymab-conjugated gold nanoparticles bind DNA in vitro and to astrocytes in culture and are anticipated will enhance the efficacy if LITT in vivo by associating with DNA released by necrotic tumors and/or by locally administered nucleosides in brain tumor environments and subsequently act as heat sink to amplify LITT impact. DISCUSSION/SIGNIFICANCE OF IMPACT: Deoxymab is a DNA-targeting, cell-penetrating autoantibody. These findings establish nucleosides as the components of DNA that promote autoantibody membrane crossing through ENT2 activity and indicate potential for use of Deoxymab-gold nanoparticles in combination with LITT for brain tumor therapy.

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The genetic risk assessment with mobile mammography (GRAMM) project: Providing genetic counseling referrals in tandem with mobile mammography for at-risk Black women

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OBJECTIVES/GOALS: The overarching goal of the GRAMM study is to address racial health disparities by increasing access to genetic counseling and testing among the Black community. Specific objectives are to determine patient acceptability of risk assessment at time of mammography and to evaluate subsequent access to and uptake of genetic counseling and testing. METHODS/STUDY POPULATION: All women presenting for screening mammography at the Ypsilanti Health Center under the University of Michigan were invited to enroll. After providing written informed consent, study participants entered family cancer and personal health information in the InheRET software tool which links to the National Comprehensive Cancer Network genetic testing guidelines. Upon completion, each participant was informed immediately if they did or did not meet the criteria to meet with a genetic counselor. For those who met the criteria, referral to genetic counseling was provided. All enrollees were invited to complete a post-assessment survey on acceptability of the service and genetics knowledge. Patients will be followed over time for completion of genetic counseling and testing. The study was approved by the Umich IRB. RESULTS/

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