Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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cytometry analysis of CSF and peripheral blood. All families met with a certified genetic counselor and genome sequencing (GS) with clinical grade analysis was performed, including parental samples when available. Clinical comprehensive oligonucleotide and SNP microarray analysis was completed for all probands. Analysis focused on primary findings related to patient phenotype and family history, and included secondary findings as defined by the ACMG list v3.0. Potentially significant variants were confirmed by Sanger sequencing in a CLIA/CAP certified laboratory prior to reporting.

Results: Patient 1 is a 13-year-old male with prior diagnoses of narcolepsy, precocious puberty, and childhood-onset schizophrenia. On clinical workup he was noted to have cardiomyopathy that was presumed to be due to medication. However, GS identified a variant of uncertain significance (VUS) in MYH7 (c.5326A>G) associated with hypertrophic cardiomyopathy. Patient 2 is a 15-year-old male who presented at age 12 with an acute febrile illness followed by new onset auditory and visual hallucinations with cognitive decline. We identified a VUS in MYRF (c.3313C>T) associated with mild encephalitis with reversible myelin vacuolization, which is typically treated with IV glucocorticoids. Patient 3 is a 5-year-old male with a history of acute mental status changes starting at age 3.5 concerning for seizures and encephalopathy. GS identified VUS is RELN (c.7634C>T) associated with familial temporal lobe epilepsy, and CAMT2 (c.665-3C>A) linked to cerebellar dysfunction with cognitive and behavioral abnormalities. Microarray analysis was normal for all three patients.

Discussion: The results for these first three patients illustrate the potential contribution of GS in this population. While definitive explanations for each patient’s phenotype were not obtained, all families received potentially significant findings in genes associated with autosomal dominant conditions, with variants in MYH7 and MYRF having direct implications for treatment. It is important to engage families in discussion of results emphasizing the meaning of a VUS and limitations of research-based sequencing. Future directions include increasing the size of the cohort, correlation of genome data with immune markers, and potential expansion to RNA sequencing.

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W101.
COVID-19 PANDEMIC STRESS AND COMT VAL158MET ON YOUTH EXTERNALIZING BEHAVIOURS: A LONGITUDINAL STUDY FROM THE ADOLESCENT BRAIN COGNITIVE DEVELOPMENT (ABCD) EUROPEAN SUBSAMPLE

Tuana Kant 1, Emiko Koyama 2, Clement Zai 3, Joseph Beitchman 1, James L. Kennedy 1

1 Centre for Addiction and Mental Health, University of Toronto; 2 Centre for Addiction and Mental Health

Background: Youth externalizing problems is one of the leading risk factors for violence and death in youth. The interaction between genetics and increased stress has been associated with an increased risk for externalizing behaviors. COVID-19 pandemic is a major current environmental stressor, with increasing both inter and intra violence and aggression. Previous studies demonstrating an influence of catechol-o-methyltransferase (COMT) Val158Met on youth externalizing behaviors suggest that youth with higher genetic risk may be more susceptible to exhibiting increased externalizing behaviors due to the pandemic stress. This study examines the possible influence of Val158Met and stress from the pandemic on youth externalizing behaviors in a longitudinal sample.

Methods: Participants were 4098 children (2185M:1913F) of European ancestry, confirmed genetically using ancestry PCA, and recruited longitudinally as part of the Adolescent Brain Cognitive Development (ABCD) study. Val158Met (rs4680) genotypes were obtained from the Smokescreen® Genotyping Array.

Externalizing Problems were analyzed using the externalizing behavior scores from Child Behavior Checklist collected before COVID (until 2020 February) and during COVID (after March 2020). Stress scores were analyzed using the collected questionnaires from the families during the pandemic. Data analyses were performed using PLINK and R. Linear fixed effects model - repeated measures were used, with collection time, genotype, and COVID-19 stress scores as fixed factors, and site ID and subject ID as random factors.

Results: The interaction between genotype and collection time was significant (p=0.017): Val carriers scored higher on externalizing behaviors at both time points, however, Met/Met carriers showed a significant increase in their scores during the pandemic while Val carriers scored similarly in both times. When COVID-19 stress scores were entered into the model, the gene x collection time interaction was marginally significant (p=0.071), with youth with higher stress scores reporting higher externalizing behaviors regardless of their genotype.

Discussion: To our knowledge, this is the first study to demonstrate the effects of the stress from the COVID-19 pandemic with Val158Met genotype on youth externalizing behaviors during the pandemic. Results propose that youth with Met/Met genotype are more susceptible to exhibiting increased externalizing behaviors during the pandemic. This emphasizes the importance of studying the effects of COVID-19 on children’s behaviors with increased genetic risk.
and may serve as a base for developing novel personalized prevention and treatment techniques for youth.

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W102.
ADVERSE CHILDHOOD EXPERIENCES AND MENTAL HEALTH: INVESTIGATING GENE ENVIRONMENT CORRELATIONS AND GENETIC CONFOUNING

Jessie Baldwin, Jean-Baptiste Pingault

University College London

Background: Children who experience adversities have an elevated risk of developing mental health problems. However, the extent to which adverse childhood experiences (ACEs) cause mental health problems remains unclear, as previously observed associations may partly reflect genetic confounding. In this Registered Report, we investigated gene-environment correlations and genetic confounding of the associations between ACEs and mental health.

Methods: Participants included over 11,000 children from the Avon Longitudinal Study of Parents and Children (ALSPAC) in the UK and the Adolescent Brain and Cognitive Development (ABCD) Study in the USA. ACEs (including maltreatment, domestic violence, and parental psychopathology, substance abuse, criminality, and separation) were prospectively measured through parent reports in childhood. Internalizing and externalizing problems at age 9/10 were assessed through parent reports. To index genetic liability to mental health problems, we derived polygenic scores for a range of psychiatric disorders.

Results: Regarding gene-environment correlations, children with higher polygenic scores for mental health problems had a small increase in odds for ACEs (pooled odds ratio=1.07, 95% CI=1.03-1.10). In contrast negative control polygenic scores (for handedness and cataracts) were not associated with exposure to ACEs (pooled odds ratio=1.00, 95% CI=0.96-1.04). Regarding genetic confounding, polygenic scores for mental health problems explained on average, 3-5% of the associations between ACEs and internalising problems and 5-6% of the associations between ACEs and externalising problems. However, these results likely underestimate the magnitude of genetic confounding as polygenic scores for mental health problems only capture a very small amount of heritability in internalising and externalising outcomes. To address this, we conducted a genetic sensitivity analysis using latent polygenic scores capturing SNP heritability in internalising and externalising problems (6% and 9%, respectively). This sensitivity analysis suggested that genetic confounding accounted for a large average proportion (>60%) of the associations between ACEs with internalising and externalising problems, in both cohorts. Notably though, some individual ACEs (e.g., childhood maltreatment, parental mental illness) remained associated with mental health problems independent of genetic confounding.

Discussion: Children at higher genetic risk of psychopathology are more vulnerable to experiencing adversities. Future family-based research is needed to understand whether such gene-environment correlations are passive or evocative in nature. Furthermore, our findings suggest that elevated risk of mental health problems in children exposed to ACEs is at least partially due to pre-existing genetic risk. Therefore, in addition to preventing ACEs, interventions should address heritable vulnerabilities in children exposed to adversity to reduce their risk of psychopathology.

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W103.
ASSESSING THE UTILITY OF PHARMACOGENETIC TESTING IN A COHORT WITH TREATMENT-RESISTANT SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER

Natasha Verzosa1, Hilary Williams1, Reza Rafizadeh3, Ankit Narang2, Prescilla Carrior1, Ric Procysyn1, Randall White1, Guillaume Poirier-Morency3, Sanja Rogic5, Andrew Mungall5, Patrick Sullivan7, William Honer4, Paul Pavlidis6, Robert Stowe9, Chad Bousman3

1University of British Columbia; 2Lower Mainland Pharmacy Services, BC Mental Health and Substance Use Services; 3University of Calgary; 4University of British Columbia, BC Mental Health and Substance Use Services (PHSA); 5Michael Smith Laboratories, University of British Columbia; 6Michael Smith Genome Sciences Centre at BC Cancer; 7Center for Psychiatric Genomics, University of North Carolina, Karolinska Institute; 8Michael Smith Laboratories, Centre for Brain Health, University of British Columbia; 9Centre for Brain Health, University of British Columbia

Background: The University of British Columbia MAGES (Metabolic and Genetic Explorations in Refractory Schizophrenia) project is a pilot, multimodal -omics and psychiatric genetic counselling project conducted in participants with treatment-resistant schizophrenia (SCZ) or schizoaffective disorder (SZAD). Study participants were recruited from the BC Psychosis Program, the tertiary inpatient adult refractory psychosis care unit for British Columbia, Canada, where patients typically have a high incidence of intolerance to, and/or lack of efficacy, to multiple antipsychotics and other psychotropic drugs. Consequently, we hypothesized that pharmacogenetic differences might contribute significantly to their poor response or intolerance to these agents.

Methods: Linked-read Illumina whole genome sequencing (WGS) at ~ 40X coverage was performed in 25 MAGES participants at Canada’s Michael Smith Genome Sciences Centre. Actionable pharmacogenetic (PGx) variants were extracted from VCF and BAM files using GATK and Stargazer (for CYP2B6, CYP2D6, CYP2C9, CYP2C19, CYP3A5, UDT15, SLC01B1, TPMT, and VKORC1), and HLAScan, and HLA-Genotyper (for HLA-A *31:01, and HLA-B *15:02, *57:01, and *58:01). Current medication profiles were obtained,