Objectives: Few studies have examined the impact of geography on risk factors for suicidal ideation (SI) and suicide attempts (SA). This study used a national representative sample to study how geography may influence the relationships of risk factors for SI and SA in commercially insured children and youth.
Methods: The sample was a nationwide retrospective cohort study of 124,424 patients <25 years using commercial claims from four major insurance companies (Aetna, Humana, Kaiser Permanente, and UnitedHealthcare) in the US. The index visit was a mental health or substance use (MH/SUD) outpatient encounter between January 2014 and June 2015. SI and SA were defined by having an ICD-9 diagnosis code within one year after the index visit. Risk factors in the models were demographic and clinical risk factors, including prior psychiatric diagnoses, prescriptions, and healthcare services utilization. Patients' geographic regions were assigned to one of the nine divisions defined by the US Census Bureau. We used survival analysis to evaluate the effects of geography on risk factors for SI and SA.
Results: At each follow-up time period (post 7-, 30-, 90-, 180-, and 365-day), rates of SI and SA varied by geographic division ($p<0.001$). The Mountain Division consistently had the highest rates for both SI and SA (5.44%-10.26% for SI; 0.70%-2.82% for SA). Having MH emergency department (ED) visits in the past year increased the hazard ratio of SI by 28%-65% for children and youth residing in the New England, Mid-Atlantic, East North Central, West North Central, and East South Central Divisions. The main effects of geographic divisions were significant for SA ($p<0.001$). Risk of SA was lower in New England, Mid-Atlantic, South Atlantic, and Pacific (HRs=0.57, 0.51, 0.67, and 0.79, respectively) and higher in the Mountain Division (HR=1.46).
Conclusions: Children and youth residing in the Mountain Division had the highest prevalence of SI and SA and the highest risk of SI after having MH ED visits. Studies of indicators of access to MH ED care and other social determinants of health may clarify the reasons for SI and SA geographic differences.

Disclosure of Interest: None Declared

O0077

Genetic Elucidation of Ultrasonography Fetal Anomalies in Children with Autism Spectrum Disorder

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Introduction: Autism spectrum disorder (ASD) is a highly heritable neurodevelopmental disorder affecting 1-2% of the population worldwide. Recent large-scale whole-exome sequencing (WES) studies identified hundreds of rare, highly penetrant genetic variations associated with ASD. Many of these genetic variations underlie particular genetic syndromes characterized by a variety of congenital anomalies in addition to the core ASD symptoms. Recently, we reported about certain ultrasonography fetal anomalies (UFAs) associated with later development of ASD (Regev *et al.* Brain 2022).
Objectives: To identify genetic mutations associated with UFAs in children with ASD.
Methods: We conducted a cross-sectional study of all children diagnosed with ASD registered at the Azrieli National Centre for Autism and Neurodevelopment (ANCAN) who have both fetal ultrasound and WES data. We used an integrative in-house bioinformatics pipeline specifically designated to identify gene-disrupting variants (GDVs) in a panel of >1200 genes associated with ASD according to SFARI gene database. Then, we compared the prevalence of GDVs in these genes between children with and without UFAs. Finally, we applied the Gene Analytics tool to disrupted genes in children with specific fetal anomalies to identify biological pathways associated with both ASD and these fetal anomalies.
Results: Overall, 115 ASD children were included in this study, of which 49 (42.6%) of them had UFAs in their ultrasound scans (Figure 1). Children with and without UFAs did not differ in their sociodemographic and clinical characteristics except for a significantly lower proportion of males in the UFA group (63.4% vs. 84.8%, respectively; $p=0.011$). Notably, **children with UFAs were more likely to carry GDVs in ASD genes than their counterparts** even after adjustment to the sex differences between the groups (aOR=2.27, 95%CI: 1.05-4.93), and this association was the most prominent with GDVs in the most notable ASD genes (i.e., those with SFARI gene score=1). Also, the study shows **higher prevalence of children with GDVs in most anatomical systems, with UFAs in fetal size (14.8% vs. 1.6%, p=0.012, cases vs. controls) and the head&brain (16.7% vs. 4.9%, p=0.040, cases vs. controls)** being the most prominent (Figure 2). In addition, **children with UFAs had significantly more co-occurring mutations, and the number of mutations in a single fetus was significantly correlated with the number of UFAs (r=0.20, p=0.035)**.
Image:

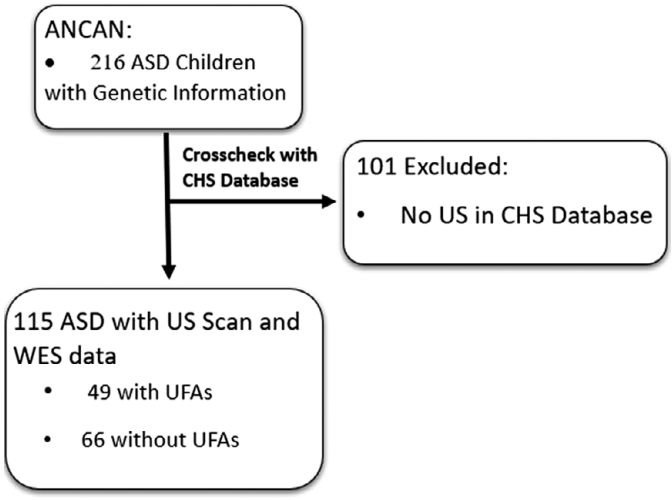
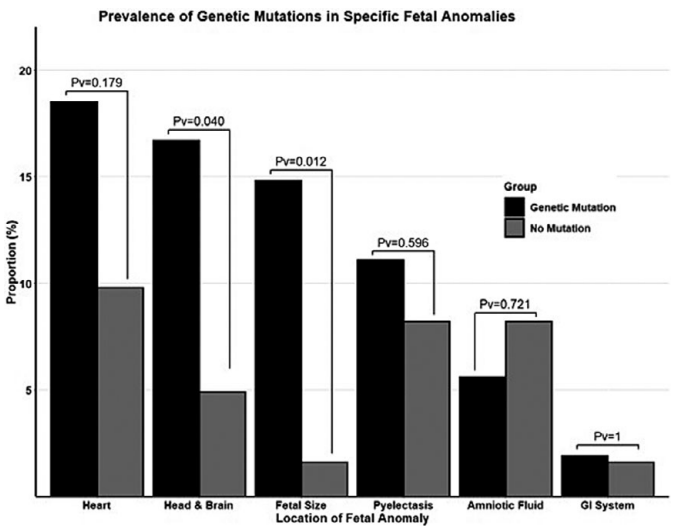


Image 2:



Conclusions: Our findings suggest distinct genetic mechanisms for ASD subtypes that are characterized by unique UFAs. These findings may form a basis for future prenatal screening approaches for ASD using both ultrasound and genetic testing. Our findings suggest distinct genetic mechanisms for ASD subtypes that are-characterized by unique UFAs. These findings may form a basis for future prenatal screening approaches for ASD using both ultrasound and genetic testing.

Disclosure of Interest: None Declared

O0078

Impact of selected single nucleotide polymorphisms in OXTR and AVPR1a genes on their expression in persons with ASD.

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Introduction: Autism spectrum disorder is a heterogeneous group of disorders that affects virtually every population, regardless of their ethnic or socioeconomic origin. In recent years, the attention of researchers has been drawn to the participation of the oxytocinergic and vasopressinergic systems in the development of autism spectrum disorders. A relatively large number of studies have investigated the association of SNPs in these genes with the development of ASD, however, there is a lack of studies in the literature focusing on their actual effect on expression and on the effect of their expression on the risk of ASD.
Objectives: The aim of this study was to assess the levels of expression of OXTR and AVPR1a genes and evaluate their links with both risk of ASD and genotypes of the most studied polymorphisms.
Methods: The study included 132 people, 77.5% of whom were male (n = 100). 113 participants (85.6%) were diagnosed with autism spectrum disorders confirmed by the ADOS-2 test conducted by a certified diagnostician. In this group, men constituted 76.1% of the population (n = 77). The remaining 28 people did not have a diagnosis of autism spectrum disorders, and in the ADOS-2 study they obtained the result below the cut-off level. The mean age in the whole group was 14.4 years (95% CI: 13.92-14.93).
Results: Significant decrease in expression of the OXTR gene was found in case of rs53576 where presence of the alternative allele (G) was linked to the 20% decrease in expression (2^(-ΔΔCt) = 0.8). In case of AVPR1a alternative allele (T) of SNP rs10877969 was linked to the 20% increase in the gene expression(2^(-ΔΔCt) = 1.197). SNPs rs2254298 (2^(-ΔΔCt) = 0.97) and rs7294536 (2^(-ΔΔCt) = 0.97) did not influence expression of the appropriate genes in significant way. In comparison between the test and control group in participants with confirmed diagnosis of ASD 13% lower expression of AVPR1a was found (2^(-ΔΔCt) = 0.87).
Conclusions: Genotype of SNPs rs53576 and rs10877969 significantly influenced the levels of expression of the genes OXTR and AVPR1a respectively. In case of rs2254298 and rs7294536 observed effects were negligible. Presence of ASD diagnosis was linked to the 13% lower expression of AVPR1a. Abnormalities in AVPR1a expression seem to be more important for the development of autistic traits than the more attention-grabbing gene abnormalities for the oxytocinergic system.

Disclosure of Interest: None Declared

O0079

Mental Health and Life Events among United States adolescents with Substance Use Disorders

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Introduction: Substance use during adolescence is linked to adverse biopsychosocial events, including poor mental health, cognitive deficits, low academic performance, and delinquency (Deas & Brown J Clin Psych 2006; 67 18; Armstrong & Costello JCCP 2002; 70 1224; Cox et al. JSH 2007; 77 109-115; Chassin JJSU 2008; 165-183). Identifying risks for these events is critical, given they are associated with adverse outcomes in adulthood.
Post-pandemic, rates of adolescent depression and anxiety have more than doubled (Racine et al. JAMA Ped 2021; 175 1142-1150). Adolescents often use substances, most commonly alcohol and cannabis, to manage mental health (Colder et al. JCCP 2019; 87 629).
Cannabis is increasingly viewed by adolescents as safe, while alcohol is viewed negatively (SAMHSA 2021). Non-disordered alcohol use (ND-AU), alcohol use below diagnostic criteria level, has adverse developmental impacts for adolescents, including increased risk-taking behavior and heavy substance use in adulthood (Marshall Alcohol Alcohol. 2014; 49 160-164).
With growing normalization of cannabis use, important questions still remain whether non-disordered cannabis use (ND-CU) among adolescents is linked to adverse life events.