

Introduction: Accumulating studies have pointed out that gut-blood and blood-brain barrier dysfunctions due to the alterations in permeability may play a role in the pathophysiology of neurodevelopmental disorders. Tight junctions are crucial components of these barriers and some peptides including claudin-5, occludin, zonulin and tricellulin are important components of these structures.

Objectives: This study aimed to investigate the relationship between these molecules and attention deficit hyperactivity disorder (ADHD) in children and adolescents.

Methods: A total of 57 children with ADHD and 60 controls aged between 6 and 12 years were included in the study. The severity of ADHD symptoms was assessed through a parent-rated questionnaire and Conner's Continuous Performance Test. Serum levels of biochemical variables were measured using enzyme-linked immunosorbent assay kits.

Results: Serum claudin-5 and tricellulin levels were significantly lower in the ADHD group compared to the control group. The difference between the groups in terms of serum claudin-5 and tricellulin levels remained significant after controlling for confounding factors such as age, gender and autistic characteristics. There was no significant difference between the groups in terms of serum zonulin and occludin levels. (Table 1)

Table 2. Serum claudin-5, occludin, zonulin and tricellulin levels of ADHD and controls

	ADHD (n=57)	Controls (n=60)	Statistical Analysis	ANCOVA ^c <i>p</i>	<i>F</i>	<i>p</i>	η_p^2
	Mean $\pm$ SD	Mean $\pm$ SD	<i>z/t</i>				
Claudin-5 *(ng/mL)	2,14 $\pm$ 0,71	2,47 $\pm$ 0,71	-3,702	<i>p</i> < 0,001 ^a	10,196	0,002	0,083
Occludin *(ng/mL)	3,75 $\pm$ 7,17	2,99 $\pm$ 2,75	-0,136	<i>p</i> = 0,892 ^a	0,264	0,608	0,002
Zonulin *(ng/mL)	4,82 $\pm$ 5,89	5,06 $\pm$ 5,53	-0,076	<i>p</i> = 0,939 ^a	0,008	0,930	< 0,001
Tricellulin (ng/mL)	3,04 $\pm$ 0,56	3,34 $\pm$ 0,71	-2,552	<i>p</i> = 0,012 ^b	6,650	0,011	0,56

Conclusions: These results suggest that claudin-5 and tricellulin may be involved in the etiopathogenesis of ADHD. Alterations in these peptides may affect the brain by leading a dysregulation in intestinal or blood-brain barrier permeability that eventually affects the gut-brain axis. The causal relationship between these peptides and ADHD requires further investigation.

Disclosure of Interest: None Declared

O0075

Do children with ADHD symptoms become socially isolated? Longitudinal within-person associations in a nationally-representative cohort

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doi: 10.1192/j.eurpsy.2023.280

Introduction: Social isolation in childhood can be detrimental to physical and mental health. Children with neurodevelopmental disorders, such as attention deficit hyperactivity disorder (ADHD), may be particularly at risk for becoming socially isolated. Similarly, isolated children have limited opportunities to observe, model, and learn age-appropriate interpersonal interactions with other children which could increase ADHD behaviours.

Objectives: This study examined longitudinal associations between ADHD symptoms and social isolation across childhood. We tested the direction of this association across time, while accounting for pre-existing characteristics, and assessed whether this association varied by ADHD presentation, informant, sex, and socioeconomic status.

Methods: Participants included 2,232 children from the Environmental Risk (E-Risk) Longitudinal Twin Study. ADHD symptoms and social isolation were measured at ages 5, 7, 10, and 12. We used random-intercept cross-lagged panel models to assess the directionality of the association across childhood.

Results: Children with increased ADHD symptoms were consistently at increased risk of becoming socially isolated later in childhood, over and above stable characteristics ($\beta=0.05-0.08$). These longitudinal associations were not bidirectional; isolated children were not at risk of worsening ADHD symptoms later on. Children with a hyperactive ADHD presentation were more likely to become isolated, compared to an inattentive presentation. This was evident in the school setting, as observed by teachers, but not by mothers at home.

Conclusions: Our findings highlight the importance of enhancing peer social support and inclusion for children with ADHD, particularly in school settings. We add explanatory value over and above traditional longitudinal methods as our results represent how individual children change over time, relative to their own pre-existing characteristics.

Disclosure of Interest: None Declared

O0076

Effects of geography on risk for suicidal ideation and suicide attempts among commercially insured children and youth in the US

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doi: 10.1192/j.eurpsy.2023.281

Introduction: To study the effects of geography on risk for suicidal ideation and suicide attempts among commercially insured children and youth in the US

Effects of geography on risk for suicidal ideation and suicide attempts among commercially insured children and youth in the US

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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doi: 10.1192/j.eurpsy.2023.282

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 bio-informatics 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:

