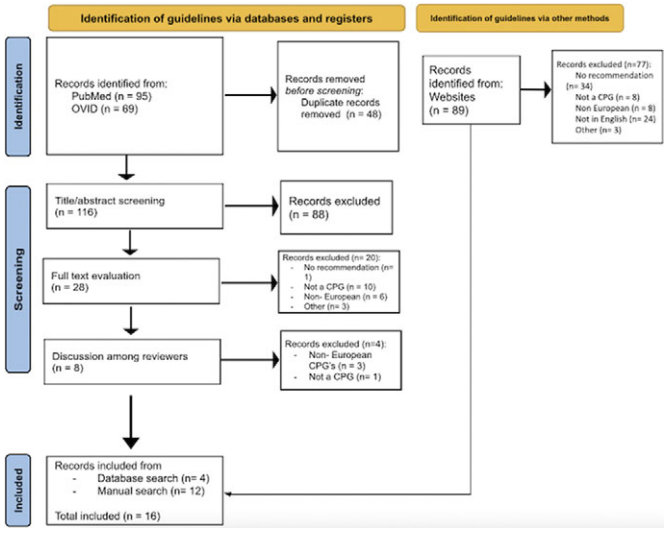
Methods: A scoping review was conducted across scientific databases (PubMed/MEDLINE and Ovid) and grey literature sources (Image 1. Flow diagram). Inclusion criteria centred on European CPGs published in English from 2010 onward with specific recommendations on genetic testing in mental disorders. Quality assessment was performed using the International Centre for Allied Health Evidence (iCAHE) checklist. Data extraction focused on guideline characteristics, target populations, and genetic test recommendations.
Results: Sixteen CPGs met the inclusion criteria, displaying considerable heterogeneity in quality and content, and covering a limited range of mental disorders. Six guidelines addressed neurodevelopmental disorders. Most recommended genetic testing in Autism Spectrum Disorder (ASD) when indicators such as intellectual disability (ID) or dysmorphic features were present; however, one guideline recommended routine testing. Only one guideline included recommendations for genetic testing in ID; routine access to Fragile X testing, chromosomal microarray, and whole genome sequencing was recommended as standard care.
Eleven guidelines provided recommendations on genetic testing in neurodegenerative disorders. In dementia, consensus on routine testing was generally limited to young-onset cases or those with distinct genetic profiles. APOE genotyping was generally discouraged. Guidelines for diagnostic testing for Huntington's Disease (HD) were consistent. Access to predictive testing with appropriate genetic counselling for at-risk adults was also recommended.

Image:



Conclusions: Based on our findings and the wider literature, we recommend considering genetic testing for: 1) all patients with ID, 2) patients with ASD exhibiting features suggestive of a genetic cause, such as ID and dysmorphic traits, and 3) patients with dementia with a young age of onset or a family history indicative of a Mendelian disorder. For HD, testing should be informed by phenotypic features and family history. Establishing harmonised, evidence-based guidelines is essential to integrate testing effectively. Key considerations include clinical utility, patient autonomy, and access to genetic counselling to ensure informed and supportive care.

Disclosure of Interest: None Declared

EPV0879

Season of birth/C-reactive protein gene interaction differentially affects negative symptoms domains in patients with schizophrenia

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Introduction: Schizophrenia is a severe psychiatric disease caused by genetic and environmental factors or their interactions that can contribute across multiple disease domains, including negative symptoms (NS), a core feature of schizophrenia.
Objectives: To study the association between season of birth (SOB), a well-replicated risk factor for schizophrenia, and NS domains avolition/apathy (AA) and diminished expression (DE) and to search for an interaction effect of SOB and rs2794521 genetic variants of the inflammatory marker C-reactive protein (CRP) on these domains.
Methods: The study included 2475 patients with schizophrenia. Patients born during the months of December to February were considered to be winter-born (n=636) and patients born in other months were considered to be non-winter-born (n=1839). Genotypes for CRP rs2794521 were obtained for 2437 patients. NS factors were calculated based on the Positive and Negative Syndromes Scale.
Results: There was a significant effect of SOB on AA scores (p=0.009), which remained after adjustment for sex and illness duration. Patients born in winter had higher scores compared with those born in other seasons. No significant effect of SOB on DE scores was observed. An association between the CRP rs2794521 *G*-allele and AA scores was found (p=0.044) in the winter-born group, with the carriers of the *G*-allele having higher scores. There was no effect of the *G* allele on DE scores in this group and on AA or DE scores in the non-winter group.
Conclusions: The results provide new evidence about the effect of SOB and SOB/CRP gene interaction on schizophrenia NS domains.

Disclosure of Interest: None Declared

EPV0880

The association between oxytocin receptor gene polymorphism, childhood adversity and negative symptoms of schizophrenia

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Introduction: Neurohormone oxytocin plays an important role in the pathogenesis of mental illness, and also moderates the relationship between stress factors, especially those acting in the early stages of development, and the development of mental disorders. Literature data indicate that environmental risk factors significantly increase the risk of schizophrenia and the severity of its clinical presentation.

Objectives: To study the association between the oxytocin receptor (OXTR) rs468302 and rs7632287 polymorphisms and negative symptoms of schizophrenia, taking into childhood adversity (CA), i.e. events that could adversely affect the psychoemotional state and development of the child in the period up to 18 years. CA includes abuse in the family, alcohol or drug addiction in parents, mental disorders.
Methods: The study included 592 patients with schizophrenia (items F20. according to ICD-10). Information about the presence of CA was obtained from case histories and patient interviews. Analysis of covariance was used for statistical data processing; in post-hoc pairwise comparison, Tukey's test was used.
Results: A significant effect of the interaction between CA and OXTR gene polymorphism rs7632287(G\A) on the severity of negative symptoms in patients with schizophrenia was revealed. For rs4686302 (C\T) polymorphism the association was found at the trend level. In patients without CA, polymorphisms did not have a significant effect.
Conclusions: The OXTR rs468302 and rs7632287 polymorphisms, previously associated with phenotypes related to social behavior, may be associated with negative symptoms of schizophrenia, and the association is mediated by the presence of a history of psychotraumatic events acting at an early stage of development.

Disclosure of Interest: None Declared

EPV0881

Exploring genetic sources of a decreased cognitive performance in psychometric schizotypy

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Introduction: Schizotypy is seen as subclinical part of the psychosis liability continuum. While several studies have attempted to confirm the relationship between schizotypal traits and genetic predisposition to schizophrenia using polygenic risk scores (SZ-PRS), the association of SZ-PRS with other features of schizotypal individuals resembling schizophrenia symptoms remains unexplored.
Objectives: This study aimed to assess the contribution of SZ-PRS and PRS for other relevant traits to cognitive functioning in schizotypy.
Methods: Healthy subjects (n=1468) were divided into low, negative, positive, and high mixed schizotypy groups based on a cluster analysis of the Schizotypal Personality Questionnaire data. Of them, 247 individuals had genome-wide information and completed a comprehensive cognitive battery, from which a cognitive index (CogI) was derived. PRS for schizophrenia, bipolar disorder, educational attainment, intelligence (IQ), neuroticism, and risk-taking were calculated with LDpred2-auto tool. The association of the CogI with PRSs was examined with stepwise multiple linear regression controlling for age and two ancestry-related principal components.
Results: The groups differed in the CogI (p=0.015). The high schizotypy individuals (n=49) had a lower CogI than the low (n=73, p=0.01), negative (n=54, p=0.08), and positive (n=64, p=0.09) ones. SZ-PRS (β=-0.16, p=0.012) and IQ-PRS (β=0.13, p=0.014) predicted CogI in low schizotypy; IQ-PRS (β=0.42, p<0.001) in negative schizotypy; risk-taking PRS (β=-0.27, p<0.001) in positive schizotypy; and none of the PRSs predicted cognition in high schizotypy.
Conclusions: We did not find traits whose PRS might explain the lower cognitive performance in high schizotypy. Thus, nongenetic factors deserve more attention in future research.

Disclosure of Interest: None Declared

EPV0882

Characterization of SLC6A1 mutations associated with schizophrenia using SH-SY5Y-based cell lines Ekaterina Marilovtseva1

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Introduction: SLC6A1 is a GABA transporter which, being expressed in neurons and glial cells, removes GABA from extracellular space, preventing the spread of the inhibitory transmission within the brain. Recently, A93T, R211C, and W495L *de novo* mutations in SLC6A1 have been demonstrated to be involved in schizophrenia pathogenesis. However, the mechanism of action of SLC6A1 in schizophrenia is still to be determined.
Objectives: To establish a series of SH-SY5Y-based cell lines expressing wt *SLC6A1* and its forms with single A93T, R211C or W495L mutations and their combinations, and to further characterize the properties and the subcellular localization of the resulting proteins.
Methods: The chosen variants of *SLC6A1* tagged with N-terminal FLAG were cloned into a lentiviral plasmid under the TRE promoter and used for transfection of HEK293T with further SH-SY5Y transduction. *SLC6A1* expression was initiated by adding 20 μg/mL of doxycycline to the cells. After 48 hours of treatment the cells were either used for qPCR and Western blot analysis, or stained.
Results: All cell lines expressed *SLC6A1* forms efficiently. SLC6A1 with single mutations, $SLC6A1^{R211C;W495L}$, and $SLC6A1^{A93T;\ R211C;\ W495L}$ were present by the same ≈67kDa form as wt SLC6A1, while $SLC6A1^{A93T;R211C}$ resulted in an additional band at ≈130kDa, indicating either the presence of PTM, or the formation of a homodimer. $SLC6A1^{A93T;W495L}$ gave no protein product, probably, due to its proteolytic degradation. Interestingly, wt SLC6A1, $SLC6A1^{R211C}$, and $SLC6A1^{A93T;R211C}$ were detected in neurites, while $SLC6A1^{A93T}$, $SLC6A1^{W495L}$, $SLC6A1^{R211C;W495L}$, and $SLC6A1^{A93T;R211C;W495L}$ were mainly found in cytoplasm, which might indicate that these mutations might affect the function of the protein.
Conclusions: Having established a series of SH-SY5Y-based cell lines expressing SLC6A1 with schizophrenia-associated mutations, we demonstrated the effect of the latter on the protein's subcellular localization. Based on our observations, we speculate that R211C has the mildest effect on the localization and function of SLC6A1 and can even partially compensate that of A93T, but not W495L. We also suggest that SLC6A1 with the A93T;W495L combination undergoes proteolytic degradation, most likely, due to the defects in its structure.

Disclosure of Interest: None Declared