EPV0558

A comparison of taxon-like schizotypal clusters of non-clinical individuals on polygenic scores for schizophrenia and related phenotypes

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Introduction: Schizotypy is conceptualized to be on the continuum of the risk for psychosis. However, previous studies that used the dimensional approach to schizotypy failed to confirm the expected relations between schizotypal traits and polygenic risk scores (PRS) for schizophrenia. A taxonic approach is an alternative way of looking at schizotypy, but to the best of our knowledge it has not been used to explore the genetic architecture of this construct.

Objectives: The present study aimed to fill this gap by comparing groups with different profiles of schizotypal traits on PRS for schizophrenia and related phenotypes.

Methods: To find clusters with different combinations of schizotypal traits, we conducted data mining of an ethnically homogeneous cohort of 1377 healthy individuals completed the Schizotypal Personality Questionnaire. Four clusters emerged, termed low, positive, negative, and high mixed schizotypy. Approximately equal groups from each cluster were selected for genotyping. After quality control, PRS for schizophrenia, depression, neuroticism, and educational attainment were calculated for 320 individuals (mean age = 31.74, SD 12.25 years, 59% women) based on the summary statistics of the largest genome-wide association studies of the respective traits. The groups from different clusters were then compared on PRS.

Results: The schizotypy groups were similar in age and sex composition but differed in educational attainment and neuroticism (as measured by the Eysenck Personality Inventory), with the high mixed schizotypes having the lowest education and highest neuroticism scores among the schizotypy groups. There were no statistically significant differences between the groups in any PRS. However, the high mixed schizotypy group showed the largest PRS for schizophrenia, neuroticism, and depression. At a nominally significant level, it differed from negative and positive schizotypes in schizophrenia PRS and from low schizotypy in neuroticism PRS. The positive and negative schizotypal groups had non-significantly lower schizophrenia PRS than low schizotypy subjects.

Conclusions: Our study showed no reliable difference between groups with different schizotypal profiles in PRS of schizophrenia and related phenotypes. At the same time, a number of trends were observed suggesting that only the high mixed schizotypy might be viewed as a condition with an elevated genetic risk of schizophrenia. This is in line with Meehl's quasi-dimensional model of schizotypy and warrants further investigation in larger samples. This work was supported by the Russian Foundation for Basic Research under Grant 20-013-00230.

Disclosure of Interest: None Declared

EPV0559

Development of a cellular model to study L-DOPA decarboxylase deregulation in the pathogenesis of schizophrenia

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Introduction: Schizophrenia (SZ) is an inherited mental illness that affects 1% of the world's population. Schizophrenia is a common functional psychosis with some unifying features that appears to have a universal distribution. Much of the research on SZ seeks to identify physiological, biochemical, or genetic features that differ between patients and healthy individuals. Biochemical factors represent an imbalance of certain biochemical substances in the brain, especially neurotransmitters. Early studies focused on the brain biochemistry of patients with SZ in terms of dysregulation of the neurotransmitter network. There is evidence that elevated dopamine concentrations are associated with positive symptoms (i.e., hallucinations, delirium) of the disease. For example, L-DOPA decarboxylase (DDC) is an enzyme involved directly in dopamine and serotonin synthesis and indirectly in noradrenaline synthesis. Therefore, the DDC gene can be considered a candidate gene for schizophrenia and its activity is a good candidate for functional analysis via epigenetic repression.

Objectives: We aimed to create a cellular model with a deregulated DDC gene.

Methods: We constructed two lentiviral vectors, one expressing the dCas9-KRAB-MeCP2 repressor under the control of a synthetic tetracycline inducible promoter, and the other carrying a cassette expressing two sgRNAs with spacers against the DDC promoter. The SH-SY5Y cell line was sequentially stably transduced with both lentiviral constructs, and cells carrying both constructs were selected by the fluorescence of the GFP and RFP reporter proteins encoded in the lentiviral construct backbones.

Results: Methyl-sensitive real-time PCR followed by high-resolution fusion showed methylation of the DDC promoter. Correspondingly, real-time PCR showed a two-fold decrease in DDC expression in SH-SY5Y during tetracycline-induced expression of the CRISPR repressor.

Conclusions: We developed a cellular model to study the contribution of DDC deregulation to SZ-related molecular mechanisms.

Disclosure of Interest: None Declared

EPV0560

Case report of schizophrenia in a patient with de novo mutation in the SLC6A1 gene

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Introduction: Schizophrenia is a severe mental disorder mainly caused by genetic risk factors. Many studies have demonstrated that both multiple genetic variants and rare mutations are associated with schizophrenia risk. The next step is to study the causal effect of the gene on the phenotype. Recently, a large family-based study identified de novo mutations, which may increase liability to schizophrenia (Rees et al 2020). In particular, a mutation in the GABA transporter (SLC6A1) gene (rs756927822 C/T) was identified in one patient from our subsample.

Objectives: Here, we present a case report of this patient and describe the procedure of derivation of induced pluripotent stem cells (iPSCs) from fibroblast cultures.

Methods: Clinical, psychometric and neuropsychological methods were used. iPSCs were derived from patients' and both unaffected parents' fibroblasts. Human fibroblasts, cultured in fibroblast medium, are infected with lentivirus vectors expressing the transcription factors Oct4, Sox2, c-Myc, and KLF4. All iPSCs were immunocytochemical stained for intracellular (Oct4, Sox2) and extracellular (SSEA4, Tra-1-81, Tra-1-60) pluripotency markers. An qPCR analysis for pluripotency markers (TDGF1, Sox2, Oct4, REX1, LIN28, NANOG, KLF4, GDF3, DPPA4, DNMT3) was performed. All four iPSC lines formed embryoid bodies before the differentiating into three germ layers. Differentiation was confirmed by immunostaining for mesoderm (aSMA), ectoderm (Nestin, Desmin) andendoderm (FoxA2, Pax6) markers.

Results: A 47-year-old male patient was presented to psychiatry at the age of 16. There was no personal or family history of psychiatric disorder, the premorbid functioning was normal, the patient had no somatic diseases, showed high performance in sport (mountain skiing). On his first admission, he was diagnosed with schizoaffective psychosis. The patient showed signs of mania and catatonia. Neuropsychological testing revealed a decrease of cognitive functioning (short-term and associative memory). The patient was followed up for more than 20 years. The diagnosis was changed for schizophrenia at the age of 43 years. There was a deterioration in cognitive function (the apparent decrease in performance on neurocognitive tests (attention, memory, executive functions) from the first examination (1997) till last one (2019). The patient refused or was not able to perform most of the tasks. During follow-up, the patient shows good adherence to treatment.

Conclusions: For this patient, obtained lines might be valuable for investigating the disease mechanisms and screening candidate drugs.

Disclosure of Interest: None Declared

Guidelines/Guidance

EPV0561

DEVELOPMENT OF A CLINICAL GUIDELINE FOR FAMILY-CENTERED COLLABORATIVE CARE IN PATIENTS WITH CHRONIC MENTAL DISORDERS

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Introduction: Background: Chronic mental illnesses have long periods, are recurring, and require continuous care and, becoming chronic, they double the problems of patients and their family. The study's purpose is, thus, the development of guidelines for family-centered collaborative care of patients with chronic mental illnesses referring to the medical centers (1).

Methods: This mixed methods study is based on the stages of the guideline adaptation provided by the Guidelines International Network (2).

Results: After reviewing and gathering evidence from a qualitative study on key participants and reviewing the literature, which includes a search for articles related to participatory family-centered care of patients with chronic mental disorders and a review of available books, a clinical guide Related and upstream documents of the country were 531 recommendations were extracted and sent to a panel of experts for evaluation.

Conclusion: Providing a family-centered collaborative care guideline will improve the quality of life of these individuals and their families, improve the quality of care, and reduce fragmented health care(3,4).

Objectives: Development of a clinical guideline for family-centered collaborative care in patients with chronic mental disorders-

Methods: This mixed methods study is based on the stages of the guideline adaptation provided by the Guidelines International Network .

Results: After reviewing and gathering evidence from a qualitative study on key participants and reviewing the literature, which includes a search for articles related to participatory family-centered care of patients with chronic mental disorders and a review of available books, a clinical guide Related and upstream documents of the country were 531 recommendations were extracted and sent to a panel of experts for evaluation.

Conclusions: Providing a family-centered collaborative care guideline will improve the quality of life of these individuals and their families, improve the quality of care, and reduce fragmented health care

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