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Adverse psychological outcomes in Brugada syndrome: About a Tunisian familial pedigree from Sfax

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Introduction: Patients with Brugada Syndrome (BS), a rare inherited cardiac channelopathy, with an increased risk of developing arrhythmias, syncope and sudden cardiac death, also present serious adverse psychological outcomes that require medical support to improve their health and well-being as well as those of their families.
Objectives: Here we report psychological concerns of a Tunisian patient who presented to our genetic counselling, with his three children, for molecular exploration of BS type 1.
Methods: Clinical, electrical, biological and psychological characteristics of the patient and his offspring were identified. Cytogenetic exploration using RHG banding and molecular screening of SCN5a gene mutations using High Resolution Melting and sequencing were carried out. Subsequently, genetic counselling was undertaken for all the family members and psychological concerns were reported.
Results: A 51-year-old married man with an academic career was born from a consanguineous couple, with a family history of sudden cardiac death. He was diagnosed with BS1 based on the pathognomonic ST-segment elevation in leads V1–V3, after experiencing palpitations and syncope. He was treated by implantable cardioverter defibrillator. The patient was also being treated for diabetes and dyslipidemia. His children, a girl and two boys, were investigated by ECG, which revealed no electrical disorders. However, both boys reported chest pain on exertion. The 18-year-old girl presented with primary amenorrhea and infantilism, along with a Turner syndrome formula. Molecular analysis revealed none of the targeted mutations in the SCN5a gene. Psychologically, the patient had a phobia of death and reported painful sensations of imminent death at each palpitation. He was anxious about the clinical outcome of his children. The children reported anxiety about their autosomal dominant fathers' disorder.
Conclusions: Approximately 16% of BS patients experience depression and anxiety. More attention needs to be indorsed to the psychological distress of BG patients and their families.

Disclosure of Interest: None Declared

EPV0544

ZNF536 dysfunction enhances spontaneous differentiation of the SH-SY5Y cell line into a neuronal-like phenotype

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Introduction: Schizophrenia (SZ) is a common psychiatric neuro-developmental disorder with a complex genetic architecture. Genomic association studies indicate the involvement of transcription factors in the pathogenesis of SZ. A recent GWAS showed a significant association of ZNF536 with SZ. To date, the molecular functions of ZNF536 are poorly understood and its possible role in the pathogenesis of SZ is unclear.
Objectives: The aim of this work was to develop a model cell line for study ZNF536-mediated pathogenic mechanisms associated with SZ.
Methods: To assess the spatial interaction of ZNF536 with SZ risk loci, we used the Capture-C method. For ZNF536 deletion, SH-SY5Y was sequentially transduced with two lentiviral vectors. The first expressed Cas9 under the control of a tetracycline regulated promoter and the second expressed a pair of sgRNAs for ZNF536 deletion. Puromycin was used to select transduced cells. Stably transduced cells were then treated with oxytetracycline to induce Cas9 expression. In parallel, SH-SY5Y were transduced with lentiviral constructs of Cas9 and sgRNA carrying a spacer lacking targets in the human genome to obtain a negative control. Individual clones were obtained by the limiting dilution method. The ZNF536 deletion was confirmed by PCR and Sanger sequencing.
Results: A spatial interaction of ZNF536 with SZ risk loci was found, suggesting its involvement in SZ pathogenesis. Using the CRISPR/Cas9 system, we obtained several clones with heterozygous deletion of ZNF536. We observed that their growth and proliferation were significantly slowed down. In addition, the mutant clones spontaneously differentiate into a neuron-like phenotype in low-serum medium.
Conclusions: We established a cellular model to study ZNF536-mediated mechanisms associated with SZ.

Disclosure of Interest: None Declared

Guidelines/Guidance

EPV0545

Korean Medication Algorithm Project for Bipolar Disorder 2022: Treatment Strategy According to Safety and Tolerability

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Introduction: Accordingly, the Korean Medication Algorithm Project for Bipolar Disorder (KMAP-BP) working committee, composed of domestic experts, developed Korea's first KMAP-BP in 2002 and later in 2006, 2010, and 2010. A revised version of KMAP-BP was announced every four years four times in 2014 and