R. Confounders included ancestry, BMI, age, sex, and 6 cell types. We tested both scores in our sample: smokers and non-smokers.
Results: In contrast to our expectations, none of the regression analyses showed a significant association with depression (MADRS-score). Nonetheless, a significant association was seen with biological sex for both analysis (overall: p=0.036, non-smokers: p=0.026). A reduced model with only this predictor explained 5% and 4% of the variance of the summary score calculated (R^2), respectively (overall: p=0.013; non-smokers: p=0.019). One of the ancestry components was marginally significant too in the non-smoker summary score (p=0.065). This was not the case anymore in the reduced model.
Conclusions: Our results show that caution is still in place when using methylation risk scores as specificity and sensitivity might not yet be optimized. The score built for depression incidence does not seem fitting for depression severity at this moment. The use of DNA methylation, a marker that is generally sensitive to confounding factors, for a risk score, might pose more challenges in the context of reliable summary statistics, in particular also for cross-trait examination, which is currently a typical use of polygenic risk scores.

Disclosure of Interest: None Declared

EPV0537

Behavioral and neurocognitive phenotypes in Crigler-Najjar syndrome in Tunisia

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Introduction: Crigler-Najjar 1 (CN1) due to exon 3 mutations of the UGT1A1 gene is a not rare genetic disease in Tunisia with a founder effect. CN1 syndrome is very severe, and most of CN1 Tunisian patients die soon after birth, within a maximum of one year, due to kernicterus. Liver transplantation, which is the only available therapeutic method for CN1, remains unreachable.
Objectives: The aim of this study was to report behavioral and neurocognitive phenotypes in CN1 patients who survived to school enrollment.
Methods: We have selected all patients evaluated from 2004 to 2010, both clinically and molecularly, for a deficiency of bilirubin-UGT enzyme activity leading to a pathological elevation of unconjugated bilirubin with a suspicion of CN1 syndrome. Direct sequencing of targeted PCR amplification products was performed for molecular analysis of UGT1A1. Behavioral and mental features of patients were studied through our genetic counselling.
Results: We identified 15 patients with the homozygous c.1070 A>G Tunisian mutation. Their age at diagnosis ranged from one week to 9 months for 13 patients. Six of them died within a month of molecular investigation. Only two boys were of school age, i.e. 6 and 9 years. The first had been hospitalized at 3 months year-old for a prolonged jaundice treated with phenobarbital and phototherapy. His psychomotor and neurological development was normal, with school attendance at the age of six. The second patient presented with an unexplored jaundice at the age of 3 days, which was later complicated by seizures and treated with phenobarbital. Despite neurological and motor sequelae associated to language impairments with slurred speech, he attended school at the age of six.
Conclusions: The neurological and behavioral profile of CN1 patients depends on familial and medical management. Quick diagnosis, close follow up and early liver transplantation can improve prognosis.

Disclosure of Interest: None Declared

EPV0540

Interaction analysis of monoaminergic polymorphisms and childhood environment related to personality functioning in patients with Borderline Personality Disorder

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Introduction: Neurobiological studies have shown that genetic variations affecting the intensity of monoamine neurotransmission play an important role in aggressive behavior and borderline personality traits. Also, the effect of family environment has been repeatedly shown on aggressive behavior and interpersonal functioning. Population-based longitudinal studies pointed out interactions between the so-called monoaminergic sensitivity alleles and childhood adversities.
Objectives: Our study aimed to analyze the associations between the most studied variable number tandem repeats of monoaminergic genes and the different psychological factors in adult patient and healthy control groups, checking for the moderating effects of the parental occupation and education, childhood abuse and trauma.
Methods: The recruited 73 patients with BPD diagnosis and 98 healthy controls were assessed by the Structured Clinical Interview for DSM-5. Participants filled out online questionnaires including the Level of Personality Functioning Scale – short version (LPFS-SR) and the Buss-Perry Aggression Questionnaire (BPQ). Childhood social environment and traumatic experiences were assessed by the Barratt Simplified Measure of Social Status and the Early Trauma Inventory or the Childhood Trauma Questionnaire. Genomic DNA samples were obtained either from peripheral blood, saliva or buccal swabs using the desalting technique. Functional dopaminergic and serotonergic polymorphisms were chosen based on previous findings, implicating them as sensitivity gene variants, e.g., the variable-number tandem-repeats of the dopamine D4 receptor, serotonin transporter and the monoamine oxidase-A (MAO-A) genes. Since the MAO-A gene is located on the X chromosome, sex-stratified analyses were also carried out.
Results: Family environment indexed by the Barratt Simplified Measure Social Status had significant effect on anger, hostility and interpersonal functioning ($p < 0.01$). In the pooled sample of patients and controls, individuals carrying the high activity alleles of MAOA had elevated scores on the BPQ subscales. When analysis

was limited to female participants, the genetic effect stayed significant only at the anger scale of the BPQ.
Conclusions: Family environment had pronounced effect on aggressive behavior and personality functioning, interaction with common monoaminergic genetic variants was detected only in women.
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EPV0541

Pain and gain of predictive genetic testing: Particular case of fragile X syndrome

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Introduction: The purpose of predictive genetic tests is to identify carriers or the onset of a disease in pre-symptomatic individuals. Prediction is linked to a negative psychological impact (anxiety, depression, etc.), depending on the perception of risk, the severity of the disease, and the availability and effectiveness of treatments.
Objectives: Here, we report on genetic counselling during predictive genetic testing offered to an Arab family affected by fragile X condition (FXS) caused by the unstable expansion of a CGG repeat (CGGR) in the FMR1 gene.
Methods: A 10-year-old boy who harbored a mental retardation was referred to our genetic counselling for genetic testing as he was suspected to be affected by FXS. Screening of FMR1 gene mutations was conducted for the index case and his mother. A predictive genetic testing for the family members (brothers, sisters and others) was offered, focusing on knowledge of genetics and medical risks of FXS.
Results: FMR1 molecular analysis showed a full mutation (300 to 2000 CGGR) for the boy and a large premutation (100 CGGR) for the mother. During genetic counselling, the family was informed about the significance of the genetic results. In FXS initiated by an expansion of over 200 CGGR. While mental retarded males usually harbor the full mutation, the mother carry a premutation (70 to 200 CGGR). The deficiency of FMR protein (FMRP) in the neurons of affected males leads to brain developmental abnormalities. Some pre-mutated children may show signs of the autism spectrum disorder and females may develop FMR1-related premature ovarian insufficiency. An increased risk of a late onset fragile X tremor ataxia syndrome is identified in pre-mutated men (55 to 200 CGGR) and less in women.
Conclusions: The reduction or loss of FMRP leads to multisystem damage. Neuropsychiatric disorders such as mental retardation, speech and language delay, autism spectrum disorder, sensory hyperexcitation, social anxiety, abnormal eye contact, shyness and aggressive behaviour are common in individuals with the mutation. Affected women are often under-diagnosed because mental retardation is not constant, but minor disorders including a borderline IQ with learning difficulties and emotional disturbances have been reported. Conditions associated with fragile X premutation, a term proposed by the European Fragile X Network (FXPAC), seem to be characterized by many physical and psychological health symptoms. Anxiety, depression, sleep disorders and mood disorders are more common in permutated individuals. However, new reports suggested that FXS patients could be at unusually low risk of cancers, because FMRP is overexpressed in multiple cancer tissues.

Disclosure of Interest: None Declared

EPV0542

Dysmorphic physical appearance and psychosocial burdens in Klippel-Feil condition

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Introduction: Klippel-Feil abnormality (KFA) is an association of bone defects characterized by a triad: fusion of the cervical vertebrae and consequent short neck, low hairline and a limited motion in the neck. KFA may be a feature of another disorder, such as MURCS association. Familial mutations in the GDF6 (KFS1 8q22), MEOX1 (KFS2 17q21), GDF3 (KFS3 12p13) and MYO18B (KFS4 22q11) genes cause inherited KFA.
Objectives: The aim of this study was to report dysmorphic features and psychological burdens in two sisters with Klippel-Feil condition.
Methods: Two sisters with amenorrhea and dysmorphic clinical features were examined at our genetic counselling. Assessment of dysmorphic and behavioral features and karyotyping using RHG banding were performed.
Results: Familial history revealed consanguineous parents and seven other healthy sisters. Physical examination shown typical triad of KFA. Karyotyping showed 46,XX formula in both patients. The first 22-year-old sister had body asymmetry with size difference between the two sides at the level of bones, pectus excavatum of the sternum, an ascent of the left scapula, scoliosis, dental position abnormalities and facial dysmorphism. The second 28-year-old sister had size difference between the two legs and scoliosis, vitiligo and facial dysmorphism. Anxious and depressed, the two sisters had normal learning abilities but shared many personal psychological concerns regarding their physical appearance and their amenorrhea. They were also exposed to significant discrimination and stigma making them feel excluded and ignored because of their visible difference.
Conclusions: Physical appearance has a profound impact on a person's life. To our knowledge, there is no reports that describe specific psychological burdens of KFA. Self-esteem, body image, and quality of life is negatively impacted in the case of dysmorphic physical appearance, always associated to social discrimination. Patients with KFA should be assessed not only for associated congenital defects but also for psychological distresses.

Disclosure of Interest: None Declared