specific correction of the altered gene without affecting the rest of the genome.

Objectives: The aim of this study was to report the current CRISPR/ Cas9 genome editing clinical trials in neurodevelopmental and mental disorders.

Methods: We conducted a search via the ClinicalTrials platform to describe clinical trials that have been conducted using the CRISPR/ Cas9 genome-editing tool in neurodevelopmental disorders.

Results: Our research revealed three clinical trials that used the CRISPR/Cas9 tool for diagnostic and therapeutic purposes. The first study aimed to investigate the pathological role of KMT2D mutations in 40 Kabuki syndrome patients in order to facilitate the identification and characterization of therapeutic strategies to improve symptoms, to identify the consequences of KMT2D mutations on epigenetic marker changes and cellular structural changes and to finally attempt gene correction by CRISPR/Cas9. The therapeutic approach was an epigenome editing approach aimed at increasing the expression of the wild-type KMT2D allele to restore the functional activity of a histone H3-lysine 4 (H3K4)methyltransferase (MLL4) in treated mesenchymal stem cells. The second clinical trial aimed to validate gene editing based on CRISPR/Cas9 technology combined with AAV delivery for the correction of the most common MECP2 mutations in Rett syndrome both in vitro and in vivo. The third GENEPI clinical trial aimed to identify acetylation profiles as epigenetic markers to assess the causality of CREBBP and EP300 variants in Rubinstein-Taybi syndrome, which is considered as a genetic model of neurodevelopmental abnormality with an epigenetic component.

Conclusions: CRISPR/Cas9 clinical trials in polygenic conditions, such as psychiatric disorders, could be envisaged at the level of the epigenetic component of these pathologies. This therapy could be applied ex vivo to perform tissue-specific gene editing.

Disclosure of Interest: None Declared

EPV0535

Female virilization related to congenital adrenal hyperplasia and psychological distress

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Introduction: In females, congenital adrenal hyperplasia (CAH), a spectrum of inherited genetic conditions related to the disruption of adrenal steroidogenesis, is among the most common conditions leading to inappropriate virilization. For adolescent and adult women,

progression of hirsutism may have many psychological concerns. **Objectives:** To explore the psychological distress of a young Tunisian woman who sought medical help and psychological support at a late stage, after suffering from genital ambiguity and severe virilization. **Methods:** Harboring phenotypic male transformation at puberty, our patient attended genetic counselling for cytogenetics assessment. Clinical, biological, psychological and genetic explorations were thus carried out. Results: A 17-year-old female was born from first-degree consanguineous parents, and had healthy siblings (a sister and three brothers). After a single menstrual episode at puberty, she developed amenorrhea and an unexpected progressive virilization, including hirsutism with an inappropriate beard that she had to shave every day and a male voice. Clinical examination revealed a male morphotype with an enlarged clitoris that resemble a penis, male-type pubic hair, underdeveloped of breasts, abnormal cutaneous hyperpigmentation, and a short stature. Pelvic ultrasound revealed a small uterus, but with no visualized gonads. Genetic exploration showed a female 46,XX karyotype and the absence of Y chromosome sequences. Diagnosis of a non-classic CAH was confirmed. Psychological assessment found that the psychological development of the sexual identity corresponded to the assignment of the female sex. A severe psychological suffering due to the non-acceptance of her virile appearance impaired the quality of her daily personal and social life. Stigmata of a depressive syndrome were also revealed.

Conclusions: Particular attention to the psychological assessment of patients with CAH is recommended, as changes in physical appearance have a detrimental impact on psychological and mental well-being.

Disclosure of Interest: None Declared

EPV0536

DNA methylation risk scores for depression, not today

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Introduction: After the success of polygenic risk scores (PRS) that embed a useful summary of genomic information in a comprehensive score, the wish to develop summary statistics for DNA methylation had become more pressing. Developing such a score faces challenges, as the score has to be specific and sensitive as well. Epidemiological research on DNA methylation and depression would benefit from such score.

Objectives: Here, we test a score trained on incident depression (case-control), i.e., a list of published weights for particular CpGs, for its validity in the context of depression severity as measured using MADRS in our sample with depressed patients only.

Methods: DNA methylation was assessed using the Illumina Infinium MethylationEPIC 850k BeadChip on a sample of 119 patients with a diagnosis of MDD. After data cleaning, 113 participants were included in the analysis (M_{age} = 47 years, 57.98% women, M_{MADRS} =27.7). Data processing was conducted using the RnBeads package. From the published reference for the overall sample, a list of 196 CpGs was provided, 170 of these were present in our dataset and used for the score. The list of non-smokers comprised 144 CpGs, of which 124 were available. The score per individual was built using M-values, using the formula: S(weight*DNA methylation value). The score was tested in association with depression and other typical confounders using multiple regression in