Introduction: Three-dimensional chromatin interactions regulate gene expressions. The significance of de novo mutations (DNMs) in chromatin interactions remains poorly understood for autism spectrum disorder (ASD).
Objectives: To investigate the genomic architecture of ASD in terms of non-coding de novo mutations and 3-dimensional chromatin interactions
Methods: We generated 813 whole-genome sequences from 242 Korean simplex families to detect DNMs, and identified target genes which were putatively affected by non-coding DNMs in chromatin interactions.
Results: Non-coding DNMs in chromatin interactions were significantly involved in transcriptional dysregulations related to ASD risk. Correspondingly, target genes showed spatiotemporal expressions relevant to ASD in developing brains and enrichment in biological pathways implicated in ASD, such as histone modification. Regarding clinical features of ASD, non-coding DNMs in chromatin interactions particularly contributed to low intelligence quotient levels in ASD probands. We further validated our findings using two replication cohorts, Simons Simplex Collection (SSC) and MSSNG, and showed the consistent enrichment of non-coding DNM-disrupted chromatin interactions in ASD probands. Generating human induced pluripotent stem cells in two ASD families, we were able to demonstrate that non-coding DNMs in chromatin interactions alter the expression of target genes at the stage of early neural development.
Conclusions: Taken together, our findings indicate that non-coding DNMs in ASD probands lead to early neurodevelopmental disruption implicated in ASD risk via chromatin interactions.

Disclosure of Interest: None Declared

EPP0456

Emotionally Unstable Personality Disorder and Severity of Suicide Attempt are related to Epigenetic Hypermethylation of Brain-Derived Neurotrophic Factor in Women

J. Jokinen[1]*, E. Jamshidi[1], Å. Nilsonne[2], A. Wilczek[2], A. Boström[1] and M. Åsberg[2]

[1]Umeå University, Umeå University, Umeå and [2]Karolinska Institutet, Stockholm, Sweden
*Corresponding author.
doi: 10.1192/j.eurpsy.2023.765

Introduction: Brain-derived neurotrophic factor (BDNF) has been associated with both emotionally unstable personality disorder (EUPD) and suicidal behavior. No study has yet investigated BDNF-associated epigenetic alterations in severely impaired EUPD and suicidal patients.
Objectives: The main goal of the present study was to investigate whether epigenetic dysregulation in BDNF, CRP, IL-1, IL-2 and IL-6 were associated with EUPD and severity of suicidal behavior.
Methods: The discovery cohort consisted of 97 women with emotionally unstable personality disorder (EUPD) with at least two serious suicide attempts (SA) and 32 healthy women. The genome-wide methylation pattern was measured by the Illumina EPIC BeadChip and analyzed by robust linear regression models to investigate mean BDNF methylation levels in a targeted analysis conditioned upon severity of suicide attempt. The validation cohort consisted of 60 female suicide attempters, stratified into low-(n=45)and high-risk groups (n=15) based on degree of intent-to-die and lethality of suicide attempt method, and occurrence of death-by-suicide at follow-up.
Results: Mean BDNF methylation levels exhibited hypermethylation in relation to EUPD(p=0.0343, percentage mean group difference ~3.8%). Similarly, this locus was confirmed as hypermethylated in an independent cohort of women with severe suicidal behavior (p=0.0469). Results were independent of age and BMI.
Conclusions: This study elicits emerging evidence of epigenetic dysregulation of BDNF in relation to phenotypes known to increase risk of suicide (lethality of suicide-attempt method and presence of EUPD diagnosis with history of recent SA). Further studies investigating epigenetic and genetic effects of BDNF on severe suicidal behavior and EUPD are needed to elucidate the role of epigenetic regulatory mechanisms and neurotrophic factors in relation to suicide risk.

Disclosure of Interest: None Declared

EPP0457

BDNF expression in brain regions of Anorexia Nervosa mouse model, a biomarker of diagnostic and prognostic?

N. Ramoz[1]*, J. Cao[1], C. Tezenas du Montcel[1], V. Tolle[1], P. Gorwood[1,2] and O. Viltart[1,3]

[1]Institute of Psychiatry and Neuroscience of Paris, INSERM U1266; [2]CMME, GHU Sainte-Anne Hospital, Paris and [3]Université de Lille, Lille, France
*Corresponding author.
doi: 10.1192/j.eurpsy.2023.766

Introduction: Anorexia nervosa (AN) is a complex mental disorder mainly characterized by a voluntary food restriction and excessive physical activity resulting in dramatic weight loss. Changes in the brain-derived neurotropic factor (BDNF) have been reported in AN patients compared to controls. According to meta-analysis, functional variant rs6265 Val66Met of the *BDNF* gene has been found genetically associated to AN. We also reported an association of this functional variant and electrodermal response to images of thinness suggesting an association between rs6265 and a reward effect of weight loss in AN. In animal models, BDNF modulates negatively the central control of food intake and its injection in rodents induces weight loss and anorexia. Thus, besides its function on neuronal survival, synaptic plasticity and mood, BDNF was also reported to have a metabolic effect via both central nervous system and peripheral organs, which makes BDNF a good candidate for AN diagnosis biomarker.
Objectives: Our study investigates the levels of expression of Bdnf, gene and protein, taking advantage of the mouse AN-like model by measuring Bdnf levels in specific brain areas and blood in food-restricted and refeed animals.
Methods: We used a mouse AN-like model combining a phase of chronic food restriction (50%) during 15 days followed by an *ad libitum* refeeding period of one week. Female mice have or not access to a running with wheel to create a similar metabolic environment that those patients suffering from AN during restriction and recovery once hospitalised. The Bdnf mRNA and protein levels were measured in samples of blood and brain regions (prefrontal

https://doi.org/10.1192/j.eurpsy.2023.766 Published online by Cambridge University Press

cortex, hippocampus, hypothalamus, dorsal striatum, nucleus Accumbens, ventral tegmental area and amygdala) using quantitative PCR and ELISA methods in the different groups of mice (ad libitum, ad libitum with wheel, food restriction and food restriction with wheel). Statistical analysis will compare the measures for different samples by one-way or two-way ANOVAs depending the group of animals or brain regions and blood.
Results: To date, no difference of the level of transcription for *Bdnf* was observed between the different groups of mice (ad libitum, ad libitum with wheel, food restriction and food restriction with wheel) in the prefrontal cortex, hippocampus and hypothalamus. We expect significant differences of Bdnf expression in the other brain regions of interest for the food restricted animals with or without the wheel compared to ad libitum animals. We expect also differences in the level of expression of Bdnf in fasted animals compared to the refeed animals.
Conclusions: The BDNF could represent a potential biomarker of AN for the diagnostic and the prognosis in the evolution to the remission when weight recover and thus will allow a better understanding of the aetiology of AN. This study is supported by Fédération pour la Recherche sur le Cerveau.

Disclosure of Interest: None Declared

EPP0458

Behavioral signs of CHARGE syndrome and CHD7 mutational spectrum

N. Bouayed Abdelmoula* and B. Abdelmoula

Genomics of Signalopathies at the service of Medicine, Medical University of Sfax, Sfax, Tunisia
*Corresponding author.
doi: 10.1192/j.eurpsy.2023.767

Introduction: CHARGE syndrome is a genetic entity caused by mutations in the chromodomain helicase DNA-binding protein 7 gene (CHD7) at 8q12.1. There are pleiotropic signs among individuals with this disorder. Diagnosis is clinical using medical criteria. CHD7 gene mutations are usually found in 90% of affected patients.
Objectives: The aim of this study was to report behavioral signs of CHARGE syndrome and their phenotype-genotype correlations.
Methods: Four Tunisian males from Sfax (Tunisia) with clinical features suggestive of CHARGE syndrome were examined at our genetic counselling at the medical University of Sfax. Assessment of facial dysmorphic and behavioral features, karyotyping using RHG banding and molecular screening of CHD7 mutations were performed. Molecular analysis was made using direct Sanger sequencing of the entire CHD7 gene.
Results: Molecular genetic analysis revealed two deletions of the CHD7 gene at exon 3 for the first patient and at exon 8 for the second. The two genetic alterations were associated to retarded growth development and genital hypoplasia. Sensory impairments included for the first visual defects and for the second auditory and olfactory defects. Besides constant delayed psychomotor development, the two patients shared receptive and expressive communication disorders, anxiety, attention deficit, cognitive impairment and intellectual disability. There were no aggressive traits nor major autistic features. Learning disabilities were also present for the two patients.
Conclusions: The CHD7 gene controls the developmental pathways as a transcriptional regulator in the nucleoplasm through chromatin organization. Mutational alterations lead according to the affected domains, and the structure of the nonfunctional CHD7 protein, to the perturbation of the regulation of the developmental pathways' genes expression. CHD7 is demonstrated as an important component of neurogenesis through two neuronal determination factors: Sox4 and Sox11. While nonsense, frameshift and missense mutations are most common, deletions and duplications are less frequent. Moreover, while exon 3 is commonly altered, mutations of exon 8, which is related to the CHD7 protein chromodomain, are very rare. Phenotype-genotype correlations according to the type of genomic alteration of CHD7 gene are rarely published, particularly concerning behavioral and psychological features of CHARGE association. Here, physical disorders of our two patients seem to be different but behavioral features seem to be common. Multidisciplinary care is thus required for CHARGE syndrome and molecular analysis must be indicated because the type of the genomic alterations may be a key step for a more accurate management of physical and behavioral disorders.

Disclosure of Interest: None Declared

EPP0460

"… wise, amazed, temp'rate, and furious, Loyal and neutral, in a moment": first heritability analysis of affective temperaments reports remarkably high SNP-based heritability

X. Gonda[1,2]*, D. Torok[3], N. Eszlari[3], D. Gyorik[3], A. Millinghoffer[4], G. Bagdy[3] and G. Juhasz[2,3,5]

[1]Department of Psychiatry and Psychotherapy, Semmelweis University; [2]NAP3.0 Neuropsychopharmacology Research Group, Hungarian Brain Research Program, Semmelweis University; [3]Department of Pharmacodynamics, Semmelweis University; [4]Department of Measurement and Information Systems, Budapest University of Technology and Economics and [5]SE-NAP 2 Genetic Brain Imaging Migraine Research Group, Hungarian Brain Research Program, Semmelweis University, Budapest, Hungary
*Corresponding author.
doi: 10.1192/j.eurpsy.2023.768

Introduction: Depression shows a moderate heritability of 37-42%, which can be up to 75% in severely depressed samples 75%. At the same time SNP-based heritability of depression in GWAS-s is around 8-9%. Heterogeneity of the depressive phenotype may contribute not only to the lack of understanding its genetic background but may also hinder the identification of novel targets. Thus clinically relevant intermediate endophenotypes are needed for. The affective temperaments in the Akiskal model may be considered high-risk states or subclinical manifestations of mood disorders. Considering their strong genetic and biological background, high heritability in family studies, and their temporal stability, they may prove to be relevant endophenotypes for depression.
Objectives: The aim of the current study was to investigate the genetic determinants and heritability of affective temperaments based on a GWAS approach.
Methods: 775 subjects aged between 18-60 years recruited in Budapest, Hungary provided genetic samples and completed

https://doi.org/10.1192/j.eurpsy.2023.766 Published online by Cambridge University Press