Genetics and Molecular Neurobiology

EPP306

Evaluation of Mitochondrial DNA (mtDNA) Copy Number Alterations and Clinical Parameter Correlations in Patients with Methamphetamine Use Disorder

H. M. Aytac[1,2*], Y. Oyaci[1,3], M. Pehlivan[4], S. I. Azizoglu[2], O. Guclu[2] and S. Pehlivan[1,3]

[1]Institute of Graduate Studies in Health Sciences, Istanbul University; [2]Department of Psychiatry, Basaksehir Cam and Sakura City Hospital, University of Health Sciences; [3]Department of Medical Biology, Istanbul Faculty of Medicine, Istanbul University and [4]Department of Hematology, Basaksehir Cam and Sakura City Hospital, University of Health Sciences, Istanbul, Türkiye
*Corresponding author.
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Introduction: Methamphetamine use disorder (MUD) and associated conditions impose a significant burden not only on affected individuals and their families but also on communities. Neurotransmitter system imbalances, mitochondrial dysfunction, oxidative stress, and activation of the inflammasome have all been implicated in methamphetamine-induced neurotoxicity. However, whether MUD is associated with peripheral mtDNA alterations remains uncertain.
Objectives: This study aimed to investigate the relationship between mtDNA copy number and clinical parameters in individuals diagnosed with MUD, comparing them with healthy controls.
Methods: Our study is a case-control research involving 52 patients diagnosed with MUD based on DSM-5 criteria and 52 healthy controls. Peripheral blood samples were collected, and leukocytes were isolated using the ELK Biotech Genomic DNA Extraction Kit for genomic DNA extraction. DNA samples were diluted to a concentration of 0.5-2 ng/µl for mtDNA copy number analysis, which was performed using the ScienCell qPCR Assay Kit. Two qPCR reactions were carried out for each sample using mtDNA and SCR primer sets. Known mtDNA copy number samples were used as references, and mtDNA copy numbers for each sample were calculated using the comparative $^{\Delta\Delta}$Cq method.
Results: When comparing the mtDNA copy numbers between patients diagnosed with MUD and the control group, the mtDNA copy number in individuals with MUD was found to be significantly lower than that of the control group (p=.001). After controlling for age and gender, clinical parameters (suicide attempt, non-suicidal self-injury, duration of disorder, withdrawal symptoms, psychosis) and scale scores were compared based on mtDNA copy numbers. Among these, only substance use duration showed a statistically significant difference between the groups (p=.045). Additionally, in this study, a significant negative correlation was found between mtDNA copy numbers and the duration of disorder in MUD patients (r=-.369, p=.008).
Conclusions: This is the first study examining the relationship between peripheral mtDNA alterations and clinical parameters in individuals diagnosed with MUD. A previous study showed that individuals with MUD exhibited decreased mtDNA copy numbers and increased mtDNA damage compared to healthy individuals in the Chinese population. Consistent with these findings, it was suggested that methamphetamine could lead to mitochondrial dysfunction and a reduction in mtDNA copy numbers in cell lines and animal models. In conclusion, individuals with MUD show decreased mtDNA copy numbers in peripheral blood samples, potentially related to increased autophagy. In this context, the reduction in mtDNA copy numbers could be used as a biomarker for MUD, and preventing this reduction may be beneficial in the clinical treatment of addiction.

Disclosure of Interest: None Declared

EPP307

Polygenic risk score for autoimmune disorder SLE predicts current depression but independently of exposure to recent stress

A. Berezvai[1], D. Torok[1,2,3], S. Krause[1,4], G. Bagdy[1,2], G. Juhasz[1,2] and X. Gonda[2,5*]

[1]Department of Pharmacodynamics, Faculty of Pharmacy; [2]NAP3.0-SE Neuropsychopharmacology Research Group, Hungarian Brain Research Program; [3]Doctoral College, Pharmaceutical Sciences and Health Technologies Division; [4]Doctoral College, Mental Health Sciences Division and [5]Department of Psychiatry and Psychotherapy, Semmelweis University, Budapest, Hungary
*Corresponding author.
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Introduction: Inflammation has emerged in recent year as one potential contributor pathway in the background of several neuropsychiatric disorders, including depression. It is also increasingly understood that inflammation may exert its role via mediating the effect of stress in the etiology of such conditions. Therefore, understanding the role of inflammation in the background of depression would offer novel insight into the involved processes facilitating the identification of related biomarkers, novel treatment targets, as well as possibilities for early screening, risk identification, and prevention and intervention. In spite of these promising possibilities, currently we know little about the shared genetic risk in case of autoimmune or inflammatory conditions and depression.
Objectives: Our present analyses aimed at investigating, using polygenic risk scores, if genetic predisposition to inflammatory or autoimmune disorders predicts depression scores and if recent exposure to life stressors interacts with the effect of genetic variation.
Methods: For establishing polygenic risk scores (PRS) for different inflammatory/autoimmune conditions, we pre-existing GWAS summary statistics were used for systemic lupus erythematosus (SLE) (7219 cases, 15991 controls), autoimmune thyroid disease (AT) (859 cases, 324074 controls), and atrophic gastritis (AG) (180 cases, 456168 controls). The NewMood database (N=1820) was used as target data. Brief Symptom Inventory Depression Scale scores reflecting current depressive symptom severity was used as outcome depression phenotype. PRS calculations were performed with LDpred2. Linear regression models performed with R (4.1.3) were used to investigate the main effect of the PRS and the interacting effect of recent stress and PRS on current depression score.
Results: The main effect analyses showed that SLE-PRS had a significant effect on depression (beta=0.2389, p=0.0175) while AT-PRS (beta=0.4094, p=0.9763) and AG-PRS (beta=0.4741, p=0.5795) did not show significant main effects. Interaction analyses did not show significant effect in case of any of the examined autoimmune/inflammatory disorders (SLE-PRS x recent stress: