M32. MITOCHONDRIAL GENETIC RISK IN OCD AND RELATED SUBPHENOTYPES
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Background Obsessive-compulsive disorder (OCD) is a severe neuropsychiatric disorder that has strong genetic risk, but the precise factors remain to be identified. Mitochondria play crucial roles in neurons, such as Ca²⁺ regulation, redox signaling, development, synaptic plasticity, and apoptosis. The importance of mitochondria in neurons is evident from the reported comorbidity between mitochondrial diseases and neuropsychiatric symptomatology. Here we examined the role of nuclear-encoded oxidative phosphorylation related genes in OCD risk and its sub-phenotypes.

Methods We selected 28 genes involved in oxidative phosphorylation or in oxidative stress, mitochondrial biogenesis, inflammation and apoptosis. A total of 59 SNPs were analyzed in 477 OCD subjects. Logistic regression was used for OCD risk analysis and linear regression was used to test association with the sub-phenotypes of interest. Given the complexity of the OCD phenotype, we also tested for association with symptom-defined subphenotypes based on YBOCS symptom dimension scores calculated using the YBOCS, in addition to age at onset and overall symptom severity. We used a permutation based test to examine the hypothesis that our set of mitochondrial genes, collectively, was associated with OCD risk.

Results From case-control analysis, we observed nominally significant association for the SNPs rs4011457 in the NDUFS7 gene and OCD risk (N=856, P(uncorrected)= 0.004). Also, nominally significant evidence for association was observed for the SNP rs3820189 in the 5’of the MFN2 gene and YBOCS total score (N=346; P(uncorrected)= 0.002) and for the SNP rs4246944 in the PPIF gene and Sex/Religion factor (N=371; P(uncorrected)= 0.002). A permutation-based test of all 59 SNPs jointly showed significant association with OCD (P(perm)=0.003).

Discussion To the best of our knowledge, this is the first study to show evidence that nuclear-encoded mitochondrial genes may influence OCD.

Disclosure: Nothing to Disclose.