M33. GENETIC VARIATION AND EPIGENETIC MODIFICATION OF SKA2: ASSOCIATIONS WITH OBSESSIVE-COMPULSIVE DISORDER DISEASE RISK AND SYMPTOM SEVERITY

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Background Obsessive-Compulsive Disorder (OCD) has a strong genetic component, is highly comorbid with Major Depressive Disorder (MDD), and is often triggered by environmental stress. Epigenetic modifications are thought to play a significant role in complex psychiatric disorders and may impact the relationship between genes and the environment via the hypothalamic-pituitary-adrenal (HPA) axis. The SKA2 gene interacts with the glucocorticoid receptor, is implicated in mediating HPA axis function, but has yet to be examined in OCD. We hypothesized that genetic and epigenetic variation in SKA2 may play a role in OCD disease risk and symptom severity.

Methods A sample of n=64 OCD patients, divided equally by presence/absence of comorbid MDD, and age and gender matched, were selected. Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score was used to measure disease severity. Genotyping for the SKA2 rs7208505 marker was performed using the Taqman allele specific assay method and DNA methylation levels were quantified using bisulfite pyrosequencing. Methylation percentage was corrected for genotype using previously established methods. Genotypes for rs7208505 were compared to controls of European ancestry (n=365; 1000 Genomes Project Consortium) using Pearson's chi-squared test. The relationship among the rs7208505 variant, methylation corrected, symptom severity, and MDD status was modeled using linear regression.

Results The SKA2 rs7208505 genotype distributions significantly differed between OCD patients and controls ($\chi 2$=8.66, p=0.013). Genotypes were associated with symptom severity (p=0.011), in that patients with the CC genotype had lower Y-BOCS scores than the CT/TT genotypes. While OCD patients diagnosed with MDD had more severe Y-BOCS scores (p=0.023), neither genetic nor epigenetic variation of rs7208505 was associated with comorbid MDD status. Methylation corrected for genotype was not significant in the regression model (p>0.05).

Discussion These results provide some evidence that SKA2 genetic variation may be associated with OCD risk and symptom severity. Methylation corrected for genotype was not associated with OCD symptom severity; however, patients with TT and CT genotypes had more severe Y-BOCS scores than the CC genotype carriers. Further work will include replication in larger samples and interrogating additional genetic and epigenetic variations in SKA2.

Disclosure: Nothing to Disclose.