

MEETING ABSTRACTS

SINGLE NUCLEOTIDE POLYMORPHISMS IN THE GENES ENCODING AChE AND ITS miR-608 REGULATOR CO-MODULATE ANXIETY AND BLOOD PRESSURE

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Cholinergic-regulated phenotypes including anxiety, cardiac and immune-related properties show inter-individual variability which might be affected by genomic Single Nucleotide Polymorphisms (SNPs) in the corresponding protein coding genes and their targeting microRNAs (miRs), but the combined impact of such SNP pairs is unknown. We have recently shown that the rs17228616 SNP in the Acetylcholinesterase (AChE) gene reduces the affinity of AChE mRNA to the primate-specific miR-608 and elevates both AChE levels in brain and blood as well as trait anxiety and blood pressure (1) while affecting PTSD-related neural circuits and downregulating numerous brain miR-608 targets (2). Others reported that the rs4919510 SNP in the miR-608 gene reduces miR-608 levels *in vitro* and limits the risk of sepsis following head injury *in vivo* (3). To explore the combined effect of these two SNPs, we tested 444 healthy 30 years old US donors and 101 Israeli ex-prisoners of the 1973 war (EWP), 76 of whom returned with post-traumatic stress disorder (PTSD). Genotyping combined with R-statistics of the corresponding biomedical evidence demonstrated that the rare allele of the AChE SNP was more abundant among non-PTSD EWP donors compared to PTSD patients in this cohort (33 vs 19%, Chi-square 0.03). Moreover, we found in both of these cohorts interaction between the effect of the two SNPs on blood pressure, inflammation and anxiety-related parameters, with the miR-608 SNP stratifying the corresponding impact of the rare allele of the AChE SNP on these parameters. Our findings indicate an interaction between the SNPs in the AChE and miR-608 genes, possibly reflecting modified impact of this primate-specific miR on its numerous downstream targets.

References

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