EVIDENCE FOR ASSOCIATION OF AKT1 GENE VARIANTS WITH BOTH SCHIZOPHRENIA AND BIPOLAR DISORDER

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Objectives: Akt1 gene has been associated with genetic etiology of schizophrenia (SCZ). SNPs and haplotypes with significant association were identified in different ethnic schizophrenia. In bipolar disorder (BD), these variants have not been studied. The aim of this study was to investigate the Akt variants both in SCZ and BD. We wished to determine whether the two disorders show similar patterns of association.

Methods: This case-control study included 788 subjects: 384 unrelated SCZ; 130 unrelated BD, and 274 unrelated healthy controls (HC) for six SNPs of the Akt1 gene located at the region spanning 36.9 kb. Genotyping was achieved with the HRM method and primers were designed by Primer3. Genotypic, allelic and haplotypic distribution between SCZ, BD and HC population were evaluated. Analyses were performed with Plink v.1.06.

Results: The analysis identified a significant global distortion in SCZ (p< 0.0005) and a weak association in BD (p< 0.01). A four-SNP haplotype (TCGA) showed a significant association with SCZ (p< 0.0007) and BD (p< 0.006). This haplotype include the Emamian et al's core haplotype (3-SNP 2/3/4/, TCG). Interestingly, SCZ and BD share this distorted haplotype. Other multi-SNP haplotypes also showed significant association with both diseases. No distortion was observed between SCZ and BD population, and when SCZ and BD were combined, the global p-value improved (p< 0.00005).

Conclusions: Our findings support the role of Akt1 in genetics of both SCZ and BD. The established association in both populations are consistent with the overlap model of these nosologies.