SYNERGISTIC INTERACTION BETWEEN TAU KINASE GENES (CDK5R1 AND GSK3B) IN PARKINSON’S DISEASE PATIENTS OF INDIA

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Introduction: Parkinson’s disease (PD) is etiologically complex. Microtubule associated protein tau (encoded by the gene MAPT), is primarily a neuronal protein that is involved in the organization and integrity of the microtubules, thereby regulating axonal transport. MAPT is a strong candidate in PD susceptibility. Previously we reported that under a common haplotype background (A,A,C,+) constructed by the markers rs1467967, rs242557, rs2471738 and del-In9, the SNP rs7521 of MAPT modifies the age at onset of PD among Indians.

Aim: Aberrant tau phosphorylation can disrupt axonal transport, which is an underlying mechanism in neurodegeneration. Glycogen synthase kinase-3β (GSK3B) and cyclin-dependent kinase 5 (CDK5) are the two major protein kinases involved in abnormal phosphorylation of tau. In this study we tried to determine their potential role in PD pathogenesis.

Methods: Two functional SNPs of GSK3B (rs334558 and rs6438552) and rs735555 of CDK5 regulatory subunit 1 (CDK5R1) were genotyped in 373 PD cases and 346 healthy controls of eastern India. Apart from single locus and haplotype analyses we also examined the combined effects between the two genes and PD susceptibility.

Results: The C,C and T,C haplotypes of GSK3B were moderately associated with increased risk and protection respectively for late onset PD. Moreover, individuals carrying the C/C genotype at rs6438552 and rs735555 had increased risk of developing PD than those without this genotypic combination [OR=1.871, 95% CI=1.181-2.964, p=0.009].

Conclusions: GSK3B and CDK5R1 appear to determine the risk profile for PD among Indians. Further studies are warranted to confirm these results in additional cohort of patients.