Objective: Intellectual disability (ID) is defined as significantly subaverage intellectual functioning with deficits in adaptive behavior. For ~40% of individuals, cause for disability remains unknown and these are categorized as idiopathic ID (IID). Various behavioral problems co-occur with ID and thus serotonergic neurotransmission, known to control emotion, mood and drive, has received immense attention. Synaptic serotonin (5-HT) level is primarily maintained by metabolizing enzyme MAOA and serotonin transporter (SLC6A4) which helps in reuptake of the neurotransmitter. Since functional genetic polymorphisms have a potency to affect activities of these proteins, in the present investigation polymorphisms in these genes (MAOA-u VNTR, rs6323, 5-HTTLPR and STIN2) have been analyzed in IID individuals associated with various behavioral problems.

Methods: Families (N=189) with IID probands were recruited following DSM-IV. After obtaining informed written consent for participation, peripheral blood was collected for isolation of genomic DNA used for PCR-based genotyping of target sites followed by family-based statistical analyses of data.

Results: Significant association of MAOA rs6323 "T" allele with female IID (P=0.016) and a trend towards association with female IID patients exhibiting behavioral problems (P=0.046) was noticed. Non significant over transmission of the 5-HTTLPR "L" allele was also observed in female IID probands with behavioral problems (P=0.076). Synergistic epistatic interaction, with a sex-bias, was noticed between MAOA and 5-HTT (P< 0.05).

Conclusions: From the data obtained it could be summarized that serotonergic system may have some role in the etiology of behavioral problems of female IID individuals.