Abstract

Background
In Schizophrenia, Molecular genetics may provide the clinician with a useful tool in deciding which trinucleotide repeat expansion (TNR) expansion does not cause or play role in Schizophrenia (SCZ). Beside this data suggests that differences in TNR expansion in normal and Schizophrenia (SCZ) patient sample may help to create clinically meaningful genetic-based subgroups in Schizophrenia. Study of TNR polymorphism based on ethnicity may give insight into the genetic specifications at the loci studied in that population.

Aim
To study the association of the trinucleotide repeat expansion (TNR) polymorphisms of six gene loci encoded in our study as - \textbf{Sam1} (CTG-B33), \textbf{Sam2} (CTG37), \textbf{Sam3} (NOTCH4), \textbf{Sam4} (DTNBPl), \textbf{Sam5} (GLUR6), \textbf{Sam6} (CTG-B1) with Schizophrenia, if any by comparisons between normal individual and Schizophrenia patient samples at these loci.

Subjects and Methods
The sample comprised of forty (40) North- Indian patients with DSM-IV diagnosis of Schizophrenia. There were also 40 control (normal) samples – twenty (20) males and twenty (20) females who were healthy blood donors. DNA was isolated from blood. Genotypes were determined using polymerase chain reaction (PCR) and direct sequencing and agarose gel electrophoresis for allelic discrimination between normal and Schizophrenic subjects of our study. The 40 Schizophrenic patients were categorized on the basis of-
1. Sex - 20 Males and 20 Females. Study was -
   Inter-gender: Normal Female vs. Schizophrenic Female.
2. Disease intensity: 20 Schizophrenic (Mild-Avg.) and 20 Chronic
   Schizophrenic patients.

Introduction:
Molecular genetics is about 20-25 years old as a field of study in medicine. In 1980s, clinicians observed inherited differences in polymorphic TNR repeats. The discovery of the genetic variation in genes in the late 1980s was considered to be of major importance in psychiatric diseases as most microsatellite DNA markers containing multiple tandem copies of Di, Tri and Tetra nucleotide sequences were being considered for the appearance of many neuropsychiatric diseases. This hypothesis was being endorsed with positive results reported in many studies especially in Caucasian populations. Most of the multiple tandem copy studies reported trinucleotide repeat (TNR) expansions in 1980s, however, molecular genetic study of microsatellite DNA markers' properly began only about 10 years ago.

Until now several polymorphisms in the genes have been associated with SCZ, however, relatively few of these results have been replicated in independent samples.

In this thesis, the polymorphism of genes affecting brain development - CTG-B33, CTG-B37, NOTCH4, AAT21, GLUR6 and CTG-B1 were chosen for molecular genetic studies. The study focused on association of TNR expansion polymorphism with Schizophrenia by observing difference of TNR expansions between Schizophrenic patients and healthy controls at these loci. Effects on disease intensity and gender bias were also studied.