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Letter to the Editor

Exploring genomics: The way forward in curbing schizophrenia

The modern science of genomics now permits the study of DNA from individual genes to the genome. Genome sequencing has led to the development of a new area of DNA research, loosely called post-genomics.

Most of the traits are not under the control of a single gene, but are controlled by several genes, which have an additive effect, so that the trait has a continuous distribution. Such traits are referred to as quantitative traits and a locus controlling them is termed as quantitative trait locus (QTL). If the chromosomal location of a QTL is known, DNA markers close to that QTL can be used to check the disease susceptibility by identifying individuals that carry the favorable allele at the QTL. Out of the different kinds of molecular markers, single nucleotide polymorphisms (SNPs) are singled out as promising markers in near future.¹ A 'SNP' is a DNA sequence variation occurring when a single nucleotide—A, T, C or G—in the genome differs between members of a biological species or paired chromosomes in an individual. Almost all common SNPs have only two alleles. It is the most common source of genetic variation in the human genome, accounting for about 90% of sequence differences. SNPs initially arise via rare spontaneous mutations which is so low that the chances of a further mutation at the same site on the same individual chromosome are negligible. Hence, any decay in association between a SNP and linked QTL is entirely due to recombination.

Schizophrenia is a severe psychiatric disorder characterized by distortion of reality, delusions, hallucinations, altered emotional reactivity, disorganized behavior, social isolation and cognitive impairment. It is the third-leading cause of disability among individuals aged between 15 and 44 years with a worldwide prevalence estimated to be approximately 1%.² Though the etiology of schizophrenia is not well understood but it has been postulated as a complex disease influenced by both genetic & environmental factors. Further, schizophrenia is a highly heritable disease with an estimated heritability as high as 80%.³ The drugs commonly used to treat schizophrenia offer important relief from some but not all symptoms and can cause serious adverse effects in many individuals.

Hence, the proposed approach for genomic selection will be as follows:

The candidate genes on which the genomic selection is to be applied are selected based on complementary information from linkage, association, gene expression, brain imaging, and model organism studies of schizophrenia, as well as knowledge of

biological systems particularly relevant to schizophrenia leading to identification and screening of appropriate SNPs of concerned genes. Then association of this SNP variation (with the help of suitable statistical model) with both the qualitative diagnosis of schizophrenia and quantitative endo-phenotypes for schizophrenia will be evaluated thereby helping in development of commercial chip for validated SNPs in further application.

Thus, by the refinement of the observed associations with each endo-phenotypes, identification of the underlying causal genetic variants and elaboration of their molecular interactions, the field of genomic selection will aid in understanding the genetics and neuropathology of schizophrenia thereby curbing this public health menace to a great extent.

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