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chizophrenia is a very complex disease that affects millions of patients worldwide, with no restriction of gender, ethnicity or socioeconomic levels. The chronicity and the side effects caused by the medications; antipsychotics, antidepressants, anticonvulsants; lead to a heavy burden and loss of quality of life to the patient and all those around him. The complexity of the treatment is not a matter of chance. The physiopathology is poorly understood, there is no specific biomarker and the diagnosis is still made by descriptive symptoms in an almost checklist fashion. Epidemiological studies have already shown the intricate entanglement between genetical and environmental factors in the development of schizophrenia and psychotic disorders. The heritability of 80% but a concordance of only 40% in identical twins is only a hint of the genetic complexity involved in the development of the disorder. Following the most prevalent theory of the dopaminergic transmission as one of the causes for psychotic symptoms, geneticists examined thoroughly the genes involved in this process. One of these candidate sequences is the NTAD cluster, comprised by the NCAM1, TCC12, ANKK1 and DRD2 genes.

Following this line of reasoning, Cordeiro and Vallada published in the present issue of Arquivos de Neuro-Psiquiatria a paper trying to clarify the influence of the Taq1A polymorphism in the pathogenesis of schizophrenia in a Brazilian sample. It is indeed the first of the kind in this population and follows several other papers with the advantage of a larger sample. Parsons et al. found the same higher prevalence of A2 allele in the subjects but with only 165 controls and 119 subjects. This study is notable for another reason; the population studied is of Basque ancestry with very low levels of miscegenation and heterogeneity. Aslan et al. couldn’t replicate the same results in a Turkish sample; the allelic frequency is completely different from the other western studies cited and no association between the A2 allele and schizophrenia was found.

These three papers are good representatives of how difficult and complex can be the interpretation of results. Heterogeneity of the studied population due to miscegenation, small samples with insufficient statistical power, stratification, or even the primary hypothesis are the causes for such discrepancy in results. It is clear now that the genes involved...
have small or no impact when taken individually and only a multiple gene approach can bear better results. The gap between gene expression and behavior is still far from being closed; genetics are one side of the bridge, identifying the genes responsible for disease are a important step and with this paper Cordeiro and Vallada clarified this point.

Perhaps it is the time to change the stratification of subjects, considering not only gender and clinical subtypes but other findings such as imaging (MRI and PET), immunological profile and response to treatment. This war has to be fought in several different fronts with all weapons that we have available.

References


