Genetics and psychiatry

The previous year marked the celebration of the 50th anniversary of the description, in 1953, of the double helix of the DNA structure by Watson and Crick. In the same period of time, as Watson and Crick’s breakthrough, chlorpromazine was synthesised in Couvoisier’s laboratory and used in clinical practice by the psychiatrists Delay and Deniker. The use of chlorpromazine by changing dramatically the picture of mental illness is considered as the third revolution in psychiatry, after the delivery of patients from the chains by Pinel (1745-1826) and the theory of Freud (1856-1939).

The term genetics was already used by Bateson in 1902, while the differentiation between the concept of genotype and phenotype was provided in 1909 by the Danish botanist Mohanssen, who was the first to introduce the term gen-. The question about the role of heredity in the etiology of psychiatric disorders, mainly the major ones - schizophrenia and affective disorder - has occupied medical thinking since the 19th century (the method for studying twins was proposed by Galton in 1875). Based on empirical observations, even at the time of Kraepelin, it was reported that these disorders were frequently presented in the families of patients.

Since 1960, the systematic investigation of the contribution of genetic factors in the pathogenesis of psychiatric disorders was significantly advanced, grace to the utilization of more strict diagnostic criteria, the use of carefully selected control groups and mainly the application of molecular biology techniques in psychiatric genetics.

Family studies have demonstrated the familial component of major psychiatric disorders, as well as of the disorders of the schizophrenic and affective spectrums and have verified the previous empirical observations that the morbidity risk is significantly higher among the relatives of patients in comparison with the relatives of normal controls.

Twin studies have shown that familiality of psychiatric disorders is mainly due to the influence of heredity, by demonstrating that the concordance for these disorders was higher in monozygotic (MZ) twins, who share identical genetic material, in comparison to dizygotic (DZ) twins, who share only half of their genes; the findings were consistent either the twins (MZ and DZ) had been reared together or apart. However, the fact that the concordance rate in MZ twins is less than 100%, as would have been the case if the disorders were only due to genetic factors, supports also the hypothesis that environmental influences are also implicated in the manifestation of the diseases. Finally, adoption studies have verified the hypothesis of genetic contribution, by demonstrating that psychiatric disorders are more frequently expressed among the biological rather than the adoptive relatives of patients.

The results of the association and linkage studies of major psychiatric disorders with various genetic markers and candidate genes in different chromosomal regions, as well as those regarding whole genome scans were positive for a lot of the respective studies, while other studies presented negative conclusions or were not able to verify previous findings. This is believed to be related to problems with the exact definition of the phenotype, due to the multiformity of its clinical expression, as well as with the genetic and clinical heterogeneity of mental illness. In diseases with classical mendelian transmission the genotype usually corresponds directly to the phenotype, while this is not the case for diseases such as the major psychiatric disorders, with multigenic-multifactorial mode of transmission. It seems that in this kind of disorders a number of genes interact with environmental factors and contribute to the manifestation of the disease. What is inherited in the end, is not the certainty that someone will develop the disorder, but a susceptibility which may be manifested through subclinical characteristics, and which is translated into disease if it exceeds a threshold during the person’s life-time.

In our days, psychiatry, based on the dramatic progress in the field of neurosciences and the completion of the mapping of the human genome as well as on the progress in pharmacogenetics and, particularly, its most promising area of pharmacogenomics, seems to be entering its fourth revolution.

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REFERENCES