

## Something about Genetics in Psychiatry

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Genetics in psychiatry is based on the application of the achievements and methods of population's genetics, immunogenetics, cytogenetics, molecular genetics and pharmacogenetics. Methods of genealogy are already known, and so are the twins method, methods of adoption. Especially present are the methods of DNA recombination discovering the location of genes on chromosomes and creating genetic maps. For now, it can be said that chromosomes 6, 22 and 8 are in the center of attention of geneticists examining the genetic background of schizophrenia[1]. Some studies also suggest an association could be made between HLA-A9 and paranoid schizophrenia. The manic-depressive disorders are more associated with a gene on the short arm of chromosome 11 and the X chromosome. Mental disorders are polygenic and conditioned multifactorial. It is because of the interaction of a number of genetic and environmental factors. The conclusion of most studies is that for the repetition of psychiatric disorders in families heritable factors are more deserving than environmental factors (e.g. studies in families with adopted children), although it is impossible to clearly separate the effects of genetic factors from the effects of environmental factors. The first studies that have attempted to detect predisposition genes for complex diseases were studies of genetic connectivity. They were based on the search of loci - markers in families, which were passed on through generations in the same way as the disease. In the search for the association of complexed hereditary diseases and certain variations of genes in a candidate, the evaluation of endophenotyp can be of a great benefit. Complexed diseases are characterized by a very diverse clinical picture and valuable data could be obtained if we individually evaluate each isolated characteristic of phenotype. The aim of the evaluation of endophenotype in the case of psychiatric disorders, is to penetrate into the mechanisms of the brain functioning and connect them with the hereditary basis. An important advantage of the endophenotype evaluation is also, that it can work in small groups of respondents. Endophenotype evaluation includes an assessment of cognitive deficits, EEG abnormalities, and data obtained by the method of neuroimaging. Considering the current cognition about the genetics of psychiatric disorders, especially schizophrenia [2],

it can be said that no single gene by itself causes brain dysfunction. Many gene variants that have proved to be risky for psychiatric disorders have also been found in many healthy individuals. Strength of correlation of the detected genetic polymorphisms is estimated to be relatively low. This means:

1. COMT genes' polymorphisms (catecho-O-methyltransferase), but also many other genes, modulate cognitive functions, but they do not represent the primary cause of disease[3],
2. genetic risk variants for psychiatric disorders are also found in many healthy people,
3. "Strength" of correlation of detected genetic polymorphisms and diseases is estimated as relative.

Except for the primary sequence of nucleotides in our genome, there is also likely a hidden genetic code, which does not determine the sequence of amino acids in proteins, but it determines the time when a gene turns on or off (rewrites or not). The problem with this code is that it is more or less changeable. It is because of the modification of the genome (DNA). The modification with metillization of cytosine in CpG dinucleotide turns off the gene, whereas the acetylation of histones alters the structure of chromatin and turns on the genes. Epigenetics studies[4] such modifications of genomes. Epigenetics may explain the large variability of phenotypes in human population, and why monozygotic twins are not quite identical. They do not differ in the sequence of nucleotides in DNA, but they have different modifications of DNA, because they occur and change by the effect of environmental factors. Changes of epigenetic sample are the result of the effect of environmental factors, especially nutrition, as well as chemicals that we are exposed to, social contacts, family relationships, etc. Effects of environmental factors alter epigenetic pattern in our genome and may induce abnormal gene function. Except for epigenetic modifications, there is recently recognized the importance of functional DNA sequences that do not code proteins. These sequences encode small RNA molecules that have a regulatory role – they modulate posttranslational the level of gene expression. It is assumed that functional non coding DNA sequences make up 3-4% of the human genome, as opposed to coding, which make up only 1-2%. Micro RNAs are the products of non coding genes and are

complementary to specific mRNA molecules that regulate[5]. Binding with mRNA creates double-stranded complexes that degrade or inactivate. The importance of this mechanism is particularly evident in neurons considering their morphology. Body of the cell is significantly away from the synaptic endings, so these ends must have supplies of mRNA molecules that could be translated into proteins if necessary. New mRNA's synthesized in the nucleus travel at a specified speed along the nerve fibers and dendrites. Lipids and their mediators are involved in the regulation of gene expression[6]. The brain in its dry state consists almost exclusively of lipids. Some of the lipids are particularly abundantly present in the brain and we need to discover the mechanisms by which the brain is able to retain such amount of certain lipid molecules. Lipidomics could provide a molecular list of cellular signaling pathways of complexed diseases. Signaling by lipids is extremely complexed and very difficult to study. Lipids and their mediators in the brain are represented as:

- long-chain unsaturated fatty acids AA and DHA (they determine the dynamic properties of neuronal membranes, regulate ion channels and signal transduction, activate transcription factors and regulate gene expression),
  - endocannabinoids (they regulate behavior, sedation, euphoria, appetite, memory),
  - sterols (cholesterol) (they regulate the dynamics of lipid rafts - signal transduction),
  - sphingolipids (myelin),
  - gangliosides (vitaly important but an unknown role).
- The enzymes that metabolize the membrane's phospholipids are related to the cell membrane and they colocalize with monoaminergic receptors, and are therefore crucial for signal transmission, but also for the creation of long-term memory.

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