3. GENETIC ASPECTS OF MIGRAINE.

Author: Morari Ecaterina

Scientific advisor: Cemortan Igor, MD, PhD, Associate Professor, Head Department of Molecular Biology and Human Genetics, *Nicolae Testemitanu* State University of Medicine and Pharmacy of the Republic of Moldova

Introduction. Migraine is a common neurological disorder which affects 15–20% of the population and usually begins at puberty, but has the greatest impact on people aged 35 to 45 years. Migraines present a severe headache with associated symptoms of nausea, vomiting, photo and phonophobia. The pain can localize on one side of the head. It can be aggravated by physical activity. There are migraines without aura (MO) and migraine with aura (MA) which include many other subtypes.

Aim of study. To investigate the molecular and genetic mechanisms of migraine and their impact on the quality of human life.

Methods and materials. From a variety of articles from PubMed, NCBI databases, Medlineplus.gov, Americanmigrainefoundation.org we selected and analyzed 25 sources describing the genetic manifestations of migraine in more detail

Results. Familial hemiplegic migraine (FHM) is the only known autosomal dominant subtype of migraine with aura. There are mutations in the calcium-channel gene CACNA1A which is present on chromosome 19p13. Four missense mutations were detected in the conserved regions of this gene. This gene usually encodes the pore-forming α1 subunit of the neuronal voltage-gated Cav2.1 channel. The different migraine phenotypes are associated with deletion of the CACNA1A gene. Another involved in increasing the risk of migraines is MTHFR gene which is localized on chromosome 1p36.2 and encodes the enzyme methylenetetrahydrofolate reductase, normally involved in the metabolism of vitamin B9 (folic acid). The MTHFR enzyme catalyses the reduction of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate which is needed for the conversion of homocysteine to methionine. The C677T mutation of the MTHFR gene is quite widespread. For example, it occurs in 35-55% of representatives of the European (Caucasian) race. Missense mutations in this gene lead to protein deficiency or defective protein synthesis. This will lead to an increased level of homocysteine in plasma and a decrease in the amount of methionine. The clinical consequences of elevated plasma homocysteine levels include damage to endothelial cells, spontaneous activation of trigeminal nerve cells, and changes in blood coagulation properties. It is believed that spontaneous activation of trigeminal nerve cells, leading to inflammation of the meninges and blockage of cerebral vessels, is the cause of migraine-related pain. Thus, homocysteine dysfunction can clearly increase the patient's propensity to develop migraines. In this case, the patient is forced to be motionless, since any exposure to light or noise makes the headache unbearable

Conclusion. Migraine is a complex brain disorder that occurs when homeostasis is lost, which leads to activation of the trigeminal vascular system and a cascade of events, the manifestation of which depends on mutations in the MTHFR and CACNA1A genes.

Keywords. Migraine, genetics, brain disorder, mutations.