Epilepsy

GENETIC CASES OF DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHIES IN RUSSIAN POPULATION

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OBJECTIVE: Developmental and epileptic encephalopathies (DEE) are the group of serious neurologic disorders characterized by severe forms of epilepsy, disturbances of intellectual and motor functions. Currently, on January 2022, OMIM includes 99 genetic variants of DEE.

METHODS: Next Generation Sequencing (NGS) was performed with the “Hereditary epilepsies” panel, clinical and whole exome sequencing on the platforms IlluminaNextSeq 500, Illumina HiSeq 1500 и Illumina HiSeq 2500 (USA).

RESULTS: At the period 2019-2021 among the group of children with early onset epileptic encephalopathies the subgroup of 38 patients with DEE was identified: DEE1(ARX gene mutations)– 1 girl, DEE2(CDKL5)– 1 girl, DEE4(STXBP1)– 2 infants, DEE5(SPTAN1)– 3 boys, DEE6(SCN1A)– 8 infants, DEE7(KCNQ2)– 2 cases, DEE9(PCDH19)– 2 girls, DEE11(SCN2A)– 1 girl, DEE13(PCDH19)– 3 boys, DEE14(KCNT1)– 5 children, DEE16(TBC1D24)– 3 girls, DEE18(SZT2) – two sisters, DEE25(SLC13A5)– 1 boy, DEE36(ALG13)– 1 girl, DEE53(SYNJ1)– 1 boy, DEE74(GABRG2)– 1 girl and DEE91(PPP3CA)– 1 boy. 14 types of mutation were not previously described, including those in genes ARX(610CA, Arg204Ser), CDKL5(284delA, Asn95fs), KCNQ2(1742GA, Arg581Gln), KCNT1(1066CT, Arg356Trp), KCNT1 (1439AG, Asp480Gly), PCDH19(1236CA, Asp412Glu), PPP3CA(702CA, Asp234Glu), SCN1A(1224delC, Phe408fs), SCN2A(623TC, Val208Ala), SCN8A(656TC, Leu219Pro), STXBP1(C.*96TA, frameshift mutation), SYNJ1 (1042CT, His348Tyr), SZT2(compound-heterozygous sisters: 2371CT, Arg791Cys & 4360GA, Val1454Ile) and TBC1D24(1499CT, Ala500Val).

CONCLUSIONS: Modern genetic assessment by means of NGS with the "Hereditary epilepsies" panel, clinical and whole exome sequencing is required for all the children with pharmacoresistant epileptic encephalopathies of unknown etiology. For some of the above forms of DEE targeted pharmacotherapy approaches were recently elaborated.