

ANALYSIS OF COGNITIVE FUNCTIONS AND NEURODEGENERATIVE DISEASES SELECTION SIGNALS IN CENTRAL EURASIAN POPULATION THROUGH TIME

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Background: Natural selection in Human favored the development of cognitive functions such as memory, attention, planning, problem solving, since these skills increased the chances of survival and reproduction. At the same time, current human lifespan led to increasing the cases of neurodegenerative diseases. Most of all manifest themselves in old age, and causal mutations pass for generations influencing on natural selection and genetic load. GWAS studies of modern population made possible to study the population of past eras.

Our aim was to evaluate selective signals of cognitive functions and neurodegenerative diseases in ancient and modern populations of the Central Eurasian region.

Materials and methods: We downloaded from the AADR the 1240K-captured genome data of 470 ancient individuals from Central Eurasia. For modern population analysis, we used genome data of 2,500 individuals from 1000G. Whole-genome data of 898 modern Kazakh individuals were taken from our resource. The SmartPcAv.16,000, ADMIXTUREv1.3.0, and pcadaptv4.3.5 packages were used to determine the population structure and assess the selection signals. For annotation and interpretation of SNP selection candidates we've used BioMart3.22 package, Gowinda1.12, Revigov1.8.1.

Results: After quality control and filtration of ancient genome data (total genotyping rate was 0.721805, 416,508 SNPs), ancient DNAs were divided to millennium time periods: 12000 -5000 (21 samples), 5000-4000 (58), 4000-3000 (139), 3000-2000 (153), 2000-500 (99) years ago. The modern Kazakh DNA genotyped data (654,027 SNPs) were imputed, and subset SNPs from 1,240k compiled 863k. The analysis of SNP candidates for selection was done in separate subgroups. The analysis applied a q-value cutoff ($q < 0.05$) to minimize false positive results. Significantly, 413 SNP selection candidates were revealed in total. After interpretation and annotation SNP variants, the phenotypes associated with cognitive functions were selected. In total, selection signals analysis revealed 91 SNPs of 42 genes, that could be involved in selection of cognitive features in populations through time.

Conclusion: Such cognitive functions as stress sensitivity, memory, attention, logic, chronotype were predominantly selectable phenotypes during Bronze and Iron Ages. The characteristics of recent times have become an increase in susceptibility to diseases such as Alzheimer's disease, Parkinson's disease, autism, epilepsy, bipolar disorder, depression, insomnia, and neuroticism.