



Session P10 - Neuromuscular disorders

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Posters P10

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Introduction: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterized by the degeneration of upper and lower motor neurons. The frequency of mutations in ALS patients has been extensively investigated in populations of various ethnic origins. Patients and methods: All investigated ALS patients (n=107) were of Hungarian origin. Repeat sizing of *C9orf72* and *ATXN2* genes and targeted next generation sequencing (NGS) were used to comprehensively assess genetic variation in 35 major ALS genes. The cohort was previously screened for *SOD1* and *TARDBP* genes, with negative results. Variants from whole-exome sequencing data of other studies (200 individuals of Hungarian or Austrian origin) were used as in-house control database. Results: Pathogenic repeat expansions in the *C9orf72* gene were detected in 10 patients (9.3%); intermediate polyQ lengths (27-33) in the *ATXN2* gene were identified in 9 (8.4%) patients. Using panel sequencing, 31 rare, potentially pathogenic variants were detected in 16 genes. According to the NGS results, the most frequently mutated genes were *NEK1* (5.6%), *NEFH*, *SQSTM1* (3.7%), *KIF5A*, *SPG11* (2.8%), *ALS2*, *CCNF*, *FUS*, *MATR3*, *TBK1* and *UBQLN2* (1.9%). Furthermore, potentially pathogenic variants were found in *ERBB4*, *FIG4*, *GRN* and *SIGMAR1* genes in single patients. Conclusion: Combining targeted NGS and repeat sizing, potentially causative variants were detected in 41% of patients including patients with variants considered to be of uncertain significance (VUS). Our findings highlight the necessity for large-scale multi-center studies on ALS patients to better understand the underlying genetic causes. Funding: Hungarian Brain Research Program (Grant No. 2017-1.2.1-NKP-2017-00002).