Abstract:

Autism spectrum disorders are a complex and heterogeneous group of difficulties affecting the physical and psychological state of an individual on many different levels. The prevalence of autism is also notable, estimated at 0.5–3.5 % of the population. Not only environmental factors but also genetic factors are involved in the etiology of autism spectrum disorders. Large proportion of these genetic aspects is represented by copy number variants. Depending on their location in the genome and the specific genes affected, these variants can have different clinical consequences. Some of these abnormal variants are observed significantly more often in individuals with autism spectrum disorders.

The main focus of this diploma thesis is to use selected cytogenomic methods (karyotyping, fluorescent *in-situ* hybridization and array comparative genomic hybridization) to detect abnormal variants in the genome of individuals with autism spectrum disorder and then to evaluate these findings according to clinical impact. The paper includes a detailed enumeration, evaluation and analysis of abnormal variants found in a cohort of individuals with autism or other neurodevelopmental difficulties. It focuses on the affected chromosomal loci and the function of individual genes. The paper also summarizes the characterization of the studied patient population with regard to the prevalence of autism between genders or the burden of neurodevelopmental disorders on individuals and entire families. Case reports of selected patients are also presented at the end of the thesis.

The paper also investigates the relationship between genetic aspects, autism and many other neurodevelopmental disorders (e.g. attention deficit hyperactivity disorder, depressive disorder, obsessive-compulsive disorder, schizophrenia or epilepsy). A hypothesis was tested to determine whether abnormal genetic variants are more common in patients with autism and these comorbid conditions than in patients with isolated autism. Our data did not support this hypothesis, but may suggest a possible trend of a 2.24-fold higher likelihood of an abnormal variant occurring in patients with neurodevelopmental comorbidities than in patients without these associated difficulties. The possible influence of the considerable range of variability that characterizes autism spectrum disorders on these results is discussed.