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ASSOCIATION OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS WITH THE SOLUTE CARRIER FAMILY (SODIUM/HYDROGEN EXCHANGER) ISOFORM 9 (SLC9A9)

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Introduction: Attention-deficit/hyperactivity disorder (ADHD) is a multifactorial, highly heritable developmental disorder which affects 3-7% of school-aged children. ADHD is characterized by behavioral symptoms of impulsivity, hyperactivity and/or inattention. Individuals with diagnosed ADHD meet the DSM-IV diagnostic criteria for one of the three main subtypes of ADHD: combined type, predominately inattentive type or predominately hyperactive-impulsive type. The role of solute carrier family 9 (sodium/hydrogen exchanger) isoform 9 (SLC9A9) in ADHD was recently suggested in a genome-wide association study for ADHD. The SLC9A9 protein, which is localized on the late recycling endosomes, may play an important role in maintaining cation homeostasis which is important for normal functioning of neuronal cells.

Materials and methods: We aimed to analyze two single nucleotide polymorphisms (SNPs), rs9289659 and rs4839604, near the 3'-untranslated region of the *SLC9A9* gene. The study included 93 medication free children with ADHD, with an average age of 9 years (ranging from 4 to 20 years), recruited sequentially from the Polyclinic Kocijan/Hercigonja, Zagreb. ADHD was diagnosed with psychiatric interview, according to the DSM-IV criteria, separate interviews with the children and their parents, psychological interview, psychological tests, physical examination and the short version of the Conners' Rating Scale for Parents. Children without psychiatric diagnoses and free of medication served as control group (N = 131), with an average age of 13 years (ranging from 6 to 18 years). SNPs were genotyped with the ABI Prism 7000 Sequencing Detection System apparatus. The association of these two polymorphisms with ADHD features was evaluated using the χ^2 -test in Sigma Stat 3.5.

Results: We found an association between rs9289659 genotypes and the symptoms of inattention in children diagnosed with ADHD. An association with ADHD features was also found for rs4839604 genotypes, particularly for predominately inattentive type and combined type. A significant difference was found in rs4839604 allele frequencies between healthy control subjects and patients with predominately inattentive type. There were no differences in genotype frequencies between male and female patients and male and female control subjects.

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Conclusions: The SLC9A9 protein may be linked to the symptom-based phenotypes observed in ADHD patients. Our study suggests an association of rs9289659 with DSM-IV inattentive symptom subscales and in case of rs4839604 with inattentive and total symptom subscales. These data should be further investigated on a larger sample to confirm or refute these findings.