Mental Health Research Institute, Tomsk, Russia
Boyarko E.G., Fedorenko O.Y., Boiko A.S., Semke A.V., Ivanova S.A.

The role of SLC6A2 and SLC18A2 genes in the development of antipsychotic-induced hyperprolactinemia

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- In Russia, the problem of side effects caused by the use of neuroleptics has high social significance.
- In psychiatry is common drug-induced hyperprolactinemia, which is important to consider during pharmacotherapy. A side effect of hyperprolactinemia is characteristic of almost every neuroleptic.
- Early studies have shown that among the side effects of antidepressants reuptake inhibitors of serotonin and norepinephrine have hyperprolactinemia.
- Genetic features are the cause of 20 to 95% of all adverse reactions of the human body for drugs. Identification of patients with these characteristics allows to predict the pharmacological response to medicince and thus increase the efficacy and safety of these drugs.

Hamner M.B., Arana G.W. , 1998; Magharious W. et al., 1998; Dickson R.A. et al., 2000; Seredenin SB, 2004; Nakonezny P. et al., 2007

- Previously shown the association of gene synaptic vesicular monoamine transporter SLC18A2 with diseases that are determined neurotransmitter dysfunction, including schizophrenia and bipolar disorder and the development of tardive dyskinesia and alcohol dependence.
- In 2015 polymorphic variants of SLC6A2 gene included in the number of new genomic candidates associated with the response to pharmacotherapy clozapine in schizophrenic patients.

Gutiérrez B. et al., 2007; Fehr C. et al., 2013; Zai C.C. et al., 2013; Xu Q. et al., 2015

In this study, the hypothesis was postulated that noradrenaline transporters may contribute to the development of hyperprolactinemia, which is not only a side effect of antidepressant therapy, but antipsychotic therapy too.

SLC6A2

SLC18A2

noradrenaline

hyperprolactinemia
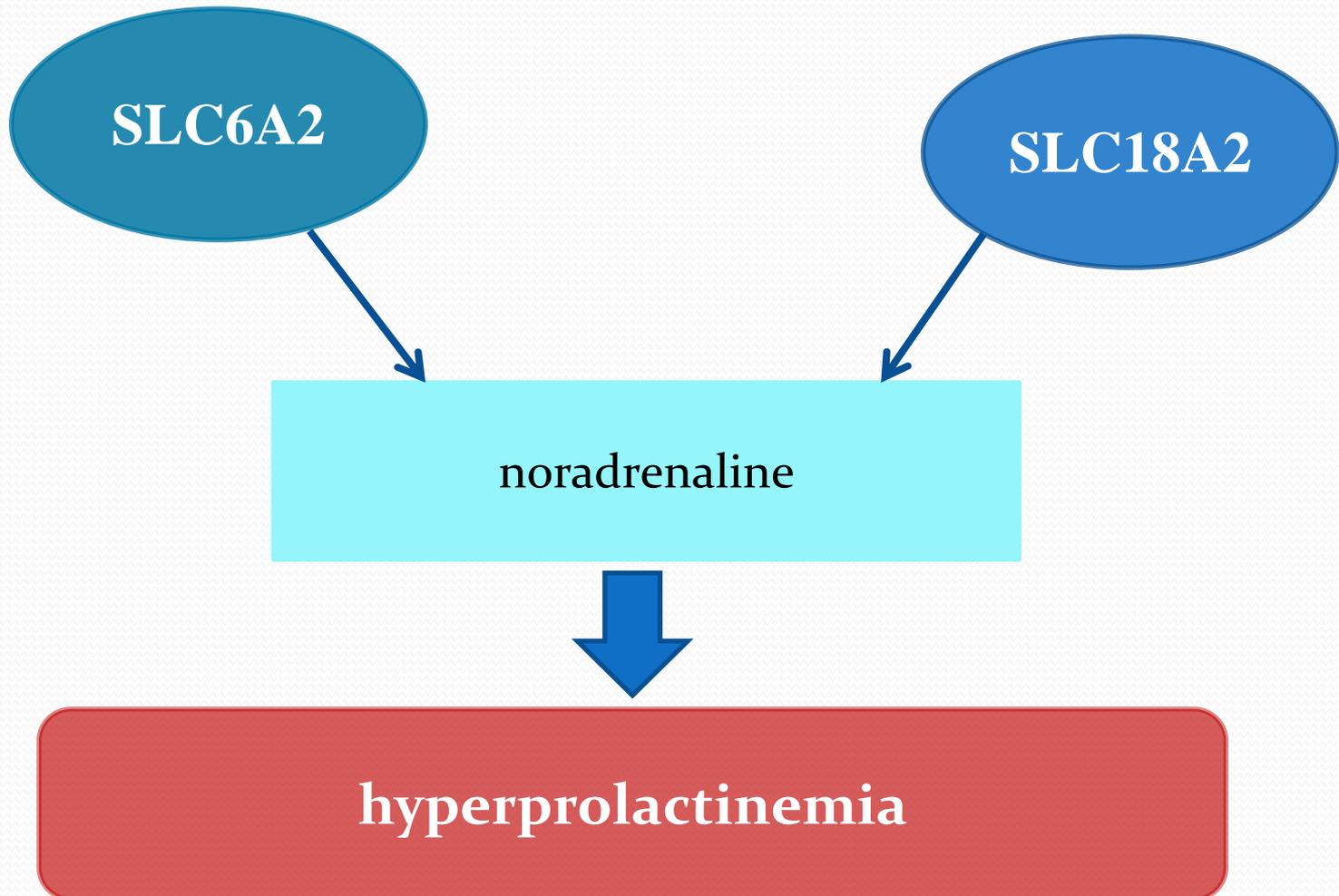
- The tasks of the study were to investigate the association of SLC6A2 and SLC18A2 gene's polymorphisms the development of hyperprolactinemia caused by long-term antipsychotic therapy in the Russian population in Siberia

Genotyping of polymorphisms of the
    gene SLC6A2 *:* rs1805066, rs933556, rs9940195, rs2242446, rs36024, rs1532701, rs40434, rs13333066, rs187714 and
    gene SLC18A2 : rs363224 was carried

PATIENTS and METHODS

445 patients with paranoid schizophrenia (224 female and 221 male) aged 18 to 65 years (mean age 42,1 ± 1,4 years) were examined.

The concentration of prolactin in the serum was determined by solid-phase enzyme immunoassay using a reagent kit PRL Test System (Monobind Inc., USA).

Genotyping of polymorphisms of the gene SLC6A2 and gene SLC18A2 was carried out by The MassARRAY® Analyzer 4 by Agena Bioscience ™, a set of SEQUENOM Consumables iPLEX Gold 384

Hyperprolactinemia was found in 50.79% of schizophrenic patients included in the study. Prevalence of females in the group with hyperprolactinemia (63.8%), indicating that the female gender is a risk factor on the development of this side effect of antipsychotic therapy.

patients with schizophrenia
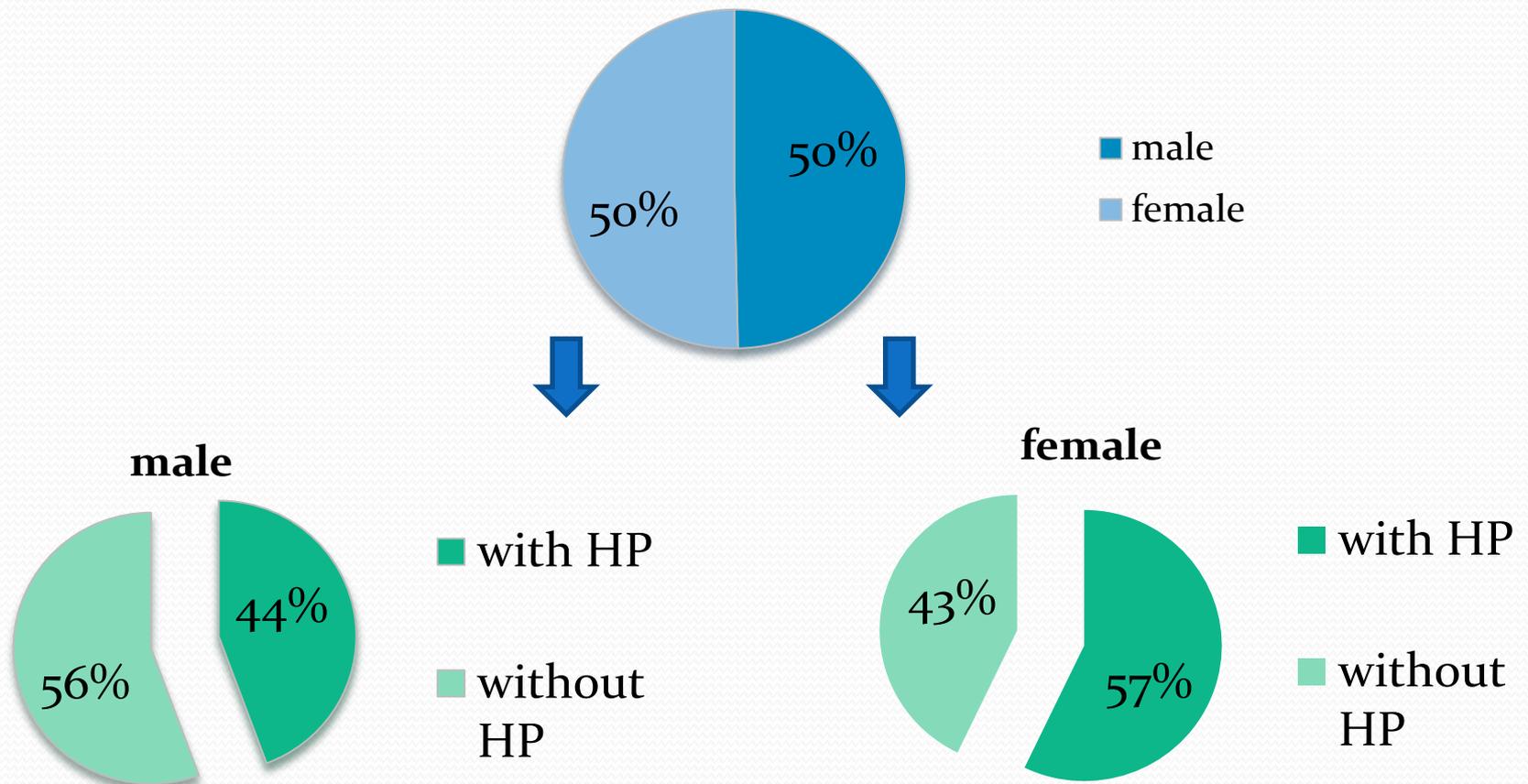
male

female

The analysis showed a significant association of the polymorphism rs1805066 (noradrenaline transporter gene SLC6A2) with the development of hyperprolactinemia in patients with schizophrenia females (p < 0.05)
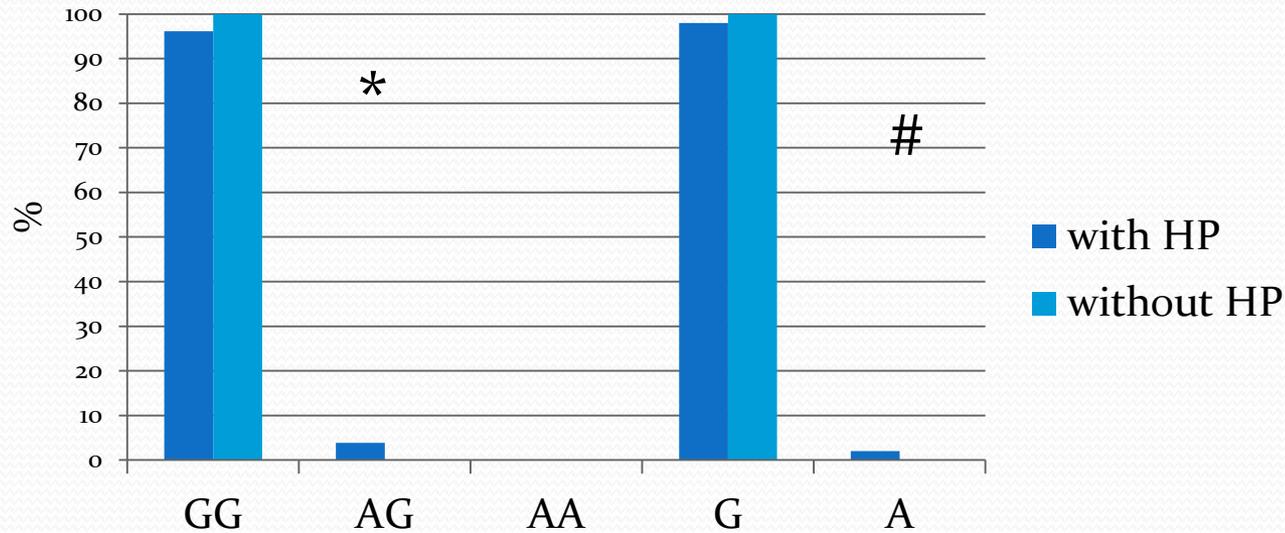
* – p<0,05 (genotypes)
# – p<0,05 (alleles)

For other polimorphisms of SLC6A2 gene statistically significant associations with giperprolatinemiey in patients with schizophrenia was not.

For gene of vesicular monoamine transporter SLC18A2 statistically significant associations with giperprolatinemiey in patients with schizophrenia was not.

CONCLUSIONS. The results suggest an association of SNP rs1805066 with hyperprolactinemia in women with schizophrenia, and confirms the participation of SLC6A2 gene in the development of drug-induced hyperprolactinemia in schizophrenia.

Thanks for your attantion!