## Summary

Our work is focused on the role of NR1 subunit of N-methyl-D-aspartate receptor in pathophysiology of schizophrenia. In animal model using separately or in combination, antisense oligodeoxynucleotide (aODN) for NR1, NR2A and NR2B subunit of NMDAR, we affected expression of these proteins in rat hippocampus. We assessed prepulse inhibition of acoustic startle reaction (PPI) in rats and protein expression of NMDAR subunits and expression of PSD proteins. There were significant differences in expression of PSD-95 and NR1 between groups. Application of aODN (NR2A, NR2B) was associated with a significant decrease of PSD-95. PPI and expression of NR2A, NR2B and PSD-93 were not changed after aODN application.The next part of the work concentrates on a human post mortem study. To assess actual changes in the expression of the NR1 subunit and its isoforms, we measured absolute differences in the levels of mRNA/protein for panNR1, as well as the individual mRNA/protein isoforms in the post mortem left/right hippocampus of patients with schizophrenia in comparison with non-psychiatric subjects. There were no significant differences in the panNR1 subunit mRNA expression, but the absolute left/right differences were much more pronounced in the patients with schizophrenia. The expression of splice variants in the mRNA level indicated decrease of the NR1-4b and NR1-2b isoform in the hippocampus of schizophrenic patients. Expression of NR1 and NR1 $^{C1}$ showed significant interactions of laterality and sex. Protein levels of the NR1 subunit in the left hippocampus in male schizophrenic patients were lower than controls. The last part of the work is focused on the role of regulator of G protein signalization 4 (RGS4) in pathophysiology of schizophrenia. To elucidate this role of RGS4 we silenced RGS4 using siRNAs in human neuroblastoma cell lines and we studied the effects of differential RGS4 expression by microarray.The cell lines with downregulated expression of RGS4 showed 67 genes with changed expression. We have detected two functional subgroups of genes which might be implicated in schizophrenia pathophysiology: histone genes and genes for transcription factors. The changes in TF expression observed in our experiment might be a side effect of the neuroblastoma cell line used. We did not detect changes in expression of any of the genes directly connect with neurotransmiter systems associated with schizophrenia.