P.1.a.016 **Emotionally painful stress causes changes in L1 insertion pattern in the hippocampus in rats with different nervous system excitability**

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Stress can induce structural changes in the brain and contribute to a variety of chronic diseases from post-traumatic stress disorder to depression. The hippocampus is a highly plastic brain region particularly susceptible to the effects of environmental stress. A genomic stress response partly consists in changes in insertion activity of transposable elements. Retrotransposons account for ~45% of the mammalian genome. Mechanisms of action of stress and the formation of posttraumatic stress disorder (PTSD) in human are associated with retrotransposons (LINE1, L1) activity in various tissues. Endogenous retrotransposition of L1 elements has been proposed as one potential mechanism generating neuronal genome diversity. They are capable of inserting into new genomic locations, which can result in deleterious outcomes. The greatest interest is the study of these processes in the brain due to individual variability of neural processes to effective pharmacotherapy path finding. The purpose of this work was to investigate the effect of stress on the LINE1 insertion pattern in the hippocampus.

We used the model of emotional stress for the PTSD-like state formation in two lines of rats with genetically determined differences in the level of excitability of the nervous system (low and high) to study of emotionally painful stress (3 types: short-term, long-term and massive stress) effect on LINE1 retrotransposon insertion polymorphism in the dentate gyrus of the hippocampus. L1 insertions in the promoter of gene GRIN1 [glutamate receptor ionotropic N-methyl-D-aspartate (NMDA) subtype, subunit 1] examined by two-step PCR (general and directed). Glutamate NMDA receptors play a key role in synaptic plasticity, synaptogenesis, excitotoxicity, memory acquisition and learning. These receptors mediate neuronal functions in glutamate neurotransmission. NMDAR-mediated neurotransmission in the hippocampus is implicated in cognitive and emotional disturbances during stress-related disorders. NMDA receptor subunit 1 is a core molecule in the NMDA receptor complex. GRIN1 expression is associated with neurotransmission efficiency and state of the nervous system. We suppose that L1 retrotransposon insertions to promoter of GRIN1 gene will alter GRIN1 expression.

It was shown that L1 insertion pattern depends on the level of excitability of the nervous system, intensity and duration of stress exposure. The most variable spectrum of L1 transposable elements activity (L1 insertion pattern) is detected under the influence of massive stress in the rats with low excitability of the nervous system.

We assume that L1 retrotransposon insertions take part in the regulation of expression of candidate genes associated with the stress response and the formation of psychopathology.

P.1.a.017 **Genetic variants in kinesin family member 13A (KIF13A) affect susceptibility to schizophrenia in Korean population**

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Introduction: Several independent studies have localized one putative susceptibility locus on the short arm of chromosome 6 for schizophrenia. Kinesin family member 13A (KIF13A) gene located at chromosome 6p23, encodes a member of the kinesin family of microtubule-based motor proteins that function in the positioning of endosomes. This family member can direct mannose-6-phosphate receptor-containing vesicles from the trans-Golgi network to the plasma membrane, and it is necessary for the steady-state distribution of late endosomes/lysosomes. In neurons, kinesins generate and drive the axonal transport and have been suspected to play important roles in neuronal pathfinding and migration and synaptic plasticity. Recent studies showed the involvement of KIF13A protein in some higher brain functions including anxiety. Variations in the KIF13A protein or expression may affect the transport or the abundance of specific synaptic vesicles. For some brain regions, including the hippocampus, many studies have found molecular evidence in support of a synaptic pathology of schizophrenia. Therefore, in the present study, we investigate whether genetic polymorphisms of KIF13A gene are associated with schizophrenia in Korean population.

Methods: Seven single nucleotide polymorphisms (SNPs) of the KIF13A gene considering their heterozigosity and minor allele frequency were genotyped in 177 schizophrenia patients and 303 control subjects. SNP genotyping was conducted using direct sequencing. All patients were evaluated by the operational criteria checklist for general psychopathology. We used a multiple logistic regression model to calculate odds ratios (ORs), their 95% confidence intervals (CIs) and corresponding p values, controlling for age and gender as covariables, to analyze the associations between schizophrenia and SNPs, and associations between SNPs and clinical symptoms. In the logistic regression analysis for each SNP, we compared three different models of gene expression (co-dominant model, dominant model and recessive model). To avoid chance findings due to multiple testing, a Bonferroni correction was applied.

Results: The genotype and allelic frequencies of rs9396812 showed significant association between schizophrenia and controls [rs9396812, $p = 0.009$, OR = 1.72, 95% CI=1.00–2.96 in the co-dominant model (A/A vs G/G) and $p = 0.003$, OR = 1.97, 95% CI=1.25–3.09 in the recessive model (A/A vs G/G + A/G)]. We also assessed the association of the seven SNPs of KIF13A gene with specific clinical symptoms (hallucinations and delusions) of the schizophrenia patients. The genotype distribution of the rs12215837 of KIF13A gene was associated with persecutory delusion in the co-dominant model (OR = 2.51, 95% CI = 1.17–5.41, $p = 0.031$) and the dominant model (OR = 2.17, 95% CI=1.05–4.49, $p = 0.032$). The distribution of genotype and allele frequencies did not differ significantly between schizophrenia patients with hallucinations.

Conclusions: Our findings suggest that KIF13A gene polymorphisms may play a role in the susceptibility to schizophrenia in Korean population. In particular, KIF13A gene polymorphisms