factor-2 (FGF2) a trophic factors widely distributed in the adult brain, activates CREB and regulates cell proliferation via phosphorylation of CREB. FGF2 is involved in regulating synaptic plasticity. Improve memory increase endogenous FGF2, suggesting that increases in FGF2 activity may be the underlying mechanism of action for memory enhancement. FGF2 expression can be modulated by psychoactive drugs. There is evidence that also NGF mediates multiple biological phenomena. Synapsin plays an important role in synaptic transmission and neural development. So it plays an important role in hippocampally based behaviors.

Haloperidol is a classical antipsychotic drug while olanzapine is an atypical antipsychotic drug commonly used for the treatment of schizophrenia and other psychosis. Atypical antipsychotics, such as olanzapine and risperidone, exert less selective activity on various neurotransmitter receptors. Sertindole is an antipsychotic drug with a unique pharmacological profile. Clozapine is the reference drug for atypical antipsychotics.

Mice were treated chronically with haloperidol (0.125 and 0.25 mg/kg, n=10), olanzapine (1 and 2 mg/kg, n=9–10), clozapine (1.25 and 2.5 mg/kg, n=8–10), risperidone (0.25 and 0.50 mg/kg, n=9–10), sertindole (1.3 and 2.5 mg/kg, n=8–10) for 15 days. Since the genes involved in neurite remodeling are among the primary targets of regulation, the effects of chronic administration of drugs on FGF2, synapsin and NGF levels in the hippocampus of mice were determined using quantitative real-time polymerase chain reaction (RT-PCR).

Our results suggest that administration of the conventional antipsychotic haloperidol and atypical antipsychotic clozapine, olanzapine, risperidone and sertindole increased the expression of FGF2, synapsin and NGF and in the mice hippocampus. Thus chronic administration of clozapine olanzapine, risperidone and sertindole may promote neuroplasticity via the up-regulation of neutrophic factors.}

PM451
A decrease in protein level and a missense polymorphism of KIF17 are associated with schizophrenia
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Abstract
It has been shown that the dysfunction of N-methyl-D-aspartate (NMDA) receptors-mediated neurotransmission plays a role in the pathophysiology of schizophrenia. Especially, GluN2B, a subunit of NMDA receptors, associated trafficking complex is altered in the prefrontal cortex of schizophrenia. The kinesin superfamily motor protein 17 (KIF17) is known as a transporter of NR2B. Previous studies showed that a structural variant of KIF17 gene is associated with a schizophrenic phenotype. Therefore, here we investigated KIF17 levels in postmortem prefrontal cortex in schizophrenia and the association of a missense polymorphism (ile341Val) in KIF17 with schizophrenia. The protein expression of KIF17 in schizophrenic postmortem brains was significantly lower than that in controls. Next, the association of missense polymorphisms (rs631375, rs13375609, rs522496 and rs2296225) of KIF17 gene in 567 schizophrenia and 710 healthy subjects was examined. Both genotypic distribution and allelic frequency of rs2296225 polymorphism were significantly different between the chronic schizophrenia subjects and controls. However, our findings described above were not replicated with the independent subjects (555 schizophrenia and 814 healthy controls). Furthermore, the two alleles of rs2296225 polymorphism did not affect the mRNA expression of KIF17. These results suggest that the dysfunction of KIF17 might be involved in the pathophysiology of schizophrenia.

PM452
Gender-specific associations of the brain-derived neurotrophic factor Val66Met polymorphism with neurocognitive and clinical features in schizophrenia
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Abstract
Objective: To explore associations of the brain-derived neurotrophic factor (BDNF) Val66Met polymorphism with cognitive functioning and psychopathology in patients with schizophrenia.

Methods: We included 133 subjects (71 females [53.4%] and 62 males [46.6%]) meeting the DSM-IV criteria for schizophrenia who were in the post-acute stage of the disease. BDNF Val66Met genotypes were identified via polymerase chain reaction. The computerized neurocognitive function battery, Positive and Negative Syndrome Scale (PANSS), Calgary Depression Scale for Schizophrenia (CDSS), Social and Occupational Functioning Scale (SOFAS), and the Subjective Well-Being Under Neuroleptic Treatment (SWN-K) were administered. Gender-stratified sub-analysis was also conducted to identify gender-specific patterns in the findings.

Results: In male patients, no significant difference in any measure by BDNF genotype was evident. In female patients, scores on the CDSS (p-value = 0.045) and total PANSS (p-value < 0.001) and all subscales were significantly higher in valine (Val) carriers. In addition, scores on the SOFAS (p-value = 0.008) and SWN-K (p-value = 0.025) were significantly lower in Val carriers. In terms of neurocognitive measures, female patients with the Val allele had significantly poorer reaction times (p-value = 0.004) and fewer correct responses (p-value = 0.001) on the Continuous Performance Test (CPT) and the Trail Making Test (parts A and B) (p-value = 0.048 and 0.033, respectively). After adjustment of PANSS total scores and log-transformed CDSS scores, CPT outcomes were significantly poorer in female patients than in those without the Val allele (p-value = 0.015 and 0.018, respectively).

Conclusion: Gender-specific associations of the Val allele with poor neurocognitive function and more severe psychopathology were evident. Further studies are required to explore the mechanisms of these differences and the potential utility of the BDNF genotype as a predictor of outcome in patients with schizophrenia.

PM453
Association between CSF1R gene polymorphism and the risk of schizophrenia in Korean population
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Abstract
Introduction: There is considerable evidence to support the involvement of inflammatory and immunological processes in the pathogenesis of schizophrenia. The presence of cytokine
receptor abnormalities in schizophrenia may help explain prior epidemiologic data relating the risk for this illness to altered rates of autoimmune disorders, prenatal infection and familial leukemia. Colony stimulating factor 1 receptor (CSF1R) gene encodes a tyrosine kinase growth factor receptor for CSF1, the macrophage and monocyte specific growth factor. CSF1R gene is located at chromosome 5q32, a region that was suggested to be linked to childhood onset schizophrenia. CSF1R gene mutation has been associated with microglial development. In this study, we investigated the genetic association between schizophrenia and single nucleotide polymorphisms (SNPs) of the CSF1R gene.

Methods: 219 Korean schizophrenia patients and 379 control subjects were enrolled for this study. We genotyped four SNPs (rs216138, rs10079250, rs2228422 and rs1986027) of the CSF1R gene by direct sequencing. All patients were evaluated by the Operational Criteria Checklist for Psychotic Illness. Multiple logistic regression models (that is, co-dominant, dominant, and recessive) were performed to generate odds ratios, 95% confidence intervals, and p values.

Results: The genotype frequencies of rs1986027 showed significant association between schizophrenia and control groups (p=0.011 in the co-dominant model (T/T vs. C/C); p=0.003 in the recessive model (T/T vs. C/C + C/T)). For the SNP rs10079250, significant association was found in the recessive model [(C/C vs. T/T + C/T); p=0.035]. There was no significant association between other two SNP polymorphisms and schizophrenia.

Conclusions: Our study is the first to report an association of the CSF1R gene polymorphisms with schizophrenia. We found significant association between CSF1R polymorphism and schizophrenia in Korean population.

Key Words: CSF1R, cytokine, schizophrenia, association.

PM454

Association analysis between (AAT)n repeats in the cannabinoid receptor 1 (CNR1) gene and smooth pursuit eye movement (SPEM) abnormality in Korean patients with schizophrenia.

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Abstract

Objective: According to previous studies, the cannabinoid receptor 1 (CNR1) gene could be an important candidate gene for schizophrenia which is located on chromosome 6q14-q15. The association between CNR1 polymorphisms and schizophrenia is actively being investigated, and some studies have linked the AAT-trinucleotide repeats in CNR1 gene with the risk of schizophrenia. Meanwhile, smooth pursuit eye movement (SPEM) has been regarded as one of the most consistent endophenotype of schizophrenia.

In this study, we investigated the association between the AAT-trinucleotide repeats in CNR1 gene and smooth pursuit eye movement abnormality in Korean patients with schizophrenia.

Methods: We measured SPEM function in 187 Korean patients with schizophrenia (84 male, 83 female) and they were divided according to SPEM function into two groups, good and poor SPEM function groups. We also investigated allele frequencies of AAT-repeat polymorphisms on CNR1 gene in each group. A logistic regression analysis was performed to find the association between SPEM abnormality and AAT-trinucleotide repeats in each group.

Results: The natural logarithm value of signal/noise ratio (Ln S/N ratio) of good SPEM function group was 4.34±0.29 and that of poor SPEM function group was 3.21±0.70.

In total, 7 types of trinucleotide repeats were identified, each containing 7, 10, 11, 12, 13, 14, and 15 repeats, respectively. (AAT)7 allele was most frequently observed, with a frequency of 30.5%. The frequencies of the other repeat alleles (in the decreasing order) were as follows: (AAT)12, 30.5%, (AAT)11, 24.3%, (AAT)10, 19.8%, and (AAT)9, 11.1%.

However, no significant associations were found between the number of AAT-repeat polymorphisms of the CNR1 gene and SPEM function.

Conclusions: No significant associations were found between AAT-trinucleotide polymorphisms and SPEM abnormality in Korean patients with schizophrenia.

PM455

Genetic variants in Chromogranin B is associated with the Risk of Schizophrenia in Korean male population

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Abstract

Schizophrenia is a devastating mental disorder with high heritability estimate up to 80%. Secretory pathway of peptide hormones and neuropeptides in brain is regulated by chromogranin proteins. Chromogranin B (CHGB), a member of chromogranin family gene, is proposed as one of the candidate genes for the risk of schizophrenia. In a genome wide association study performed in a Japanese population, genetic variant (microsatellite: D20S95) near CHGB could be a potential genetic marker for the schizophrenia development.

In the current study, 15 SNPs of CHGB were genotyped in 310 schizophrenia patients and 604 healthy controls to investigate the association with the schizophrenia susceptibility. Statistical analysis has revealed that four genetic variants (rs446659, rs6133278 (D145N), rs910122 (R178Q), rs28281) were associated with the reduced risk of schizophrenia (OR=0.72–0.78, p=0.002–0.02). In the subgroup analysis, five genetic variants (rs236141, rs446659, rs6085323, rs910122 (D178Q), rs28281) and a haplotype (ht3) showed more protective effect on the schizophrenia in male subjects (OR=0.52–0.74, p=0.002–0.05), but not in female subjects.

Our results demonstrated that genetic variants in CHGB showed gender-specific effect to the reduced risk of schizophrenia, which could be a useful preliminary result for further study.

Keywords: Single nucleotide polymorphisms (SNPs), Chromogranin B (CHGB), schizophrenia, gender-specific marker, male

PM456

Aberrant cortico-cerebellar connectivity of the default mode network in individuals at ultra-high risk for psychosis: a resting-state fMRI study

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