palate. In this study, we investigated the association between coding region single nucleotide polymorphisms (cSNPs) of ADAMTS20 gene and schizophrenia in a Korean population.

**Methods:** Six cSNPs (rs10506226, rs10880473, rs7310011, rs7297737, rs7302446 and rs11182088) in 276 schizophrenia patients and 406 control subjects were genotyped using Sequenom iPLEX-Gold assay. The associations of SNPs were analyzed based on logistic regression using multiple inheritance models (log-additive, dominant, and recessive models).

**Results:** In our study, significant associations between rs7302446, rs7297737 and rs7310011 and schizophrenia were shown in the dominant models (p = 0.0057, OR = 1.27, 95% CI = 1.17–2.57 for rs7302446; p = 0.0043, OR = 1.75, 95% CI = 1.19–2.58 for rs7297737; p = 0.006, OR = 1.71, 95% CI = 1.17–2.52 for rs7310011). We also found a significant association between rs11182088 and schizophrenia in the log-additive (p = 0.004, OR = 1.44, 95% CI = 1.12–1.85) and dominant models (p = 0.048, OR = 1.57, 95% CI = 1.15–2.16). Additionally, in the analysis of haplotypes, the ATGCTG, ATGCTA and CCATAA haplotypes consisting six cSNPs were associated with schizophrenia (p = 0.0006, 0.044, and 0.020, respectively).

**Conclusion:** These results suggest that the ADAMTS20 gene contributes to the susceptibility of schizophrenia.

---

**PM449**

Hot genes in schizophrenia: case-control, pharmacogenetics and exploratory analyses in two independent samples

Stefano Porcelli, Soo-Jung Lee, Changsu Han, Ashwin A. Patkar, Diana De Ronchia, Anna Rita Atti, Alessandro Serretti, Chi-Un Pae

1Department of Biomedical and NeuroMotor Sciences, University of Bologna, Italy; 2Department of Psychiatry, The Catholic University of Korea College of Medicine, Seoul, Republic of Korea; 3Department of Psychiatry, Korea University College of Medicine, Seoul, Republic of Korea; 4Department of Psychiatry and Behavioural Sciences, Duke University Medical Center, Durham, NC, USA.

**Founding:** This study was supported by a grant from the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea (HI12C0003).

**Abstract**

We investigated the effects of genetic variants within PPP3CC, RORA, SP4, ST8S1A2 and ZNF804A genes in a Korean sample of 176 SCZ patients and 326 healthy controls and an Italian sample of 83 SCZ patients and 194 healthy controls. The PANSS was used to assess psychopathological severity and antipsychotic response (AR). Several clinical features were recorded in both samples. In the Korean sample RORA rs10483383 was associated with SCZ (p = 0.03) as well as haplotype rs2282888-rs2237304-rs10272006-rs12673091 within SP4 gene (p = 0.02). In the Italian sample 3 PPP3CC variants (rs11780915 p = 0.006; rs10108011 p = 0.01; rs2249098 p = 0.0004), ZNF804A rs1344706 (p = 0.02) and SP4 rs12673091 (p = 0.02) were associated with SCZ. The haplotype rs11780915-rs10108011-rs2249098 within PPP3CC gene and the haplotype rs7603001-rs1344706 within ZNF804A gene was associated with SCZ as well (respectively p = 0.03 and p < 0.02). Further, several RORA variants were associated with AR (Korean sample: rs1871858 p = 0.02; rs12900122 p = 0.06, rs17204440 p = 0.02, haplotype rs1020729-rs1871858 p = 0.01; Italian sample: rs12900122 p = 0.003). In the Italian sample also 2 SP4 variants (rs2282888 p = 0.02; rs10272006 p = 0.02) and ST8S1A2 rs4777989 (p = 0.04) were associated with AR. Exploratory analyses suggested that: 1) PPP3CC, ST8S1A2 and SP4 genes may be implicated in the develop and severity of psychotic symptoms, 2) RORA gene may play a role in AR, particularly of negative symptomatology, as well as ZNF804A gene. Considering limitations linked to the sample size and candidate genes approach, our results further support a role for these gene in SCZ, as well as in AR. Analyses in well phenotyped samples could help researchers to refine the role of these genes for further, focused investigations.

---

**PM450**

Effects of olanzapine, clozapine, risperidone and saddletype on FG2, synapsin and NGF expression in the hippocampus of naive mice

Guner Ulak, Esen Gumuslu, Oguz Mutlu, Merve Erdem, Ipek Komsuoğlu Celikyurt, Furuzan Akar, Faruk Erden

1Department of Medical Genetics, Medical Faculty, Kocaeli University, Kocaeli, Turkey. 2Department of Medical Pharmacology, Psychopharmacology Lab., Medical Faculty, Kocaeli University, Kocaeli, Turkey.

**Abstract**

Some atypical antipsychotic drugs have unique actions, which may contribute to enhanced neurogenesis. Fibroblast growth factor (FGF) is a major mammalian growth factor that is involved in the growth and differentiation of neural progenitor cells and it is regarded as a potent activator of neurogenesis in the hippocampus of adult rats. In the present study, we investigated the effects of olanzapine, clozapine, risperidone and saddletype on FG2, synapsin and NGF expression in the hippocampus of naive mice.

---

**PM448**

Investigation of maternal effects, maternal-fetal interactions and parent-of-origin effects (imprinting), using mothers and their offspring with schizophrenia

Byung Dae Lee, Hee Jeong Jeong, Young Min Lee, Eunsoo Moon, Je Min Park

Pusan National University Hospital, Republic of Korea

**Abstract**

**Objective:** Many complex genetic effects, including epigenetic effects, may be expected to operate via mechanisms in the interuterine environment. A popular design for the investigation of such effects, including effects of parent-of-origin (imprinting), maternal genotype, and maternal-fetal genotype interactions, is to collect DNA from affected offspring and their mothers (case/mother duos) and to compare with an appropriate control sample. We investigate the effects of estimation of maternal, imprinting and interaction effects using multimodal modeling using parents and their offspring with schizophrenia in Korean population.

**Methods:** We have recruited 27 probands(with schizophrenia) with their parents and siblings whenever possible. For best estimation of diagnosis, we have used medical records and a Korean version of DIGS (Diagnostic Interview for Genetic Studies) & FICIS (Family Interview for Genetic Studies). We have used lifetime dimensions of psychosis scale(LDPS) for measuring psychotic features. We analyzed 96 SNPs of 17 functionally only relevant genes and 21 neuronal genes in chromosome 18 for DNA samples that was checked for the data quality and genotype error. We used EMIM analysis program for the estimation of maternal, imprinting and interaction effects using multimodal modeling

**Summary of results:** Of analyzed 96 SNPs, significant SNP(rs 324420) will be suggested in EMIM analysis for child genetic effects(p = 1.5 x 10^-4) and child genetic effects allowing for maternal genetic effects(p = 5.3 x 10^-5) with very stringent multiple comparison Bonferroni correction. Additionally, analysis results for maternal genetic effects (and maternal genetic effects allowing for child genetic effects) will be presented.

**Conclusions:** Epigenetics and gene-environment interactions are represented underlying statistical genetics. Our results are the pilot study for investigating epigenetic mechanism in the cause of schizophrenia. And it will help to understand and use the EMIM statistical genetics analysis program with many limitations including small pedigree numbers.
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 psychoses. 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 and in the mice 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 neutropic factors.

PM451

A decrease in protein level and a missense polymorphism of KIF17 are associated with schizophrenia

Akiyto Hishimoto1, Shuken Boku1, Hiroki Ishiguro2, Woraphat Ratta-apha2, Ichiro Sora1
1Kobe University Graduate School of Medicine, Japan, 2Yamanashi University, Japan

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

Sung-Wan Kim, Ju-Yeon Lee, Hae-Ju Kang, Seon-Young Kim, Kyung-Yeol Bae, Jae-Min Kim, Il-Seon Shin, Jin-Sang Yoon*
Department of Psychiatry, Chonnam National University Medical School, Gwang-ju, Korea

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 (CDS), Social and Occupational Functioning Scale (SOFAS), and the Subjective Well-Being Under Neuroleptic Treatment (SWM-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 CDS (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 CDS scores, CPT outcomes were significantly poorer in female patients with 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

Won Sub Kang1, Young Jong Kim’, Jong Woo Paik2
1Department of Neuropsychiatry, School of Medicine, Kyung Hee University, Seoul, Republic of Korea,
2Department of Neuropsychiatry, School of Medicine, Kyung Hee University, Seoul, Republic of Korea,

Abstract

Introduction: There is considerable evidence to support the involvement of inflammatory and immunological processes in the pathogenesis of schizophrenia. The presence of cytokine