the studied polymorphisms via the restriction fragment length polymorphism method. Clinical factors such as gender, age, duration of illness, and final medication dosage were noted as well. The researchers measured psychopathology biweekly, using the Positive and Negative Syndrome Scale (PANSS) five-factor model scale (positive, negative, excitement, cognitive, and depressive). A mixed model regression approach (SAS Proc MIXED) was used to analyze the effects of genetic and clinical factors on PANSS performance after aripiprazole treatment.

**Results:** We found that the A1/A1 (T/T) genotype of DRD2/ANKK1 Taq1A (rs1800497) polymorphism predicted superior aripiprazole treatment response specifically for positive and excitement symptoms. Otherwise, the T/T and T/C genotype groups of 5-HT2A T102C (rs6313) polymorphism predicted superior aripiprazole treatment response specifically for negative symptoms. Furthermore, the C/C genotype of 5-HT1A C-1019G (rs6295) polymorphism predicted superior aripiprazole treatment response specifically for cognitive and depressive symptoms. Finally, the clinical factors including dosage of aripiprazole and duration of illness were found to influence PANSS performance upon aripiprazole treatment.

**Conclusions:** Our study shows DRD2, 5-HT1A, and 5-HT2A gene polymorphisms and clinical factors modulate aripiprazole efficacy in different symptom dimensions of schizophrenia.

**Keywords:** rs1800497, rs6295, rs6313, aripiprazole, schizophrenia

**PM515**

The association between serotonin receptor gene polymorphisms and hyperprolactinemia in antipsychotic drug-treated schizophrenic patients

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**Abstract**

Hyperprolactinemia (HPRL) is a common side effects of antipsychotic drugs. It is primarily attributed to blockade of DRD2 within the pituitary gland. Although dopamine is considered the primary prolactin (PRL) release inhibiting factor, the activity of PRL producing lactotrophs is also regulated by the serotonergic: thyrotrophin releasing hormone, vasoactive intestinal polypeptide and serotonin (5-HT).

The aim of our study was to investigate the association between 5-HT receptor variants and hyperprolactinemia in antipsychotic drug treated patients with schizophrenia.

The study group included 446 Caucasian persons (M 221/F 225) with a clinical diagnosis of schizophrenia, who were treated with classical and/or atypical antipsychotic drugs. Prolactin level was determined with ELISA method. The upper limits for normal PRL concentration were set at ≤20 ng/ml for men and ≤25 ng/ml for women. We selected a subset of 29 SNPs, that would accurately represent the majority of SNPs for the following serotonin receptors genes: HTR1A, HTR1B, HTR2A, HTR2C, HTR3A, HTR3B, HTR6. DNA extraction and genotyping were conducted according to standard protocols and blind to the clinical status of the subjects. The software “R” and SPSS were used for statistical analysis.

None of the studied autosomal markers was found to be associated with HPRL. However, a statistically significant association was established between various HTR2C polymorphisms and HPRL. As a result of the analysis of association between HPRL and haplotypes of X-chromosome SNPs, the most statistically significant association was found for a combination of the rs569959G and rs17326429A alleles.

It is unlike, that our results are invalidated by the binding potential of the antipsychotic drug used by the patients. We found no clear evidence that the studied HTR2C variants correspond to lack of constitutive activity of this receptor.

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**PM516**

Association of DNA Methylation of Taq1A in the DRD2 with Response to Aripiprazole in acute schizophrenia

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**Abstract**

**Background:** Epigenetic modification including DNA methylation may have effects on response to antipsychotics in schizophrenia. The Taq1A is located 10kb downstream of DRD2, and causes an amino substitution within the 11th ankyrin repeat of ankyrin repeat and kinase domain containing 1 (ANKK1). We investigated the effects of the DNA methylation of Taq1A in DRD2 on the response to aripiprazole and plasma levels of homovanillic acid (HVA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) in antipsychotic-free acute schizophrenic patients.

**Methods:** Subjects were 34 Japanese patients with schizophrenia, and were treated with aripiprazole for 6 weeks. The Positive and Negative Syndrome Scale (PANSS) was used for assessment of clinical symptoms. Plasma levels of HVA and MHPG were measured using high-performance liquid chromatography before and after the treatment. The DNA methylation levels of all CpG sites ranging from -162 C to +260 C of 5’ region of ANKK1 gene were determined by sequencing using next-generation sequencer.

This study was approved by the ethics committee of Medical University, and the patients consented to participate after having been informed of the purpose of the study.

**Results:** Aripiprazole decreased PANSS scores after the 6 weeks. Plasma levels of HVA (p=0.01) and MHPG (p=0.002) decreased in responders after the 6 weeks treatment, but not in non-responders. In responders, DNA methylation of Taq1A was significantly higher than non-responders at 3 CpG sites. Furthermore, methylation levels of Taq1A were correlated with changes in plasma levels of HVA and MHPG in 4 and 3 CpG sites, respectively.

**Conclusion:** This is the first study of the association between the DNA methylation of Taq1A in DRD2 and the response to aripiprazole, suggesting that methylation of Taq1A at specific sites may have effects on the response to antipsychotics. Because of the small sample size, further studies are needed to confirm these results.

**PM517**

Transition into overt psychosis in individuals at ultra-high risk for psychosis: possible roles of multidimensional schizotypy and basic symptoms

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**Abstract**

This is the first study of the association between the DNA methylation of Taq1A in DRD2 and the response to aripiprazole, suggesting that methylation of Taq1A at specific sites may have effects on the response to antipsychotics. Because of the small sample size, further studies are needed to confirm these results.
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Abstract

Background: Individuals at ultra-high risk (UHR) for psychosis are understood to be the putative prodrome of overt psychosis, although there is still a possibility of false positives. The aim of the present study is to examine the potential links between multi-dimensional schizotypy, basic symptoms and emerging psychosis as defined by positive symptoms in individuals at ultra-high risk (UHR) for psychosis.

Method: Sixty-one UHR individuals and 41 healthy controls were participated in baseline assessments. For multi-dimensional schizotypy assessments, Chapman’s perceptual aberration scale, magical ideation scale, revised physical and social anhedonia scales, schizotypal ambivalence scales, and Eysenck’s impulsiveness scale were used. Basic symptoms were assessed by using the schizophrenia-specific items of the Frankfurt complaints questionnaire (FCQ).

Results: Individuals at UHR showed higher schizotypy scores and basic symptoms at baseline. The transition rate of overt psychosis was 36.4 % at 4 years of follow-up. Cox regression analysis showed that the basic symptoms (HR 1.456, p = 0.025) and impulsiveness (HR 1.175, p = 0.039) were significant predictors of transition into overt psychosis in UHR individuals $[\chi^2(4) = 14.242, p = 0.007]$. 

Conclusion: The addition of the self-reported basic symptoms and impulsiveness may be useful for a risk enhancement or stratification strategy in individuals at ultra-high risk for psychosis.

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PM518

Medication Adherence in schizophrenia: Focus on therapeutic relationship

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Abstract

Introduction: Poor adherence to medication is one of the leading causes of relapse in schizophrenia. Several determinants have been proposed as reasons for noncompliance. Insight and Quality of doctor-patient relationship seems to be important determinants in compliance. Only few studies investigated the role. We examined the relationships between medication adherence and clinical variables with schizophrenia in Korea.

Method: 81 clinically stable outpatients diagnosed as schizophrenia were participated. To evaluate medication adherence, Korean version of medication adherence rating scale(KMARS) was used. Korean version of Scale To Assess the Therapeutic Relationship(STAR-K) was used to check quality of therapeutic alliance. STAR-K consists of two subscales, ‘positive collaboration’ and ‘Non-supportive clinical input’. Insight to illness was assessed with Korean version of Scale to Assessment of Unawareness of Mental disorder(K-SUMD). There are 3-items in KSUMD, each item evaluate awareness in mental disorder(item1), the achieved effects of medication(item2) and consequences of mental disorder(item3). Correlations and regression analyses were calculated between KMARS, STAR-K and K-SUMD

Results: KMARS total score was correlated with STAR-K total score(r=0.235, p<0.05), STAR-K non-supportive clinical input(r=0.367, p<0.01), K-SUMD item1(r=-0.228, p<0.05) and item2(r=-0.256, p<0.05). The regression performed testing K-SUMD(item1), K-SUMD(item2) and STAR-K non-supportive clinical input as independent variables and KMARS total score as a dependent variable. Result shows that K-SUMD(item2) and STAR-K explained 13.2% of the variance. (p=0.001)

Conclusions: Good therapeutic alliance was associated with better therapeutic adherence in outpatient clinic. Especially, non-supportive attitudes of clinicians linked to lower adherence. Making patients feel that the clinicians are supportive could improve the adherence rate. Considering insight into illness, awareness in mental disorder and achieved effects of medication was associated with adherence rate.

Moreover, subjective response in medication was not associated with insight. It suggests that patients with high awareness in need for treatment, the response of medication could influence small portion in adherence.

PM519

Early Cannabis Use Effects on Frontal Cortical Gamma Oscillations in First Episode Psychosis

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Abstract

Cognitive control – a system that modulates the operation of other cognitive in the service of goal-directed behavior – is a core deficit in schizophrenia and its association with frontal cortical gamma oscillatory disturbances suggests a way to integrate molecular findings and models of cognition. Here we present data from first episode patients and address the role of concurrent cannabis usage in cognitive control impairments and its neuropsychological markers. 62 healthy controls were compared to 101 first episode patients performing the Preparing to Overcome Prepotency (POP) task, a cued stimulus-response reversal task, which in chronic schizophrenia patients, has been shown reduced engagement of prefrontal gamma activity. Psychosis subjects included patients with schizophrenia, schizoaffective disorder as well as other psychosis spectrum disorders, and had a variable history of cannabis usage. Patients showed impaired performance and complex spectral alterations of EEG activity. This included reduction of gamma activity in the frontal electrodes during high-control trials. However in the patient group, significant variability was explained by cannabis usage history. In particular a greater gamma power impairment was observed for subjects who had greater lifetime cannabis usage and heavy earlier cannabis use (<16 years old) appeared to exert a more deleterious effect than later use or more minimal use. The findings of this study suggest that the presence and time course of cannabis use history in first episode psychosis has a significant deleterious impact on frontal cortical gamma oscillations in the context of a cognitive control task. Cannabis effects during development are recognized as a critical area in psychosis research, possibly implicated in the genesis, presentation of the disorder and/or serving as an important confounding factor. The present data highlights how the development of specific and accurate models of cognitive impairment in psychosis