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 (rs6319) 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 statisically 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 rs569959*G and rs17326429*A 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 Fukushima 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**

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. 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.