PM444
Effectiveness of Integrating Cognitive Remediation Program into Everyday Clinical Practice of Schizophrenia at Psychiatric Rehabilitation Settings
Alexander John1, Helen Ayres2, Milan Dragovic3, Kim Yeak2
1University of Western Australia, Australia, 2Bentley Health Service, Australia

Abstract
Cognitive deficits (CD) in schizophrenia are recalcitrant to treatment as usual. Whilst there has been considerable interest in recent years for evaluating the efficacy of cognitive remediation (CR) programs in schizophrenia at research settings, scant attention has been paid to evaluate the effectiveness of CR programs at everyday clinical practice settings.

Method: We evaluated retrospectively short-term cognitive, occupational and accommodation outcomes of consecutive patients with schizophrenia admitted over a 5 year period at a tertiary-care inpatient public psychiatric rehabilitation facility in Western Australia. The Brief Assessment of Cognition in Schizophrenia (BACS) was utilised to assess cognition. Patients were divided into 3 groups based on their participation in the neuroplasticity based auditory CR program of PositScience; those who did not participate (non-trainers), those who completed less than 20 hours of training (incomplete-trainers) and those who completed 20 or more hours of training (complete-trainers).

Results: The mean age of the patients was 32.1 years, 68.5% were males, nearly 80% had treatment-resistant illness, 65% were on clozapine and comorbidity was highly prevalent (72%). Thirty-seven patients were classified as non-trainers, 17 as incomplete-trainers and 34 as complete-trainers. The 3 groups did not differ in measured demographic and clinical parameters. Compared to their admission scores, complete-trainers had significantly improved scores at discharge on verbal memory (p=0.012), motor speed (p=0.009) and the composite score (p=0.006). Furthermore, 24%, 22% and 36% of patients changed from unemployed to the employed group in the non-trainers, incomplete-trainers and complete-trainers groups respectively from admission to discharge.

Conclusion: Our study demonstrates that CR program can be integrated effectively into the interventions provided for people with schizophrenia at public psychiatric rehabilitation settings. Significant improvements in cognitive and functional outcomes revealed in this study indicate the need for further translational research in the field of CR in schizophrenia.

PM445
A family of primary familial brain calcification due to mutation in platelet-derived growth factor-B gene
Teruo Hayashi, Giovanni Coppola, Andrea Legati, Tadashi Nishikawa Seiunkai Nishikawa Hospital, Japan

Abstract
Primary familial brain calcification (PFBC) is a neuropsychiatric disorder characterized by abnormal deposits of calcium in the basal ganglia and cerebellum. PFBC can present with a spectrum of symptoms resembling those seen in dementia and schizophrenia. Mutations in some genes have been found to cause PFBC: namely, the SLC20A2 gene that codes for the sodium-dependent phosphate transporter and the PDGFRB gene that codes for the platelet-derived growth factor (PDGF) receptor β. A recent study found that mutations of PDGFB, which encode the ligand peptide PDGF-B for the PDGF receptor β, also cause PFBC. Here we report the first Japanese family of PFBC carrying a mutation of PDGFB. CT scans revealed a symmetrical calcification over the basal ganglia in two members of the family. One family member complained auditory hallucination at 16 years old, and had been treated for schizophrenia. The other family member complained memory and gait disturbances in his late 60s. The mutation in PDGFB (c.445C>T, p.Arg149*) that causes the substitution of an arginine with a stop codon at amino acid 149 of the PDGF-B protein (p.Arg149*) was consistently detected in both cases. No mutations in SLC20A2 were detected. This finding indicates that the PDGF pathway plays a crucial role in pathogenesis of PFBC, and that dysfunction of the PDGF signaling may lead to psychiatric symptoms that are associated with dementia and/or schizophrenia.

PM446
The relationship between MMN and COMT Val108/158Met genotype in schizophrenia
Sho Horikoshi, Tetsuya Shiga, Hiroshi Hoshino, Haruka Ochiai, Keiko Kanno-Nozaki, Kazuko Kanno, Haruka Kaneko, Itaru Miura, Hirooki Yabe
Department of Psychiatry, Fukushima Medical University

Abstract
Background: Mismatch negativity (MMN) is a component of auditory event-related potentials that reflect automatic change detection in brain, showing qualities of endophenotypes in schizophrenia. MMN deficiency is one of the robust findings in the patients, and reflects cognitive and functional decline. The Catechol-O-methyltransferase (COMT) is a key enzyme involved in regulating dopamine transmission within the prefrontal cortex. Preliminary study suggested that COMTVal108/158Met genotype is related to cognitive function in schizophrenia. Both related to cognitive function, however, no studies have reported the relationship between MMN and COMTVal108/158Met genotype in schizophrenia. In this study, we examined the relationship between them.

Method: Duration MMN was measured, and COMTVal108/158Met polymorphism was detected by polymerase chain reaction-restriction fragment length polymorphism in 49 schizophrenia patients. (Val/Val, 21; Met carriers 28). The amplitude and latency of MMN were compared between the Val/Val and Met carriers.

Results: The MMN amplitudes in schizophrenia patients were no difference between Val/Val and Met carriers. The MMN latency of Met carriers was shorter than that of Val/Val carriers.

Conclusions: It is known that the enzyme containing Met has less activity and presumably greater synaptic dopamine than the Val/Val enzyme. Therefore, these results mean that the dopamine activity in prefrontal cortex accelerates pre-attentive auditory change detection.

PM447
Association between coding single nucleotide polymorphisms in ADAMTS20 gene and schizophrenia in a Korean population
Hae Jeong Park, Jong Woo Kim, Youngjong Kim
Kyunghee Univ. Hospital, Republic of Korea

Abstract
Objective: In support of the neurodevelopmental hypothesis of schizophrenia, patients with schizophrenia have been shown to have a higher incidence of minor physical anomalies (MPAs) than healthy controls, especially in the craniofacial region. A disintegrin-like and metalloprotease with thrombospondin type 1 motif, 20 (ADAMTS20) has been implicated in craniofacial abnormalities and in particular the development of cleft lip and
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 = 1.72, 95% CI = 1.17–2.52 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, ATGCCTA 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.

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) & FICG (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^-4) 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.

PM449
Hot genes in schizophrenia: case-control, pharmacogenetics and exploratory analyses in two independent samples
Stefano Porcelli1, Soo-Jung Lee2, Changsu Han3, Ashwin A. Patkar4, Diana De Ronchia5, Anna Rita Atti5, Alessandro Serretti5, Chi-Un Pae6,7,8,9
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, ST8SIA2 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 rs10438333 was associated with SCZ (p=0.03) as well as haplotype rs2282888-rs2273004-rs10277006-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 were 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; rs10277006 p=0.02) and ST8SIA2 rs4777989 (p=0.04) were associated with AR. Exploratory analyses suggested that: 1) PPP3CC, ST8SIA2 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 sertrindole on FGF2, synapsin and NGF expression in the hippocampus of naive mice
Guner Ulak1, Esen Gumuslu1, Oğuz Mutlu1, Merve Ertan1, İpek Komsuolu Çelikyurt1, Furuzan Akar1, Faruk Erdem1,2
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