## P22.03

HLA antigenes in schizophrenia: relation to eye movement disturbances

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Region coding HLA antigens on chromosome 6q21 was shown to be associated with both the vulnerability to schizophrenia and the presence of eye movement disturbances (EMD). The aim of the study was to investigate how individual HLA antigens in schizophrenic patients may be related to the intensity of two kinds of EMD: fixation and smooth pursuit. First, the incidence of HLA antigens was compared between 40 schizophrenic patients (17 male, 23 female) and 198 healthy control subjects (112 male, 86 female). In schizophrenic patients, the intensity of EMD was assessed by infrared reflectometry and quantified on 0–3 scale. Significant correlation was obtained between some EMD and antigens A3, A24, A28, B18, CW3, DR3, DR11, DRW51 and DRW52. Out of these, antigens A3, A24, A28, CW3 and DR3 have been also found to occur with different frequency in schizophrenic patients than in healthy subjects. These five antigens seem most promising for future studies on the pathogenesis of schizophrenia as being associated both with schizophrenia as well as with eye movement disturbances, an endophenotypic neuro-physiological marker of this illness.

## P22.04

No association between norepinephrine transporter gene (1287 A/G) polymorphism and schizophrenia

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**Objective:** Norepinephrine can be implicated in the pathogenesis of schizophrenia. Increased levels of brain norepinephrine were found in schizophrenic patients, especially during period of psychotic relapse. Norepinephrine transporter (NET) regulates the level of norepinephrine, so norepinephrine transporter gene would be a candidate gene for studies of schizophrenia.

**Methods:** The study was performed on patients with schizophrenia n=198 (male n=118, female n=80). Control subjects were blood donors n=211 (male n=111, female n=100), who were not psychiatrically assessed. A silent polymorphism 1287 A/G of NET located in exon 9 was analysed by PCR-RFLP method.

**Results:** There were no differences in the frequency of genotypes between patients and controls. In the frequency of the alleles we also did not find any differences (32% for allele A for schizophrenic patients, 33% for controls, for allele G 68% for schizophrenia, 66% for controls respectively). Dividing the patients according to the gender, no differences in the frequency of either genotypes or alleles were found.

**Conclusion:** In our study we have not confirmed an association between the studied polymorphism of norepinephrine transporter gene and schizophrenia.

## P22.05

The significance of the hereditary factors in the clinical-nosological differentiation of the schizoaffective psychosis

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The conception of the nosological independence of schizoaffective disorder has been called in question, widely discussed in psychiatric science for many years and has been remained contradictory. One of the ways to the solution of this problem might be the study of the hereditary parameters of this disease.

**Objective:** The analysis of the genetic data, which could serve as a proof of independence of schizoaffective disorder.

**Materials and Methods:** There were investigated the clinical characteristics of the family background of the 121 patients with schizoaffective disorder due to ICD-10. According to the clinical-nosological differentiation the 59 patients had been diagnosed as the nosologically independent schizoaffective disorder, the 62 patients were diagnosed as shift-like schizophrenia, with the picture of the schizoaffective episode. In the both group were investigated 170 and 206 the first-degree relatives correspondingly. Clinical-genetical and clinical-psychopathological methods were applied during the research work, and the special maps of clinical-genetic examination of patients developed in MHRC were filled in. According to the ICD-10, the presence and the frequencies the incidence of personality disorders (accentuation of character, psychopathic personality), affective disorders, schizophrenia, and other mental disturbances in the relatives were analyzed.

**Results:** The comparative analysis data showed the prevalence of affective pathology in the relatives of patients with schizoaffective disorders (8.8% opposite to 4.9% in the families of the patient with schizophrenia). Schizophrenia occurred slightly more frequently in relatives of schizophrenic patients (9.8% to 8.2%) including shift-like schizophrenia (3.7% to 2.4%). Psychopatic personality disorders were observed in the relatives with the same frequency (45.3% to 45.1%), but in the group of schizophrenic patients they were more severe attaining the level of psychopathia (12.1% to 5.9% correspondingly, $p<0.05$ of the investigated groups of patients may be used in differentiation of a schizoaffective disorde).

**Conclusion:** The obtained data about statistically significant differences in the family background where the clinical parameters are taken into account might be used in the differentiation diagnosis between schizoaffective disorder and a shift-like schizophrenia.

## P22.06

The C677T polymorphism of the methylenetetrahydrofolate reductase (MTHFR) gene is associated with depression, but not anxiety

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**Background:** A previous case-control study has suggested that homozygosity for the MTHFR C667T polymorphism (TT genotype) is associated with depression, while no such studies have examined the association with anxiety.

**Objective:** To investigate the associations between the MTHFR C667T polymorphism and depression and anxiety in a general population sample.

**Method:** The study population included 4,849 subjects aged 46–48 years (47 % men) and 4,338 aged 70–72 years (43 % men) from Hordaland county, Norway. Average participation rate was 77 %. The MTHFR genotypes were analysed by real time PCR.

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Anxiety and depression were measured by the Hospital Anxiety and Depression Scale. Odds ratios for having anxiety or depression were estimated for the TT genotype with the CC + CT genotypes as reference.

**Results:** The MTHFR-TT genotype was associated with a significantly increased risk of depression (OR=1.62 CI: 1.09–2.41), whereas the risk for anxiety was not different from that of the reference group (OR=1.01 CI: 0.74–1.37).

**Conclusion:** Our data support the previous finding that the MTHFR-TT genotype confers increased risk of depression. The lack of association between the MTHFR-TT genotype and anxiety needs to be replicated.

## P22.07

Association between major depressive disorder and a specific haplotype of the CRH binding protein gene

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Recent research suggests that central CRH hyperdrive is an important neurobiological risk factor for developing major depression. The availability of free CRH in the CNS is tightly regulated by the expression of CRH binding protein (CRHBP). Therefore, the gene encoding for CRHBP is an important functional candidate gene for central CRH hyper drive and for the liability to develop major depression.

We present a systematic study of single nucleotide polymorphisms (SNPs) in the CRHBP gene, and their role in the liability for major depression. Eleven SNPs occurring in the general population were identified, 7 of which were subsequently genotyped in a well diagnosed sample of 92 patients with recurrent major depressions and matched controls. Two SNPs within the CRHBP gene were significantly associated with the disease. An expectation-maximization (EM) algorithm estimating haplotypes combining all 7 SNPs, estimated a specific haplotype to be present in 48% of the patients versus 24% of the controls. This represents a highly significant association. We conclude that the CRHBP gene is likely to be involved in the genetic vulnerability for major depression.

## P22.08

Interleukin-1beta gene promoter polymorphism and risk to functional psychosis

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**Objectives:** Interleukin-1beta is a citokine implicated both in the inflammatory response and development of central nervous system. Genetic association between interleukin-1beta gene (IL-1B) and schizophrenia has been described in previous studies. However, little is known about the role of this gene conferring risk for other functional psychosis.

**Method:** For this study we examined 88 bipolar patients (DSM-III-R), 73 schizophrenic patients (DSM-IV) and 170 healthy controls, all of them of Spanish origin. The polymorphism AvaI (-511), located in the promoter region of IL-1B gene, was analized in all subjects and the genotypic and allelic frequencies were calculated for each diagnostic group and controls.

**Results:** A significant excess of allele 1 was detected in schizophrenics compared to controls (P=0.01). Although similar tendencies were found for the total bipolar group, only patients with psychotic symptoms showed significant increase of allele 1 (P=0.01).

**Conclusions:** These results suggest: i) a possible role of allele 1 of IL-1beta gene in the vulnerability to schizophrenia and other functional psychosis and ii) schizophrenia and bipolar disorder could share some genes of risk, as has been suggested in the continuum hypothesis. Acknowledgments: This study was supported by a grant from Fundació "La Caixa" (99–111–000).

## P22.09

Th1 and Th2 relationship in schizophrenia – immunological, immunogenetic and therapeutic investigations

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We have hypothesised immunological abnormalities characterised by a decreased Th1 and an increased Th2 immune response in a distinct group of schizophrenic patients. To prove this hypothesis we performed biochemical, immunogenetic, and clinical investigations: Cytokine production by in-vitro stimulated lymphocytes; Molecular genetics of candidate Th1/Th2-related genes: IFN-gamma, IL-4, IL-12, IL-13 (patients/controls n=170 each); Clinical study using a COX2 inhibitor added to an antipsychotic medication (n=50 patients).

Our results suggest a subgroup of schizophrenic patients with reduced IFN-gamma production and increased IL-4/IL-13 production. The IL-13 gene A1082G promotor polymorphism, accompanied with more pronounced Th2 response, was more frequent in patients. Patients receiving the COX2 inhibitor showed a markedly faster reduction of psychotic symptoms, than patients of the placebo group.

Our complex but systematic results may have great impact for the identification of a subgroup of schizophrenia with immune-related pathophysiology and for the development of an immune-mediated therapy strategy in schizophrenia.

# P23. Geropsychiatry

## P23.01

States of loss of sense in late age and their role in creation of lingering depressive responses

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The purpose of the given operation was installation of link between experiences of sense of life and development of lingering depressive disorders in late age. The methods were applied: the special questionnaire, semi-structured interview, psycho biographical method with registration of significant acts of the person during all life, statistical method Fisher. 35 patients of late age (from 62 till 75 years) male and female with presence of experiences of loss of sense of life were researched. As a result of comparative researches is detected, that corrupting of higher personal senses of social and spiritual levels as a result of corrupting former outlook, ideals, loss of the close man, the dismissal with favourite operations result ined to creation of disorders of acclimatization as lingering depressive responses, dysthymias. Being superimposed on the primary psychogenic depressive disorders, which have arisen under influence of a serious stress, the secondary depressive disorders caused by losses

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