XXIV Paulo International

Medical Symposium

Schizophrenia - Epidemiology and Biology

June 18th to 20th, 2012

Oulu, Finland

Program and abstracts

Organisers:

Oulu Psychiatric Epidemiology Society (OPES)
Department of Psychiatry, University of Oulu, Finland

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Oulu 2012

Dear colleagues,

Welcome to the Paulo International Medical Symposium 2012 entitled Schizophrenia – Epidemiology and Biology. The conference will be held in Oulu, Finland from 18th to 20th June, 2012. The conference is organized by the Oulu Psychiatric Epidemiology Society (OPES) in collaboration with the University of Oulu. The conference venue is the Hotel Lasaretti.

During the conference days we are pleased to offer lectures, posters and discussion on high quality international research in epidemiology and biology of schizophrenia. During your visit we hope you can also enjoy the midnight sun in the largest city in northern Finland!

Welcome to Oulu and to the Midnight Sun Science Festival!

With best regards,

Organizing committee

Jouko Miettunen
Erika Jääskeläinen
Antti Alaräisänen
Marianne Haapea
Tanja Nordström
Matti Penttilä
Ina Rissanen
Pauliina Juola
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Juha Veijola
Pirjo Mäki
Matti Isohanni

Acknowledgements

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The Paulo Foundation
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The Finnish Medical Association

PROGRAM

Sunday 17th June 2012

16:00-19:00 Registration desk open
19:00-21:00 **Welcome Reception, Aurora Hall**

Monday 18th June 2012

8:00 Registration desk opens
8:45-9:15 *Coffee*

9:15-9:30 **Opening of the symposium, Aurora Hall**
Adjunct Professor Jouko Miettunen and Dr Erika Jääskeläinen,
Oulu Psychiatric Epidemiology Society

Session 1 **Aurora Hall** - Chair: Matti Isohanni, co-chair: Antti Alaräisänen
9:30-10:30 **Translational epidemiology – linking clues from schizophrenia epidemiology with experimental neuroscience**
Professor John McGrath (Australia)
10:30-11:30 **The outcome of schizophrenia revisited: Are there international differences?**
Dr Josep Maria Haro (Spain)

11:30-12:30 *Lunch*, Lasaretti Restaurant

12:30-13:30 **Poster session 1, Yrjö Hall** - Chair: Juha Veijola, co-chair: Marianne Haapea

Session 2 **Aurora Hall -** Chair: John McGrath, co-chair: Jouko Miettunen
13:30-14:30 **Signs of infection and inflammation in early life and risk of schizophrenia**
Professor Christina Dalman (Sweden)
14:30-15.30 **Altered learning and memory mechanisms in schizophrenia**
Professor Carol Tamminga (USA)
15:30-16:00 *Coffee*

Parallel oral sessions

Oral session 1 **Aurora Hall -** Chair: Christina Dalman, co-chair: Erika Jääskeläinen
16:00-16:30 James MacCabe: Decline in verbal IQ between age 13 and 18 and risk for schizophrenia in adulthood: a Swedish longitudinal cohort study
16:30-17:00 Vera Morgan: Clustering of neuropsychiatric outcomes in children of women with psychosis: a western Australian retrospective e-cohort study using record-linked data

Oral session 2 **Merikoski Hall** - Chair: Juha Veijola, co-chair: Pauliina Juola
16:00-16:15 Pirjo Mäki: Childhood and adolescence symptoms predicting psychosis in the general population based Northern Finland Birth Cohort 1986
16:15-16:30 Susanne Gage: Cannabis use and psychotic experiences in ALSPAC teenagers – a longitudinal study
16:30-16:45 Maria Niarchou: Speed of processing deficits predict non-clinical psychotic experiences in children and adolescents; longitudinal analyses in a large birth cohort
16:45-17:00 Sarah Sullivan: Psychotic symptoms and social functioning: a longitudinal study

Oral session 3 **Linna Cabinet** - Chair: Brian Miller, co-chair: Tanja Nordström
16:00-16:15 Tuomas Jukuri: Default mode network in young people with familial risk for psychosis – the Oulu Brain and Mind Study
16:15-16:30 Tuukka Raij: Auditory verbal hallucination and imagery of the hallucination differ by stronger activation of the supplementary motor area during imagery

16:30-16:45 Timothea Toulopoulou: Prefrontal deviations in function but not volume are putative endophenotypes for schizophrenia

16:45-17:00 Matti Isohanni: Lifespan development in schizophrenia from womb to grave - results from the Northern Finland 1966 Birth Cohort

19:00-01:00 **Conference Dinner, Maikkula Estate**

Tuesday 19th June 2012

8:30 Registration desk opens

9:00-9:30 *Coffee*

Session 3 **Aurora Hall** - Chair: Jaana Suvisaari, co-chair: Erika Jääskeläinen

9:30-10:30 **Psychosis and diagnosis: Are symptoms part of the cause?**
Professor Jim van Os (Netherlands)

10:30-11:30 **Is relapse in schizophrenia an immune-mediated phenomenon?**
Assistant Professor Brian Miller (USA)

11:30-12:30 *Lunch*

12:30-13:30 **Poster session 2, Yrjö Hall** - Chair: Pirjo Mäki, co-chair: Matti Penttilä

Session 4 **Aurora Hall** - Chair: Jim van Os, co-chair: Ina Rissanen

13:30-14:30 **Gene-environment interactions in psychosis: time to take it seriously**
Professor Inez Myin-Germeys (Netherlands)

14:30-15.30 **Back to the environment – prenatal and childhood risk factors for schizophrenia**
Professor Mary Cannon (Ireland)

15:30-16:00 *Coffee*

Parallel oral sessions

Oral session 4 **Aurora Hall** - Chair: Brian Kirkpatrick, co-chair: Antti Alaräisänen

16:00-16:30 Risto Näätänen: The mismatch negativity (MMN) - an index of cognitive deterioration, the common core of all major neuropsychiatric diseases – a review

16:30-17:00 Juha Veijola: Progression in brain tissue loss in subjects with schizophrenia. The Northern Finland 1966 Birth Cohort study

17:00-17:30 Alan Mackay-Sim: Patient-derived stem cells: access to the cell biology of schizophrenia

Oral session 5 **Merikoski Hall** - Chair: James MacGabe, co-chair Jouko Miettunen

16:00-16:15 Vladeta Ajdacic-Gross: Disentangling the heterogeneity and complexity of psychosis syndromes: methodological promises

16:15-16:30 Anthony Ahmed: Psychosis phenotypes and the structure of personality: evidence of a dimensional model of psychotic experiences

16:30-16:45 Virva Siira: The role of long-term manifestation of personality traits and heritability as vulnerability indicators for psychopathology

16:45-17:00 Michael Fitzgerald: The role of long-term manifestation of personality traits and heritability as vulnerability indicators for psychopathology

17:00-17:15 Niklas Granö: JERI - Early detection and intervention model for adolescents at risk for psychosis: Can transition to psychosis be prevented?

17:15-17:30 Marius Lahti: Cardiovascular morbidity, mortality, and pharmacotherapy in patients with schizophrenia

Oral session 6 **Linna Cabinet** - Chair: Vera Morgan, co-chair: Sanna Huhtaniska

16:00-16:15 Aye-Mu Myint: Immune activation induced kynurenines imbalance is associated with response to treatment with antipsychotics

16:15-16:30 Tayfun Uzbay: Possible role of agmatine in schizophrenia

16:30-16:45 Jaana Suvisaari: Proline and schizophrenia
16:45-17:00 Esben Agerbo: Modelling the contribution of family history and variation in single nucleotide polymorphisms to risk of schizophrenia: a Danish national birth cohort-based study
17:00-17:15 Mary C. Clarke: Evidence for a skewed developmental trajectory among first-degree relatives of schizophrenia patients
17:15-17:30 Adrianna Mendrek: Sex-specific differences in neurocognitive function in schizophrenia

19:00-21:00 **City Reception, City Hall**

Wednesday 20th June 2012

8:30 Registration desk opens
9:00-9:30 *Coffee*

Session 5 **Aurora Hall** - Chair: Christos Pantelis, co-chair: Marianne Haapea
9:30-10:30 **What underlies the onset of psychosis?**
Professor Philip McGuire (UK)
10:30-11:30 **A conceptual model of schizophrenia**
Professor Brian Kirkpatrick (USA)

11:30-12:30 *Lunch*

12:30-13:30 **Poster session 3, Yrjö Hall** - Chair: Matti Isohanni, co-chair: Erika Jääskeläinen

Session 6 **Aurora Hall** - Chair: Peter Jones, co-chair: Jouko Miettunen
13:30-14:30 **Reward prediction error learning dysfunction in psychosis: linking dopamine, learning and delusions**
Dr Graham Murray (UK)
14:30-15.30 **Neuroimaging markers of illness onset in psychosis: the search for a moving target**
Professor Christos Pantelis (Australia)
15:30-16:00 *Coffee*

Session 7 **Aurora Hall** - Chair: Graham Murray, co-chair: Antti Alaräisänen
16:00-17:00 **Most adult psychiatric disorders begin in childhood, but when should we treat them?**
Professor Peter Jones (UK)

17:00-17:15 **Closing of the symposium, Aurora Hall**
Adjunct Professor Jouko Miettunen and Dr Erika Jääskeläinen,
Oulu Psychiatric Epidemiology Society

Poster session presentations

Monday, 18th June

P01 Doi N. Impact of epidemiology on molecular genetics of schizophrenia. I. Persistence criterion for nuclear susceptibility genes

P02 Doi N. Impact of epidemiology on molecular genetics of schizophrenia. II. Mitochondrial DNA hypothesis for schizophrenia

P03 Boyle SP. Investigations for a putative diagnostic biomarker in schizophrenia

P04 Solismaa A. No association between M1 and M2 gene polymorphisms and subjective depression anxiety or sympathicotonia tension like symptoms during clozapine treatment

P13 Partti K. Lung function, respiratory diseases and symptoms, and smoking in psychotic disorders

P14 Tanasiewicz M. State of the oral cavity in schizophrenic inpatients during therapy with atypical and classical neuroleptics

P15 Niittyvuopio-Jämsä L-M. Childhood vitamin D supplementation and risk and prognosis of schizophrenia

P23 Riekki T. Schizotypal and affective traits in the offspring of antenatally depressed mothers – relationship to parental history of psychosis

P24 Schweizer U. Selenoprotein-deficiency impairs cortical parvalbumin+ interneuron function in mice: another cause for schizophrenia?

P25 Zumárraga M. Gamma-aminobutyric acid in the plasma of schizophrenic patients, bipolar patients and healthy controls

P26 Pujol-Lopez Y. Effect of different antipsychotic compounds on cytokines and tryptophan metabolites after different immune challenges in astrocytes culture

P35 Göktalay G. Effects of baseline prepulse inhibition on morphine induced conditioned place preference

P36 Kayir H. Baseline prepulse inhibition does not correlate with anxiety in elevated plus-maze test

P37 Di Lorenzo R. Hyperhomocysteinemia in schizophrenia: a possible marker of chronic dysfunction or a confounding factor?

P38 Daryani A. Serological survey of Toxoplasma gondii in schizophrenia patients referred to psychiatric hospital, Sari City, Iran

Tuesday, 19th June

P05 Miettunen J. Temperament in individuals with psychotic disorders before and after the onset of illness

P06 Ahmed A.O. Latent structure of schizophrenia-spectrum personality disorders: taxometric detection and construct validation

P07 Kyllönen M. Latent class analysis of risk factors for schizophrenia and other psychoses

P08 Haapea M. Improving participation rates in population based schizophrenia research by using home interviews

P09 Keskinen E. Interaction between parental psychosis and risk factors during pregnancy and birth for schizophrenia

P16 Ajdacic-Gross V. Assessing psychosis dimensions and symptoms in the ZInEP Epidemiological Survey

P17 Mazumder AH. Positive and negative symptoms of schizophrenia in Bangladesh

P18 Penttilä M. Association between duration of untreated psychosis and short- and long-term outcome in schizophrenia within the Northern Finland 1966 Birth Cohort

P27 Cowling D. Ageing in schizophrenia: a review

P28 Juola P. A systematic review and meta-analysis of recovery in schizophrenia

P29 Hirvonen N. First-episode positive and negative symptoms as predictors of symptom remission in schizophrenia: a systematic review and meta-analysis
P30 Rissanen I. Use of antipsychotic medication and suicidality – the Northern Finland Birth Cohort 1966
P39 Garcia-Rizo C. Cannabis use and energy intake homeostasis in first episode psychosis
P40 Manrique-Garcia E. Cannabis, schizophrenia and other non-affective psychoses: 35 years of follow-up of a population-based cohort
P41 Moilanen K. Unwantedness of pregnancy, parental psychosis and subsequent risk of schizophrenia in the offspring in the Northern Finland 1966 Birth Cohort
P42 Dantas CR. Deficit and non-deficit schizophrenia do not differ regarding season of birth in Brazilian southern and southeast regions

Wednesday, 20th June
P10 Gale CK. The effect of recent adverse events and psychotic symptomatology among people with schizophrenia
P11 Hurtig T. Psychotic-like symptoms and social and academic achievement in adolescents
P12 Haravuori H. Life event characteristics of adolescents treated for non-affective psychosis were similar to adolescents with other severe mental disorders
P19 Yoshii H. Stigma toward schizophrenia among parents of junior and senior high school students in Japan
P20 Lin S-H. Qualitative and quantitative minor physical anomalies in Taiwanese patients with schizophrenia disorder
P21 Jones P. Efficiency of early motor development and the window of risk for adult schizophrenia: making connections
P22 Kobayashi H. Delayed neurodevelopment predicts later deterioration of response speed during executive function in schizophrenia
P31 Huhtaniska S. Longitudinal studies on associations between use of antipsychotics and brain morphometric changes in schizophrenia – a systematic review
P32 Moilanen J. Brain morphology of subjects with schizophrenia spectrum disorder with and without antipsychotic medication – the Northern Finland 1966 Birth Cohort study
P33 Jääskeläinen E. Association between duration of untreated psychosis and progression of brain volume change in schizophrenia – the Northern Finland 1966 Birth Cohort
P34 Kettunen K. Structural MRI study of childhood- and adolescent-onset schizophrenia as a part of Kellokoski Adolescent Inpatient Follow-Up Study (KAIFUS)
P43 Kukkohovi L. Learning and generalization in schizophrenia, other psychoses, siblings, and controls. The Northern Finland 1966 Birth Cohort study
P44 Rönkkö E. The effect of typical and atypical antipsychotic medication on basal ganglia mediated learning and medial temporal lobe mediated stimulus generalization in schizophrenia. The Northern Finland 1966 Birth Cohort study
P45 Mendrek A. Preliminary functional imaging results show that cue-induced cravings elicit orbitofrontal activations in patients with cannabis abuse/dependence
P46 Mäntylä T. Activation of the prefrontal cortex during automatic reality monitoring of naturalistic stimulation differentiates psychotic and healthy subjects
P47 Huossa V. Whole brain network analysis of schizophrenia

ABSTRACTS

BIOGRAPHS AND ABSTRACTS

Invited speakers

TRANSLATIONAL EPIDEMIOLOGY – LINKING CLUES FROM SCHIZOPHRENIA EPIDEMIOLOGY WITH EXPERIMENTAL NEUROSCIENCE

PROFESSOR JOHN MCGRATH
(AUSTRALIA)

John McGrath, AM, MBBS, MD, PhD, FRANZCP. John McGrath received his medical degree from the University of Queensland. After working as a community-based psychiatrist, he moved into full-time research, becoming the Director of the Queensland Centre for Mental Health Research in 1990. He holds appointments at the University of Queensland, Department of Psychiatry, the Queensland Brain Institute, and Griffith University. His research aims to generate and evaluate nongenetic risk factors for schizophrenia. He has forged productive cross-disciplinary collaborations linking risk factor epidemiology with developmental neurobiology (e.g. using animal models to explore candidate exposures). In addition, he has supervised major systematic reviews of the incidence, prevalence and mortality of schizophrenia. He has won several national and international awards including the Premier's Award for Medical Research, a Queensland-Smithsonian Fellowship, a Rockefeller Foundation Bellagio Residency, and the Organon Senior Research Award. The Australian government awarded John a Centenary Medal in 2003 and in 2007 he was appointed a Member of the Order of Australia (AM). He is on the editorial boards of several international journals.

O01 PROFESSOR JOHN MCGRATH. TRANSLATIONAL EPIDEMIOLOGY – LINKING CLUES FROM SCHIZOPHRENIA EPIDEMIOLOGY WITH EXPERIMENTAL NEUROSCIENCE

Schizophrenia epidemiology can provide us with valuable information to guide research directions. However, while epidemiology is useful for generating candidate risk factors, it cannot always deliver studies that prove causality. We argue that the field needs more translational research that links schizophrenia epidemiology with molecular, cellular, and behavioral neuroscience. Cross-disciplinary projects related to candidate genetic or nongenetic risk factors not only can address the biological plausibility of these factors, but they can serve as catalysts for discovery in neuroscience. This type of cross disciplinary research is likely to be more efficient compared to clinically dislocated basic neuroscience. As an example, details of a program of translational research based on the links between advanced paternal age and offspring mental health will be presented. We need to build shared discovery platforms that encourage greater cross-fertilization between schizophrenia epidemiology and basic neuroscience research.

THE OUTCOME OF SCHIZOPHRENIA REVISITED: ARE THERE INTERNATIONAL DIFFERENCES?

DOCTOR JOSEP MARIA HARO
(SPAIN)

Josep Maria Haro, psychiatrists and Ph.D. in Public Health, is the Research Director of Saint John of God Health Park in Barcelona, Spain. After his medical studies, he was trained in Epidemiology and Public Health at the Johns Hopkins School of Hygiene and Public Health (Baltimore, MD, USA). Later he got his specialization in psychiatry at the Clinic Hospital of Barcelona. During the past fifteen years he has worked both in clinical medicine and in public health research and has published more than one hundred scientific papers. His areas of investigation have been epidemiology of mental disorders and schizophrenia. In schizophrenia, he has been interested in the consequences of the disorder in patient functioning and quality of life and the impact on society overall. He has also conducted research on treatment outcomes, both in observational and randomized studies. Lately, he has focused on the role of observational research in the assessment of the effects of new treatments and has participated in the development of new methodologies to improve the designs of these studies. As a researcher in the epidemiology of mental disorders, he has conducted studies on the prevalence of disorders in the general population and the treatment of mental disorders in primary care. Dr. Haro is an active member of several scientific and professional organizations in the field of psychiatry and public health. He is one of the founding members of the PSICOST group, a group of researchers in the field of mental health care costs. He is also a member of the Spanish Public Health Society and principal investigator of one of the members of the CIBERSAM network. He is currently the European coordinator of the EC FP7 project Roadmap for mental health and wellbeing research in Europe (ROAMER). In 2011 he won the Best Investigator Award of the Spanish Society for Biological Psychiatry.

O02 Dr Josep Maria Haro. The outcome of schizophrenia revisited: Are there international differences?

The International Pilot Study of Schizophrenia (IPSS) and the Determinants of Outcome Study (DOS) of schizophrenia, which were conducted over 25 years ago by the World Health Organization (WHO), found regional differences in the incidence and outcomes of schizophrenia. Patients living in less developed areas had better outcomes than patients in economically developed areas. These findings were criticized due to a number of reasons such as differences in study methodology and lack of information on social issues. Although numerous projects since then have reported on the geographical and cultural variations in outcome, we do not know if the political and economic changes that have taken place in the last decades have changed this scenario. Using data from the World-SOHO study we have analyzed international differences in the course of schizophrenia with a consistent methodology across geographies.

The results show that the clinical outcomes of schizophrenia seem to be worse in Europe compared to other regions. The frequency of clinical remission was lower in the three European regions (60-65%) than in the regions of East Asia, Latin America and North Africa/Middle East (79-84%). However, regional differences in functional remission followed a different pattern. While it was more likely for patients in Latin America to achieve functional remission compared with South Europe, there were no clear differences with East Asia or North Africa/Middle East. We will discuss these findings in relation to cultural, economical and health services availability differences.

SIGNS OF INFECTION AND INFLAMMATION IN EARLY LIFE AND RISK OF SCHIZOPHRENIA

PROFESSOR CHRISTINA DALMAN
(SWEDEN)

Professor Christina Dalman is the Head of Division of Public Health Epidemiology, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden. She is senior researcher in psychiatry appointed by the Swedish Research Council, Associate Professor in Epidemiology, MD, and PhD in Social Medicine. Dr Dalman has expertise in psychiatric epidemiology and has a vast experience in large record linkage studies with longitudinal follow up in combination with sub-analyses of biological data. Her work focus on vulnerability and risk factors for psychiatric disorders with special regard to serious and long standing conditions such as psychotic disorders. The overall aim is to disentangle etiological factors but also to achieve knowledge on how to prevent mental ill health.

O03 Professor Christina Dalman. Signs of infection and inflammation in early life and risk of schizophrenia

There is some support of an association between early life inflammation and/or infection and increased risk of schizophrenia later in life. An overview of the evidence from different research fields will be presented: 1) Epidemiological studies of exposure to different kinds of infections, autoimmune disorders and inflammatory markers during fetal life and childhood, based on both biological samples and register data. 2) Animal studies dealing with maternal immune activation (MIA) and off-springs´ immune dysregulation in relation to brain morphology and functioning. 3) Studies of the involvement of immune-related genes in the etiology of schizophrenia. Possible underlying mechanisms will be discussed as well as associations to other known risk factors of schizophrenia. Similarities and differences between schizophrenia and autism spectrum disorders (ASD) with regard to infectious/inflammatory etiology will be presented.

ALTERED LEARNING AND MEMORY MECHANISMS IN SCHIZOPHRENIA

PROFESSOR CAROL TAMMINGA
(USA)

Dr. Tamminga holds the Lou and Ellen McGinley Distinguished Chair and the McKenzie Chair in Psychiatry at the University of Texas Southwestern Medical School; she is the Chairman of the Department of Psychiatry and the Chief of the Schizophrenia Division at UTSW. She received her M.D. degree from Vanderbilt University and completed residency training in psychiatry at the University of Chicago. She served on the University of Chicago faculty from 1975 to 1979 and moved to the NINDS for training in Neurology in 1978. After joining the faculty at the University of Maryland Medical School in 1979, she practiced research, clinical care and teaching there until joining the faculty at UT Southwestern Medical School in 2003. Dr Tamminga has served on the Board of Scientific Counselors of the National Institute of Mental Health and the National Institute of Drug Abuse, as Council member and President of the American College of Neuropsychopharmacology, as a Member and Chair of the Psychopharmacological Drugs Advisory Committee of the FDA as well as consultant for the Orphan Products Development Review Group, FDA. She is currently the Deputy Editor of the American Journal of Psychiatry and on the editorial board of several other journals in the field. Dr Tamminga was elected to the Institute of Medicine of the National Academies of Sciences in 1998 and has served on several IOM committees in that capacity. The goal of Dr. Tamminga's research is to examine and understand the mechanisms underlying schizophrenia, especially its most prominent symptoms, psychosis and memory dysfunction, in order to build rational treatments for the illness. She evaluates the function of the living human brain in individuals with and without schizophrenia, using brain imaging techniques. Then, building on this knowledge, she uses human postmortem brain tissue to translate the functional alterations from the living human patient into molecular observations of the illness. Her ultimate goal is to base novel pharmacologies for psychosis and memory dysfunction on these observations and to use the altered in vivo imaging and postmortem molecular changes as biomarkers and targets for identifying novel active pharmaceuticals.

O04 PROFESSOR CAROL TAMMINGA. ALTERED LEARNING AND MEMORY MECHANISMS IN SCHIZOPHRENIA

The hippocampal formation is one of the most extensively studied regions of the brain, with well described anatomy and basic physiology; moreover, aspects of human memory mediated by hippocampus are well characterized. In schizophrenia, alterations in hippocampal anatomy, perfusion and activation are consistently reported; impairments in declarative memory function, especially in the flexible use of event memories (e.g., in the service of memory-based inference), are common. Postmortem molecular changes suggest a selective reduction in glutamate transmission in the dentate gyrus (DG) and in its efferent fibers, the mossy fiber pathway. A reduction in DG glutamatergic output and in its information processing functions could generate two co-occurring outcomes in hippocampus: (a) a change in homeostatic plasticity processes in CA3, accompanied by increased activity due to reduced afferent stimulation from DG onto CA3 neurons, a process that could increase the '*pattern completion*' functions of CA3; and (b) the loss of DG-specific mnemonic functions, namely '*pattern separation*', a change that could increase the prevalence of illusory pattern completion and reduce discrimination between present and past experiences in memory. The resulting increase in 'runaway' CA3-mediated *pattern completion* could result in cognitive 'mistakes', generating psychotic associations and resulting in memories with psychotic content. Tests of this model could result in novel approaches to the treatment of psychosis and declarative memory alterations, and novel animal preparations for basic schizophrenia research.

PSYCHOSIS AND DIAGNOSIS: ARE SYMPTOMS PART OF THE CAUSE?

PROFESSOR JIM VAN OS
(NETHERLANDS)

Jim van Os is Professor of Psychiatric Epidemiology and Chairman of the Department of Psychiatry and Psychology at Maastricht University Medical Centre, Maastricht, The Netherlands, and Visiting Professor of Psychiatric Epidemiology at the Institute of Psychiatry, London, UK. He trained in Psychiatry in Casablanca (Morocco), Bordeaux (France) and finally at the Institute of Psychiatry and the Maudsley/Bethlem Royal Hospital in London (UK) and after his clinical training was awarded a three-year UK Medical Research Council Training Fellowship in Clinical Epidemiology at the London School of Hygiene and Tropical Medicine. He is on the editorial board of several European and US psychiatric journals such as Acta Psychiatrica Scandinavica, European Psychiatry, Psychological Medicine, Schizophrenia Research, Schizophrenia Bulletin, Early Intervention in Psychiatry and The Journal of Mental Health. Jim van Os is coordinator of a €12M EU FP7 IP project on gene-environment interactions in schizophrenia, and is also active in clinical gene-environment interaction research in depression and bipolar disorder. He is a member of the Psychosis Group of the DSM-V Task Force, and was co-chair of the APA DSM/ICD conference Deconstructing Psychosis. In 2011, he was elected member of the Royal Netherlands Academy of Arts and Sciences. He is Director of Psychiatric Services at Maastricht University Medical Centre and runs a service for treatment-resistant depression and first episode psychosis. Areas of interest include the clinical, cognitive and genetic epidemiology of bipolar disorder, schizophrenia and depression, in particular the study of variation in overlapping dimensions of these disorders in the general population and the underlying cognitive factors and gene-environment interactions driving this variation. Treatment studies focus on implementation of Assertive Outreach and CBT in routine mental health settings, and aspects of patient-professional carer communication.

O05 PROFESSOR JIM VAN OS. PSYCHOSIS AND DIAGNOSIS: ARE SYMPTOMS PART OF THE CAUSE?

We will present a model of the onset of psychosis that takes into account how contextual factors impact on underlying states that in turn give rise to symptoms that in turn impact on each other and manifest epidemiologically as quantitative deviations from health.

IS RELAPSE IN SCHIZOPHRENIA AN IMMUNE-MEDIATED PHENOMENON?

ASSISTANT PROFESSOR BRIAN MILLER
(USA)

Dr. Brian Miller is an Assistant Professor of Psychiatry on a research tenure track at Georgia Health Sciences University (GHSU). He earned his BS in mathematics from Vanderbilt University, MD/MPH from The Ohio State University, and PhD in medical science from the University of Oulu. He completed general psychiatry residency (chief resident 2009-10) and psychotic disorders fellowship at GHSU. During his training, Dr. Miller was recognized with the Laughlin Fellowship from the American College of Psychiatrists, and young investigator awards from the International Congress on Schizophrenia Research, Society of Biological Psychiatry, NIMH New Clinical Drug Evaluation Unit, and APA Research Colloquium for Junior Investigators.

Dr. Miller's PhD thesis was on paternal age as a risk factor for psychosis and mortality in the Northern Finland 1966 Birth Cohort. His current research focuses on cytokines as a potential state and relapse predictive marker in schizophrenia.

O06 Assistant Professor Brian Miller. Is relapse in schizophrenia an immune-mediated phenomenon?

Clinical course in schizophrenia is often characterized by recurrent relapses, which are associated with adverse outcomes. Immune system abnormalities, including inflammation, have been one of the more enduring findings in the field. Several recent findings suggest that relapse in some patients with schizophrenia may be an immune mediated effect. These associations raise the possibility of immune-based treatments for relapse (and/or relapse prevention) in a subset of patients with schizophrenia. Immune system abnormalities in patients with first-episode psychosis and/or relapse of chronic schizophrenia -- including cytokines, the acute phase response, leukocyte subsets, autoantibodies, and markers of blood-brain barrier dysfunction -- will be reviewed. Limitations of the current literature and future research directions will be discussed.

GENE-ENVIRONMENT INTERACTIONS IN PSYCHOSIS: TIME TO TAKE IT SERIOUSLY

PROFESSOR INEZ MYIN-GERMEYS
(NETHERLANDS)

Inez Myin-Germeys (º1972) is professor of ecological psychiatry at Maastricht University, The Netherlands. She also heads the Division Mental Health within the school of Mental Health & Neuroscience at the same university. Inez Myin-Germeys has studied Theoretical Psychology at the University of Louvain in Belgium, and obtained her PhD at the department of Psychiatry and Neuropsychology in Maastricht. She has obtained several prestigious personal fellowships from the Dutch Medical Council as well as from NARSAD. Her work focuses on the application of experience sampling technology in the study of severe mental illness, specifically psychosis. Research topics include the phenomenology of severe mental illness, the study of psychological models in real life, gene-environment interactions, underlying biological pathways, as well as the translation to clinical practice. Inez Myin-Germeys has published over 100 papers in psychiatry and psychology journals including top-ranked journals such as Archives of General Psychiatry, Biological Psychiatry, American Journal of Psychiatry, British Journal of Psychiatry, and Schizophrenia Bulletin. She has supervised over 20 PhD projects.

O07 Professor Inez Myin-Germeys. Gene-environment interactions in psychosis: time to take it seriously

Inconclusive results from molecular genetic studies in schizophrenia have generated interest in more realistic yet more complicated models of disease aetiology including gene-environment interactions. The findings of epidemiological GxE studies have been suggestive of widespread gene-environment interactions in the aetiology of psychotic disorder. However, whereas genome-wide association studies have brought about a revolution in the search for molecular genetic variation underlying psychiatric disorders, a similar development at the level of the environment is highly needed. The experience sampling method (ESM) may be well placed to improve our understanding of environmental risk. ESM is a structured diary technique that captures mental states as well as contextual information in the flow of daily life, allowing for a prospective, repeated measure of proximal environmental factors. Alternatively, experimental approaches may be well suited to improve our understanding of reactivity to the environment in G*E studies.

In order to demonstrate the power of these approaches, I will focus on an interaction between molecular genetic variation in COMT and environmental stress as well as exposure to cannabis. It will be demonstrated that the Val/Val genotype predispose to a psychotic reaction to cannabis in patients with a psychotic disorder, both in an experimental design, as well as in the ESM study. In contrast, patients with the Met/Met genotype react psychotically to stress.

These results demonstrate the necessity for high quality GxE interaction studies examining the immediate effect of risk exposure conditional on specific susceptibility polymorphisms.

BACK TO THE ENVIRONMENT – PRENATAL AND CHILDHOOD RISK FACTORS FOR SCHIZOPHRENIA

PROFESSOR MARY CANNON
(IRELAND)

Mary Cannon trained in psychiatry at St John of God Hospital Dublin and the Institute of Psychiatry, London. She holds a Masters degree in Epidemiology from the London School of Hygiene and Tropical Medicine and was awarded her PhD from University of London in 2002. She is Associate Professor in Psychiatry at the Royal College of Surgeons in Ireland, Dublin, and is the holder of a Clinician Scientist Fellowship from the Health Research Board Ireland. Her research area of interest is developmental psychiatric epidemiology, in particular the study of childhood and adolescent risk factors for schizophrenia such as obstetric complications, developmental delay and cannabis use, and the interaction of environmental and genetic risk factors for psychosis. Her current research programme also focuses on psychotic symptoms in childhood and adolescence which she believes can inform us about the risk trajectory to later psychotic illnesses and could provide a significant opportunity for prevention. She is a Member of the Board of Directors of the Schizophrenia International Research Society and is a member of the Editorial Board of Schizophrenia Bulletin and The British Journal of Psychiatry. She also works as a clinical psychiatrist in Beaumont Hospital in Dublin.

O08 PROFESSOR MARY CANNON. BACK TO THE ENVIRONMENT – PRENATAL AND CHILDHOOD RISK FACTORS FOR SCHIZOPHRENIA

Although somewhat neglected in recent years, environmental risk factors for schizophrenia are well replicated and have respectable effect sizes. Genome-wide association studies, while generating much interest, show that individual "genes" explain very little of the variance associated with schizophrenia. Many of the clues from epidemiology converge on exposures during the prenatal period and early childhood. Understanding the role of prenatal and early childhood exposures in relation to risk for schizophrenia offers clues to etiopathogenesis and potential preventive strategies. In this talk I propose to focus on prenatal, perinatal and early childhood environmental risk factors. I will discuss evidence for interaction between genetic vulnerability and early environmental exposures. It is hoped that this session will help refocus attention on the importance of environmental risk factors for schizophrenia and the need for new methodological approaches to study the complex relationship between genes and the environment.

WHAT UNDERLIES THE ONSET OF PSYCHOSIS?

PROFESSOR PHILIP MCGUIRE
(UK)

Philip McGuire is Head of the Department of Psychosis Studies at the Institute of Psychiatry, King's College, London, and the Academic Director and joint Leader of the Psychosis Clinical Academic Group, King's Health Partners. He is also Director of OASIS, and of the Voices Clinic. He is the Chairman of the European Psychiatric Association Section of Neuroimaging, Associate Editor of the British Journal of Psychiatry and a Fellow of the Academy of Medical Sciences, the Royal College of Psychiatrists, the European Psychiatric Association, and the International College of Neuropsychopharmacology. He studied physiology and medicine at the University of Edinburgh, then worked as a research fellow at Yale University with Patricia Goldman-Rakic. After training in psychiatry at the Maudsley hospital, he was a Wellcome Research Fellow at the MRC Cyclotron Unit, Hammersmith Hospital with Chris Frith, then worked with Robin Murray as a Senior Lecturer, Reader and Professor in the Department of Psychological Medicine at the Institute of Psychiatry in London. He leads a clinical academic research group focused on determining the neurocognitive basis of psychosis and developing new treatments for psychosis.

O09 PROFESSOR PHILIP MCGUIRE. WHAT UNDERLIES THE ONSET OF PSYCHOSIS?

A CONCEPTUAL MODEL OF SCHIZOPHRENIA

PROFESSOR BRIAN KIRKPATRICK
(USA)

Brian Kirkpatrick, M.D., M.S.P.H., is Professor and Chair in the Department of Psychiatry at Texas A&M University and Scott & White Healthcare. He graduated from the University of Texas Medical School at Houston, then completed psychiatry residency, research fellowships, and a master's in epidemiology at the University of North Carolina Chapel Hill. He served on the faculty of the Maryland Psychiatric Research Center at the University of Maryland before moving to the Medical College of Georgia as Vice Chair of the Department of Psychiatry and Health Behavior. He became the Chair of the Department of Psychiatry at Texas A&M College of Medicine and Scott & White Healthcare in 2010. Throughout his career, Dr. Kirkpatrick has focused on schizophrenia. He is Associate Editor of Clinical Schizophrenia & Related Psychoses, and is on the Editorial Board of Schizophrenia Bulletin. Dr. Kirkpatrick has conducted epidemiological, clinical, post-mortem, and animal studies related to schizophrenia and the neurobiology of social behavior. His research focuses on negative symptoms, and on schizophrenia as a systemic disease.

O10 PROFESSOR BRIAN KIRKPATRICK. A CONCEPTUAL MODEL OF SCHIZOPHRENIA

Schizophrenia is seen primarily as a psychotic disorder in which dysregulation of dopamine signaling is the central feature of pathophysiology. However, people with schizophrenia have several neuropsychiatric problems other than psychosis, and for many patients, psychosis is not the best predictor of their level of impairment. Newly diagnosed, antipsychotic-naive patients with schizophrenia also have abnormal glucose tolerance and other metabolic problems compared to well matched controls. Many of these neuropsychiatric and metabolic problems have an increased prevalence in the first degree relatives of people with schizophrenia. The dopamine theory also has serious deficiencies: many patients' psychotic symptoms respond poorly or not at all to dopaminergic agents, and the same is true of their other neuropsychiatric problems. There is also good evidence that other neurotransmitters are involved in the pathophysiology of psychosis.

A more appropriate conceptual model of schizophrenia is that: 1) schizophrenia is not a psychotic disorder, but a disorder of essentially every brain function in which psychosis is present; 2) it is not a brain disease, but a disorder with impairments throughout the body, including the brain; and 3) some conditions that are considered to be comorbid to schizophrenia are integral parts of the illness.

REWARD PREDICTION ERROR LEARNING DYSFUNCTION IN PSYCHOSIS: LINKING DOPAMINE, LEARNING AND DELUSIONS

DOCTOR GRAHAM MURRAY
(UK)

Graham Murray is a Medical Research Council Clinician Scientist at the University of Cambridge, UK. He studied Physics and Philosophy at Oxford University, and Medicine at King's College, London, where he graduated with distinction. He worked as a junior doctor in London and Oxford before moving to Cambridge for postgraduate training in psychiatry. He gained a PhD with distinction from University of Oulu in cognitive developmental epidemiology and a research MD from University of London in cognitive neuroscience. He has been awarded prizes from the Medical Research Society, the Royal College of Psychiatrists and the European Psychiatric Association. He has two main lines of research: one takes a cognitive neuroscience approach to understanding the role of reward processing in the generation and treatment of psychiatric symptoms in a variety of psychiatric disorders, and the other involves taking a longitudinal approach to study the course of psychotic illness.

O11 Dr Graham Murray. Reward prediction error learning dysfunction in psychosis: linking dopamine, learning and delusions

There is a close link between striatal dopaminergic abnormalities and psychotic experience but the mechanisms that underpin this link are unknown. A candidate psychological process that is mediated by dopamine and that could cause psychotic experience is (dysregulated) reward prediction error learning. Yet some scholars have argued that abnormalities in reward processing could cause negative symptoms, not positive symptoms, in schizophrenia. I will present results of experiments of reward processing in psychosis and in dopaminergic drug studies in healthy volunteers and discuss how learning processes may relate to the symptoms of schizophrenia and other psychiatric disorders.

NEUROIMAGING MARKERS OF ILLNESS ONSET IN PSYCHOSIS: THE SEARCH FOR A MOVING TARGET

PROFESSOR CHRISTOS PANTELIS
(AUSTRALIA)

Professor Christos Pantelis is an NHMRC Senior Principal Research Fellow, Foundation Professor of Neuropsychiatry and Scientific Director of the Melbourne Neuropsychiatry Centre at The University of Melbourne and Melbourne Health. He also heads the Adult Mental Health Rehabilitation Unit at Sunshine Hospital. He leads a team of researchers that have been undertaking neuroimaging and neuropsychological work in schizophrenia and psychosis, and other psychiatric and neurodegenerative disorders since 1993 in Australia. His work has focused on brain structural and functional changes during the transition to psychosis. His group was the first to describe progressive brain structural changes at psychosis onset, with a seminal paper published in The Lancet in 2003. He has published over 350 papers and chapters, including papers in high-profile international psychiatry, neurology, radiology and medical journals. He published one of the first books on the neuropsychology of schizophrenia, a recently published book on “Olfaction and the Brain” and a book on “The Neuropsychology of Mental Illness”. He has been co-Chief Investigator on 2 NHMRC Program Grants (2005-2009: $7.4 million; 2009-2013: >$10 million). In 2003 he won the Selwyn-Smith Medical Research Prize of The University of Melbourne for his work on progressive brain changes in early psychosis and, most recently, he was highly commended in the 2009 Victorian Minister of Health Award for Outstanding Individual Achievement in Mental Health. He was awarded an NHMRC Senior Principal Research Fellowship, which commenced in 2010. He was awarded a 2011 NARSAD Distinguished Investigator Grant from the Brain & Behavior Research Foundation (US). He is on the editorial board of a number of journals.

O12 Professor Christos Pantelis. Neuroimaging markers of illness onset in psychosis: the search for a moving target

I will describe neuropsychological and brain imaging findings in the early stages of psychosis and schizophrenia. My talk will focus on recent clinical high-risk studies and consider whether the evidence supports these as markers of illness onset and transition. The findings suggest that there are a number of processes at psychosis onset that may represent markers of incipient illness. These neurobiological indices particularly implicate the integrity of frontal and temporal cortices. However, these brain regions are dynamically changing during normal maturation, meaning that any putative neurobiological markers identified at the earliest stages of illness may be relatively unstable. I will suggest that, while such measures may be readily identified as potential neurobiological markers of established illness, they are inconsistent at (or around) the time of illness onset when assessed cross-sectionally. Instead, identification of more valid risk markers may require longitudinal assessment to ascertain normal or abnormal trajectories of neurodevelopment. Accordingly, I assert that the current conceptualisations of potential biomarkers or 'endophenotypes' for schizophrenia may need to be reconsidered in the context of normal and abnormal brain maturational processes at the time of onset of psychotic disorders.

Selected relevant references

Gogtay, N., Vyas, N. S., Testa, R., Wood, S. J., & Pantelis, C. (2011). Age of onset of schizophrenia: perspectives from structural neuroimagingstudies. *Schizophr Bull*, 37(3), 504-513.

Pantelis, C., Wood, S. J., Velakoulis, D., Testa, R., Fontenelle, L. F., & Yucel, M. (2010). Should we redefine the concept of endophenotype in schizophrenia? *Rev Bras Psiquiatr*, 32(2), 106-107.

Pantelis, C., Yücel, M., Bora, E., Fornito, A., Testa, R., Brewer, W. J., Velakoulis, D., & Wood, S. J. (2009). Neurobiological Markers of Illness Onset in Psychosis and Schizophrenia: The Search for a Moving Target. *Neuropsychol Rev*, 19, 385-398.

Pantelis, C., Yücel, M., Wood, S. J., Velakoulis, D., Sun, D., Berger, G., Stuart, G. W., Yung, A., Phillips, L., & McGorry, P. D. (2005). Structural brain imaging evidence for multiple pathological processes at different stages of brain development in schizophrenia. *Schizophr Bull, 31*(3), 672-696.

MOST ADULT PSYCHIATRIC DISORDERS BEGIN IN CHILDHOOD, BUT WHEN SHOULD WE TREAT THEM?

PROFESSOR PETER JONES
(UK)

Peter Jones is Professor of Psychiatry & Head of the Department of Psychiatry at the University of Cambridge. He read for his first degree in anatomy and neurobiology at King's College, London, before qualifying in medicine from Westminster Medical School. Following general medical posts he began psychiatry training at the Bethlem & Maudsley Hospitals in London. After a MSc in clinical epidemiology at the London School of Hygiene & Tropical Medicine and a PhD in psychiatric epidemiology, he was appointed as Senior Lecturer at the Institute of Psychiatry and Hon. Consultant Psychiatrist in 1993. In 1997 he took-up the Chair of Psychiatry & Community Mental Health in Nottingham, moving to his present post in Cambridge in 2000. Peter's research concerns the epidemiology of mental illness, particularly the psychoses, early life course influences on adult mental health and illness, and the interface between population-based and biological investigations. He also works in treatment research with randomised trials of drug and psychological treatments. The clinical team he co-directs, www.cameo.nhs.uk, provides care for young people with first episode psychosis and won the UK Hospital Doctor Team of the Year Award in 2007.

O13 Professor Peter Jones. Most adult psychiatric disorders begin in childhood, but when should we treat them?

The study of age at onset (AAO) of mental health disorders is technically and conceptually difficult. It is important to understand their AAO distributions in order to understand causes and mechanisms of illness, and so that interventions are made at an appropriate juncture to be maximally effective and to achieve primary and secondary prevention.

This presentation reviews some of the approaches to studying AAO, sets out the evidence to support the assertion that adult mental disorders begin in adolescence and to demonstrate that perhaps half of all adult mental health disorders have begun by the teenage years. The paper then discusses whether this fits what is known about the developmental neurobiology of the brain and introduces the implications for mental health services. The fact that parts of psychiatric syndromes, including psychotic illnesses, may be common in the general population is an added complication. Findings from trials, including the EDIE-2 trial of CBT for ultra-high risk mental states will be reviewed and directions for further research and practice explored.

The conclusion is that we cannot, as yet, treat risk either safely or with conviction. We should treat the individual before us and the problems they bring, regardless of age.

ABSTRACTS

Parallel oral sessions

O14 MacCabe J.H. Decline in verbal IQ between age 13 and 18 and risk for schizophrenia in adulthood: a Swedish longitudinal cohort study

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Background: There is now clear evidence that patients with schizophrenia suffer from a variety of cognitive deficits during childhood and adolescence. However, very little is known about the course of premorbid cognition over the premorbid period.
Aims: To assess the impact of cognitive developmental trajectory in adolescence on risk for schizophrenia in adulthood.
Methods: Longitudinal cohort study using four population-based cohorts of males born in Sweden in 1953, 1967, 1972 and 1977, totaling 10,717 individuals, and followed to 31 December 2006. Scores in tests of verbal, spatial and inductive ability at age 13 and in equivalent tests at army conscription (age 18) were the exposures. Hospital admission for schizophrenia in adulthood was the outcome.
Results: Relative decline in verbal ability between age 13 and 18 was associated with increased risk of schizophrenia (adjusted hazard ratio for an increase of one standard deviation in verbal ability = 0.59 (95% confidence interval = 0.40, 0.88; p=0.009)). Decline between age 13 and 18 was a much stronger predictor of schizophrenia than absolute score at age 18. The association was not confounded by parental educational level, family history of psychosis or urbanicity, and was present in late-onset cases, indicating that this was not a prodromal effect.
Conclusions: Decline in verbal ability during adolescence, is associated with increased risk of schizophrenia in adulthood, and decline between age 13 and 18 is a stronger predictor of schizophrenia than ability at age 18 alone. This suggests an impairment of late neurodevelopment affecting the acquisition of verbal skills.

O15 MORGAN V.A. CLUSTERING OF NEUROPSYCHIATRIC OUTCOMES IN CHILDREN OF WOMEN WITH PSYCHOSIS: A WESTERN AUSTRALIAN RETROSPECTIVE E-COHORT STUDY USING RECORD-LINKED DATA

Vera A. Morgan[1,2], Maxine Croft[1,3], Giulietta Valuri[1], Stephen R. Zubrick[3], Carol Bower[3,4], Thomas McNeil[1,5], Sonal Shah[1], Patsy Di Prinzio[1], Jenny Griffith[1], John Dean[1], Assen Jablensky[1,2]
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Background: Since 1996, the Neuropsychiatric Epidemiology Research Unit has been building research capacity to investigate genetic and environmental risk factors for neuropsychiatric outcomes in the children of mothers with psychosis using record-linked data.
Aims: We will illustrate our program of research with an investigation of the risk of intellectual disability and other neuropsychiatric outcomes in case children of mothers with psychosis compared to children of unaffected mothers.
Methods: Linked Statewide birth and psychiatric case registers were used to identify an "e-cohort" of high risk children of mothers with schizophrenia, bipolar disorder and unipolar depression, and comparison children of unaffected mothers. Psychiatric status was determined for mothers, fathers and children. Other linked registers provided data on risk factors (e.g. obstetric complications) and outcomes (e.g. birth defects, intellectual disability). We will describe: (i) the building of the relational data model; (ii) the development of constructs (e.g. neonatal encephalopathy; adversity; and longitudinal measures of maternal morbidity); (iii) our adaptation of existing resources for use with electronic data (e.g. McNeil-Sjöström Obstetric Complications Scale); and (iv) the integration of material from clinical casenotes.
Results: Case children were at significantly increased risk of intellectual disability with odds ratios of 3.2 (CI 1.8-5.7), 3.1 (CI 1.9-4.9) and 2.9 (CI 1.8-4.7) in the maternal schizophrenia, bipolar and unipolar depression groups respectively. Multivariate analysis suggested familial and obstetric factors contribute independently to the risk. Although summated labour/delivery complications (odds ratio 1.4, CI 1.0-2.0) failed to reach significance, neonatal encephalopathy (odds ratio 7.7, CI 3.0-20.2) and foetal distress (odds ratio 1.8, CI 1.1-2.7) were independent significant predictors. Rates of rare syndromes in case children were well above population rates. Risk of pervasive developmental disorders was significantly elevated for children of mothers with bipolar disorder. Risk of epilepsy was doubled for children of mothers with unipolar depression.
Conclusions: Our data support growing evidence that phenotypically different neuropsychiatric disorders cluster within pedigrees and that, in part, this is likely to result from some genetic overlap between disorders and, in part, from exposure to certain types of obstetric trauma and other environmental insults. This example illustrates the capacity of our longitudinal, multigenerational, high risk e-cohort to answer questions on the relative contribution of familial liability and environmental exposures at different developmental stages in the aetiology of schizophrenia and other neuropsychiatric outcomes.

O16 MÄKI P. CHILDHOOD AND ADOLESCENCE SYMPTOMS PREDICTING PSYCHOSIS IN THE GENERAL POPULATION BASED NORTHERN FINLAND BIRTH COHORT 1986

Pirjo Mäki[1,2], Jouko Miettunen[1], Irma Moilanen[2,3], Marika Kaakinen[4,5], Anja Taanila[4,5], Tuula Hurtig[3,4], Graham Murray[6], Matti Joukamaa[7], Markus Heinimaa[8], Sebastian Therman[9], Peter B Jones[6], Juha Veijola[1,2]

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Background: The onset for psychotic disorders is often in adolescence. At least some of them are neurodevelopmental disorders. Prospective general population based reports are lacking on specific symptoms in childhood and adolescence predicting clinically treated psychosis in youth.
Aims: We studied which kind of symptoms precedes psychosis when taking account specificity.
Methods: Members (N= 6,676) of the Northern Finland Birth Cohort 1986 were examined in childhood and adolescence. The 8 –year field study included Rutter B2 questionnaire for teachers and subscales from Rutter A questionnaire for parents screening antisocial and neurotic symptoms. The 16 –year field study included a 21-item PROD-screen questionnaire screening prodromal symptoms for last six months. The Finnish Hospital Discharge Register was used to find out new cases of psychosis and non-psychotic disorders till the age of 23 years.
Results: High scores of antisocial and neurotic symptoms in Rutter B2 and in subscales of Rutter A did not associate with later psychosis. The highest prevalence of positive symptoms in the PROD-screen was in the adolescents who developed psychotic disorder (65%) compared to the subjects who developed non-psychotic disorder (36%, $p<0.001$), and to the subjects without any disorder (27%, $p<0.001$). Respective figures for negative symptoms were 55% in the psychotic adolescents, 30% in the subjects with non-psychotic disorder ($p=0.01$) and 24% in the 'healthy' ($p<0.001$).
Conclusions: Antisocial and neurotic symptoms reported by teachers and parents at age 8 did not predict psychosis. Both positive and negative features were common in adolescents especially in those who later developed psychosis.

O17 GAGE S.H. CANNABIS USE AND PSYCHOTIC EXPERIENCES IN ALSPAC TEENAGERS – A LONGITUDINAL STUDY

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Background: A consistent association between cannabis use and psychotic experiences (PEs) has been described, but confounding by childhood characteristics has been only partially adjusted for in most studies.
Aims: To investigate the association between cannabis use and incidence of PEs, with more extensive consideration of potential confounders.
Methods: We used data from the ALSPAC birth cohort (N=3303). Cumulative use of cannabis at 16 was assessed via self-report questionnaire. PEs at 18 were assessed via semi-structured interviews. Confounders (family history, IQ, depression, borderline personality traits, SDQ, and other drug use) were measured variously by questionnaire and interview.
Results: We observed a strong association between cannabis and PEs (OR: 1.48, 95%CI: 1.29, 1.71) that was relatively unchanged when adjusting for maternal and childhood confounders (OR: 1.52, 95%CI 1.24, 1.85). Associations were greatly attenuated by adjustment for other illicit drug use (OR 1.22, 95%CI 0.93, 1.58), though independent effects of cannabis and other drugs was difficult to determine due to their collinearity. This was especially true for tobacco use where collinearity meant it was not possible to examine cannabis and tobacco in the same model. There was much weaker evidence that cannabis was associated with PEs when excluding individuals who described their experiences as only ever occurring within 2 hours of using the drug (adjusted OR: 1.14, 95%CI 0.89, 1.47).
Conclusions: Associations between cannabis and PEs are robust to confounding by childhood characteristics, but further study is required to examine potential confounding by other substances, including tobacco.

O18 NIARCHOU M. SPEED OF PROCESSING DEFICITS PREDICT NON-CLINICAL PSYCHOTIC EXPERIENCES IN CHILDREN AND ADOLESCENTS; LONGITUDINAL ANALYSES IN A LARGE BIRTH COHORT

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Children reporting psychotic experiences (PEs) are at high risk of developing psychosis in adulthood. Cognitive deficits often occur in psychotic disorders particularly schizophrenia, where they tend to predate the first episode of psychosis. There is also evidence that preexisting cognitive impairment, as evidenced by low IQ, is a risk factor for PEs in children. We set out to test in which neurocognitive domains impairments are precursors of PEs, and also to determine whether, when taking IQ and other neurocognitive function into account, particular measure(s) better predict PEs than others. 6,784 individuals from the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort completed a set of comprehensive neurocognitive assessments at ages 8, 10 and 11, and a semi-structured interview for psychotic experiences at age 12. Lower performance in the domains of speed of processing (age 8) (OR: 1.24; 95% CI: 1.1-1.41), attention (age 8) (OR:1.21(1.03-1.41)) and working memory (age 10) (OR:1.15(1.02-1.3)) was associated with higher risk of developing PEs at age 12. When adjusting for IQ score at age 8 the associations persisted, although the strength was somewhat reduced. When adjusting for other cognitive domains assessed at the same age, speed of processing at age 8 (OR: 1.16(1.02-1.3)) and 11 (OR: 1.16 (1.04-1.32)) were more strongly associated with PEs. These findings suggest that defective speed of processing is a particularly strong predictor of PEs in children. Further work is required to determine whether this has implications for the higher risk of subsequent psychotic disorder associated with PEs.

O19 SULLIVAN S. PSYCHOTIC SYMPTOMS AND SOCIAL FUNCTIONING: A LONGITUDINAL STUDY

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Background: There is limited evidence regarding the longitudinal association between poor social functioning and psychotic symptoms in community samples.
Aims: To investigate whether antecedent poor social functioning and deteriorating social functioning are antecedent to psychotic symptoms at 12 years in a community sample.
Methods: Measures of social functioning (peer problems and prosocial behaviour) were collected in the ALSPAC birth cohort at ages 7 and 11 and data on psychotic symptoms at age 12. The association between psychotic symptoms and social functioning was examined using logistic regression models for each age (7 and 11) and any impact of change in social functioning between 7 and 11 years. Multiple imputation methods were used to examine the impact of missing data.
Results: Peer problems were associated with psychotic symptoms at 12 years (7 years OR 1.11 95% CI 1.04,1.19; 11 years OR 1.12 95% CI 1.05,1.19) after adjustment for confounders. Enduring peer problems between 7 and 11 years were associated with psychotic symptoms at age 12 (OR 2.40 95% CI 1.58,3.66) after adjustment for confounders. There was no evidence of an association with prosocial behaviour at either age or that a deterioration in social functioning influenced the association with psychotic symptoms. Imputing missing data did not materially affect the findings.
Conclusions: Non clinical psychotic symptoms are associated with peer problems in childhood and may represent early stage psychosis or vulnerability to future clinical psychosis. Persistently high but not deteriorating levels of peer problems were associated with later risk of psychotic symptoms.

O20 JUKURI T. DEFAULT MODE NETWORK IN YOUNG PEOPLE WITH FAMILIAL RISK FOR PSYCHOSIS – THE OULU BRAIN AND MIND STUDY

Tuomas Jukuri[1,2], Vesa Kiviniemi[3], Juha Nikkinen[3], Jouko Miettunen[1], Pirjo Mäki[1,2], Erika Jääskeläinen[1,2], Sari Mukkala[1,2], Jenni Koivukangas[1], Anja Taanila[4,5], Irma Moilanen[6], Markus Heinimaa[7], Jenny Barnett[8], Peter B Jones[8], Graham K Murray[8], Juha Veijola[1,2]
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Background: The default mode network (DMN) is active in the brain at rest and de-activated during cognitive tasks. Abnormal function in the DMN has been reported in people with schizophrenia but it´s not known whether this reflects familial risk for psychosis (FR).
Aims: Our aim was to study the activation of the DMN between FR participants and controls.
Methods: We conducted a resting state functional MRI in 72 young adults with a history of psychosis in one or both parents (Familial Risk; FR) and 72 age matched controls with no such history; both groups were drawn from the Northern Finland 1986 Birth Cohort (Oulu Brain and Mind study). Parental psychosis was established using the Finnish hospital discharge register. We pre-processed R-fMRI data using the FSL (Functional MRI of the Brain- Software Library) pipeline. We then used MELODIC (Multivariate Exploratory Linear Optimized Decomposition into Independent Components) and then probabilistic independent component analyses with model order 30, followed by a dual regression approach to assess differences between the groups. We focused only the DMN and compared group differences using non-parametric permutation tests, threshold-free cluster enhancement and correcting for multiple comparisons ($p<0.05$).
Results: FR participants demonstrated significantly lower activation compared with controls in the posterior cingulate cortex (PCC), the central node of the DMN. The size of the region was 41 mm3.
Conclusions: The activation of the DMN differs between FR and control groups. This suggests that familial risk for psychotic disorders may be mediated through genetic effects on connectivity in the PCC.

O21 RAIJ T.T. AUDITORY VERBAL HALLUCINATION AND IMAGERY OF THE HALLUCINATION DIFFER BY STRONGER ACTIVATION OF THE SUPPLEMENTARY MOTOR AREA DURING IMAGERY

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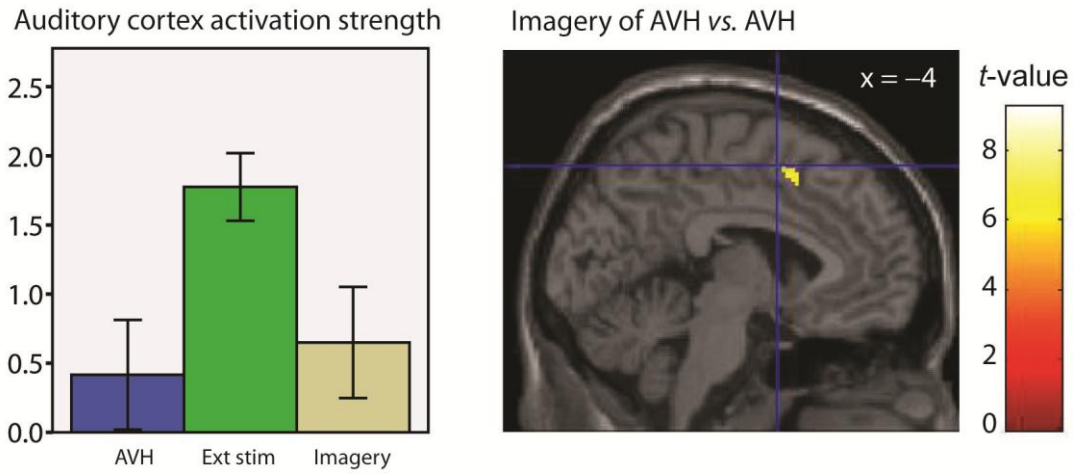
Background: Auditory verbal hallucination is one of the commonest symptoms of schizophrenia. Its neuronal underpinnings remain poorly understood. One suggested, yet unproven, mechanism is brain activation, which is similar to verbal imagery but occurs without the proper activation of the neuronal systems that are required to tag the origins of imagery in one's mind.
Aims: To test this prominent hypothesis about mechanisms of auditory verbal hallucination.
Methods: Patients with schizophrenia received external speech stimulation in 30 s blocks and signaled the onsets and offsets of their auditory verbal hallucinations during magnetic resonance imaging. During non-hallucination periods without external stimulation, patients imagined the hallucination they had previously experienced. Fifteen healthy control subjects signaled the onsets and offsets of self-paced imagery of similar voices.
Results: Both hallucination and the imagery of the hallucination were associated with similar weak activation of the fronto-temporal language-related circuitries. During both of these conditions, the auditory cortex activation was clearly weaker than during external speech stimulation ($P < 0.05$, corrected for multiple comparisons; Figure, left). In contrast, the supplementary motor area was more strongly activated during imagery than during the hallucination ($p < 0.05$, corrected for multiple comparisons; Figure, right).
Conclusions: These findings support the view that auditory verbal hallucination resembles verbal imagery rather than external stimulation in language processing. The supplementary motor area is related to the initiation of action and to the experience of intentionality. Thus decoupling of this region could contribute to the experience of non-self source of the verbal material during hallucination.



O22 TOULOPOULOU T. PREFRONTAL DEVIATIONS IN FUNCTION BUT NOT VOLUME ARE PUTATIVE ENDOPHENOTYPES FOR SCHIZOPHRENIA

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Background: Endophenotypes are biological traits, intermediate between the genes and the clinical phenotype, that increase disease susceptibility.
Aims: This study sought to systematically investigate whether prefrontal cortex grey matter volume reductions are valid endophenotypes for schizophrenia, specifically investigating a) their presence in unaffected relatives, b) their heritability c) their genetic overlap with the disorder itself, and finally d) their performance on these criteria with neuropsychological indices of prefrontal functioning.
Methods: We used a combined twin and family design and examined four prefrontal cortical regions of interest (ROIs).
Results: Not unexpectedly the superior and inferior regions were significantly smaller in patients. However this was not the case in the unaffected relatives so we could confirm that these deficits were not due to familial effects. Volume of the prefrontal and orbital cortices were moderately heritable, but neither shared a genetic overlap with schizophrenia. Total prefrontal cortical volume reductions shared a significant unique environmental overlap with the disorder, suggesting again that the reductions were not familial. By way of contrast, prefrontal (executive) functioning deficits were present in the unaffected relatives, were moderately heritable and shared a substantial genetic overlap with the disorder.
Conclusions: These results suggest that the well-recognized prefrontal volume reductions commonly found in schizophrenia could be really epiphenomena and may be attributable to or confounded by illness trajectory or duration, chronicity, medication, or substance abuse, or in fact a summation of some or all of them.

O23 ISOHANNI M. LIFESPAN DEVELOPMENT IN SCHIZOPHRENIA FROM WOMB TO GRAVE - RESULTS FROM THE NORTHERN FINLAND 1966 BIRTH COHORT

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Background: Subtle developmental (motor, emotional, structural, cognitive and behavioural) abnormalities often precede schizophrenia suggesting that some aspects of causation are established before overt psychosis.
Aim: Within NFBC 1966 to study the lifespan development for schizophrenia in a population-based cohort using developmental markers at birth and at ages 1, 16, 31, 34 and 43.
Methods: We studied developmental pathways using developmental markers in genetics, cognitive capacity, outcomes, somatic comorbidity, mortality and brain morphology. Psychiatric outcomes have been ascertained through data linkage to a national case registers, hospital charts and clinical evaluations.
Results: The schizophrenia group showed altered patterns of development over time when compared with non-psychotic subjects. There was excess mortality and metabolic syndrome in a relatively early age and phase of illness. Schizophrenia was associated with relatively poor prognosis, limited occupational capacity and many hospital readmissions. The associations between early development and post-onset cognition/brain morphology differed in various diagnostic groups supporting progressive dysfunction.
Conclusions: Our study combines the unique advantages of a large population-based birth cohort, detailed longitudinal phenotyping and DNA availability, allowing study of both genetic and environmental components in the evolution of disorder. The lifespan developmental trajectories in schizophrenia were different compared to controls. These findings emphasize both neurodevelopmental and neurodegenerative aspects of schizophrenia and the scientific value of pathway variables collected in longitudinal birth cohort studies.

O24 NÄÄTÄNEN R. THE MISMATCH NEGATIVITY (MMN) - AN INDEX OF COGNITIVE DETERIORATION, THE COMMON CORE OF ALL MAJOR NEUROPSYCHIATRIC DISEASES – A REVIEW

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Cognition is usually affected at least in the later stages of major neuropsychiatric diseases such as schizophrenia, bipolar disease, major depression, autism, dysphasia, epilepsy, multiple schlerosis, Alzheimer´s disease (and related neurodegenerative diseases), and Parkinson´s disease. Very importantly, the mismatch negativity (MMN), an automatic brain response to auditory change or, more generally, regularity violation, and/or its magnetoencephalographic (MEG) equivalent MMNm are affected in most of these cases. Furthermore, the MMN attenuation often correlates with the magnitude of cognitive decline. This suggests that the MMN has opened a unique window to the core element of the neurocognitive diseases, the cognitive impairment. In this talk, I will review MMN (MMNm) studies in these neuropsychiatric diseases and show that the abnormalities of the MMN/MMNm response are tied with the concurrent impairment of cognitive function.

O25 VEIJOLA J. PROGRESSION IN BRAIN TISSUE LOSS IN SUBJECTS WITH SCHIZOPHRENIA. THE NORTHERN FINLAND 1966 BIRTH COHORT STUDY

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Background: Growing evidence suggests that there is progressive brain volume reduction in schizophrenia. But there still remain some doubts if the results supporting progressive brain volume reduction addition.
Aim: We had an opportunity to study in a relatively long follow-up period brain changes in schizophrenia patients and control subjects in a sample comparatively robust to selection bias.
Methods: All members of the Northern Finland 1966 Birth Cohort (NFBC1966) known to have had psychotic illness and a random sample of other members of NFBC1966 were invited for a field study. The baseline study was conducted during 1999-2001 and the follow-up 9 years later, during 2008-2010. Written informed consent and adequate brain scan was obtained from 33 subjects with schizophrenia patients 33 and from 71 control subjects.
Results: The mean annual whole brain volume reduction was 0.66% in schizophrenia patients. The corresponding percentage for control subjects was 0.48 % (adjusted for sex, educational level, alcohol use, body weight change and functioning, significant level p=006). In seven schizophrenia patients without or low dose antipsychotic medication the annual brain volume loss was 0.47 % as compared to subjects using intermediate dose of antipsychotics (annual brain volume loss of 0.59 %) and to subjects using high dose of antipsychotics (annual brain volume loss of 0.79 %).
Conclusions: In this birth cohort based study on brain volumes in schizophrenia, we found continuing brain losses in a relatively late phase of the illness. Antipsychotic medication did contribute to the excessive loss in brain volume.

O26 MACKAY-SIM A. PATIENT-DERIVED STEM CELLS: ACCESS TO THE CELL BIOLOGY OF SCHIZOPHRENIA

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Background: There is a pressing need for new tools to identify the biological substrates of schizophrenia. Patient-derived neural stem cells from the organ of smell provide a means to investigate the cell biological bases of the neurodevelopmental hypothesis of schizophrenia.
The **Aim** is to identify disease-associated differences in cell biology. Our hypothesis is that patients share dysregulated cell functions that make them susceptible to altered brain development.
Methods: Olfactory stem/progenitor cells are grown from patients and controls and subjected to gene expression profiling to identify cell signalling pathways that are dysregulated in schizophrenia. Identified pathways are then investigated through functional and molecular analyses.
Results: Two of most significantly dysregulated pathways in patient cells, cell cycle regulation and cell adhesion, are concerned with cellular aspects of neurodevelopment. Detailed cell cycle analysis and protein expression studies demonstrated that patient cells have a faster proliferation rate than control cells resulting from a shorter cell cycle period brought about by a very large difference in cyclin D1 levels, a protein that regulates the timing of the start of DNA synthesis during the cell cycle. Additionally, patient cells are more motile than control cells due to dysregulated signalling through the focal adhesion kinase pathway, leading to faster dynamics of the focal adhesion complexes via which cells adhere to the extracellular substrate.
Conclusions: If the differences in patient cells operate during brain development, they could make it more susceptible to environmental stressors that, when combined, could push homeostatic regulation past the threshold of normal development.

O27 AJDACIC-GROSS V. DISENTANGLING THE HETEROGENEITY AND COMPLEXITY OF PSYCHOSIS SYNDROMES: METHODOLOGICAL PROMISES

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Background: Heterogeneity and complexity are major obstacles in research on brain systems and psychiatric diseases. In psychosis research, such as in quite a few other domains and disciplines, only unsatisfactory efforts have been made to bring study designs and methods in line with these challenges. The notion of developing simple models or elegant theories is still predominating. Epidemiological surveys and advanced statistical models offer opportunities to leave this blind alley.

Aims:

- To emphasize the advantages of epidemiological surveys vs. clinical research.
- To delineate the distinction between complexity reduction and complexity representation.
- To introduce a typology of analysis aims and related statistical models.
- To delineate different frameworks of analysis (multilevel, longitudinal).

Methods: The typology of statistical models includes causal models (e.g. regression or path analysis, SEM), classifications of variables (e.g. factor analysis), typologies / grouping of subjects (e.g. CA, cluster analysis, LCA) and network analysis tools. Their potential grows when they are used in combined models (e.g. mixture models) and within different analysis frameworks.

Results: The typology is illustrated by analyses with Zurich Study data and other databases.

Conclusions: Research on heteregeneous and complex issues such as psychosis syndromes should aim at representing complexity instead of merely reducing it. Adequate study designs and statistical models are available by nowadays. Network analysis tools promise new analysis (and theoretical) aims within a multilevel framework.

O28 AHMED A.O. PSYCHOSIS PHENOTYPES AND THE STRUCTURE OF PERSONALITY: EVIDENCE OF A DIMENSIONAL MODEL OF PSYCHOTIC EXPERIENCES

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Background: There is growing support for dimensional models of psychosis that view psychotic experiences as existing on a severity continuum ranging from normative perceptual aberrations and subclinical experiences to frank psychosis observable in psychotic disorders. The evidentiary support for a dimensional model is limited to population surveys that suggest that psychotic experiences are prevalent although asymmetrically distributed in the population. Definitive evidence of a dimensional structure requires an analysis of latent rather than manifest structure. Moreover, evidence of a dimensional structure should demonstrate that psychotic experiences represent extremes of normal personality and behavioral organization.
Aims: 1.) Investigate the latent structure of psychotic experiences by comparing the relative viability of categorical and dimensional models of psychosis; 2.) Examine the overlap of personality dimensions and psychosis using canonical correlational analysis; and 3.) Test a causal structural equation model of personality structure and psychotic experiences.
Methods: Participants were respondents to the 1992 National Comorbidity Survey (NCS) and the 2001/2002 Collaborative Psychiatric Epidemiological Surveys (CPES). We analyzed their responses to psychosis items using taxometric methods (MAMBAC, MAXEIG, and L-Mode). We submitted responses on the psychosis and personality and self-descriptors section of the NCS to structural equation modeling.
Results: Taxometric analyses produced greater support for a dimensional rather than taxonic model in the epidemiological surveys. In the NCS, psychosis subscales demonstrated significant overlap with personality dimensions-- Neuroticism and Openness.
Conclusions: Psychotic experiences are not only dimensionally distributed in the population, but can be adequately incorporated into the five-factor model of normal personality and behavioral organization.

O29 SIIRA V. THE ROLE OF LONG-TERM MANIFESTATION OF PERSONALITY TRAITS AND HERITABILITY AS VULNERABILITY INDICATORS FOR PSYCHOPATHOLOGY

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Background: Studies have shown that psychometric deviance, identified using the Minnesota Multiphasic Personality Inventory (MMPI), is associated with an underlying vulnerability to schizophrenia and the symptoms of schizophrenia.
Aims: To examine whether MMPI measured personality traits can be used as vulnerability indicators to identify risk of developing psychiatric disorders among adoptees with or without genetic risk.
Methods: 14 MMPI scales were used to assess adoptees without psychiatric diagnosis in the initial phase of the study (mean age: 23 years), who were high-risk (HR) offspring of biological mothers with schizophrenia-spectrum disorder (n=28) as well as low-risk (LR) controls (n=46). Assessments were conducted twice after a mean interval of 11 years. A variance analysis of the data collected, with genetic risk and adoptees' age as independent variables, was performed to study the variation within- and between the groups of adoptees with (n=23) and without follow-up diagnosis (n=51).
Results: Differences between the groups of adoptees without and with follow-up diagnoses were found in L, F, K, HOS, HYP and PHO, independent of genetic risk. However these same variations, with the exception of PHO, were also found in LR adoptees. No differences between groups were found among HR adoptees. In SzP low scores were associated with mental health among LR adoptees at the follow-up. High PHO had an association with follow-up diagnosis independent of genetic risk.
Conclusions: Social anxiety and phobic behavior (PHO) may be vulnerability indicator for psychiatric disorders, including schizophrenia, among adoptees with and without genetic risk.

O30 FITZGERALD M. SCHIZOPHRENIA AND AUTISM. THE CASE FOR A CONNECTION

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Background: There is a long controversial history between schizophrenia and autism.
Aim: To detail the history of the relationship between autism and schizophrenia
Methods: Literature review
Results: The overlap phenomology genetics will be discussed.
Conclusions: Adult autism can easily be confused with schizophrenia. There are very significant overlaps and differences between autism and schizophrenia.

O31 GRANÖ N. JERI - EARLY DETECTION AND INTERVENTION MODEL FOR ADOLESCENTS AT RISK FOR PSYCHOSIS: CAN TRANSITION TO PSYCHOSIS BE PREVENTED?

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Background: Jorvi Early psychosis Recognition and Intervention (JERI) - team at Helsinki University Central Hospital (HUCH) has worked since 2006 as an early detection and intervention team for adolescents at risk for psychosis. The JERI team meets with adolescents at ages between 12-22 at school or at home together with their parents and with community co worker, for example a social worker, teacher, nurse or GP, who has contacted the team for reason of unclear or undiagnosed mental health problems.
Aims: The main purpose of JERI team is to identify the possible risk of psychosis by interview instruments and to meet the client and family together with community co worker(s) to find a way to reduce stress. The model is based on idea of community and family oriented care and stress-vulnerability model of psychosis. If needed, JERI team integrates other psychiatric care as a part of treatment.
Methods: 47 subjects from period 2006-2008 and 53 subjects from period 2009-2011 have been detected to be at risk for psychosis by PROD-screen or SIPS-interview.
Results: At baseline, of total 100 at risk subjects, 5 were evaluated to have additionally an untreated psychosis. Of those 55 subjects who were not in psychosis, who were eligible at follow up and were treated by JERI intervention, 3 subjects turned to psychotic during the intervention. Hence, transition rate is 5.5 %. However, dropout percent is 42%.
Conclusions: Subjects catched and treated with JERI- intervention seem to have a relatively low transition rate to psychosis.

O32 LAHTI M. CARDIOVASCULAR MORBIDITY, MORTALITY, AND PHARMACOTHERAPY IN PATIENTS WITH SCHIZOPHRENIA

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Background: Patients with schizophrenia have excess cardiovascular morbidity and mortality. Previous studies suggest that this may be partly due to inadequate somatic treatment and care, such as non-optimal use of cardiovascular pharmacotherapy, but longitudinal studies on such etiological pathways are scarce.
Aims: We investigated the use of lipid-lowering and antihypertensive pharmacotherapy, and the risk of hospitalization for and death from coronary heart disease and stroke among patients with schizophrenia and control subjects without psychotic disorder.
Methods: Our study sample comprised 12 939 Helsinki Birth Cohort Study 1934-44 participants. This cohort was followed for over 30 adult years by using national databases on cardio- and cerebrovascular hospitalizations and mortality and on reimbursement entitlements and use of drugs for treatment of hypertension, dyslipidaemia, coronary heart disease, and diabetes.
Results: Individuals with schizophrenia had a higher risk of hospitalization for coronary heart disease (Hazard Ratio (HR) = 1.65, 95 % Confidence Interval (CI) 1.03-2.57). Mortality from this disease was markedly higher (HR = 2.92, 95 % CI 1.70-5.00), particularly among women (p = .001 for women; p = .008 for men). Women with schizophrenia had also marginally increased stroke mortality (p = .06). However, patients with schizophrenia used less lipid-lowering (Odds Ratio = 0.47, 95 % CI 0.27- 0.80) and antihypertensive drugs (HR = 0.37, 95 % CI 0.22-0.61).
Conclusions: In this longitudinal study, coronary heart disease morbidity was increased and coronary heart disease mortality markedly increased in patients, especially in women, with schizophrenia. These patients nevertheless received less antihypertensive and lipid-lowering treatment.

O33 MYINT A.-M. IMMUNE ACTIVATION INDUCED KYNURENINES IMBALANCE IS ASSOCIATED WITH RESPONSE TO TREATMENT WITH ANTIPSYCHOTICS

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Background: Immune activation was reported to be involved in pathophysiology of schizophrenia. It is hypothesized that immune activation induced increase in tryptophan breakdown and imbalance in kynurenine downstream metabolites are involved in chronicity of the disorder.
Aim: To understand the role of immune activation and tryptophan metabolites changes, the plasma cytokines, plasma tryptophan metabolites were analyzed in medication naïve and medication free patients with schizophrenia, before and after treatment with antipsychotics.
Methods: The early morning fasting plasma samples from 35 medication naïve, 18 medication free patients and 48 age and gender matched healthy controls were analyzed on admission and upon discharge after 6 weeks treatment. Cytokines were analyzed using commercially available ELISAs and tryptophan metabolites were analyzed using high performance liquid chromatography. The clinical scores were recorded also on admission and at the time of discharge.
Results: Patients with schizophrenia showed increased pro-inflammatory cytokines, tryptophan breakdown ratio and plasma 3-hydroxy-kynurenine. Plasma kynurenic acid and 3-hydroxy-anthranillic acid were reduced in the patients. The ratios between kynurenic acid to kynurenine and kynurenic acid to 3-hydroxykynurenines were reduced. The quinolinic acid showed a trend of increase. Antipsychotics could reverse the cytokines changes and kynurenines imbalance. Plasma kynurenic acid levels on admission could predict the response of both positive symptoms and depressive symptoms scores to 6 weeks antipsychotic treatment.
Conclusions: Rebalancing kynurenines through rebalancing immune system might be one of the mechanisms of antipsychotics. Initial balance in kynurenines is associated with response to antipsychotic treatment.

O34 UZBAY T. POSSIBLE ROLE OF AGMATINE IN SCHIZOPHRENIA

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Background: Agmatine is a polyamine that is formed by decarboxylation of L-arginine and accepted as a novel neurotransmitter in brain. It has been suggested that some end products of the agmatine-like polyamines may responsible for the development of schizophrenia.
Aims: We aimed to evaluate a possible relationship between agmatine and schizophrenia.
Methods: Current experimental and clinical evidences indicating a relationship between polyamines and schizophrenia was examined and focused on agmatine which is a polyamine neurotranmitter. Results obtained from publications on agmatine involved in qualified animal models of schizophrenia such as prepulse inhibition was taken into consideration. All data was interpreted together with our laboratory findings.
Results: Hypofunctioning of NMDA receptors is responsible for some symptoms of schizophrenia and agmatine blocks glutamatergic NMDA receptors. Agmatine is metabolized to polyamines and increased polyamine levels is related to schizophrenia. The assessment of sensorimotor gating, as operationally measured by prepulse inhibition (PPI) has become an important tool by which to better understand information-processing impairments in schizophrenia spectrum disorders. It was demonstrated that agmatine disrupted the PPI of the acoustic startle reflex in rats. It was also hypothesize that unbalanced and/or excessive agmatine release may be related to schizophrenia.
Conclusions: The agmatine-polyamine system merits investigation as a potential target for developing new drugs for the treatment of psychoses, such as schizophrenia. Further studies will be helpful for clarifying this matter.

O35 SUVISAARI J. PROLINE AND SCHIZOPHRENIA

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Background: Recent research suggests that proline metabolism is activated as a response to inflammatory, genotoxic and metabolic stress. Several previous studies have linked schizophrenia with polymorphisms in the gene encoding proline oxidase (POX). POX catalyzes the degradation of proline to pyrroline-5-carboxylate, and deficient POX functioning leads to hyperprolinemia.
Aims: We have previously observed in a population-based sample that people with schizophrenia, but not people with other psychotic disorders, have elevated proline compared to matched population-based controls. In this study, we examined factors associated with serum proline levels further.
Methods: We analysed proline levels in serum samples from a general population-based study in Finland. The study included all persons with DSM-IV primary psychotic disorder (schizophrenia n = 45; other non-affective psychosis n = 57; affective psychosis n = 37) and controls matched by age, sex, region of residence, and time of the year when the samples were taken. In addition to diagnostic variables, we examined the effect of the following variables on proline levels: antipsychotic medication use, type 2 diabetes, metabolic syndrome, waist circumference, insulin and triglyceride levels, systolic blood pressure, handgrip strength as a measure of muscle strength, bone broadband ultrasound attenuation, vitamin D level, and inflammatory markers CRP, interleukin-1 receptor antagonist, and soluble interleukin-2 receptor (IL-2R). For continuous variables, we examined Spearman's rank correlation coefficients (ρ), and for dichotomic variables, we tested significant differences using the Mann-Whitney test. We examined which of the variables were independently associated with elevated proline levels using a linear mixed model that took the matching of case-control pairs into account.
Results: Proline was elevated in people with schizophrenia (P=0.0002), type 2 diabetes (P=0.030) and metabolic syndrome (P=0.034). The following variables were associated with increased proline: serum triglyceride (ρ 0.22, P=0.0003), serum insulin (ρ 0.20, P=0.0011), serum urate (ρ 0.27, p<0.0001), IL-2R (ρ 0.28, P<0.0001), waist circumference (ρ=0.25, P<0.0001), handgrip strength (ρ 0.16, p=0.008) and IL-1RA (ρ=0.12, P=0.048). Vitamin D level correlated negatively with proline level (ρ=-0.12, P=0.043).
In the regression analysis, schizophrenia (P=0.0020), triglyceride level (P=0.0087), and L-2R (P=0.0012) remained independently associated with elevated proline levels.
Discussion: Schizophrenia is associated with elevated proline levels compared to age- and sex-matched controls, and this is not explained by metabolic comorbidity, poor skeletal health or vitamin D deficiency. The finding could fit with deficient proline oxidase functioning. The association with serum triglycerides and IL-2R could be related to the fact that PPARγ, produced by adipocytes in response to inflammatory stress, upregulates proline metabolism.

O36 AGERBO E. MODELLING THE CONTRIBUTION OF FAMILY HISTORY AND VARIATION IN SINGLE NUCLEOTIDE POLYMORPHISMS TO RISK OF SCHIZOPHRENIA: A DANISH NATIONAL BIRTH COHORT-BASED STUDY

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Background: Epidemiological studies indicate that having any family member with schizophrenia increases the risk of schizophrenia in the probands. However, genome-wide association studies (GWAS) have accounted for little of this variation.
Aims: The aim of this study was to use a population-based sample to explore the influence of single-nucleotide polymorphisms (SNP) on the excess schizophrenia risk in offspring of parents with a psychotic, bipolar affective or other psychiatric disorder.
Methods: A nested case-control study with 739 cases with schizophrenia and 800 controls. Their parents and siblings. Information from national health registers and GWAS data from the national neonatal biobank.
Results: Offspring schizophrenia risk was elevated in those whose mother, father or siblings had been diagnosed with schizophrenia or related psychosis, bipolar affective disorder or any other psychiatric disorder. The rate ratio was 9.31(3.85;22.44) in offspring whose 1st degree relative was diagnosed with schizophrenia. This rate ranged between 8.31 and 11.34 when adjusted for each SNP individually and shrank to 8.23(3.13; 21.64) when adjusted for 25% of the SNP-variation in candidate genes. The percentage of the excess risk associated with a family history of schizophrenia mediated through genome-wide SNP-variation ranged between -6.1%(-17.0%;2.6%) and 4.1%(-3.9%;15.2%). Analogous results were seen for each parent and for histories of bipolar affective and other psychiatric diagnoses.
Conclusions: The excess risk of schizophrenia in offspring of parents who have a psychotic, bipolar affective or other psychiatric disorder is not currently explained by the SNP variation included in this study in accordance with findings from published genetic studies.

O37 CLARKE M.C. EVIDENCE FOR A SKEWED DEVELOPMENTAL TRAJECTORY AMONG FIRST-DEGREE RELATIVES OF SCHIZOPHRENIA PATIENTS

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Objective: Obstetric complications and developmental delay are well established risk factors for schizophrenia. We have previously shown that these risk fact interact in an additive manner to further increase risk for schizophrenia. Here we examine if this these risk factors can distinguish between first-degree relatives of patients and healthy controls.
Method: The study population comprised all those born in Helsinki between 1962 and 1969 who had developmental records archived in the Helsinki City Archives. Through linkage between the Finnish Population Register, the Finnish Hospital Discharge Register and the Child Health Archives, we traced Child Health cards on 115 siblings of individuals with a diagnosis of schizophrenia and on 115 controls, individually matched to the siblings on gender and year of birth. The Child Health cards contain detailed prospective developmental data from birth, as well as an indicator of fetal distress, as measured by Apgar score. We extracted detailed developmental data from the first year of life. Our previous work has shown that the age at which individuals sit is the most sensitive measure of developmental delay among individuals who later develop schizophrenia.
Results: Here we found that age of sitting significantly distinguished our sibling high-risk group from the comparison group. Exposure to obstetric complications also significantly distinguished between the groups. Obstetric complications did not increase risk of developmental delay indicating that they are independent risk factors.
Conclusions: Our data provide evidence of a similar developmental trajectory, albeit skewed to a lesser extent, among first degree relatives of schizophrenia patients.

References:

Clarke MC, Tanskanen A, Huttunen M, Leon DA, Murray RM, Jones PB, Cannon M. Increased risk of schizophrenia from additive interaction between infant motor developmental delay and obstetric complications: evidence from a population-based longitudinal study. Am J Psychiatry. 2011;168(12):1295-302.

Cannon M, Caspi A, Moffitt TE, Harrington H, Taylor A, Murray RM, Poulton R. Evidence for early-childhood, pan-developmental impairment specific to schizophreniform disorder: results from a longitudinal birth cohort. Arch Gen Psychiatry 2002. 59(5): 449-56.

Clarke M.C, Roddy S, Cannon M Obstetric Complications and Schizophrenia. In: The Origins of Schizophrenia. Edited by Brown AS, Patterson, PH). Columbia University Press 2012 p96-119.

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O38 MENDREK A. SEX-SPECIFIC DIFFERENCES IN NEUROCOGNITIVE FUNCTION IN SCHIZOPHRENIA

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Background: Sex differences in epidemiology and clinical expression of schizophrenia have been well documented. In our study of visuo-spatial processing we observed significantly diminished brain activations in male patients and significantly greater activations in female patients, relative to the same-sex controls.
Aims: The purpose of the present investigation was to determine if the aforementioned effect reflected a generalized neurofunctional deficit in male patients and thus would be also apparent during emotional memory task.
Methods: 42 schizophrenia patients (21 women) and 42 healthy controls (21 women) underwent functional magnetic resonance imaging (fMRI) while performing an emotional memory task. The task consisted of the recognition of pleasant, unpleasant and neutral photographic pictures (scenes, faces, objects).
Results: The fMRI data analysis revealed significantly stronger activations in male patients relative to control men in several brain regions associated with processing of emotional memories, during recognition of both positive and negative images. In contrast, female patients exhibited significantly weaker activations that control women during recognition of emotional stimuli.
Conclusions: The results of the preset study show that the previously observed reversal of normal sexual dimorphism in schizophrenia patients could not be explained by a generalized deficit in neurocognitive function of male patients, but is task-dependent. In fact, sex differences in patients' cerebral activations during emotional memory were in the opposite direction to what we had observed during mental rotation in the same cohort of participants. Additional factors including circulating levels of sex steroid hormones, as well as implication of positive and negative symptoms, will be examined next.

ABSTRACTS

Poster sessions

P01 DOI N. IMPACT OF EPIDEMIOLOGY ON MOLECULAR GENETICS OF SCHIZOPHRENIA. I. PERSISTENCE CRITERION FOR NUCLEAR SUSCEPTIBILITY GENES

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Background: Genetic research of schizophrenia (SZ) based on the nuclear genome model (NGM) has been one of the most active areas in psychiatry for the past two decades. Although this effort is ongoing, the current situation of molecular genetics of SZ seems rather perplexing. Furthermore, a prominent discrepancy between persistence of the disease at a relatively high prevalence and a low reproductive fitness of patients gives a paradox. Heterozygote advantage works to sustain the frequency of a putative susceptibility gene in the mitochondrial genome model (MGM) but not in NGM.

Aims: To examine the plausibility of NGM from a stand point of epidemiology.

Methods: We deduced a criterion that every nuclear susceptibility gene for SZ should fulfill for the persistence of the disease under general assumptions of the multifactorial threshold model. The distribution of SZ-associated variants listed in the top 45 in SZGene database that could meet or do not meet the criterion was surveyed using the epidemiological data by Haukka et al. (2003).

Results: 19 SZ-associated variants that do not meet the criterion are located outside the regions where the SZ-associated variants that could meet the criterion are located. Since a SZ-associated variant that does not meet the criterion cannot be a susceptibility gene, it should be linked with a susceptibility gene in NGM, which disagrees with these results.

Conclusion: NGM for SZ today seems to be confronted with a trying situation, which may encourage us to make a paradigm shift to MGM in the genomic research of SZ.

P02 DOI N. IMPACT OF EPIDEMIOLOGY ON MOLECULAR GENETICS OF SCHIZOPHRENIA. II. MITOCHONDRIAL DNA HYPOTHESIS FOR SCHIZOPHRENIA

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Background: The nuclear genome model (NGM) for schizophrenia (SZ) today seems to be confronted with a trying situation. On the other hand, mitochondrial dysfunction (MD) in SZ has been suggested by several independent lines of evidence including disturbed oxidative phosphorylation and oxidative stress (OS). While it is still unknown whether MD in SZ is a primary pathogenic change or a secondarily induced process, it may suggest a possibility of the mitochondrial genome model (MGM) for SZ.

Aims: To examine the plausibility of MGM.

Methods: Based on MGM we propose a new hypothesis that assumes brain-specific antioxidant defenses in which trans-synaptic activations of dopamine- and *N*-methyl-D-aspartate-receptor are involved, and present ten predictions.

Results: The hypothesis predicts: (1) a higher maternal transmission, (2) that SZ-associated genes are all protective, (3) an apparent signature of positive selection in SZ-associated genes,(4) sex difference and a protective effect of estrogen, (5) that early-life exposure to environments which induce OS increases the risk of SZ in the predisposed population, (6) increased obstetric complications in the birth of patients with SZ, (7) low comorbidity between SZ and rheumatoid arthritis, (8) genomic instability in SZ, (9) inconsistency in the results of the association studies on the nuclear genome, and (10) therapeutic effects of antioxidants. Most of the predictions seem to accord with the major epidemiological facts and the results of association studies.

Conclusion: This hypothesis, although speculative to date, seems to explain various and specific aspects of SZ and the somewhat perplexing results of association studies to date.

P03 BOYLE S.P. INVESTIGATIONS FOR A PUTATIVE DIAGNOSTIC BIOMARKER IN SCHIZOPHRENIA

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Background: Schizophrenia is a major illness characterised by psychosis, cognitive impairment, apathy and social withdrawal. The exact cause of this disease is unknown but a number of factors including social, environmental and genetic factors are thought to contribute to its development. The heterogeneity of this disorder coupled with the absence of a biochemical biomarker makes both disease diagnosis and efficacious treatment challenging for the clinician. Characterisation of a diagnostic biochemical biomarker of schizophrenia would be a significant positive development and is the primary aim of this research.
Aims: This research aimed to identify a putative diagnostic biomarker for schizophrenia by investigating levels of $cPLA_2$, erythrocyte fatty acid content and biomarkers of oxidative stress in the blood of healthy control subjects and drug naive patients presenting with first episode psychosis.
Methods: Age matched trial participants were recruited from the United Arab Emirates and blood samples processed, snap frozen in liquid nitrogen and stored at -80C until analysis. Erythrocyte fatty acid profiles were determined by GC-FID, erythrocyte $cPLA_2$ was determined by ELISA and plasma malondialdehyde (MDA) was determined by LC-MS-DAD.
Results: Mean plasma MDA, erythrocyte $cPLA_2$ and fatty acid profiles were compared between the populations and principal component analysis was employed to look for similarities and differences between the two populations and thereby determine if $cPLA_2$ levels alone, or in association with altered fatty acid profiles, may be used as diagnostic criteria for schizophrenia.
Conclusions: The research highlights some future avenues in the search for a diagnostic biomarker which may augment established formal rating scales.

P04 SOLISMAA A. NO ASSOCIATION BETWEEN M1 AND M2 GENE POLYMORPHISMS AND SUBJECTIVE DEPRESSION ANXIETY OR SYMPATHICOTONIA TENSION LIKE SYMPTOMS DURING CLOZAPINE TREATMENT

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Background. Clozapine is the most effective antipsychotic agent for treatment refractory schizophrenia. During clozapine treatment, patients experience cognitive side effects such as fatigue, difficulty concentrating and memory impairment. Cholinergic neurons participate in regulation of arousal and attention. Clozapine has a high affinity for muscarinic (M) receptors and affects the cholinergic system in the CNS.
Aims. The aim of the study was to examine the possible associations between three M1 (rs542269, rs2507821 and rs2075748) and two M2 (rs8191992 and rs324640) polymorphisms and subjective depression anxiety or sympathicotonia tension like side effects during clozapine treatment. Genotype frequencies of M1 and M2 polymorphisms were also compared between patients and healthy controls.
Methods. Study population comprised 237 clozapine-treated patients with a diagnosis of schizophrenia, schizoaffective or other nonorganic and nonaffective psychosis. The patients completed the Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS) and their M1 and M2 gene polymorphisms were genotyped. The control group comprised 388 healthy blood donors.
Results. No associations were found between M1 or M2 genotype and depression anxiety or sympathicotonia tension like side effects during clozapine treatment, even when the clozapine serum concentrations were taken into account. Furthermore, no differences were found in genotype frequency distributions of M1 or M2 polymorphisms between patients and healthy controls.
Conclusions. M1 or M2 genotypes did not explain the severity of clozapine induced depression anxiety or sympathicotonia tension like side effects. The limitations were the relatively small study population and that the side effects were self assessed without any testing for cognitive performance.

P05 MIETTUNEN J. TEMPERAMENT IN INDIVIDUALS WITH PSYCHOTIC DISORDERS BEFORE AND AFTER THE ONSET OF ILLNESS

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Background: The Temperament and Character Inventory (TCI) is used to measure novelty seeking (NS), harm avoidance (HA), reward dependence RD), and persistence (P).
Aims: We aim to study the stability of temperament in individuals with psychotic disorders (with onset of illness before and after first follow-up) and in healthy controls.
Methods: As part of the 31-year follow-up survey of the prospective population based Northern Finland 1966 Birth Cohort, the TCI was filled by a large sample of individuals. A subsample of psychotic individuals, with the onset of illness before (n=16) or after (n=15) the 31-year follow-up, and healthy controls (n=117) filled in these scales again at the age of 43. We studied also the association between psychotic symptoms (measured with Positive and Negative Syndrome Scale, PANSS) and premorbid temperament.
Results: The 31-year and 43-year temperament scores correlated strongly among controls (Pearson's r: NS 0.68, HA 0.60, RD 0.56, P 0.54), whereas correlations among psychotic individuals with the onset of psychosis before first follow-up were weaker (NS 0.38, HA 0.50, RD 0.17, P 0.53). High HA before the onset of illness (at age of 31 years) associated significantly with a lower likelihood of remission and with more negative, disorganization and total symptoms in the PANSS. High NS before illness associated with a higher likelihood of remission according to the PANSS.
Conclusions: Temperament was stable among controls, and more unstable in individuals with psychoses. Premorbid harm avoidance and novelty seeking predicts the clinical outcome in schizophrenia.

P06 AHMED A.O. LATENT STRUCTURE OF SCHIZOPHRENIA-SPECTRUM PERSONALITY DISORDERS: TAXOMETRIC DETECTION AND CONSTRUCT VALIDATION

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Background: The categorical-versus-dimensional status of schizophrenia-spectrum personality disorders (PDs) has been the subject of debate among the proponents of various typological models of psychiatric disorders. The consensus among mental health professionals for dimensional models of personality pathology wanes whenever Cluster A disorders and Avoidant PD are in question because of their perceived relationship to schizophrenia, generally viewed as taxonic. Moreover, some have questioned the current nosological organization of Cluster A disorders due to equivocal evidence of the genetic relationship between Schizophrenia and Paranoid, Avoidant, and Schizoid PD.
Aim: We conducted taxometric analyses of current Cluster A disorders and Avoidant PD in epidemiological surveys.
Methods: We drew participants from the 2000 Psychiatric Morbidity Survey and the two waves of the National Epidemiologic Survey on Alcohol and Related Conditions. We analyzed participant responses using taxometric procedures that allowed us to test the comparative viability of categorical versus dimensional models. We also examined the association between latent structure and a set of criterion variables including disability, treatment history, and psychosis.
Results: Taxometric analyses supported a taxonic structure for Schizotypal PD and a dimensional structure for Paranoid, Schizoid, and Avoidant PDs. Schizotypal PD taxon membership was associated with ethnic minority status, disability cognitive functioning, psychosis, and treatment history.
Conclusions: The difference in the latent structure of schizophrenia-spectrum PDs is problematic for the current nosological scheme. Paranoid, Schizoid, and Avoidant PDs may represent phenomenologically separate entities from the rest of the schizophrenia spectrum or the latent liability is expressed as taxonic and dimensional entities.

P07 KYLLÖNEN M. LATENT CLASS ANALYSIS OF RISK FACTORS FOR SCHIZOPHRENIA AND OTHER PSYCHOSES

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Background: There are several risk factors for schizophrenia that may correlate with each other. Latent class analysis is a method that posits there is an underlying unobserved categorical variable that divides a multivariate data into mutually exclusive and exhaustive latent classes. These subtypes of statistically independent individuals can be used in further analyses.
Aim: We conducted a latent class analysis with possible risk factors for schizophrenia in a general population sample to see if certain combinations of risk factors comprise especially high risk for schizophrenia and other psychoses.
Methods: The study sample comprised of 10,675 individuals from the prospective Northern Finland 1966 Birth Cohort, including 150 (1.4%) individuals with schizophrenia and 151 (1.4%) with other psychosis.
Results: Based on the information criteria, seven latent classes best described the data. The highest prevalences for schizophrenia (4.3%) and other psychoses (5.7%) were in a class which was best described with neurological deficits as a child and problems at school. This class also had a large proportion of individuals with developmental disorder. A class of individuals with e.g. large birth weight and height was specifically at risk for schizophrenia (3.3%), but not for other psychoses (1.1%).
Conclusions: Latent Class Analysis can be used to identify individuals who are at increased risk for schizophrenia and other psychosis. Individuals with psychosis in these groups can be further studied in relation to symptom and cognitive outcome.

P08 HAAPEA M. IMPROVING PARTICIPATION RATES IN POPULATION BASED SCHIZOPHRENIA RESEARCH BY USING HOME INTERVIEWS

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Background: The participation rates in epidemiologic cohort studies have declined in recent years. Missing data is a serious problem especially in population based research reducing sample size and statistical power.
Aims: To find out if, among psychotic subjects, non-participants experience more severe clinical symptomatology than participants in a psychiatric follow-up study with 10 years of follow-up, and whether opportunity to be interviewed at home increases the participation rate.
Methods: This study is based on the Northern Finland 1966 Birth Cohort. A psychiatric field study was conducted in 1999-2001 and the follow-up in 2008-2010 in the Oulu University Hospital, Finland. The field studies consisted of magnetic resonance imaging of the brain, cognitive testing, and mental health related interviews. Altogether 91 out of 146 subjects with psychosis participated in the field study in 1999-2001, of whom 87 had non-organic psychosis. Five subjects deceased during the follow-up, and one denied the use of data. Out of 81 subjects, 54 (67%) participated in the follow-up. To study effects of home interview, PANSS, SOFAS, CGI, level of total recall and recognition, and semantic and serial cluster scores (CVLT) were compared separately between 1) participants vs. non-participants, and 2) those interviewed in the hospital vs. others (non-participants and those interviewed at home). Effect sizes (d) were calculated to compare the means.
Results: Altogether 18 (33%) participants of the follow-up were interviewed at home. The participation rates were 66% in schizophrenia and 68% in other psychoses. Of the participants with schizophrenia 14 (35%), and with other psychoses 4 (29%), were interviewed at home. When the participants were compared with the nonparticipants, no statistically significant differences occurred. When compared those interviewed in the hospital with others, those interviewed in the hospital had less negative and excitement symptoms (12.1 vs. 16.5, d -0.46, P 0.038, and 10.2 vs. 12.2, d -0.53, P 0.017), their SOFAS was higher (57.0 vs. 48.5, d 0.50, P 0.028), and level of total recall was higher (51 vs. 42, d 0.60, p 0.015), i.e. their illness was less severe.
Conclusions: In this study, we showed that the effort made in recruiting subjects with psychosis increases the participation rate and likely reduces the nonresponse bias by affecting the estimates of severity of illness in schizophrenia studies.

P09 KESKINEN E. INTERACTION BETWEEN PARENTAL PSYCHOSIS AND RISK FACTORS DURING PREGNANCY AND BIRTH FOR SCHIZOPHRENIA

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Background: The interaction between parental psychosis and early risk factors for schizophrenia during pregnancy and birth are unclear.
Aims: To investigate interactions between parental psychosis and early risk factors for schizophrenia.
Methods: The study sample comprised of 10,675 individuals from the prospective Northern Finland 1966 Birth Cohort, including 150 (1.4%) individuals with schizophrenia.
Results: High birth weight and length and higher maternal education had a significant interaction with parental psychosis in the prediction of schizophrenia. The presence of any biological risk factor increased the risk of schizophrenia significantly only among the parental psychosis group (OR 4.3; 95% CI 1.6- 11.8). The findings were confined to schizophrenia (not applicable to other psychoses).
Conclusions: Parental psychosis can act as an effect modifier on early risk factors for schizophrenia. Evaluation of the mechanisms behind the risk factors should, therefore, include consideration of the parental history of psychosis.

P10 GALE C.K. THE EFFECT OF RECENT ADVERSE EVENTS AND PSYCHOTIC SYMPTOMATOLOGY AMONG PEOPLE WITH SCHIZOPHRENIA

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Background: Childhood trauma is a suggested aetiological factor for psychosis (1). This hypothesis differs from the clinical lore that recent stressors can worsen symptomatology
Aims: To see what life events are associated with symptomatology in people with stable psychosis.
Methods: We interviewed people with stable schizophrenia or schizoaffective disorder from a community mental health centre. We used the CIS-R life events module and as outcomes total PANSS. We used analysis of variance using a logistic regression for six month PANSS scores.
Results: We identified 141 potential participants, of which 86 agreed to the interview, but a further 12 refused to complete parts of the life events section, giving 74 to 79 responders. Over their lifetime, 53 (77%) were bullied, 21 (28%) home violence, 15 (20%) run away from home, 15 (20%) homeless, 14 (18.9%) sexually abused, 10 (13.3%) work violence and four (5.3%) school explusion. Over the last six months, 15 (20.5%) reported losing items , 15 (20%) victim of a crime, 14 (18.6%) conflict with others. 14 (18.6%) death of acquaintance, 10 (13.6%) money difficulties, 10 (13.3%) death close to them, seven (9.6%) police difficulties, six (8.0%) separation from partner, six (7.8%) illness or injury, four (5.5%) being out of work and four (5.3%) being assaulted. PANSS was associated with police difficulties (Deviance 13.9, d.f. 76 P = 0.0018 and conflict with others (deviance 4.66 d.f. 73 P=0.031).
Conclusions: Among people with schizophrenia and related psychosis, sexual abuse is common, but is but the fourth most common life event. More recent events are as common, and two of these are associated with worsening psychopathology.

Reference:

Read J, Bentall RP. Negative childhood experiences and mental health: theoretical, clinical and primary prevention implications. Br J Psychiatry. 2012 Feb;200:89-91

P11 HURTIG T. PSYCHOTIC-LIKE SYMPTOMS AND SOCIAL AND ACADEMIC ACHIEVEMENT IN ADOLESCENTS

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Background and aim: Social isolation and academic problems may precede onset of psychosis years before the full-blown episode. However, earlier research relied on retrospective design in patient samples. It is important to gain knowledge of these possible associations in several groups of individuals, such as high-risk as well as community, before the onset of psychotic disorder. Our aim was to study the associations between psychotic-like symptoms and social and academic achievement in a general adolescent population.

Methods: The sample is based on a population-based prospective birth cohort, the Northern Finland Birth Cohort (NFBC) 1986. In the 15-16 -year follow-up the adolescents completed a general health and well-being questionnaire as well as the PROD-screen questionnaire that addressed prodromal symptoms of psychosis (N = 6101, 2919 boys and 3182 girls). The cross-sectional associations between positive, negative and general symptoms in the PROD-screen and several social and academic factors were studied.

Results*:* Those scoring in the upper 10th percentile in PROD negative or general symptoms scales were more likely to have no close friend, to be dissatisfied in life, to dislike going to school, and to have repeated a grade at school. Those scoring above the cut-off in PROD positive symptoms scale were more likely to be dissatisfied in life and to dislike going to school. Those exceeding the cut-offs in any PROD scales had lower mean values in grand means for grade marks for all school subjects. However, there were no differences between the study groups in educational aspirations after comprehensive school.

Conclusion: Psychotic-like symptoms in adolescence may be associated with social and academic problems.

P12 HARAVUORI H. LIFE EVENT CHARACTERISTICS OF ADOLESCENTS TREATED FOR NON-AFFECTIVE PSYCHOSIS WERE SIMILAR TO ADOLESCENTS WITH OTHER SEVERE MENTAL DISORDERS

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Background: Severe mental disorders including suicidality may require treatment in hospital. Kellokoski adolescent inpatient follow-up study (KAIFUS) was initialized to analyze characteristics of the adolescents in psychiatric hospital care and the factors affecting the long-term outcomes.
Aims: We analyzed whether the inpatients with psychosis differ from the other inpatient and comparison adolescents in their background and life event characteristics at admission.
Methods: The subjects were 202 adolescents admitted to hospital 2006–2010 and 196 comparison adolescents recruited from schools. The data included background information, DSM-IV diagnoses primarily based on K-SADS-pl interviews, and self-administered scales (BDI-21, Audit, LEC, PSSS-R).
Results: Mean age of the inpatients was 15.1 years (range 13–17) and over 70 % were females, with no differences to the comparison group. Lower SES, parental death, psychiatric treatment and substance use problems, and placing outside of home were more common among the inpatient than the comparison group. Inpatient adolescents smoked more often and perceived less support from family and friends than the comparison group. Non-affective psychosis was diagnosed in 15 inpatients. Those with psychosis differed from the other inpatients only by lower BDI-21 scores and less perceived support from friends. CGAS scores were equally low (median 27.9 vs. 30.0). The number of self-reported negative life events and severity of clinician judged psychosocial factors did not differ between the psychosis and other diagnosis groups.
Conclusions: Adolescents requiring treatment in psychiatric hospital have often experienced stressful life events. Patients with psychotic disorders are not different from other inpatients in this small sample.

P13 PARTTI K. LUNG FUNCTION, RESPIRATORY DISEASES AND SYMPTOMS, AND SMOKING IN PSYCHOTIC DISORDERS

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Background*:* Persons with schizophrenia suffer from increased comorbidity and mortality from medical disorders, such as cardiovascular disease. However, there are only a few studies that have investigated lung function and the prevalence of respiratory diseases and symptoms in persons with psychotic disorders.
Aims: To compare: 1) lung function using spirometry, 2) the prevalence of respiratory diseases and symptoms, 3) smoking in persons with psychotic disorders with the general population.
Methods: The study was based on a nationally representative sample of 8028 Finns aged 30 or over. The DSM-IV psychiatric diagnoses were based on a consensus procedure utilizing both the SCID-I interview and case note data. Lung function was measured by spirometry; moreover, information on respiratory diseases and symptoms was collected in a physician's examination, using register data and questionnaires. Smoking was quantified by measuring serum cotinine levels.
Results: Subjects with schizophrenia and other non-affective psychosis had significantly lower FEV1 % predicted (85.0%, p=.000 and 88.5%, p=.022, respectively) and FVC % predicted values (87.7%, p=.000 and 90.5%, p=.010) compared with the general population; however, no significant differences were found for the FEV1/FVC ratio, suggestive of restrictive pulmonary impairment. In the linear regression model, schizophrenia remained an independent predictor of low spirometry values after adjusting for the most common risk factors for impaired lung function. Moreover, schizophrenia was associated with increased odds for pneumonia (OR 4.9, p=.000), COPD (OR 4.2, p=.003) and chronic bronchitis (OR 3.8, p=.002), adjusted for age and sex; and significantly high cotinine levels (p=.019).
Conclusions: Schizophrenia is associated with impaired lung function and increased odds for pneumonia.

P14 TANASIEWICZ M. STATE OF THE ORAL CAVITY IN SCHIZOPHRENIC INPATIENTS DURING THERAPY WITH ATYPICAL AND CLASSICAL NEUROLEPTICS

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Background: As far as dental healthcare is concerned, that group of schizophrenic patients has serious problems with improper hygiene of the oral cavity. Additionally, those patients are usually not concerned about their own state of health.
Aim: Assessment of state of the oral cavity in schizophrenic in patients treated with atopic and classical neuroleptics and its comparison with a healthy group; assessment of efficiency of pro-hygienic activities conducted in the researched groups and the control group.
Methods: The research group comprised patients of the Psychiatric Clinical Ward of the MUS in Tarnowskie Góry. The research group comprised 100 schizophrenics (male and female), treated with atypical and classical neuroleptics. The control group comprised 50 healthy people who did not give any information about possible diagnosis of any physical illness in their cases.
Results: In case of patients from the research group all components of DMFT index reached values that indicated less than satisfactory state of the dentition, when compared to the control group.
Conclusion: Schizophrenics show significantly less interest in hygiene of the oral cavity and state of own dentition. Atypical neuroleptics can have advantageous influence on the degree of interest of the treated person on the state of hygiene of their oral cavity. Patients undergoing treatment with classical neuroleptics should be taken under particular care, as effectiveness of dental hygienic activities in that group, including hygienic training for the oral cavity, is lower than in the group which was treated with atypical neuroleptics.

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P15 NIITTYVUOPIO-JÄMSÄ L.-M. CHILDHOOD VITAMIN D SUPPLEMENTATION AND RISK AND PROGNOSIS OF SCHIZOPHRENIA

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Background: Low use of vitamin D supplementation in childhood has been associated in higher risk in schizophrenia. There are no studies of association between vitamin D and prognosis of schizophrenia.
Objective: We aimed to analyze relationship between amount of vitamin d supplementation during first year of life and risk of and prognosis of schizophrenia in general population.
Methods: The sample was based on The Northern Finland 1966 Birth Cohort and included 169 individuals of schizophrenia spectrum disorder and 9314 nonpsychotic controls. Regularity and dose of vitamin D supplementation during first year of life was collected from maternal interviews. Information on diagnosis of schizophrenia spectrum was gained from the Finnish Hospital Discharge Register. Age of illness onset, amount of hospital days due to psychosis, occupational status and death were measured as outcomes.
Results: Only for males, low dose (<2000 IU/day) of vitamin D supplementation increased the risk of schizophrenia spectrum disorder (RR 3.07, 95% CI 1.01-9.33). Though there was a trend towards association between infrequent use of vitamin D and better outcome, none of the associations reached statistical significance.
Conclusions: In this general population sample, low dose of vitamin D supplementation increased the risk of schizophrenia spectrum disorder among men. Based on this sample, infrequent use of vitamin D in childhood might be related to better outcome. However, relatively low number of cases and very low number of those using low dose or irregularly vitamin D supplementation may affect the results.

P16 AJDACIC-GROSS V. ASSESSING PSYCHOSIS DIMENSIONS AND SYMPTOMS IN THE ZINEP EPIDEMIOLOGICAL SURVEY

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Background: The ZInEP Epidemiological Survey is a subproject of The Zurich Program for Sustainable Development of Mental Health Services *(ZInEP)*. Its major aim is to generate comprehensive data about mental health in the general population of adults aged 20 to 40 years. Its design is geared to the longitudinal Zurich Study of Jules Angst. In contrast to the latter, psychosis is a prority issue in the ZInEP Epidemiological Survey.
Aims: The ZInEP Epidemiologic Survey will provide information on:

- the differentiation of subthreshold psychotic syndromes
- their association with corollary scales
- associations with neurophysiological tests and markers
- comorbid syndromes and symptoms
- the influence of stress-related effects
- further related risk factors

Methods: The Survey consists of three components.
1) Approximately 10'000 subjects representative of the canton of Zurich were screened with a computer assisted telephone interview using the SCL-27 (enriched by psychoticism, paranoia and irritability items).
2) Applying a stratified sampling procedure, 1'500 participants were selected for a comprehensive face-to-face-interview with the Mini-SPIKE covering most psychiatric syndromes. Psychotic symptoms were assessed also by the brief version of the SPQ-B, the Paranoia Checklist, and by subscales of the ADP-IV questionnaire. Additionally, we introduced psychosis related scales such as the SIA, the SIAPA, the CEQ, and the BCSS.
3) Furthermore, 250 participants of the interview-sample have been selected for a longitudinal survey. We perform a series of neurophysiological tests and assess also stress and other biological markers. Subsequently the subjects are interviewed three times in 2-month intervals.
Results and Discussion: We will present preliminary descriptive results.

P17 MAZUMDER A.H. POSITIVE AND NEGATIVE SYMPTOMS OF SCHIZOPHRENIA IN BANGLADESH

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Background: Evaluation of positive and negative symptom patterns of schizophrenia is necessary for the assessment of prognosis and treatment outcome. At present there is no relevant research in Bangladesh.

Aims: To delineate the type and frequency of positive and negative symptoms of schizophrenia and to find out possible association of socio demographic and relevant variables with positive and negative symptoms.

Methods: This was a cross sectional, analytical and descriptive study done in a tertiary care hospital located in the capital of Bangladesh. Sample size was 78. The SCID-I and pre designed socio demographic questionnaire was applied. Positive and negative symptoms were assessed by using the Positive and Negative Symptom Scale (PANSS). Statistical analysis was done through SPSS version 17.

Results: Among the patients with schizophrenia positive symptoms (57.7%) were more predominant than negative symptoms (42.3%). Among positive symptoms the most frequent was delusion (64.1%) and among negative symptoms the most frequent was blunted affect (55.1%). Again, among illiterate patient group negative symptoms (63.6%) were more predominant than positive symptoms (36.4%) and among unemployed patient group negative symptoms (62.5%) were more predominant than positive symptoms (37.5%). Among higher monthly income group of patients positive symptoms (71.4%) were more predominant than negative symptoms (28.6%).

Conclusions: Though in the current study positive symptoms were more predominant, negative symptoms were significantly associated with poverty, unemployment and lack of education. For this reason clinicians should be careful not to miss negative symptoms and their association with socio economic and educational condition.

P18 PENTTILÄ M. ASSOCIATION BETWEEN DURATION OF UNTREATED PSYCHOSIS AND SHORT- AND LONG-TERM OUTCOME IN SCHIZOPHRENIA WITHIN THE NORTHERN FINLAND 1966 BIRTH COHORT

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Background: Long duration of untreated psychosis (DUP) may relate to poor short-term outcome in schizophrenia, but especially the association between DUP and later course of illness remains unclear.
Aims: Our aim was to explore associations between DUP and short- and long-term outcomes in schizophrenia.
Methods: Among subjects with schizophrenia (n=89) in the population-based Northern Finland 1966 Birth Cohort DUP was assessed from medical records, and its associations to short- (under 2 years) and long-term clinical and social outcomes extending to 20 years after the onset of the illness.
Results: Longer DUP predicted longer length of first hospitalisation and increased the risk of rehospitalisation during the first two years. Longer DUP associated with decreased probability of disability pension, smaller proportion of time spent in hospital, and higher proportional time of work during the 10 years of follow-up.
Conclusions: Regarding early outcome long DUP may be a modest marker and proxy measure of more severe clinical phenotype. The divergent results of earlier studies and the association between long DUP and better long-term outcome in our study indicates that the length of DUP does not necessarily predict poor outcome in long follow-up. This may be due to different subgroup associations confounded by multiple and mixed individual and clinical characteristics.

P19 YOSHII H. STIGMA TOWARD SCHIZOPHRENIA AMONG PARENTS OF JUNIOR AND SENIOR HIGH SCHOOL STUDENTS IN JAPAN

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Background: Stigma toward schizophrenia is a substantial barrier to accessing care and adhering to treatment. Provisions to combat stigma are important, but in Japan and other developed countries there are few such provisions in place that target parents of adolescents. The attitudes of parents are important to address as first schizophrenic episodes typically occur in adolescence.
Aims: In overall efforts to develop an education program and provisions against stigma, here we examined the relationship between stigma toward schizophrenia and demographic characteristics of parents of junior and senior high school students in Japan. The specific hypothesis tested was that contact and communication with a person with schizophrenia would be important to reducing stigma.
Methods: A questionnaire inquiring about respondent characteristics and which included a survey on stigma toward schizophrenia was completed by 2690 parents.
Results: The demographic characteristics significantly associated with the Devaluation-Discrimination Measure were family income, occupation, presence of a neighbor with schizophrenia, and participation in welfare activities for people with mental illness ($p < 0.05$). The mean ± SD score was 32.74 ± 5.66 out of a maximum of 48 points on the Link Devaluation-Discrimination Measure.
Conclusions: Stigma toward schizophrenia among parents of junior and senior high school students was in fact significantly stronger among members of the general public who had had contact with individuals with schizophrenia. In addition, stigma was associated with family income.

P20 LIN S.-H. QUALITATIVE AND QUANTITATIVE MINOR PHYSICAL ANOMALIES IN TAIWANESE PATIENTS WITH SCHIZOPHRENIA DISORDER

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Background: Numerous studies report an increased frequency of minor physical anomalies (MPAs) in schizophrenic individuals compared with controls. However, most previous studies were limited in the method of measuring the MPAs by using qualitative measurements.
Aims: The study aimed to examine the reliability and validity of a new physical measurement scale and to investigate whether there are associations between MPAs and early/late onset stage patients with schizophrenia.
Methods: We developed a new physical measurement scale and an accompanying manual for score rating as well as standardized measurement. This scale included the mainly qualitative Waldrop scale, which was used in the vast majority of studies and mainly qualitative in nature, and some quantitative measures of the head and face area.
Results: This scale was then applied in 152 patients with early-onset schizophrenia, 213 patients with late-onset schizophrenia and 195 normal subjects. Significantly higher total MPAs score was found in schizophrenic patients than in normal subjects, with the early-onset patients having MPAs in the areas of ears, mouth, hands and feet, and with the late-onset patients having MPAs in the areas of eyes, ears, mouth, and feet. Schizophrenic patients also had longer facial width, longer skull height, longer tragion to tragion distance, longer interpupilary distance, right ear width, smaller left ear rotation, longer philtrum, narrower lip-width, and narrower palate than normal subjects.
Conclusions: This new physical measurement scale could be reliably applied in schizophrenia subjects. Our scale can be used as a biomarker for genetic-environmental dissection in future etiological studies on schizophrenia.

P21 JONES P. EFFICIENCY OF EARLY MOTOR DEVELOPMENT AND THE WINDOW OF RISK FOR ADULT SCHIZOPHRENIA: MAKING CONNECTIONS

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Background: Delays in early motor milestones and the characteristic age-incidence function suggest a developmental dimension to schizophrenia.
Objective: To test the hypothesis that precocious earlier motor development predicts a briefer window of risk for schizophrenia, with earlier mean age-at-onset (AAO).
Methods: Data come from the North Finland 1966 Birth Cohort (n=12,058). Schizophrenia cases were identified from registers. Latent class analysis (LCA) determined three latent motor developmental classes (LDC), early, regular and late. Associations between LDC and some putative causal factors were examined in the whole risk set.
Results: The risk set comprised 9,820 subjects (5,589 men); 135 (90) developed schizophrenia (AAO 15-39 years). Cumulative risk accelerated from the mid-teens, slowing by age 21 in the early LDC but increasing linearly in the late LDC until age 39; the regular LDC was intermediate. Mean AAO was youngest in the early LDC and oldest in the latest LDC. The three LDC survival functions differed (Wald 15.29, $p<0.001$), the later LDC having lower- (HRR 1.7; $p=0.02$) and the early LDC higher survival (HRR 0.5; $p=0.008$) than the regular LDC. Perinatal brain damage, maternal depression, unwantedness, lower maternal education and higher maternal and paternal age were associated with later development; males and females were very similar.
Conclusions: Prompt early neurodevelopment is associated with a shorter period of risk for schizophrenia during adult life. This may be due to a common mechanism involving efficient connectivity development during these two neuro-developmental epochs. Genetic studies of development and imaging studies of connectivity are recommended.

P22 KOBAYASHI H. DELAYED NEURODEVELOPMENT PREDICTS LATER DETERIORATION OF RESPONSE SPEED DURING EXECUTIVE FUNCTION IN SCHIZOPHRENIA

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Background: Abnormal maturation of brain systems may be found in schizophrenia. We hypothesized that brain network dysfunction should gradually develop with the progression of illness in schizophrenia and be associated with delayed neurodevelopment, and the degree of neurodevelopmental delay in infancy would predict the degree of neurodegeneration in mid-life
Aims: To measure changes over time in executive function in subjects with schizophrenia, and to examine the association between deterioration of executive function and age of learning to stand in infancy.
Methods: Control subjects and participants with schizophrenia were drawn from the Northern Finland 1966 Birth Cohort study. The first survey was conducted in 1999-2001, which included examination by structured interview as well as neuropsychological testing (The Abstraction, Inhibition, and Working Memory task and The Visual Object Learning Test). After 10 years, the same assessments as baseline were conducted for the initial cohort.
Results: Out of the initial sample, 34 subjects with schizophrenia, 14 subjects with other psychosis, and 72 healthy controls were traced successfully over 10 years. Whilst memory function in schizophrenia was stable over time, there was a marked deterioration in schizophrenia (compared to controls) of response times during executive function. Additionally, age of learning to stand significantly inversely predicted later deterioration of response times during executive function in adult schizophrenia (faster infant development linked to less subsequent cognitive deterioration).
Conclusion: Our findings suggest that infant neurodevelopment can be connected with subsequent neurodegeneration in schizophrenia.

P23 RIEKKI T. SCHIZOTYPAL AND AFFECTIVE TRAITS IN THE OFFSPRING OF ANTENATALLY DEPRESSED MOTHERS – RELATIONSHIP TO PARENTAL HISTORY OF PSYCHOSIS

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Background: Maternal depression is relatively common during pregnancy. To the authors' knowledge there have been no epidemiological reports on schizotypal traits in the offspring of antenatally depressed mothers.
Aims: Our aim was to study whether maternal antenatal depressed mood increased the incidence of schizotypal or affective traits among young adults with and without a parental history of psychosis.
Methods: In the general population-based Northern Finland 1966 Birth Cohort, mothers of the cohort members were asked at mid-gestation at the antenatal clinic if they felt depressed. Parental psychosis was detected using the Finnish Hospital Discharge Register. In the 31-year field study in the offspring seven psychometric instruments were selected to function as proxies for positive, negative and affective aspects of psychotic disorders. The final sample included 4,928 individuals (2,203 males).
Results: There were no statistically significant differences in mean scores of the schizotypal and affective scales between offspring with and without maternal depressed mood during pregnancy; nor were there differences between subjects with and without parental psychosis. The mean scores and prevalences in the schizotypal and affective scales were not statistically significantly higher in the subjects with both antenatally depressed mothers and psychotic parents than in other groups.
Conclusion: Surprisingly, the effects of maternal depressed mood during pregnancy or parental psychosis did not relate to schizotypal or affective traits in the general population-based birth cohort.

P24 SCHWEIZER U. SELENOPROTEIN-DEFICIENCY IMPAIRS CORTICAL PARVALBUMIN+ INTERNEURON FUNCTION IN MICE: ANOTHER CAUSE FOR SCHIZOPHRENIA?

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Background: Several lines of evidence suggest that redox imbalance affects parvalbumin+ GABAergic interneuron function. In particular, GSH-deficiency during postnatal interneuron development leads to a reduction of parvalbumin+ interneurons in cortex and hippocampus. Among GSH-consuming enzymes are glutathione peroxidases, a family of selenium-containing proteins. Selenium is incorporated into protein as selenocysteine, the 21st proteinogenic amino acid, and is critical for catalysis. Targeted inactivation of the major selenium transport protein in plasma and brain, selenoprotein P, reduces the activities of selenoenzymes in the brain, including glutathione peroxidase 1 (GPx1), thioredoxin reductase (Txnrd), and methionine-sulfoxide reductase. Selenoprotein P-deficient mice display a complex neurological and behavioral phenotype which can be rescued by supraphysiological dietary selenium intake. Reduced expression of selenoprotein P has been reported in prefrontal cortex of schizophrenic patients.
Aims: Find out whether selenoprotein-deficiency affects parvalbumin+ interneuron function in mice.
Methods: We have generated and analyzed a battery of transgenic mice either deficient in global cerebral selenoprotein expression or deficient for specific selenoproteins only in neurons. Parvalbumin, calretinin, and GFAP were assessed by immunohistochemistry. Molecular studies involved Affymetrics gene expression chips.
Results: GFAP is induced in cortex of models with a phenotype. Cortical parvalbumin+ (but not calretinin+) interneuron numbers are reduced in many, but not all mouse models. Together, these data support the involvement of GPx4, a GSH-dependent lipid-hydroperoxide degrading enzyme in parvalbumin+ interneuron development and function. Global gene expression changes in selenoprotein P-KO mice resemble results from cortex of schizophrenic patients.
Conclusions: Selenoprotein-deficiency may be involved in development of schizophrenia-like pathology.

P25 ZUMÁRRAGA M. GAMMA-AMINOBUTYRIC ACID IN THE PLASMA OF SCHIZOPHRENIC PATIENTS, BIPOLAR PATIENTS AND HEALTHY CONTROLS

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Background: The gamma-aminobutyric acid (GABA) mediated neurotransmission system has been implicated in schizophrenia and bipolar disorder The concentration of GABA in plasma has been suggested as an index of brain GABA activity. Studies trying to demonstrate differences in plasma GABA concentrations among schizophrenic, bipolar patients and controls have yielded inconsistent results.
Aims: To study the differences in plasma GABA concentrations among bipolar type I patients, schizophrenic patients and healthy controls; and the possible influence of clinical and demographic data.
Methods: A total 171 schizophrenic patients, 181 bipolar I patients (DSM-IV-TR), and 233 healthy controls were selected. A blood sample was obtained at 8-8.30 am, after 30 minutes of rest and 12 hours of fast. GABA in plasma was assessed by HPLC and fluorometric detection after pre-column derivatization by means of o-phthalaldehyde.
Results: The concentration of GABA in plasma was lower (ANOVA $F=32.09$; $p<0.001$) in schizophrenic patients (mean:10.42 ng/ml, 95% CI 10.07-10.78) than in controls (mean: 13.04 ng/ml, 95% CI 12.74-13.34) and bipolar patients (mean: 12.40 ng/ml; 95% CI 12.06-12.74) Gender and age did not influence these results.
Conclusions: The lower levels of plasma GABA observed in schizophrenic patients are consistent with the reduced expression of GAD67, a key enzyme in GABA synthesis, found in schizophrenic patients; and with post-mortem studies of schizophrenic patients that have revealed GABA reductions in different brain areas.

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P26 PUJOL-LOPEZ Y. EFFECT OF DIFFERENT ANTIPSYCHOTIC COMPOUNDS ON CYTOKINES AND TRYPTOPHAN METABOLITES AFTER DIFFERENT IMMUNE CHALLENGES IN ASTROCYTES CULTURE

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Background: Immune activation induces pro-inflammatory state and enhances the tryptophan degradation into kynurenine. It is hypothesized that immune activation in the brain increases tryptophan breakdown and induces imbalance in kynurenine downstream metabolites. The kynurenines have been reported to be involved in development of schizophrenia and response to treatment with antipsychotics.
Aim: To understand the detailed mechanisms of antipsychotics regarding immune activation and tryptophan metabolites changes, the effects of different antipsychotics on immunologically challenged mouse astrocytes cultures were investigated.
Methods: The astrocytes from the 2-day old mice brains were cultured with medium alone or with Lipopolysaccharide (LPS) (bacterial toxin) or Polyinosinic:polycytidylic acid (PolyI:C) (viral mimetic) which acts through Toll-like receptor-4 and -3 respectively; and with and without different antipsychotics for 72 hours at 37°C. Tryptophan metabolites in the culture supernatants were analyzed using high performance liquid chromatography. Cytokines and signaling pathways were analyzed using commercial ELISAs.
Results: Antipsychotics generally showed anti-inflammatory activity. Treatment with both LPS and PolyI:C reduced the tryptophan levels and increased the kynurenines levels. The antipsychotics seemed to suppress kynurenine levels. However treatment with LPS and PolyI:C enhanced the tryptophan breakdown. Kynurenic acid to kynurenine ratio was somewhat decreased by LPS and PolyI:C and haloperidol, clozapine and quetiapine could reverse this effect.
Conclusions: Although previous clinical study showed increase in plasma kynurenic acid and decrease in plasma 3-hydroxykynurenine after treatment with antipsychotics, current in-vitro study showed no significant effect on 3-hydroxykynurenine. Moreover, our results indicated that immune activation leads to increased neurotoxic 3-hydroxykynurenine in astrocytes.

P27 COWLING D. AGEING IN SCHIZOPHRENIA: A REVIEW

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Background: Schizophrenia is generally a lifelong condition and, despite excess mortality, most survive into old age. Very few prospective longitudinal studies have analysed trajectories from early-mid adulthood into old age.

Aim: To review current knowledge of the progression of schizophrenia into later life and the efficacy of available treatment options.

Methods: We conducted an electronic search of PubMed, PsychINFO and Scopus using the terms: (ageing OR "older adult" OR elderly OR geriatric OR "late life") AND (schizophrenia OR schizoaffective OR schizophreniform). Articles and books were also searched manually.

Results: While the course in later life is variable and the condition frequently stable, many remain symptomatic and impaired, and mortality and somatic comorbidity increase. Relatively higher rates of decline in cognitive functioning affect ability to function independently. However, many individuals have a favourable clinical course and may stop receiving treatment. Around 25% achieve full recovery in old age. There is a growing evidence base for interventions that alleviate symptoms, improve social and cognitive functioning and improve quality of life. However, inequalities exist between different age groups in the quality and range of treatment interventions currently available.

Conclusions: Early introduction of regular psychiatric and somatic assessments and prompt and adequate treatment of symptoms and comorbidities throughout the life course are essential. Cases of remission/recovery are often excluded in clinical research. This risks presenting a biased, somewhat pessimistic description of the illness course into later life. The evidence base for treatments needs to improve and future trials must endeavour to include older participants.

P28 JUOLA P. A SYSTEMATIC REVIEW AND META-ANALYSIS OF RECOVERY IN SCHIZOPHRENIA

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Background: It is widely accepted that a proportion of individuals with schizophrenia have a favorable prognosis. The precise estimates of cases with favorable outcomes are, however, less clearly understood.
Aims: We had three primary aims in this study: 1) to identify the proportion of individuals with schizophrenia and related psychoses who met recovery criteria based on both clinical and social domains. 2) Examine if recovery was associated with factors such as gender, economic index of sites, and selected design features of the study. 3) Examine whether the proportion of recovery had changed over time.
Methods: The proportion of subjects meeting our recovery criteria (improvements in *both* clinical and social domains, and evidence that improvements in at least one of these two domains had persisted for at least two years) was extracted from each study meeting our inclusion criteria. Meta-regression techniques were used to explore the association between recovery proportions and the selected variables.
Results: We identified 53 studies with data suitable for inclusion. The median proportion (25% to 75% quartiles) meeting our recovery criteria was 13.9% (8.7% – 20.9%). Studies from sites with poorer economic status had higher recovery proportions. However, there were no statistically significant differences when the estimates were stratified according to sex, decade of study intake, duration of follow-up, strictness of used diagnostic system, or other design features.
Conclusions: Approximately one in seven individuals with schizophrenia met our criteria for recovery. Despite major changes in treatment options in recent decades, the recovery rates have not increased.

P29 HIRVONEN N. FIRST-EPISODE POSITIVE AND NEGATIVE SYMPTOMS AS PREDICTORS OF SYMPTOM REMISSION IN SCHIZOPHRENIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: The identification of characteristics that predict remission is essential in schizophrenia. Poor outcome has been associated with both positive and negative symptoms at the early course of the illness. However, it is still unclear how early course symptoms associate with remission in a long-term follow-up.
Aims: The aim of this systematic review was to collate studies related to the association between baseline positive and negative symptoms and remission in first-episode schizophrenia, and to synthesize these data with meta-analytic techniques.
Methods: A systematic search to identify potentially relevant studies was conducted using seven electronic databases (PsycINFO, Pubmed, ISI Web of Science, EBSCOhost Academic Search Premier, CINAHL, SciVerse Scopus, Science Direct) and by manual literature search. Search terms included schizophrenia, baseline, outcome, and symptoms with synonymous expressions. Only original studies where baseline symptoms of subjects with first-episode schizophrenia spectrum diagnosis were used to predict remission after at least a two year follow-up were included. The articles were extracted independently by two authors using predefined criteria.
Results: The search identified 4780 unique potentially relevant articles of which preliminary 9 studies met our inclusion criteria. In most studies, more positive and negative symptoms at baseline were associated with smaller probability of remission. The median effect sizes (Cohen's d) were small, -0.15 (range -0.44 to +0.30) for positive and -0.12 (range -0.55 to +0.11) for negative symptoms.
Conclusions: Baseline positive and negative symptoms can be used to predict later remission in schizophrenia. However, the previous literature shows heterogeneous results and at most moderate effect sizes.

P30 RISSANEN I. USE OF ANTIPSYCHOTIC MEDICATION AND SUICIDALITY – THE NORTHERN FINLAND BIRTH COHORT 1966

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Background: Off-label use of antipsychotic medications is increasing which has raised concern about their safety. It has been reported that antidepressant and antiepileptic drugs may increase the risk of suicidality, but the data on antipsychotic medication are inconclusive. Population based studies on antipsychotic medication and suicidality are rare.
Aims: We wanted to find out whether there is association between the use of antipsychotic drugs and suicidality in population based sample.
Methods: Our sample was the Northern Finland 1966 Birth Cohort. Medication data was collected from nationwide medication registers and postal questionnaire (N=8,218) sent to cohort members in 1997. The presence of suicidal ideation was assessed using the Symptom Check List - 25 –questionnaire. We studied associations between suicidal ideation, adjusted for symptoms of depression and anxiety, and use of, different types of, and different doses of antipsychotic medication in different diagnostic groups (schizophrenia, other psychosis, no psychosis).
Results: According to the questionnaire 70 respondents (0.9%; 35; 50.0% males) were on antipsychotic medication. Individuals receiving antipsychotic medication had in general more suicidal ideation, although the associations diminished when taking other symptoms into account. The antipsychotic dose did not relate significantly to suicidality among the individuals who had a diagnosis of schizophrenia ($r=0.31$, $p=0.06$) or other psychosis ($r=-0.12$, $p=0.77$), but among non-psychotic persons higher doses correlated with more suicidal ideation ($r=0.81$, $p<0.001$).
Conclusions: Higher antipsychotic doses are associated with suicidal ideation among non-psychotic individuals. Our results suggest that one should take suicidal ideation into account when prescribing antipsychotic medication off-label.

P31 HUHTANISKA S. LONGITUDINAL STUDIES ON ASSOCIATIONS BETWEEN USE OF ANTIPSYCHOTICS AND BRAIN MORPHOMETRIC CHANGES IN SCHIZOPHRENIA – A SYSTEMATIC REVIEW

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Background: Relatively little is known on longitudinal changes in brain morphometry in schizophrenia after the onset of the illness. People with schizophrenia are known to have changes in their brain compared to healthy controls, but it is still unclear why these changes happen.
Aim: The aim of the current study was to systematically review previous literature on longitudinal MRI studies of antipsychotic effects on brain morphometric changes in schizophrenia and related psychoses.
Methods: Studies were systematically collected using the databases of PubMed, Scopus, Web of Knowledge, and PsycINFO. A particular study was included if subjects were scanned twice and the average scanning interval was at least two years and antipsychotic medication data was used to predict morphometric changes in schizophrenia.
Results: In total 22 studies fulfilled our inclusion criteria. The main finding of our study was that most of the reported correlations were statistically non-significant. The significant associations between antipsychotic use and brain changes were reported from various areas. In the studies with significant findings, use of antipsychotics more often associated with decrease than increase of brain volumes, even in the very few studies taking into account illness severity.
Conclusions: There are no consistent findings on brain changes and antipsychotic use in schizophrenia. The studies often included relatively small samples of schizophrenia patients and there were significant methodological differences in the studies, for instance the studies rarely focused on same research questions. New studies are needed to try to replicate previous findings.

P32 MOILANEN J. BRAIN MORPHOLOGY OF SUBJECTS WITH SCHIZOPHRENIA SPECTRUM DISORDER WITH AND WITHOUT ANTIPSYCHOTIC MEDICATION – THE NORTHERN FINLAND 1966 BIRTH COHORT STUDY

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Background: Recently many studies have been discussed possible effects of antipsychotic medication on brain morphometric changes.
Aims: We aim to compare the brain morphology of subjects with schizophrenia spectrum disorder with and without antipsychotic medication after in average ten year of illness.
Methods: Data of 65 subjects with schizophrenic psychoses (mean duration of illness 10.4 years) from the Northern Finland 1966 Birth Cohort were gathered by interview and from hospital records. Structural MRI data at age 34 years were acquired from all participants on a GE Signa system operating at 1.5T. Grey matter volume maps with voxel-based morphometry were analyzed using FSL tools.
Results: Of the subjects 17 (26%) had taken no antipsychotics during the previous year. Subject with antipsychotic medication had trend-level (p=0.056) smaller total grey matter volumes (TGM) compared with non-medicated subjects. When adjusted with sex, onset age, TGM and remission, medicated had lower volume in left parahippocampal gurys.
Conclusions: In this population based sample, we were able to study effects of antipsychotic medication in heterogeneous sample, including also currently non-medicated individuals. Antipsychotic medication may have harmful effects on brain tissue. Patients should be treated with lowest dose needed to prevent relapses.

P33 JÄÄSKELÄINEN E. ASSOCIATION BETWEEN DURATION OF UNTREATED PSYCHOSIS AND PROGRESSION OF BRAIN VOLUME CHANGE IN SCHIZOPHRENIA – THE NORTHERN FINLAND 1966 BIRTH COHORT

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Background: Long duration of untreated psychosis (DUP) associates to some brain volume differences in schizophrenia in cross-sectional analyses. It is not known how DUP relates to brain volume change over time.
Aim: Our aim was to analyse the association between length of DUP and total brain volume change in schizophrenia in a general population based sample.
Methods: All members of the Northern Finland 1966 Birth Cohort (NFBC1966) known to have had psychotic illness were invited for a field study in 1999-2001 (in average 10 year after onset of psychosis) and follow-up nine years later in 2008-2010. DUP was assessed from medical records. The total brain volume scan interval change and the DUP information were available for 32 subjects with DSM-III-R schizophrenia. We analysed the correlation between length of DUP and the mean annual whole brain reduction, adjusted for age of illness onset and sex.
Results: The mean annual whole brain volume reduction in the sample was 0.66%. The reduction was 0.76% among those with shortest DUP, 0.58% among those with median DUP, and 0.63% among those with longest DUP. There was no statistically significant correlation between DUP and annual brain volume change when adjusted for onset age and/or sex.
Conclusions: We did not find an association between long DUP and brain volume decrease in schizophrenia in 9-years follow up. Although earlier long DUP has been associated with differences in brain volume in cross-sectional analyses, the significance of DUP in brain morphology in long term is unclear.

P34 KETTUNEN K. STRUCTURAL MRI STUDY OF CHILDHOOD- AND ADOLESCENT-ONSET SCHIZOPHRENIA AS A PART OF KELLOKOSKI ADOLESCENT INPATIENT FOLLOW-UP STUDY (KAIFUS)

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Background: There is growing evidence that schizophrenia affects structure and function of the maturing brain during adolescence.
Aims: We aim to analyze the the MR images of the adolescent schizophrenia patients compared to the healthy volunteers. Regions of special interest include the size of the ventricles, the PFC (pre-frontal cortex); the ACC (anterior gingulate cortex), the basal ganglias as well as the various white matter connections.
Methods: In years 2009 – 2010, structural MRI study was carried out to inpatients recruited into KAIFUS meeting DSM-IV-TR criteria of schizophrenia. The same study protocol was offered to other Adolescent inpatient units in HUS (Helsinki and Uusimaa) District**.** Comparison group was recruited from schools. The data include background information, DSM-IV diagnoses based on K-SADS-PL interviews and psychological testing (cognitive capacity and neuropsychological interview). VBM (voxel-based-morphometry) and the DTI (diffusion-tensor-imaging) variables will be analyzed from the MR images.
Results: As a result, 22 patients aged 13 to 17 yrs were scanned with 3T MRI. 8 of the patients were male, 14 were female. 63 healthy volunteers of the same age were recruited to the structural MRI study as a comparison group. 31 of them were female, 32 male. The preliminary results of structural MRI will be analyzed during the spring 2012.
Conclusions: The conclusions, as well as the results, will be published and discussed in the poster made for the congress.

P35 GÖKTALAY G. EFFECTS OF BASELINE PREPULSE INHIBITION ON MORPHINE INDUCED CONDITIONED PLACE PREFERENCE

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Background: Recently we showed that there is a relationship between baseline prepulse inhibition (PPI) and ethanol withdrawal severity or nicotine induced locomotor sensitization. Another reliable method for measuring drug dependence is conditioned place preference.
Aim: The aim of this study was to determine a possible relationship between baseline PPI levels and development of conditioned place preference (CPP) to morphine.
Methods: Male Sprague Dawley (3-4 months) rats were put in a descending order according to their baseline PPI levels at 78 dB prepulse stimulus. The highest 1/3 and the lowest 1/3 proportions were selected as high inhibitory (HI) and low Inhibitory (LI) rats (n= 8), respectively. The CPP procedure was started one week later from baseline PPI. Conditioning sessions were conducted twice a day for four days treated with morphine (2.5 mg/kg) or saline s.c. and confined to one of the two conditioning chambers for 30 min. Actual test were conducted on day 5 approximately 24 h after the conditioning period. During the whole CPP procedure locomotor activity was also measured.
Results: There were significant differences between HI and LI groups for the PPI ($p<0.05$). Locomotor activity was also different between HI and LI groups ($p<0.05$). Low inhibitory rats showed less preference for the black striped box ($p<0.05$). However, there was no significant difference between the two groups for the morphine induced CPP ($p>0.05$).
Conclusion: Our results show that baseline PPI level has a significant impact on the natural preference in CPP test cages, however do not predict morphine induced CPP.

Acknowledgement: This research has been supported by a grant from Uludag University Scientific Research Project Office. Project Number: T-2008/4

P36 KAYIR H. BASELINE PREPULSE INHIBITION DOES NOT CORRELATE WITH ANXIETY IN ELEVATED PLUS-MAZE TEST

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Background: Prepulse inhibition (PPI) of startle reflex reflects the functioning of sensorimotor gating system. PPI is disrupted in psychotic disorders, such as schizophrenia. Anxiety is more common in psychotic patients than normal population.
Aim: Investigating the relationship between baseline PPI and anxiety measures in elevated plus-maze (EPM) test was aimed.
Methods: Baseline PPI levels of 20 adult, male Wistar rats were measured. Anxiety levels of the same animals were evaluated in EPM test. Correlations between the outcomes of PPI test, such as startle reflex amplitude and latency, percent PPI, and percent habituation, and percent closed arm exploration time in EPM test were evaluated. Further, the rats were assigned into two groups (high-PPI and low-PPI) according to their basal PPI values. High-PPI and low-PPI rats were compared for their EPM test results.
Results: There was no significant correlation between any of the PPI test outcomes and anxiety measure in EPM test (R^2 values< 0.172, p values> 0.05). Anxiety level was also similar when the rats grouped as high-PPI and low-PPI (p values> 0.05).
Conclusions: Our results show that baseline anxiety level in EPM test is independent from baseline PPI levels in rats. However, other anxiety test such as social anxiety should also be evaluated in further studies.

Acknowledgement: This study has been supported by the Scientific and Technological Research Council of Turkey (TUBITAK, project# 105S387-SBAG-3194).

P37 DI LORENZO R. HYPERHOMOCYSTEINEMIA IN SCHIZOPHRENIA: A POSSIBLE MARKER OF CHRONIC DYSFUNCTION OR A CONFOUNDING FACTOR?

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Background: Hyperhomocysteinemia may represent an increased risk for cardio-vascular and neurodegenerative diseases. Recently, hyperhomocysteinemia was related to schizophrenic disorders, although not all the studies confirmed these findings.
Aims: In a population with schizophrenic disorders, we evaluated whether homocysteine blood level was significantly higher than in a comparable control group and was correlated to selected schizophrenic features.
Methods: The blood level of homocysteine, folate and vitamin B12 was examined in a population of patients (n=100) with schizophrenia and schizophreniform disorder (DSM-IV-TR), admitted to an acute psychiatric ward (SPDC1 of Modena) from 1-12-07 to 1-12-2010, and compared to that of a control group (n=100) matched for age and gender.
We analyzed the correlation between homocysteinemia and the following variables: gender, age, years of illness, number of previous psychiatric admissions, and Brief Psychiatric Rating Scale (BPRS), Positive Negative Syndrome Scale (PANSS) and Global Assessment Functioning (GAF) scores (Spearman Kendall rank correlation, chi square, t test).
Results: We observed an elevated homocysteinemia in 48% of the patients, a reduction of folate and vitamin B12 levels in 36% and 9%, respectively. Homocysteinemia presented a positive statistically significant correlation with age and years of illness and a negative statistically significant correlation with GAF score, but not with other variables. We did not find any statistically significant difference between the homocysteine level of patients and control group one.
Conclusions: Hyperhomocysteinemia may occur in chronic schizophrenia related to poor social and relational functioning, but it could simply represent an effect of both aging and altered psychotic lifestyle.

P38 DARYANI A. SEROLOGICAL SURVEY OF TOXOPLASMA GONDII IN SCHIZOPHRENIA PATIENTS REFERRED TO PSYCHIATRIC HOSPITAL, SARI CITY, IRAN

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Background: Schizophrenia is a severe neuropsychiatric disorder of unknown etiology.
Aims: As there is little information about the association between *Toxoplasma gondii* infection and schizophrenia in Iran, we investigated the seroprevalence of *T. gondii* in these patients and compared with that obtained in control individuals.
Methods: Eighty schizophrenia patients and 99 healthy people in Sari city, Iran, 2009, were examined for the presence of IgG and IgM antibodies to *T. gondii* by enzyme linked immunosorbent assay (ELISA).
Results: Overall prevalence rates of anti-*T. gondii* antibodies (IgG/IgM) in case and control groups were 72.5% and 61.6%, respectively ($P>0.05$). IgG antibodies indicating chronic form of toxoplasmosis were found in 28 (35%) and 25 (25.3%) of case and control groups, respectively ($P>0.05$). IgM antibodies (acute form) were also seen in 9 (11.2%) and 11 (11.1%) of case and control individuals, respectively ($P>0.05$). The highest 10^{th} percentile of IgG titers in schizophrenia individuals (18.8%) was significantly higher than control group (6.1%, $P=0.02$).
Conclusions: As prevalence rate of *T. gondii* antibodies in patients with schizophrenia was high, it seems that designing a cohort study will determine the causative relationship between *Toxoplasma* infection and schizophrenia.

P39 GARCIA-RIZO C. CANNABIS USE AND ENERGY INTAKE HOMEOSTASIS IN FIRST EPISODE PSYCHOSIS

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Cannabis use is highly related to psychosis onset, however the actual state of knowledge refers the endocannabinoid system as a key player in energy intake homeostasis, involved in the control of both appetite and peripheral fat metabolism. We compared the metabolic profile of first episode patients with non affective psychosis regarding its cannabis use. We measured serum ghrelin levels in 31 male patients with a first episode of non affective psychosis. Cannabis users (N=17) showed a higher level of serum ghrelin [1170,2 pg/mL] compared with non user patients (N=14) [821,4 pg/mL]; (p=.019).Our results highlight the importance of cannabis use besides its implication in the psychotic breakout. Its use may interfere in the energy intake homeostasis from the patients, modifying its metabolic profile and the risk of cardiovascular adverse events.

P40 MANRIQUE-GARCIA E. CANNABIS, SCHIZOPHRENIA AND OTHER NON-AFFECTIVE PSYCHOSES: 35 YEARS OF FOLLOW-UP OF A POPULATION-BASED COHORT

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Background: There is now strong evidence that cannabis use increases the risk of psychoses including schizophrenia, but the relationship between cannabis and different psychotic disorders, as well as the mechanisms, are poorly known. We aimed to assess types of psychotic outcomes after use of cannabis in adolescence and variation in risk over time.
Methods: A cohort of 50 087 military conscripts with data on cannabis use in late adolescence was followed up during 35 years with regard to in-patient care for psychotic diagnoses.
Results: Odds ratios for psychotic outcomes among frequent cannabis users compared with non-users were 3.7 [95% confidence interval (CI) 2.3–5.8] for schizophrenia, 2.2 (95% CI 1.0–4.7) for brief psychosis and 2.0 (95% CI 0.8–4.7) for other non-affective psychoses. Risk of schizophrenia declined over the decades in moderate users but much less so in frequent users. The presence of a brief psychosis did not increase risk of later schizophrenia more in cannabis users compared with non-users.
Conclusions: Our results confirm an increased risk of schizophrenia in a long-term perspective, although the risk declined over time in moderate users.

P41 MOILANEN K. UNWANTEDNESS OF PREGNANCY, PARENTAL PSYCHOSIS AND SUBSEQUENT RISK OF SCHIZOPHRENIA IN THE OFFSPRING IN THE NORTHERN FINLAND 1966 BIRTH COHORT

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Background: The role of unwanted pregnancy as a risk factor for schizophrenia needs to be investigated.

Aim: We examined the interaction between unwantedness and parental psychosis as a risk for schizophrenia.

Methods: In the Northern Finland 1966 Birth Cohort mothers of 12,058 children were asked at mid-gestation whether their pregnancy was unwanted. The offspring were followed for over 30 years. Psychoses (offspring/parental) were detected using the Finnish Hospital Discharge Register. Altogether 111 cases of DSM-III-R schizophrenia were identified. Information on biological and psychosocial risks were analysed by logistic regression and chi-squared automatic interaction detection analysis (CHAID).

Results: In the logistic regression the highest adjusted odds ratio (OR) of schizophrenia was found among unwanted offspring with a psychotic parent (OR: 8.8; 95% confidence interval CI: 3.4-23.2) followed by the risk among offspring with only parental psychosis (OR: 3.3; 95% CI: 1.7-6.4) or only unwantedness (OR: 1.5; 95% CI: 0.8-2.8) compared to those without either of them. Parental psychosis was the strongest risk factor for schizophrenia by CHAID analyses. Among offspring with a psychotic parent mother's frame of mind during pregnancy and unwantedness of pregnancy predicted also schizophrenia. Among offspring without a psychotic parent gender of the child segmented the data sample into two subsets. Further, among girls, unwantedness of pregnancy predicted schizophrenia.

Conclusions: Unwantedness carries a risk factor for schizophrenia especially when interacting with parental psychosis. Being born from unwanted pregnancy may act as an additive factor for subjects already vulnerable to schizophrenia but it may also be a independent risk factor among girls.

P42 DANTAS C.R. DEFICIT AND NON-DEFICIT SCHIZOPHRENIA DO NOT DIFFER REGARDING SEASON OF BIRTH IN BRAZILIAN SOUTHERN AND SOUTHEAST REGIONS

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Background: There is a 5-10% excess of births in winter and spring among the patients with schizophrenia born in the northern hemisphere. However, in patients with the deficit syndrome of schizophrenia, there is a slight over-representation of births in summer. The data from the southern hemisphere have been less consistent.
Aims: In this study, we aimed at verifying whether the same patterns reported in the northern hemisphere are found in patients with schizophrenia born in the Brazilian south and southeast regions (latitudes 14° S to 33° S).
Methods: Seventy-six patients with schizophrenia were assessed for demographics and psychopathology and also categorized for the presence of deficit syndrome using the SDS. Patients with deficit and non-deficit schizophrenia were compared for the season of birth. In addition, we compared psychopathological variables between patients born in all four seasons.
Results: There was no significant difference in the distribution of births according to the seasons. Although two thirds of the patients with deficit syndrome were born in the summer and autumn, this over-representation did not reach statistical significance. We found no differences regarding psychopathology between patients born in all four seasons.
Conclusions: In the south and southeast regions of Brazil, there was no significant excess of births in the summer between schizophrenic patients with deficit syndrome, neither was an excess of births in winter and spring in the overall sample of patients with schizophrenia.

P43 KUKKOHOVI L. LEARNING AND GENERALIZATION IN SCHIZOPHRENIA, OTHER PSYCHOSES, SIBLINGS, AND CONTROLS. THE NORTHERN FINLAND 1966 BIRTH COHORT STUDY

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Background: In addition to positive and negative symptoms neurocognitive impairments are a core feature of schizophrenia. The medial temporal lobe (MTL) is a crucial brain region associated with declarative memory important in conscious acquisition and recollection of facts and events. The basal ganglia (BG) instead are linked to non-declarative memory functions such as gradual learning of skills and habits. Acquired equivalence is a phenomenon in which prior training to treat two stimuli as an equivalent increases generalization between them. The stimulus-response learning is mediated by the BG and the stimulus generalization by the MTL.
Methods: The Northern Finland Birth Cohort 1966 is based upon 12 068 women and their 12 058 live-born children. The modified Rutger´s Acquired Equivalence task (AE) was performed for 35 schizophrenia patients, 26 patients suffering from other psychosis, 21 siblings and 174 control subjects.
Results: The behavioral data showed significant impairment in both BG mediated learning and MTL mediated stimulus generalization in schizophrenia group compared to control subjects. Other psychosis group also showed impaired performance in both tasks compared to controls. Siblings did not differ significantly from controls in BG mediated learning but showed impairments in MTL mediated stimulus generalization.
Conclusions: In previous studies BG mediated learning has been unimpaired in schizophrenia patients whereas MTL mediated stimulus generalization has been declined. In our data schizophrenia and other psychotic patients showed impairments in both learning and generalization. In siblings learning was intact, but they showed impairments in generalization.

P44 RÖNKKÖ E. THE EFFECT OF TYPICAL AND ATYPICAL ANTIPSYCHOTIC MEDICATION ON BASAL GANGLIA MEDIATED LEARNING AND MEDIAL TEMPORAL LOBE MEDIATED STIMULUS GENERALIZATION IN SCHIZOPHRENIA. THE NORTHERN FINLAND 1966 BIRTH COHORT STUDY

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Background: Generalized cognitive impairments affecting e.g. memory and learning is a core feature of schizophrenia. Acquired equivalence (AE) is a phenomenon in which prior training to treat two stimuli as an equivalent increases generalization between them. The stimulus-response learning is mediated by the basal ganglia and the stimulus generalization by the medial temporal lobe. Antipsychotic drugs (APD) affect the performance in the AE-task. The difference between atypical APD's and typical APD's effects on cognition rely on their different receptor affinity and occupance profiles. D_2-receptor being the most important in conjuction with 5HT2A-receptor in the case of atypical APDs.
Methods: The Northern Finland Birth Cohort 1966 is based upon 12 068 women and their 12 058 live-born children. The modified Rutger´s Acquired Equivalence task (AE) was performed for 35 schizophrenia patients, 26 patients suffering from other psychosis, 21 siblings and 174 control subjects.
Results: Other psychosis group treated with typical APDs showed impairments in BG mediated learning compared to patients not treated with typical APDs. There was a similar, yet not statistically significant, trend also in the schizophrenia group. The overall trend showed that higher doses equal poorer performance on the task.
Conclusions: In previous studies APD treatment has shown to be beneficial to patient's performance in the AE-test but this was not the case in our study. The adverse effect on BG mediated learning caused by typical APD treatment was seen in our results.

P45 MENDREK A. PRELIMINARY FUNCTIONAL IMAGING RESULTS SHOW THAT CUE-INDUCED CRAVINGS ELICIT ORBITOFRONTAL ACTIVATIONS IN PATIENTS WITH CANNABIS ABUSE/DEPENDENCE

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Background: Given that drug craving is a significant predictor of drug relapse in substance abusers, numerous groups examined the neural correlates of cue-elicited craving. Relative to tobacco, alcohol and cocaine, marijuana craving has attracted far less attention thus far. To our knowledge, only one functional imaging has been performed and it involved regular cannabis smokers.
Aims: Here, we sought to explore the neural correlates of cue-elicited marijuana craving in substance abusers.
Methods: Craving was elicited using marijuana pictures while patients were scanned with functional magnetic resonance imaging (fMRI). Nine patients with cannabis abuse/dependence were recruited, with (n=4) and without (n=5) schizophrenia (DSM-IV criteria). Participants were active marijuana smokers who avoided smoking cannabis 6 hours prior to the scanning session. fMRI data were analyzed using SPM-5.
Results: Cannabis cues elicited potent cravings (mean=52%) on a visual analog scale ranging from 0 (no craving) to 100 (strongest imaginable craving). A one-sample t-test revealed that marijuana images induced significant loci of activation in the medial orbitrofrontal cortex, left hippocampus, superior parietal cortex, inferior occipital cortex, and the cerebellum. Cannabis cravings were positively correlated with medial orbitofrontal activations.
Discussion: These preliminary results show that marijuana pictures elicit potent cravings in substance abusers, and that cannabis cravings are mediated by medial orbitofrontal activations, a result consistent with the pre-clinical literature showing that this region plays a critical role in drug addiction. In the future, our group intends to explore whether the neural correlates of cannabis craving differ between patients with and without schizophrenia.

P46 MÄNTYLÄ T. ACTIVATION OF THE PREFRONTAL CORTEX DURING AUTOMATIC REALITY MONITORING OF NATURALISTIC STIMULATION DIFFERENTIATES PSYCHOTIC AND HEALTHY SUBJECTS

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Background: The most distinctive factor in psychotic disorders is reality distortion. Previous studies have suggested that attenuated prediction-error signaling in the right dorsolateral prefrontal cortex (rDLPFC) during violation of expectations in simplistic cognitive tasks is related to reality distortion symptoms. Whether the attenuated rDLPFC function is similar during the evaluation of realisticness of natural environment, however, remains unknown.
Aims: To compare the brain basis of automatic reality monitoring during naturalistic audiovisual stimulation (movie viewing) in psychotic and healthy subjects.
Methods: Patients with first-episode psychosis (n=15) and healthy control subjects (n=13) viewed a 7 minute movie clip from Tim Burton's Alice in Wonderland during functional magnetic resonance imaging. The clip was edited to contain scenes with variable realism. An independent, healthy control group (n=18) rated continuously how likely the events currently seen in the movie could happen in real life. Mean time series of the realisticness ratings was subsequently used to predict brain activation during movie viewing in the general linear model.
Results: DLPFC activity in the right hemisphere showed stronger negative correlation with realisticness of movie events in controls than in patients (FDR corrected $p < 0.05$).
Conclusions: Our findings suggest that rDLPFC signaling is related to evaluation of realisticness in natural environment. Furthermore, these results support the hypothesis of disturbed rDLPFC signaling in reality distortion, as previously shown with simplistic cognitive tasks on violation of expectations.

P47 HUOSSA V. WHOLE BRAIN NETWORK ANALYSIS OF SCHIZOPHRENIA

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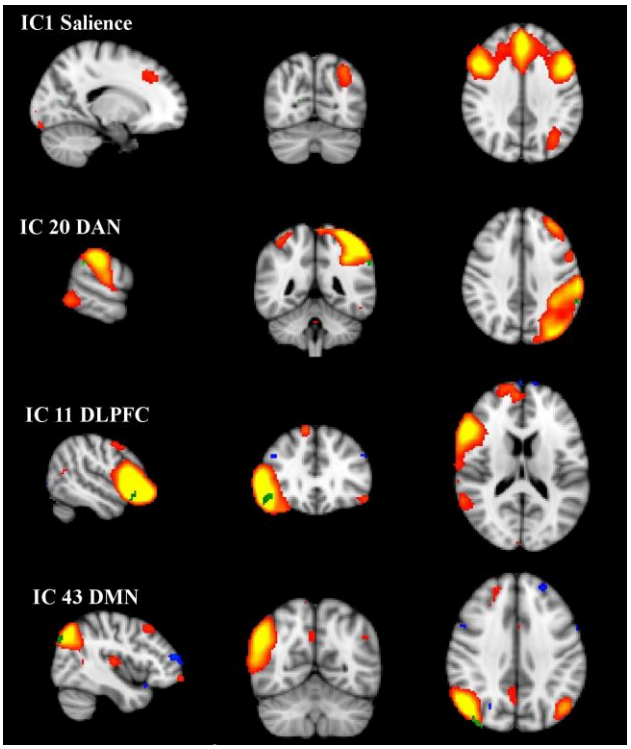
Background: Our fMRI laboratory has developed a new data concatenation method that enables the assessment of multiple brain networks covering the whole brain cortex to be analysed simultaneously [1]. The analysis enabled the correction for type I error for that follows the selection of several brain networks instead of one. We hypothesized that resting-state functional connectivity (measured using ICA and dual regression) would be altered in schizophrenia in the Northern Finland 1966 Birth Cohort (NFBC 1966) data sample.
Methods: 43 (17 ♀, 26 ♂) NFBC 1966 subjects with schizophrenia were compared to matched (age-, gender- and ethnicity) controls. Resting-state BOLD data (GE 1.5 T ,TR 1800 ms, TE 40 ms, 280 time points). MELODIC probabilistic independent component analysis (PICA) [2] using 70 components applied to detect RSNs [3]. Dual regression [4] was used to obtain spatial maps of each subject's fMRI data set. All results were then corrected twice for multiple comparisons ($P<0.05$); primarily voxel level correction for each IC was performed with typical TFCE randomize correction in FSL. The secondary inter-IC TFCE-correction for multiple IC's was performed after concatenating 4D randomize dataset into a single file in y-direction and running 10 000 iterations.
Results & Conclusion: 39 RSN's were identified and at voxel level some 25 RSN's had elevated functional connectivity compared to controls. After 2nd level concatenation correction for multiple RSN's four RSN's showed alterations. IC 1 of fronto-insular Salience and IC 11 of DLPC networks had anatomically altered functional connectivity. IC 20 Dorsal attention network and IC 43 cranial default mode network had increased functional connectivity in schizophrenic subjects compared to controls.



References

Jafri MJ, Pearlson GD, Stevens M, Calhoun VD. A method for functional network connectivity among spatially independent resting-state components in schizophrenia.Neuroimage. 2008;39(4):1666-81.
Beckmann CF, Smith SM (2004), "Probabilistic independent component analysis for functional magnetic resonance imaging", IEEE Trans Med Imaging, pp. 137-152.
Abou Elseoud et al., (2010), "The effect of model order selection in group PICA", Human Brain Mapping, pp. 1207-1216.
Filippini et al., (2009), "Distinct patterns of brain activity in young carriers of the APOE-epsilon4 allele" Proc Natl Acad Sci USA, pp. 7209-7214.

General information

Conference fee includes participation to all lectures and oral and poster presentations, abstract book, lunch and coffee, welcome reception, conference dinner, and city reception.

Conference venue: Hotel Lasaretti, Kasarmintie 13, 90101 Oulu
The conference venue is situated in culturally and historically valuable setting on the idyllic Lasaretinsaari (Island Lasaretti), appr. 2 kilometres from the city centre.
Free wireless internet (panOULU; www.panoulu.net) is available in the conference venue and in many locations in the city centre.
There is a cafeteria in the conference venue.

Registration and information desk
Registration and information desk is in the lounge of the conference venue. The opening hours are: Sunday 17th June 16:00-19:00; Monday 18th June 8:00-18:00; Tuesday 19th June 8:30-18:00, and Wednesday 20th June 8.30-18:00.

Conference dinner
The conference dinner is held in Maikkula Estate (Maikkulanrinne 21, 90240 Oulu) on Monday evening (19.00-01.00). Registration in advance is required.
Maikkula Estate is located approximately 8 kilometres South-East from the conference venue.
There is free bus transportation from the Hotel Lasaretti to Maikkula Estate and back. Timetables are provided in the information desk.

Poster sessions and presentations
Poster sessions are held each day after lunch time, between 13:30-14:30, in Yrjö Hall. Posters are present during all conference days. The presenting author is invited to give a short oral overview of the poster's content during one of the three poster sessions. At least one of the authors should be present at their poster at designated sessions. The organising committee offers a small award to the best poster of the conference.

Organisers
Oulu Psychiatric Epidemiology Society, OPES
Department of Psychiatry, University of Oulu

Organising committee
Adjunct Professor Jouko Miettunen; MD, PhD Erika Jääskeläinen; MD, PhD Antti Alaräisänen; PhD Marianne Haapea; MSc Tanja Nordström; MD Matti Penttilä; BMed Ina Rissanen; BMed Pauliina Juola; Professor Juha Veijola; Adjunct Professor Pirjo Mäki; Professor Matti Isohanni.

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Transportation

The distance from the Oulu airport to the city centre is about 15 kilometres. There is an airport bus (bus #19) from the airport to Oulu city centre and from Oulu city centre to the airport. The timetable of the bus can be found from www.koskilinjat.fi. The price for one way ticket from airport to city centre is approximately 5 Euros. The taxi drive from/to the airport costs approximately 40 Euros. There is taxi stop outside the airport, and taxi can also be ordered by phone: +358 600 30081 (from Finnish mobile phone 0600 30081).
The Oulu train station is located in the city centre.

Transportation inside Oulu

Taxi: The number of taxi of Oulu is +358 600 30081 (from Finnish mobile phone 0600 30081).

Public bus: One way bus ticket costs 3.20 Euros. The timetables of busses can be found from www.koskilinjat.fi, and are also available in the information desk at the conference venue.

Information about Oulu
http://www.oulu.com/
http://www.oulutourism.fi/en

The weather in Oulu during the conference is likely to be sunny and warm, appr. +20 degrees Celsius, but with chance of rain. During the Midsummer it does not get dark in the Northern Finland.

The currency of Finland is Euro. The time zone is GMT+2.

Shopping in Oulu: The city centre's shopping streets are Kirkkokatu (pedestrian street called Rotuaari), Isokatu, Uusikatu, Kauppurienkatu, Pakkahuoneenkatu, and Hallituskatu. When you find the pedestrian street Rotuaari, you will also find the Market Hall and Market Square. You can get to the Market Hall and Market Square easily from the Rotuaari by walking along the Kauppurienkatu towards the sea.

MAPS

Hotel Lasaretti

The following parts of Hotel Lasaretti are used during the conference:

1. Reception, info desk
2. Hotel rooms
3. Lasaretti Restaurant
4. Sauna-cabinet as a speakers' room
5. Aurora Hall
6. Merikoski Hall
8. Linna Cabinet
11. Yrjö Hall

City Center


Tuiranranta
Koskikeskus
Hotel Lasaretti
8156
Merikoskenkatu
Hupisaaret
Lammassaari
Kasarmintie
Salmelanti
Nahkatehtaankatu
Makasiinikatu
Väljastehtaankatu
Linnankatu
Isokatu
Oikokatu
Ojakatu
Kajaaninkatu
8156
Uusikatu
Tulliväylä
Hallituskatu
City Hall
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847
Lävistäjä
Heikinkatu
Aleksanterinkatu
Torikatu
Asemakatu
Pakkahuoneenkatu
OULU
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