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ABSTRACTS

3rd European Conference on Schizophrenia Research: Facts and Visions

PL-01 A 100 years of schizophrenia: from Bleuler to DSM-V/ICD-11

PL-01-001
A 100 years of schizophrenia: from Bleuler to DSM-V/ICD-11

A. Jablensky (The University of Western Australia, Perth, Australia)

Abstract: Schizophrenia is a disorder with variable phenotypic expression and poorly understood complex etiology, involving a major genetic contribution, as well as environmental factors interacting with the genetic susceptibility. The disorder occurs in diverse populations at comparable rates and, although its incidence has not changed much over the past two centuries, the disease concept originated in late nineteenth century with Kraepelin's proposal to integrate catatonia, hebephrenia and *démence precoce* into a single nosological entity under the name of *dementia praecox*. Kraepelin emphasised that "we meet everywhere the same fundamental disorders in the different forms of *dementia praecox*…in very varied conjunctions, even though the clinical picture may appear at first sight ever so divergent". However, it was Eugen Bleuler who coined the term "schizophrenia" in 1908, and modified significantly Kraepelin's original concept by stating in 1911 that schizophrenia "is not a disease in the strict sense, but appears to be a group of diseases…Therefore we should speak of schizophrenias in the plural". Bleuler introduced a fundamental distinction between *basic* (obligatory) and *accessory* (supplementary) symptoms of the disorder and acknowledged that "schizophrenia must be a much broader concept than the overt psychosis of the same name", thus foreshadowing the notion of schizophrenia spectrum disorders. As defined currently in ICD-10 and DSM-IV, the clinical concept of schizophrenia is supported by empirical evidence that its multiple facets outline a broad syndrome with likely heterogeneous genetic underpinnings and a still incompletely understood pathophysiology. However, the study of endophenotypes cutting across the conventional diagnostic boundaries is likely to reveal unexpected shared genetic associations with features of autism, bipolar disorder and certain neurological diseases. The mapping of clinical phenomenology on specific brain dysfunction is now becoming feasible and the resulting functional psychopathology may in the future substantially recast the present nosology.
Policy of full disclosure: None.

PL-02 Schizophrenia treatment and prevention: facts and visions

PL-02-001
Schizophrenia treatment and prevention: facts and visions. Providing the best treatment today and developing better treatments for tomorrow

R. Tandon (University of Florida, Gainesville, USA)

Abstract: The introduction of second-generation antipsychotics and cognitive therapies for schizophrenia over the past two decades generated considerable optimism about possibilities for recovery. To what extent have these developments resulted in better outcomes for affected individuals? What is the current state of our science and how might we address the many unmet needs in the prevention and treatment of schizophrenia? In this presentation, I briefly trace the evolution of various treatments for schizophrenia and summarize current knowledge about available pharmacological and psychosocial treatments. I consider the frequent efficacy-effectiveness gap in the provision of available treatments and note the significant variability in individual treatment-response and outcome. I believe a careful appraisal of current clinical knowledge and its disciplined application will substantially improve patient outcomes today—an individualized treatment approach which emphasizes careful monitoring and ongoing collaborative decision-making is outlined. Looking to the future, I note that the evolution of both pharmacological and psychosocial treatments thus-far has been based principally on serendipity and intuition. In view of our improved understanding of the etiology and pathophysiology of schizophrenia, there is an opportunity to develop prevention strategies and treatments based on this enhanced knowledge. In this context, I discuss potential psychopathological treatment targets and enumerate current pharmacological and psychosocial development efforts directed at them. Considering the stages of schizophrenic illness, I review approaches to prevent progression from the pre-symptomatic high-risk to the prodrome to the initial psychotic phase to chronicity. I evaluate the potential contribution of pharmacogenomics and other biological markers in optimizing individual treatment and outcome in the future.
Policy of full disclosure: None.

PL-03 Social cognition and schizophrenia

PL-03-001
Social cognition and schizophrenia

M. F. Green (UCLA and VA Greater Los Angeles, Los Angeles, USA)

Objective: This presentation will cover 4 topics: (1) how social cognition is defined and measured in schizophrenia research; (2) its relationship to community outcome and its role as a mediator; (3) how measures from social neuroscience can be adapted for use in schizophrenia research, and (4) the development of a training intervention for social cognition.
Methods: Several types of methods will be discussed, including cross-sectional and longitudinal studies of prediction of outcome from performance measures, case control studies of behavioral and neuroimaging paradigms from social neuroscience, and a randomized controlled trial of a training intervention.

Results: Social cognition can be reliably measured in schizophrenia and it can be divided into meaningful subcomponents, such as emotion processing, social perception, theory of mind, and attributional bias. It shows consistent relationships to daily functioning that tend to larger than the relationships between non-social neurocognition and functioning. Also, it acts as a mediator between neurocognition and community functioning in statistical models of outcome. Studies from fMRI show that schizophrenia patients do not activate the same brain networks as controls during a mental state attribution task and during a test of empathic accuracy. Lastly, a new 12-week training intervention has shown some promise for improving aspects of social cognition (e.g., emotion perception and emotion management) in patients.
Conclusion: Social cognition is a rapidly emerging area of research in schizophrenia with a clear growth in number of publications. It holds considerable explanatory power for understanding the determinants and mechanisms of outcome, identifying underlying neural substrates of social processes that might be dysfunctional in schizophrenia, and the development of novel interventions that will facilitate recovery for patients.
Policy of full disclosure: I have served as a consultant for: Abbott Laboratories, Amgen, Cypress, Lundbeck, and Teva. I have served as a speaker for Otsuka and Sunovion.

S-01 Developments in DSM-V and ICD-11 with respect to schizophrenia

S-01-001
Trends, perspectives and problems of classification systems

N. Sartorius (Association for the Improvement of Mental Health Programmes, Geneva, Switzerland)

Abstract: The imminence of the 11th Revision of the International Classification of Diseases (ICD) and the 5th Revision of the Diagnostic and Statistical Manual of the American Psychiatric Association makes it timely and useful to recall some of the problems inherent in the classification of mental disorders and some of the contextual factors that influence the process of its revision and use. Among the former the two most important are the continuing scarcity of findings that would allow the move from the description of mental disorders to the definition of mental diseases and the problem of separating the diagnosis of a disorder from the definition of a "case" for epidemiological investigations and the provision of mental health care. Among the many issues related to the context of the revision the most prominent are those related to the use of the classification for public health purposes, for the development of treatment guidelines, the education in psychiatry and the orientation of future research. The presentation will address these issues and list the challenges that have to be overcome if the classification of mental disorders is to be useful.
Policy of full disclosure: None.

S-01-002
Defining schizophrenia: from Kraepelin to DSM-V

R. Tandon (Department of Psychiatry, University of Florida College of Medicine, Newberry, USA)

Abstract: Although dementia praecox or schizophrenia has been considered a unique disease entity for the past century, its definitions and boundaries have changed considerably over this period. Despite changing definitions, the construct of schizophrenia does convey useful information: (i) patients diagnosed as having schizophrenia do have *some real disease*—they experience both suffering and disability; (ii) a diagnosis of schizophrenia does suggest a *distinctive clinical profile*—a characteristic long-term course; an admixture of positive, negative, and cognitive symptoms; likelihood of benefit from antipsychotic treatment; and (iii) schizophrenia satisfies criteria for a valid diagnostic entity better than almost any other psychiatric diagnosis. On the other hand, the concept of schizophrenia has serious shortcomings. First, it is not a single disease entity—it has multiple etiological factors and pathophysiological mechanisms. Second, its clinical manifestations are so diverse that its extreme variability has been considered by some to be a core feature. Third, its boundaries are ill-defined and not clearly demarcated from other clinical entities. In DSM-V, several proposed revisions to address these limitations are being field-tested. For example, instead of current subtypes and course specifiers, the heterogeneity of schizophrenia might be significantly explained by the interplay between variations in: (a) illness dimensions and intermediate phenotypes; and (b) distinct stages of schizophrenic illness. Better delineation of schizoaffective disorder and clarification of the nosological status of catatonia are two additional major initiatives. The DSM-V approach to providing a more useful description of schizophrenia will be summarized.
Policy of full disclosure: None.

S-01-003
Recent developments on the way to ICD-11

W. Gaebel (Department of Psychiatry and Psychotherapy, Medical Faculty, LVR-Klinikum Düsseldorf, Heinrich-Heine-University, Duesseldorf, Germany)

Objective: To describe the current topics in the development of the revised criteria for psychotic disorders in ICD-11 with a special review of the current discussion in the newly formed WHO Working Group on Psychotic Disorders for the development of ICD-11.
Methods: Review of the current discussion on the reclassification of schizophrenia and other psychotic disorders including novel aspects of conceptualizing schizophrenia based on genetic or other neurobiological evidence. Report on the work of the international Working Group on Psychotic Disorders installed by the World Health Organisation in early 2011.
Results: Genetics and other neurobiological findings in schizophrenia research do not yet result in novel classification criteria for psychotic disorders. Therefore, clinical symptoms will remain the mainstay of diagnostic assessments of people with psychotic disorders. The WHO Working Group on Psychotic Disorders has so far decided that the structure of the psychotic disorders chapters needs some revision as to a revision of the transient psychotic disorders and the introduction of schizophreniform disorder. Discussions are currently underway to develop optimized definitions of all categories of psychotic disorders including course specifiers.
Conclusion: The Working Group on Psychotic Disorders has identified several key aspects of the classification of psychotic disorders which warrant further literature reviews in order to identify the best available evidence, especially regarding the defining clinical criteria like key symptoms of schizophrenia, i.e., the classificatory value of first-rank symptoms, and duration criteria, course specifiers and issues pertaining to the inclusion of functional impairments or cognitive dysfunctions in diagnostic algorithms. Further topics of ongoing discussions are the potential inclusion of a psychosis risk syndrome in ICD-11, how to deal with schizophrenia subtypes and whether dimensional assessments would be necessary and feasible as has been proposed for DSM-5.

Policy of full disclosure: Personal financial relationship 2010 until now:
Wolfgang Gaebel has received symposia support from Janssen-Cilag GmbH, Neuss, Lilly Deutschland GmbH, Bad Homburg and Servier, Munich. He is a member of the Scientific Advisory Board of Lundbeck International Neuroscience Foundation (LINF), Denmark.

S-02 Suicide and suicidal behavior in recent onset psychotic disorders

S-02-001
Risk and suicidal behavior in recent onset psychotic disorders

M. Nordentoft (Psychiatric Centre Copenhagen, Faculty of Health Sciences, University of Copenhagen, Gothenburg, Denmark), M. Pompili, P. Mortensen, C. Pedersen, T. M. Laursen

Objective: Previous estimates of life-time risk of suicide in schizophrenia and schizophrenia spectrum disorders were based on short term follow-up or selected samples. We wanted to analyze the absolute risk of suicide in schizophrenia in a national Danish incident cohort, compared to a representative sample of the non-psychiatric population.
Methods: We extracted individual data from Danish longitudinal registers and carried out a prospective study of incident cases with schizophrenia followed up to 36 years. Persons born in Denmark 1955–2006 were followed from their first contact with schizophrenia until suicide, death from other causes, emigration or disappearance, or 31 December 2006. For each participant, five age and sex-matched controls without any history of mental disorder were included. We also analyzed suicide risk in a recent cohort of patients with first onset schizophrenia in the period 2000–2006 and compared suicide risk among patients and the non-psychiatric population.
Results: Among men with schizophrenia, the absolute risk of suicide in percent was 6.47(95% CI: 5.78–7.25). Among women with schizophrenia the risk in percent was 4.87 (95% CI: 4.00–5.93). The co-occurrence of a suicide attempt increased the risk approximately two fold. In the most recent cohort, the rate ratio for suicide was 38 for men and 34 for women during an up to 6 years follow-up period.
Conclusion: Absolute risk of suicide was analyzed in the hitherto largest complete national sample with the longest follow-up. Schizophrenia was associated with high risk of suicide, and this risk was markedly increased in patients who also had a history of suicide attempt.
Policy of full disclosure: None.

S-02-002
Development of suicidal behavior in first episode psychosis

I. Melle (Psychosis Research Unit, Oslo University Hospital, Oslo, Norway), J. O. Johannessen, J. I. Røssberg, I. Joa, U. Haahr, S. Friis, T. K. Larsen, S. Opjordsmoen, E. Simonsen, P. Vaglum, B. Rund, T. McGlashan

Objective: The risk of suicide is high in early psychosis. Initial results from the present early intervention study indicated that early intervention reduces severe sicidalityat start of first treatment.
Methods: Five year follow-up of initial study participants.
Results: There were no differences between the Early Detection (ED) and the No-Early Detection (No-ED) sites in deaths (13/5%) and suicides (7/3%). For the 186 patients with suicidality data at 5-year follow-up, there were no differences in severe suicidality (plans and attempts) between the sites. The rate of severe suicidality in the ED group fluctuated around 5-–10% at all time points, while the rate in the NoED group decreased from 20% before treatment start to the same levels as the ED group. A K mean cluster analysis indicated four groups of development across samples and time-points: A main group with no suicidal ideation at all; one group with stable low levels; one group with moderate levels of suicidality before start of treatment, no apparent suicidality during the two-year treatment program but subsequent increase in suicidal ideation; and one group had severe suicidality before treatment start but low levels from that point onward. This group's median duration of untreated psychosis (DUP) were over the combined samples median while the other were not ($P = 0.03$, median test).
Conclusion: This indicates that suicidality is a significant, complex and treatment responsive problem; that pre-treatment severe suicidality with risks of psychological and physical sequela is associated with longer DUP rather than patient characteristics and that early intervention programs may prevent this complication to early psychosis.
Policy of full disclosure: None.

S-02-003
Self-disorders and suicidality in recent onset psychotic disorders

E. Haug (Innlandet Hospital, Ottestad, Norway)

Objective: A recent hypothesis is that suicidality in schizophrenia may be linked to the patients' altered basic self-awareness or sense of self, termed self-disorders (SDs). The aim was to investigate whether SDs in first episode schizophrenia spectrum disorders are related to suicidality and whether this relationship is independent of or mediated by depression or other standard clinical measures.
Methods: SDs were assessed in 49 patients with first-episode schizophrenia by means of the Examination of Anomalous Self-Experience (EASE) instrument. Symptoms severity and functioning were assessed using the Structured Clinical Interview for the Positive and Negative Syndrome Scale (SCI-PANSS), Calgary Depression Scale for Schizophrenia (CDSS), and Global Assessment of Functioning—Split Version (GAF-S). Suicidality was measured by CDSS item 8.
Results: Analyses detected a significant association between current suicidality, current depression and SDs as measured by the EASE. The effect of SDs on suicidal ideation appeared to be mediated by depression.
Conclusion: The interaction between anomalous self-experiences and depression could be a rational clinical target for the prevention of suicidality in the early phases of schizophrenia, and supports the rationale for including assessment of SDs in early intervention efforts.
Policy of full disclosure: None.

S-02-004
Insight, subjective experiences and suicidal behavior in first episode psychosis

E. Barrett (Oslo University Hospital, Oslo, Norway)

Objective: Suicidal behaviour is prevalent in psychotic disorders. Insight has been found to be associated with increased risk for suicidal behaviour, but not consistently. A possible explanation for this is that insight has different consequences for patients depending on their beliefs about psychosis. The present study investigated whether a relationship between insight, negative beliefs about psychosis and suicidality was mediated by depressive symptoms, and if negative beliefs about psychosis moderated the relationship between insight and suicidality in patients with a first episode of psychosis (FEP).

Methods: One hundred ninety-four FEP-patients were assessed with a clinical interview for diagnosis, symptoms, functioning, substance use, suicidality, insight, and beliefs about psychosis.
Results: Nearly 46% of the patients were currently suicidal. Depressive symptoms, having a schizophrenia spectrum disorder, insight, and beliefs about negative outcomes for psychosis were independently associated with current suicidality; contradicting a mediating effect of depressive symptoms. Negative beliefs about psychosis did not moderate the effect of insight on current suicidality.
Conclusion: The results indicate that more depressive symptoms, higher insight, and negative beliefs about psychosis increase the risk for suicidality in FEP-patients. The findings imply that monitoring insight should be part of assessing the suicide risk in patients with FEP, and that treating depression and counteracting negative beliefs about psychosis may possibly reduce the risk for suicidality.
Policy of full disclosure: None.

S-03 Brain imaging in the early stages of schizophrenia

S-03-001
Structural and functional brain alterations in individuals at ultra-high risk for psychosis: an overview and future directions

J. S. Kwon (Department of Psychiatry, Seoul National University College of Medicine, Seoul, Korea; Department of Brain and Cognitive Sciences, WCU Program, College of Natural Sciences, Seoul National University, Seoul, Korea)

Abstract: Schizophrenia arises through multiple processes including early/late neurodevelopmental changes occurring at least from initial stage of psychosis, and neurodegenerative change after onset of psychosis. Hence, the prodromal phase of schizophrenia has drawn great attention since 1990s and many neuroimaging researches have been applied to subjects at high risk for psychosis. The neuroimaging studies of high risk subjects present clues to further understanding of psychopathology and pathophysiology of psychosis.
We established the Seoul Youth Clinic and have provided multidimensional evaluation and intervention for young people at putatively prodrome of psychosis, i.e. ultra-high risk (UHR) subjects. For these UHR subjects, various methods were performed including neuropsychological tests, and structural/functional neuroimaging at baseline and follow-ups. UHR subjects showed cortical thinning in the distributed area of cerebral cortices and midline neurodevelopmental anomalies. They also showed abnormal early auditory processing and deficits in top-down attentional control in neurophysiological studies. In recent fMRI studies, we have found that UHR subjects exhibit altered resting state functional connectivity, and that functional deficits associated with spatial working memory processing emerge in the UHR subjects before the onset of schizophrenia.
Our findings illustrate that structural and functional brain abnormalities precede the psychosis onset. Further longitudinal follow-ups are vital to validate the interpretation of our findings, and to reveal differences in these abnormalities between those who will convert to psychosis later and those who will not.
Policy of full disclosure: None.

S-03-002
Brain alterations and cognitive correlates in individuals at ultra-high risk psychosis

E. Meisenzahl (Klinikum der Universität München, Munich, Germany), N. Koutsouleris

Abstract: Structural brain abnormalities have been described in individuals with an at-risk mental state for psychosis. Compared with healthy controls, ARMS participants show grey matter volume losses in fronto-temporo-limbic structures. Brain alterations associated with the early at-risk mental state may relate to an elevated susceptibility to psychosis, whereas alterations underlying the late at-risk mental state may indicate a subsequent transition to psychosis.
Deficits in executive functioning have been described as a core feature of schizophrenia and have been linked to patterns of fronto-temporo-limbic brain alterations. We found the ARMS subjects to be specifically impaired in their TMT-B performance versus HC. Brain-cognition associations involving the insular cortices were observed in the HC, but not in the ARMS individuals. Conversely, TMT-B correlations in the VMPFC, the cerebellum, the fronto-callosal white matter were detected in the ARMS, but not the HC group. The VMPFC was linked to the temporo-limbic cortices in HC, whereas the connectivity pattern in the ARMS involved the left temporal and dorsolateral prefrontal cortex, the cerebellum, the right SMA and extended portions of the fronto-callosal white matter. These findings suggest that executive deficits are already present in the ARMS for psychosis and may be subserved by structurally altered networks of interconnected cortical and subcortical brain regions in line with the disconnectivity hypothesis of schizophrenia.
Policy of full disclosure: None.

S-03-003
Brain alterations in individuals at ultra-high risk for psychosis: emotional correlates

A. Aleman (Neuroimaging Center, University Medical Center Groningen, Groningen, The Netherlands; Department of Psychosis Studies, Friesland Mental Health Care, Leeuwarden, The Netherlands), E. Opmeer, E. Liemburg, R. Nieboer, L. Wunderink

Abstract: In this study we investigated the neural correlates of social cognitive and emotional processing in subjects at ultra-high risk (UHR) for psychosis. We hypothesized that this group would be characterized by difficulties with emotion regulation and with functional abnormalities in brain activation patterns during regulation of emotions. We compared regional brain activation during two conditions: attend and reappraisal, in response to IAPS pictures. The reappraisal condition required active emotion regulation. Individuals with an at risk mental state (i.e. ultra-high risk for psychosis) were identified through mental health services using the CAARMS interview. Functional MRI activation was compared to an age- and education-matched control group. The preliminary results show that UHR individuals are less proficient in using the reappraisal strategy to downregulate negative affect. Concurrently, less activation was observed for the UHR group in dorsolateral and mediodorsal prefrontal cortex, an area that has previously been shown to be involved in emotion regulation. We tentatively conclude that UHR subjects may be compromised in their ability to regulate negative emotions, which is reflected in a reduced cognitive control of emotion through the frontal cortex. Future research should establish whether this pattern of abnormal activation is predictive for transition to clinical psychosis.
Policy of full disclosure: None.

S-03-004
Fronto-striatal interactions in individuals at ultra-high risk for psychosis

O. Howes (Psychiatric Imaging, Clinical Sciences Centre & Institute of Psychiatry, London, UK)

Objective: Alterations in both frontal and striatal functioning have been linked to the cognitive impairments seen in schizophrenia. However, it is not clear when these become apparent in the development of the disorder, or how they relate to each other. We sought to determine which is primary by studying people at risk for psychosis.
Methods: We used PET and fMRI imaging in the same individuals to study both striatal dopamine synthesis capacity and the neural substrates of performance during tasks designed to index frontal executive functions that are impaired in schizophrenia. Thirty subjects at high clinical risk of psychosis (all meeting the CAARMS criteria for an at risk mental state [ARMS]) who show prodromal signs of schizophrenia and twenty matched controls received the measures. The ARMS subjects received clinical follow-up to determine who developed psychosis. The striatal regions of interest were the whole striatum (S), and limbic (LS), associative (AST) and sensorimotor (SMST) striatal subdivisions.
Results: Striatal dopamine synthesis capacity was significantly elevated in the associative striatum ($P < 0.05$) and was linked to poorer cognitive performance in the ARMS subjects. Furthermore it was also linked to alterations in brain activation during working memory and executive tasks ($r = 0.732$, $P < 0.001$). The inter-relationship between striatal dopamine synthesis capacity and frontal activation was significantly different between ARMS and controls ($P < 0.0001$).
Conclusion: These findings indicate that frontal and striatal abnormalities both predate the onset of schizophrenia in people with prodromal signs of schizophrenia, and that these show an altered inter-relationship to that seen in matched controls. This evidence suggests that fronto-striatal interactions play a role in the development of executive cognitive impairments, and that treatments targeting these circuits may thus be beneficial.
Policy of full disclosure: None.

S-04 Advances in animal models of schizophrenia: genes, environment, and prevention to biological foundations

S-04-001
A mouse model for the study of synergistic interactions between prenatal immune activitation and peri-pubertal stress in the development of schizophrenia-relevant disease

U. Meyer (ETH Zurich, Schwerzenbach, Switzerland), S. Giovanoli, J. Feldon

Objective: Converging evidence from human epidemiological studies and parallel experimental investigations in animals indicates that prenatal exposure to infection may be a relevant environmental risk factor for schizophrenia and related disorders. However, if prenatal infection does indeed play a significant role in the etiology of schizophrenia, then it likely does so by interacting with other genetic and/or environmental susceptibility factors. Besides prenatal infection, exposure to stressful situations in peri-pubertal stages of life has been repeatedly suggested to represent a significant postnatal environmental factor in the development of psychotic disorders. Against this background, the present study was designed to test the hypothesis whether prenatal viral-like immune challenge may synergistically interact with peri-pubertal stress to facilitate the emergence of schizophrenia-like behavioral abnormalities in adulthood.
Methods: We combined a well established mouse model of prenatal (gestation day 9) immune challenge by the viral mimic Poly[I:C] (= polyriboinosinic-polyribocytidilic acid, a synthetic analogue of double-stranded RNA) with a model of exposure to peri-pubertal stress induced by a sub-chronic variable stress protocol applied in peri-puberty. The stress protocol included electric foot shock exposure (3 times, 0.25 mA), forced swimming (2 times, 1 min each), repeated changing of home cage embedding (5 times), 22-h food deprivation, and exposure to restrained stress (45 min). These stressors were applied on alternate days between postnatal days 30 and 40. The single and combined effects of prenatal immune activation and peri-pubertal stress on schizophrenia-relevant behavioral functions were assessed when the animals reached adulthood (i.e., from postnatal day 70 onwards).
Results: We found that peri-pubertal stress led to significant behavioral and pharmacological abnormalities specifically in animals which had been subjected to prenatal Poly[I:C]-induced immune challenge at low intensity (1 mg/kg, i.v). These alterations included impairments in sensorimotor gating in the form of prepulse inhibition (PPI) disruption, cognitive deficits in the form of reversal learning impairment, and potentiated sensitivity to the psychotomimetic drugs amphetamine and dizocilpine (MK-801). Importantly, neither prenatal Poly[I:C] treatment at the chosen dose alone nor peri-pubertal stress alone induced such behavioral abnormalities.
Conclusion: Our initial experimental research supports the biological plausibility for synergistic interactions between prenatal immune challenge and postnatal stress in the precipitation of brain dysfunctions relevant to schizophrenia. In accordance with an environmental two-hit model of schizophrenia etiology, prenatal immune challenge may render the brain more vulnerable to postnatal stress, thereby facilitating the development of full-blown psychotic disturbances associated with schizophrenia. Additional experimental research is now underway in our laboratory to explore the relevant cellular and molecular mechanisms mediating the synergistic interactions between mild prenatal immune challenge and peri-pubertal stress in the disruption of adult behavioral functions. Initial evidence suggest that transient up-regulation of activated microglia cells and accompanied increases in pro-inflammatory cytokine release may be critically involved, as supported by synergistic effects between prenatal immune challenge and peri-pubertal stress emerging in immunohistochemical and cytokine protein analyses in peri-pubertal subjects. Such transient neuroinflammatory processes may readily offer a target for early immunomodulatory interventions aiming at preventing the disruption of adult brain functions following combined exposure to prenatal immune activation and peri-pubertal stress.
Policy of full disclosure: None.

S-04-002
Prevention of schizophrenia-relevant brain and behavioral pathology by adolescent antipsychotic drug administration in an infection-based rat model of schizophrenia

I. Weiner (Tel-Aviv University, Israel)

Objective: The concept of schizophrenia as a neurodevelopmental disorder whereby the primary pathogenic event occurs in utero but symptoms emerge in adolescence/early adulthood, raises two questions critical for diagnosis and treatment. Are active brain changes occurring between the neurodevelopmental aberration and its overt manifestation, and can these changes be prevented by early intervention. Our objective was to address these questions in the prenatal immune stimulation model that is based on the association of prenatal infection and increased risk of schizophrenia.
Methods: Pregnant rats were injected on gestational day 15 with the viral mimic polyriboinosinic-polyribocytidylic acid (poly-I:C) or saline. Male and female offspring of polyI:C- and saline-treated dams received one daily injection of the atypical antipsychotic drug (APD) clozapine (7.5 mg/kg) at one of three developmental windows: postnatal days (PNDs) 34-47, PNDs 48-61, or PNDs 62-78. Beginning

at about PND 90 the offspring underwent behavioral testing (latent inhibition and amphetamine-induced activity) and in vivo structural imaging.
Results: Prenatal polyI:C-induced interference with fetal brain development led to aberrant postnatal brain development as manifested in decreased hippocampal and increased lateral ventricles (LV) volumes as well as disrupted latent inhibition and excessive amphetamine-induced activity. Hippocampal volume loss and LV volume expansion as well as the behavioral abnormalities were prevented in the offspring of poly I:C mothers who received clozapine during the asymptomatic period of adolescence (PND 35–47). Administration at the later windows, PNDs 48–61 or 62–78, exerted sex- and region-specific effects, with clozapine being ineffective in males but partially effective in females.
Conclusion: (1) Prenatal insult leads to postnatal brain and behavior pathology; (2) Treatment with atypical APDs can prevent both brain and behavioral pathology; (3) There is a sex-dependent pattern of efficacy that fits our previous developmental data showing that the development of both structural and behavioral abnormalities are delayed in females; (4) In both sexes, the earlier the intervention, the more effective is the prevention.
Policy of full disclosure: None.

S-04-003
DISC1 modulates immune response in the brain

M. Pletnikov (Johns Hopkins University, Baltimore, USA)

Objective: Our studies indicate that Disrupted-In-Schizophrenia-1 (DISC1) may be involved in the mechanisms of fetal brain immune activation in response to environmental infectious factors (Abazyan et al. 2010). We sought to elucidate the molecular mechanisms whereby DISC1 and its variants could modulate immune responses in the brain cells.
Methods: We used a neuroblastoma cell line, Neuro2a (N2a), to assess cytokine-induced signaling. N2A cells were transiently transfected with mutant DISC1 or GFP and subsequently stimulated with a pro-inflammatory cytokine, TNF-alpha.
Results: As expected, TNF-alpha induced degradation of IkB-alpha that inhibits activation of NF-kB by preventing its translocation into the nucleus. We found that mutant DISC1 significantly delayed a recovery of IkB-alpha expression levels even 60 min post stimulation, suggesting a prolonged activation of NF-kB-dependent cytokine signaling. We also analyzed TNF-alpha-induced transcriptional activity of NF-kB using luciferase assay. We found that mutant DISC1 decreased transcriptional activity of NF-kB in response to TNF-alfa treatment.
Conclusion: We are assessing if mutant DISC1-produced delay in degradation of IkB-alpha is an upstream compensatory response to primary alterations in transcriptional activity of NF-kB or the other way around. The findings indicate that altered DISC1 functions could contribute to neuroimmune dysfunction in schizophrenia.
Policy of full disclosure: None.

S-04-004
Combining pharmacological and genetic approaches to animal models of schizophrenia: experimental approaches in dopamine receptor deficient mice

P. Moran (University of Nottingham, Nottingham, UK),
M. O'Callaghan, C. Bay-Richter, C. O'Tuathaigh, J. Waddington

Objective: Animal models are becoming increasingly important to our understanding of how genetic abnormalities contribute to the symptoms of schizophrenia. At their most simplistic these models reproduce the abnormal function of a gene found in the disease and examine the behavioural and neural consequences with a view to back-translation of this information to the disease. More recently animal models have begun to use an approach that combines genetic manipulation, pharmacological challenge, and complex behavioural evaluation. We used this approach to investigate the role of dopamine D2 receptors (DRD2) in the behavioural effects of antipsychotic drugs. It has been suggested that schizophrenia symptoms may reflect an abnormality in the appropriate allocation of salience to environmental stimuli and that antipsychotic drugs restore appropriate salience allocation by DRD2 blockade.
Methods: Mice with genetic deletion of DRD2 (DRD2-/-) were used to assess whether these receptors are necessary for antipsychotic drugs to modify salience allocation. Salience allocation abnormality was modelled in mice as experimental or pharmacological abolition of the learning phenomenon latent inhibition (LI).
Results: Both haloperidol and clozapine restored experimentally extinguished LI in wild-type but not in DRD2−/− mice, indicating a requirement for DRD2. D-amphetamine (AMPH) abolished LI similarly in both backgrounds, and remarkably, both clozapine and haloperidol reversed AMPH abolition of LI in DRD2−/−, demonstrating that antipsychotics can influence salience allocation disruption in the absence of DRD2.
Conclusion: These findings indicate that while DRD2 can be necessary for antipsychotics to restore abnormal salience allocation, there is also an additional, non-DRD2-dependent mechanism that is unmasked in the presence of AMPH. Using a combined genetic and pharmacological approach in conjunction with a specific behavioural measure has identified both DRD2 and non DRD2 dependent influences on behaviour that would not have been detectable using either approach alone.
Policy of full disclosure: The authors gratefully acknowledge the support of The Wellcome Trust.

S-05 The future of psychiatric genetics beyond GWAS

S-05-001
The future of the GWAS

T. Schulze (Department of Psychiatry and Psychotherapy,
Georg August University, Goettingen, Germany)

Objective: The community of psychiatric genetic researchers entered the twenty-first century with high hopes. Genome-wide association studies (GWAS) were hoped and touted to be the philosopher's stone in finally unraveling the genetic basis of psychiatric disorders. This proved to not be the case. While some vulnerability variants have robustly been identified, they only explain a very small fraction of phenotypic variance.
Methods: This presentation will give a critical evaluation of GWAS in psychiatry, putting them in the context of complex genetic research in general. The use of polygenic modeling and targeted follow-up of genome-wide significant findings will be discussed.
Policy of full disclosure: None.

S-05-002
Proteomics and biomarkers

D. Martins-de-Souza (University of Cambridge, Cambridge, UK)

Objective: The main goal of the Human Genome Project (HGP) relied on the hope that identifying and sequencing all human genes may

reveal answers about most of human diseases. Whilst the HGP indeed generated a huge amount of useful data, it has not provided the direct answers expected initially. There was still a lack about which molecular targets would be the best to invest efforts on. Further studies were proposed for the post-genomic era. Genotyping techniques and genome wide association studies (GWAS) have generated important leads about schizophrenia. However, considering that schizophrenia is a disorder composed by several genetic differences of small effect, the findings are hardly replicated. Additionally, the environmental factor, which seems to play a pivotal role in the development of the disease, cannot be genetically predicted. Microarray-based transcriptomic studies have been carried out as an alternative and complementary strategy in an attempt to increase our knowledge about schizophrenia etiology. Transcriptomics has also provided leads on potential pathways and biomarkers for the disease. One challenge, however, was to translate the findings into the level of proteins or protein pathways, which are the final and functional biochemical products. Proteomics has emerged in this context as a promising strategy since it deals with effects on proteins, which better reflect the dynamic nature of cellular physiology. Proteomics is supposedly to be able to answer questions about the biochemical pathophysiology of schizophrenia as well as on the identification of biomarkers for diagnosis or predictive value for disease risk or therapeutic response. On the other hand, due the more complex nature of proteins, proteomic methodologies are not in the same level of development as genomic or transcriptomic technologies.
Methods: Diverse tissues such as post-mortem brains, liver and pituitary as well as freshly collected blood and cerebrospinal fluid have been analyzed using proteomic methodologies such as two-dimensional gel electrophoresis (2DE), two-dimensional difference gel electrophoresis (2D-DIGE) and shotgun mass spectrometry.
Results: Proteomic analyses have been applied extensively over the past 10 years in studies of several tissues from schizophrenia patients, resulting in increased insight into the affected molecular pathways. In addition, proteomic approaches have led to the identification of a molecular panel of peripheral biomarkers.
Conclusion: The advantages, limitations and needs of proteomics are commented here, based in the results obtained in schizophrenia studies. Above of all, proteomics is likely to be an interesting complement to other methodologies rather than the final solution for molecular characterization of schizophrenia and even other psychiatric disorders.
Policy of full disclosure: None.

S-05-003
Back to the phenotype or endophenotype?

O. Gruber (Department of Psychiatry and Psychotherapy, Georg August University, Goettingen, Germany)

Objective: Background: Genome-wide association studies in psychiatry have had less success in identifying genes involved in the pathogenesis of psychiatric disorders (based on current diagnostic classification systems) than was originally expected. Classification of psychiatric disorders is mainly based on the phenotype, i.e. psychopathological symptoms observed in the patients. More recent approaches have focused on neurobiological markers that may qualify as endophenotypes, i.e. that may be more closely related to and that may facilitate the identification of susceptibility genes of psychiatric disorders.
Methods: In this talk, a combination of functional MRI studies in healthy subjects, patients with schizophrenia and affective disorders and in their healthy first-degree relatives will be presented. This combination of investigations permits to identify pathophysiological abnormalities in functional brain circuits of psychiatric patients, to test for their possible role as endophenotypes, and to search the genome for genetic factors that may be involved in the occurrence of these endophenotypic markers relevant for a psychiatric disorder.
Results: First results from a large cohort of more than 300 subjects will be presented. Patients with schizophrenia and patients with bipolar disorder, but not patients with unipolar depression revealed altered brain activation in different prefrontal and parietal brain areas during working memory. In specific decision-making tasks, all patient groups showed (in part diagnosis-specific) alterations in brain regions involved in reward processing and other motivational processes. Significant genome-wide associations of (patho)physiological neuroimaging markers with genetic polymorphisms will be reported.
Conclusion: The endophenotypic approach in functional neuroimaging may help to identify genes involved in the pathogenesis of psychiatric disorders and may provide important information for the development of valid animal models for further research.
Policy of full disclosure: None.

S-06 Efficacy and mechanisms of cognitive behavior therapy for psychosis: results of the POSITIVE network

S-06-001
Cognitive behavioral therapy versus supportive therapy for persistent positive symptoms in psychotic disorders: major results of the POSITIVE study

S. Klingberg (Psychiatry and Psychotherapy, University of Tübingen, Tuebingen, Germany), A. Wittorf, C. Meisner, W. Wölwer, G. Wiedemann, J. Herrlich, A. Bechdolf, B. Müller, G. Sartory, M. Wagner, G. Buchkremer

Objective: Cognitive behavioral therapy (CBT) is recommended in evidence based treatment guideline. However, it is an open question whether treatment effects are due to CBT-strategies.
Methods: We conducted a multicenter randomized clinical trial comparing CBT with Supportive Treatment (ST). $n = 330$ patients with psychotic disorders have been included. They received individual outpatient treatment of 20 sessions. Primary outcome was the PANSS positive syndrome score. The study implemented a systematic recruitment, single-blind assessments, controlled for adherence, and was analysed using advanced statistics.
Results: We found a significant difference between CBT and ST regarding positive symptoms at the post-treatment assessment. Additional results will be presented.
Conclusion: CBT has specific treatment effects which can be observed in addition to unspecific effects of ST.
Policy of full disclosure: This study was publicly funded by the German Ministry of Education and Research (grant No. 01GV0618).

S-06-002
The therapeutic alliance in CBT for pychoses: course and predictive value for outcome

A. Wittorf (Universitätsklinik Psychiatrie und Psychotherapie, Tuebingen, Germany), S. Klingberg

Objective: The therapeutic alliance is viewed as an important factor for the outcome in psychotherapy. However, regarding cognitive-behavioural therapy for psychosis (CBTp) there are only few studies

which addressed the association between alliance and outcome. Thus, we investigated whether the course of therapeutic alliance is predictive for symptom change during the course of CBTp.
Methods: The data presented here are part of the POSITIVE-study (ISRCTN29242879), a randomised clinical trial comparing CBTp and supportive therapy. Questionnaire-based ratings of the therapeutic alliance were repeatedly obtained throughout the course of study therapies. Patient and therapist alliance ratings were examined separately. Outcome was measured with the Positive and Negative Syndrome Scale (PANSS). Data analyses comprised cluster analytic procedures and repeated measurement analyses of variance.
Results: Neither patient nor therapist alliance ratings showed a differential course throughout study treatments. Irrespective of the treatment condition, we previously (Wittorf et al. 2010, Journal of Nervous and Mental Disease, 198, 478–485) found a cluster with a positive alliance rating and a cluster with a more neutral rating for therapist and patient ratings, respectively. Baseline symptoms and insight differentiated between these types of clusters. However, our present analyses showed no significant interactions between a patient's cluster affiliation and the change of positive and negative symptoms from pre to post treatment.
Conclusion: Our findings indicate that CBTp does no harm to the integrity of the therapeutic alliance. However, the course of alliance did not predict symptom outcome. This finding is compatible with a threshold model whereby the absence of negative alliance ratings might be a precondition for treatment adherence and symptom change in psychotherapy for psychosis.
Policy of full disclosure: None.

S-06-003
Cognitive biases and cognitive deficits in patients with positive symptoms: relationship with symptoms and with symptom change during psychotherapy

M. Wagner (University of Bonn, Germany)

Objective: In theoretical models, social-cognitive biases (i.e. attribution bias, reasoning bias) and emotional processes are hypothesized to mediate the formation and maintenance of persecutory delusions and positive symptoms of psychosis in general. The present study aims at studying the relationship between different forms of bias with general cognitive deficits and specific psychopathological symptoms across the course of psychotherapy.
Methods: The POSITIVE-study is a randomized controlled trial comparing cognitive behavior therapy (CBT) and supportive therapy for the treatment of persistent positive symptoms. The majority of the 330 patients recruited into this multicenter study were assessed with a traditional neuropsychological battery (comprising measures of memory attention and executive function) and were also studied with several social-cognitive tasks addressing attributional style, cognitive impulsivity, emotional perception and understanding of intentions.
Results: Social-cognitive and neuropsychological measures were largely independent of each other. As expected, delusional symptoms were related to more aberrant social-cognitive biases and to negative affect and negative self-schemata. Longitudinal analyses about change of social-cognitive biases over time are ongoing.
Conclusion: Data confirm that social-cognitive measures capture unique aspects of information-processing which are unrelated to traditional neuropsychology but which are linked with delusions. These links may hint at mechanisms relevant for the efficacy of CBT in treating positive symptoms.
Policy of full disclosure: None.

S-06-004
Cognitive behavior therapy in adolescents with persistent psychotic symptoms: results of randomised controlled trial

A. Bechdolf (University of Cologne Psychiatry, Germany), T. Tecic, G. Lehmkuhl, P. Walger, K. Mueller, G. Wiedemann, D. Stoesser, S. Klingberg

Objective: Treatment as usual (TAU) supplemented by cognitive-behavioral therapy (CBT) leads to greater clinical improvement in adult patients with schizophrenia than TAU alone. Until now no cognitive-behavioral therapy for patients with "early onset psychosis" (EOP, a first episode of psychosis between 14 and 18 years) has been developed. The present project's goal is to develop a modified cognitive-behavioral treatment (mCBT) for patients with EOP and to evaluate the acceptance, tolerability and efficacy.
Methods: 49 patients were screened of which 25 were included in a randomised controlled trial. Thirteen patients were randomised into the intervention group (mCBT + TAU) and 12 into the control group (TAU). MCBT was delivered in 20 individual sessions (plus five sessions with relatives) over a period of 9 months. Assessments were performed at baseline and monthly during treatment until treatment stopped using the PANSS Positive-Scale, Global Functioning Scale (GAF) and Quality of Life (MSLQ).
Results: The average age was 17.2 years. There were no significant differences between groups regarding demographic and clinical features at intake. Eighty percent of planned sessions were conducted. At the descriptive level by the end of treatment more patients in mCBT + TAU were in remission than in TAU (75% vs. 50%). Differences in GAF between groups (62.3 vs. 58.9, $P = 0.13$) were in favour of mCBT. MSLQ Scores descriptively revealed advantage for the intervention group (67.4 vs. 61.6, $P = 0.18$). The effect sizes in the mCBT group were moderate for GAF ($d = 0.35$) and MSLQ ($d = 0.45$).
Conclusion: The pilot study has shown that mCBT is feasible, acceptable and tolerable in adolescents with schizophrenia. The effect sizes for mCBT were moderate in several secondary outcome parameters but no statistically significant differences between the treatment groups emerged It is likely that due to the small sample size a statistical significant difference could not be detected.
Policy of full disclosure: None.

S-07 Insight in psychosis: cognitive and neural basis, and implications for treatment

S-07-001
Is there a neurological basis for poor insight in schizophrenia?

A. David (Institute of Psychiatry, London, UK), N. Bedford, B. Wiffen, J. Gilleen

Abstract: Lack of insight or unawareness of illness and deficits is a problem common to many neuropsychiatric disorders. It has been most intensively studied in the psychoses. Lack of insight can be conceptualised in a number of ways: (i) phenomenologically—as a set of beliefs or attitudes occurring in the context of psychopathological abnormalities (e.g. an aspect of delusions); (ii) psychosocially—involving self or other deception (denial) or the expression of culturally shared beliefs; (iii) neuropsychiatrically—as a result of cognitive impairment with neurophysiological correlates. Support for the last of these comes clinical studies in neurological disorders and the syndrome of anosognosia and also from studies showing that lower insight scores in schizophrenia patients tend to be associated

with cognitive impairments, both generalised and specific (i.e. executive functioning). Similarly, a literature is emerging from structural neuroimaging which indicates correlates between low insight and brain anatomy—both generalised and specific (i.e. the cortical midline system). New findings from functional imaging may improve our understanding of how brain-function might be relevant to lack of insight in psychosis. However, it is likely that phenomenological and psychosocially mediated process co-exist with neurophysiological processes related to awareness of illness and that a complete understanding of insight in psychosis will require integration of all three.
Policy of full disclosure: None.

S-07-002
The association between self-reflective processing and insight in psychosis in schizophrenia patients: an fMRI study

L. van der Meer (Lentis Medical Health Center, Groningen, Netherlands), M. Pijnenborg, A. Aleman

Objective: The study of self has become increasingly popular in cognitive neuroscience. Several studies investigated the neural correlates of self-reflection. Self-reflection refers to the evaluation process used to decide if certain environmental cues apply to one's self. Accurate representation of one's traits, abilities and attitudes is important in evaluating one's behavior and in comparing it with others' behavior. Deficient self-reflection may hamper proper self-monitoring, resulting in wrong attributions, and may result in problems in social interaction and insight in illness. Functional neuroimaging research revealed that a set of regions known as Cortical Midline Structures (CMS) is critically involved in these self-reflection processes. Furthermore, it was demonstrated that patients with brain damage in these CMS, have difficulties in evaluating their problems and often overestimate their capacities and performance on cognitively demanding operations. A recent meta-analysis of fMRI studies on self-reflective processing by van der Meer et al. (2010)* confirmed the involvement of the CMS, and more specifically the importance of two regions within the medial prefrontal cortex (MPFC). The ventral MPFC is specifically involved in self-reflective processing, whereas the dorsal MPFC is involved in self- as well as other-reflective processing. A model was developed in which the vMPFC is involved in tagging information relevant for 'self', whereas the dMPFC is involved in decision making processes in self- and other-referential processing.
Methods: This model was the starting point in an fMRI study in 40 patients with schizophrenia. More specifically, the relationship between brain activation during self-reflection and illness insight was investigated.
Results: Preliminary results suggest that schizophrenia patients show a deviant pattern of activation in self-reflective processing. Results concerning the relationship with insight will be presented.
Conclusion: More knowledge on the neural basis of self-reflective processing in schizophrenia may provide information in the specific problems of these patients and may help to design new treatment strategies.
Policy of full disclosure: None.

S-07-003
Neuropsychological dysfunction and poor insight in psychosis

A. Aleman (Neuroimaging Center, University Medical Center Groningen, Gronningen, Netherlands), P. Quee, R. Bruggeman, M. Pijnenborg

Abstract: More than 40 studies have been published over the past decades regarding neurocognitive function and poor insight in psychosis. Statistically significant, albeit small in magnitude, relationships between cognitive impairment and poor insight have been established. These are most pronounced for executive functioning, and in particular mental flexibility. Some recent studies have began to explore the role of social cognition, e.g. emotion recognition and theory of mind. Studies from our center have demonstrated associations of insight with social cognitive measures, over and above a contribution of neurocognition. This supports theories that imply a role for deficient emotion recognition and mentalizing in reduced insight. Reduced levels of empathy may also predict poor insight, independent from cognition. Implications of these findings for theories of reduced insight in psychosis will be discussed.
Policy of full disclosure: None.

S-07-004
Treatment of insight in schizophrenia: meta-analysis

M. Pijnenborg (Department of Psychotic Disorders, GGZ Drenthe, Assen, Netherlands), R. Donkersgoed, A. Aleman

Abstract: The percentage of persons with schizophrenia who have only limited insight into their illness is rather large (50–80%). Insight is regarded as consisting of the following three dimensions: awareness of mental illness, relabeling of symptoms and need for treatment. Limited insight has a negative impact on the outcome of the disease. Poor treatment compliance in patients mediates this relationship between, but there is also a direct association between insight and outcome. Given the negative impact of limited insight on relevant outcomes of schizophrenia, insight is logical target for treatment. We performed a meta-analysis on the effectiveness of psychosocial and pharmacological treatment options to enhance insight in schizophrenia. An inclusive literature search was performed in PubMed, ISI Web of Science, and EMBASE. The search terms used (language not specified) were "Insight", "Awareness", "Denial", "Cognitive Therapy", "Treatment", "Psychosis", and "Schizophrenia". A cross-reference search of eligible articles was performed to identify studies not found in the computerized search. Randomized controlled trials assessing the efficacy treatment on insight in schizophrenia were included in the meta-analysis. Effect sizes (Cohen *d*) of each study were calculated. The overall mean standardized mean difference was calculated under a random effects model with 95% confidence intervals. Results of the meta-analysis will be presented. Clinical implications will be discussed.
Policy of full disclosure: None.

S-08 Neuroprotective strategies in schizophrenia

S-08-001
Neuroprotection in schizophrenia: novel candidates and perspectives

Josef Priller (Department of Neuropsychiatry, Charité-Universitätsmedizin Berlin, 10177 Berlin, Germany)

Erythropoietin (EPO) is a glycopeptide hormone, which is primarily produced in the kidney, but also in the brain by astrocytes. Because of its cytoprotective actions, EPO is considered to be a potent drug candidate for a variety of neuropsychiatric disorders, including schizophrenia. However, the clinical use of EPO as a neuroprotectant is complicated by its hematopoietic effects.
We have identified endogenous EPO splice variants in the human and murine brain and kidney. Importantly, we found that all EPO splice

variants are devoid of hematopoietic activity in vitro and in vivo. The EPO splice variants exerted the same neuroprotective activities as EPO in models of cerebral ischemia (oxygen-glucose deprivation of primary neuronal cell cultures and middle cerebral artery occlusion in mice). In addition, they had effects on adult neural stem cells, which were distinct from EPO. In line with these findings, EPO splice variants do not appear to signal through the classical EPO receptor.
Our data suggest that EPO splice variants are interesting novel drug candidates for neuroprotection in schizophrenia, since they share the cytoprotective properties of EPO without exerting hematopoietic side-effects.

S-08-002
Brain-derived neurotrophic factor: also playing a neuroprotective role in schizophrenia?

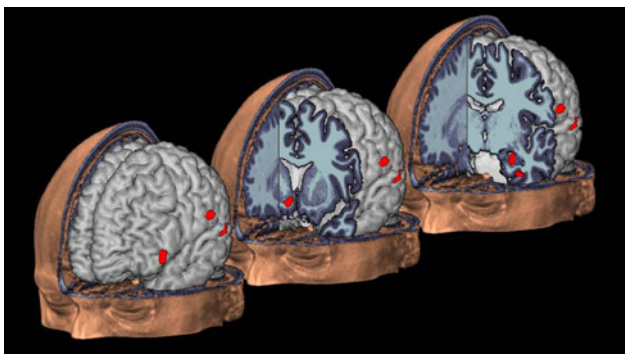
R. Hellweg (Charité-Universitätsmedizin, Berlin, Germany)

Abstract not received in due time.

S-08-003
EPO treatment preserves gray matter in discrete brain regions of chronic schizophrenic patients

T. Wüstenberg (Charité-Universitätsmedizin, Berlin, Germany), M. Begemann, C. Bartels, O. Gefeller, S. Stawicki, D. Hinze-Selch, A. Mohr, P. Falkai, J. B. Aldenhoff, M. Knauth, K.-A. Nave, H. Ehrenreich

Objective: Neurodevelopmental abnormalities together with neurodegenerative processes contribute to schizophrenia, an etiologically heterogeneous, complex disease phenotype that has been difficult to model in animals. The neurodegenerative component of schizophrenia is best documented by magnetic resonance imaging (MRI), demonstrating progressive cortical gray matter loss over time. No treatment exists to counteract this slowly proceeding atrophy. The hematopoietic growth factor erythropoietin (EPO) is neuroprotective in animals.
Methods: 32 human subjects, suffering from chronic schizophrenia, were treated weekly with high-dose EPO for as little as 3 months in a placebo-controlled study. MRI and voxel-based morphometry (VBM) were applied to test for treatment related changes in brain structure.
Results: Here, we show that EPO treatment halts the progressive atrophy in brain areas typically affected in schizophrenia, including hippocampus, amygdala, nucleus accumbens, and several neocortical areas. Specifically, gray matter protection is highly associated with improvement in attention and memory functions.
Conclusion: These findings suggest that a neuroprotective strategy is effective against common pathophysiological features of schizophrenic patients, and strongly encourage follow-up studies to optimize EPO treatment dose and duration.
Policy of full disclosure: Prof. Dr. Dr. Hannelore Ehrenreich holds a user patent for the treatment of schizophrenia with EPO.



S-08-004
EPO: a new treatment for cognitive dysfunction and depressive symptoms in patients with affective disorder?

K. Miskowiak (Copenhagen University Hospital, Denmark)

Objective: Depression and bipolar disorder are associated with reduced neural plasticity and cognitive dysfunction. Current drug treatments for these affective disorders have insufficient effects in a large group of patients and fail to reverse cognitive deficits. There is thus a need for more effective treatments which aid cognitive function. Erythropoietin (Epo) is involved in neuroplasticity and may be a candidate for future treatment of affective disorders. We therefore investigated the effects of EPO administration to healthy and depressed individuals to clarify (1) if Epo has direct actions on neurocognitive function independent of effects on hematocrit (2) and if so, whether such actions would be compatible with increased neural plasticity and an antidepressant action.
Methods: We used functional magnetic resonance imaging to explore the effects of a single dose of Epo (40,000 IU) versus saline on neural and cognitive response during hippocampus-dependent picture memory and emotional face processing tasks in healthy and depressed individuals. Blood tests were taken before and after Epo/placebo administration.
Results: We demonstrated that a single dose of Epo directly improves neurocognitive function in healthy and depressed individuals in the absence of effects on changes in hematocrit. Epo also reduced neurocognitive processing of negative emotional information in these groups similar to effects seen with conventional antidepressants.
Conclusion: Our findings highlight Epo as a candidate agent for management of cognitive dysfunction and mood symptoms in affective disorders.
Policy of full disclosure: None.

S-09 Novel therapeutic targets for treating schizophrenia

S-09-001
Novel approaches for treating schizophrenia

G. Gründer (Department of Psychiatry, Psychotherapy and Psychosomatics, RWTH Aachen University, Aachen, Germany)

Abstract: Two decades of searching for the "miracle antipsychotic" with efficacy against all heterogeneous phenomena associated with the complex group of diseases called schizophrenia has proved at least partly disappointing. Although the superior tolerability of the second-generation antipsychotics with regard to EPS is beyond doubt, new detrimental side-effects such as metabolic complications have been associated with the use of some of these compounds. Moreover, recent effectiveness-studies, despite their methodological pitfalls, have raised concerns about the clinical meaningfulness of their fairly modest clinical advantages. Furthermore, it has not been shown unequivocally that any of the available second-generation antipsychotics is superior to the compounds from the first generation with regard to improvement of the cognitive deficits associated with schizophrenia, and the effects of all compounds in this domain are small.
Here we propose to deconstruct the disease "schizophrenia" into various phenomenological components, which should be targeted independently with separate molecules or specifically designed multi-target drugs. Experimental evidence suggests that the best approach for treating positive symptoms is still the administration of a D2

antagonist/partial agonist. Negative symptoms seem not to respond to dopamine agonists/psychostimulants but to glutamatergic drugs (agonists at the glycine binding site of the NMDA receptor and inhibitors of the glycine transporter type 1, GlyT1). Especially GlyT1 inhibitors represent a very promising approach for the treatment of negative symptoms, when these drugs are used in conjunction with a D2 antagonist antipsychotic. Multiple drugs are currently being investigated for the treatment of the cognitive deficits associated with schizophrenia. These include drugs that modulate NMDA and AMPA receptor function, agonists at the muscarinic and the nicotinic acetylcholine receptor, α5 benzodiazepine receptor agonists, D1 dopamine receptor agonists, among others. We suggest that these drugs should be used in a "rational polypharmacy" approach in order to treat the different dimensions of schizophrenia independently.

Policy of full disclosure: Dr. Gründer has served as a consultant for Astra Zeneca (London, UK), Bristol-Myers Squibb (New York, NY), Eli Lilly (Indianapolis, Ind), Lundbeck (Copenhagen, Denmark), and Otsuka (Rockville, Md.). He has served on the speakers' bureau of Astra Zeneca, Bristol-Myers Squibb, Eli Lilly, Janssen Cilag (Neuss, Germany), Otsuka, Pfizer, Servier (Paris, France), and Wyeth. He has received grant support from Alkermes, Bristol-Myers Squibb, Eli Lilly, and Johnson & Johnson. He is co-founder of Pharma-Image—Molecular Imaging Technologies GmbH.

S-09-002
Methodological challenges of demonstrating cognitive improvements with broad spectrum agents: a novel approach

A. H. Kalali (Quintiles Global CRO Medical and Scientific Service, San Diego, USA), Y. Geffen, M. Davidson, M. R. Hufford, R. M. Gendreau, S. G. Rao, R. Zablocki, J. D. Kranzler (BioLineRx Limited, Jerusalem, Israel)

Objective: There are numerous methodological challenges related to the development of treatments to address the cognitive impairments associated with schizophrenia. Current consensus guidance from FDA and the NIH recommends use of the MATRICS Consensus Cognitive Battery (MCCB) to assess potential cognitive improvement in stable schizophrenic patients. CYP-1020 is a potential broad-spectrum agent that combines dopamine antagonism with GABAergic activity. Because CYP-1020 appears to be acting in a broad spectrum manner, providing beneficial cognitive and antipsychotic effects soon after treatment has begun, we explored evaluating its therapeutic utility starting with acutely ill patients with schizophrenia.

Methods: Evidence for broad-spectrum activity is derived from the EAGLE study, which was conducted at approximately 40 sites in US, Romania and India. In this 6-week double blind study, 363 patients were randomized equally to treatment with 10 mg/day CYP-1020, 20–30 mg/day of CYP-1020, risperidone (2–8 mg/day) or placebo. The study was designed to demonstrate significant superiority of CYP-1020 to placebo on the total score of the PANSS. The effect on cognition as measured by the BACS was an exploratory end point.

Results: The total PANSS scores change (LOCF) indicated that treatment with CYP-1020 high dose (LS mean −23.6; 95% CI −28.4; −18.8), was statistically superior to placebo ($P = 0.002$); (LS mean −14.4; 95% CI: −19.1; −9.7). Risperidone treatment also was associated with significant improvement (LS means −26.2; 95% CI −31.0; −21.3) compared to placebo. Treatment with CYP-1020 yielded statistically superior cognition results as measured by the BACS composite score based on LOCF. The age- and gender-corrected change from baseline on the BACS composite score for the CYP-1020 high dose group was LSM = 12.8, SE = 1.58, as compared to a placebo group change of LSM = 8.4, SE = 1.63 and a change with risperidone treatment of LSM = 8.2, SE = 1.46 ($P < 0.03$ vs. placebo and risperidone).

Conclusion: In this acute study, CYP-1020 demonstrated comparable antipsychotic activity to risperidone versus placebo, while simultaneously demonstrating superior pro-cognitive results compared to both placebo and risperidone. Moving forward, a hybrid clinical trial design will assess antipsychotic efficacy and cognitive functioning of CYP-1020, including both a 6-week acute treatment phase with CYP-1020, placebo or risperidone, followed by a 6-month chronic treatment phase of CYP-1020 or risperidone using both the PANSS and MCCB. This trial should be able to more fully characterize CYP-1020's long-term antipsychotic efficacy and impact on cognition.

Policy of full disclosure: The presenter Dr. Amir H. Kalali is a consultant to BioLineRx. The authors Yona Geffen et al. are employees of BioLineRx.

S-09-003
Selective phosphodiesterase inhibitors as a target for cognition enhancement in schizophrenia

J. Prickaerts (Department of Psychiatry and Neuropsychology, School for Mental Health and Neuroscience, Maastricht University, Maastricht, The Netherlands)

Abstract: Cognitive dysfunction is one of the first and earliest symptoms of schizophrenia. Thus targeting cognition might be an effective strategy to treat schizophrenia while at the same time slowing down the occurrence of affective and positive symptoms. Our understanding of the neurobiological processes underlying cognition is continuously improving, leading to the identification of targets for the development of cognition-enhancing drugs. One class of drugs is the phosphodiesterase (PDE) inhibitors, which have been identified as possible cognition enhancers about a decade ago. PDEs differ in the substrate, i.e. cyclic adenosine monophosphate (cAMP) and/or cyclic guanosine monophosphate (cGMP), being hydrolyzed. Since these cyclic nucleotides have been suggested to play specific roles in processes of memory, selective PDE inhibitors preventing the breakdown of cAMP and/or cGMP could improve memory. Studies with different timing of treatment with specific PDE inhibitors indicated that distinct underlying signaling pathways for early and late consolidation processes exist corresponding to specific time-windows for memory consolidation. There is evidence that the underlying mechanisms of PDE inhibition on the observed behavioral effects are independent of possible cerebrovascular effects. Most likely the underlying mechanisms are a cGMP/PKG pathway for early consolidation processes and a cAMP/PKA pathway for late consolidation processes. Recently, the effects of specific PDE inhibitors are explored on other cognitive domains including acquisition processes/short-term memory and information processing. It will be shown that elevation of central cGMP levels as well as cAMP levels after treatment with a specific PDE inhibitor improve acquisition processes/short-term memory. The effects of specific PDE inhibitors on information processing by using a sensory gating paradigm indicate that elevation of both cGMP and cAMP with a specific PDE inhibitor improves sensory gating, whereas elevation of cGMP alone has no effect. In a translational approach we also investigated the effect of PDE5 inhibition on cognition in humans. Within the context as described above, the latest results of specific inhibitors of PDE2, PDE4, PDE5 and PDE10 on cognitive processes will be presented and discussed for treating cognitive impairments.

Policy of full disclosure: The data presented have no conflicting interests.

S-09-004
LY2140023 Monohydrate: preclinical and clinical update on the development of an mGluR2/3 agonist treatment for schizophrenia

J.-C. Gomez (Eli Lilly and Company Lilly Corporate Center, Indianapolis, USA)

Abstract: While dopamine has been viewed as the key neurotransmitter mediating the symptoms of schizophrenia over the last 5 decades, there is accumulating evidence implicating dysregulation of the glutamatergic system as a prominent contributant to the pathophysiology of the disease. Understanding the role of glutamate in schizophrenia may provide a new direction for the development of innovative and hopefully more effective drug therapies for schizophrenia. As an overview of our research, I will summarize data from several preclinical animal models of schizophrenia identifying metabotropic glutamate (mGlu) 2/3 receptors as potential antipsychotic targets, and present data from several recent clinical trials assessing the role of the mGlu 2/3 receptor agonist LY2140023 monohydrate, an oral prodrug of LY404039, as a possible therapeutic agent in the treatment of schizophrenia.
Policy of full disclosure: I am full time employee and stockholder of Eli Lilly and Company.

S-10 Cognitive behavior therapy for psychosis: what do we know about its effectiveness and neural correlates?

S-10-001
The effects of CBT in persons with ultra high risk: the Dutch EDIE trial

M. van der Gaag (VU University + EMGO Institute, Amsterdam, Netherlands)

Objective: CBT might postpone or even prevent a first psychotic episode in people who are at ultrahigh risk for developing psychosis.
Methods: A randomised controlled trial in four research sites was performed with CBT targeted at cognitive bias that play a role in the development of psychosis. 201 parsons were included.
Results: The final results will be in on September 1st 2011.
Conclusion: Screening the general help-seeking population for people with an at risk mental state is more productive then using a referral strategy. Screening is less biased to young males. The effects of the intervention are awaited.
Policy of full disclosure: None.

S-10-002
Targeting social and symptomatic outcomes using CBT for psychosis: effectiveness, strategies and mediators

D. Fowler (Faculty of Health Clinical Psychology, University of East Anglia, Norwich, UK)

Abstract not received in due time.

S-10-003
Effectiveness of CBT in a German outpatient setting. Short and long term results of a controlled randomised trial

T. Lincoln (Phillips-Universität Marburg Fachbereich Psychologie, Germany), M. Ziegler, S. Mehl, E. Luellmann, M.-L. Kesting, S. Westermann, W. Rief

Objective: RCTs have shown that CBT reduces positive symptoms of psychosis. However, studies are needed to demonstrate its effectiveness in unselected samples in routine clinical practice settings.
Methods: 80 patients with DSM-IV schizophrenia spectrum disorders seeking outpatient treatment for psychosis were randomized to a cognitive-behavioural intervention (CBTp, $n = 40$) or a wait-list (WL, $n = 40$). The CBTp-group was assessed at baseline, post-treatment and one-year follow-up. The WL-group was assessed at baseline, after a 4-month waiting-period, post-treatment and after 1 year. The main outcome measure was the Positive and Negative Syndrome Scale.
Results: By post-treatment, the treatment-group showed significant improvement over the wait-list group for positive symptoms and overall psychopathology. There was no improvement for negative symptoms. The number of dropouts during the treatment phases was low (11.3%). The majority of the participants perceived the treatment as helpful (98%) and considered themselves improved (92%). Significant pre-post effect sizes varied between .77 for general psychopathology and .38 for delusional conviction. At post-assessment, 69% had reliably improved in at least one PANSS domain. The positive effects of treatment on the main outcomes could be maintained at one-year follow-up.
Conclusion: Patients with psychosis seeking help in clinical practice settings benefit from CBTp. The efficacy of CBTp can be generalized to clinical practice despite differences in patients, therapists and deliverance.
Policy of full disclosure: None.

S-10-004
How does CBT effect the brain of patients of schizophrenia: a multicenter fMRI study

T. Kircher (Marburg, Germany)

Abstract: In recent years, CBT for schizophrenia has shown its effectiveness in a multitude of clinical trials and meta-analyses. It has been included as therapy of choice—besides antipsychotic medication and social rehabilitation—in all major treatment guidelines. However, a number of questions remain about its effectiveness in particular subsamples, about the mediating effects and its effect on brain plasticity. In this presentation, an overview will be given on novel research on brain changes due to CBT in a large multicenter trial. The presentations will include an overview of the current clinical implementations and latest research on CBT in psychosis.
Policy of full disclosure: None.

S-11 Motor symptoms as an intrinsic component of schizophrenia pathobiology

S-11-001
Spontaneous involuntary movements as an integral component of network dysfunction in schizophrenia

J. Waddington (Royal College of Surgeons, Dublin, Ireland), K. Tomiyama, N. Koshikawa

Objective: Whether the pathobiology of schizophrenia extends beyond its defining symptoms, to involve diverse domains of abnormality in the manner of a systemic disease, has long been debated. Studies of neuromotor dysfunction have been confounded by treatment with antipsychotic drugs.

Methods: This challenge has been illuminated by a new generation of studies on first episode schizophrenia before initiation of antipsychotic treatment and by opportunities in developing countries to study chronically ill patients who have remained antipsychotic-naïve due to limitations in provision of psychiatric care. Building from studies in antipsychotic-naïve patients, this presentation focuses on involuntary movements.
Results: The presence and characteristics of involuntary movements in untreated vis-à-vis treated psychosis indicate such movements to be an intrinsic feature of the disease process and implicate dysfunction in cortical-basal ganglia-cortical circuitry. Additionally, recent studies in mice mutant for genes associated with risk for schizophrenia indicate a phenotype that includes orofacial dyskinesia.
Conclusion: Involuntary movement disorder in schizophrenia joins other markers of subtle but pervasive cerebral and extra-cerebral, systemic dysfunction and complement current concepts of schizophrenia as a disorder of disconnectivity in developmentally determined cortical-basal ganglia-thalamo-cortical/cerebellar networks.
Policy of full disclosure: None.

S-11-002
Dyskinesia and Parkinsonism in antipsychotic naive schizophrenia, first-degree relatives and controls; prevalence and methods of measurement

J. Koning (Amersfoort, Netherlands)

Objective: Movement disorders such as dyskinesia and Parkinsonism have frequently been reported in (drug-naive) patients with schizophrenia. Therefore movement disorders may be related to schizophrenia. Siblings of patients with schizophrenia also appear to have subtle forms of movement disorders. This suggests that motor abnormalities may also be related to the risk of developing the disease. Subtle forms are not always detected with the use of the standard observation-based clinical rating scales, which are less sensitive than mechanical instrument measurement.
Methods: First a systematic search was conducted to identify studies reporting on dyskinesia and Parkinsonism assessed in antipsychotic-naive patients with schizophrenia and controls and separately in non-ill first-degree relatives and controls. Second, in a clinical study we compared the presence and severity of dyskinesia and Parkinsonism in 42 non-psychotic siblings of patients with nonaffective psychosis and in 38 controls as measured by mechanical instruments and clinical rating scales.
Results: Antipsychotic-naive schizophrenia was found to be strongly associated with dyskinesia and Parkinsonism compared to controls. Dyskinesia and Parkinsonism were also significantly more prevalent in healthy first-degree relatives of patients with schizophrenia as compared to healthy controls. Based on the clinical study, there were no significant differences in movement disorders between siblings and controls on the basis of clinical assessments. However, mechanical measurements indicated that siblings compared to controls displayed significantly more dyskinesia and Parkinsonism signs.
Conclusion: The results suggest that movement disorders, and by inference abnormalities in the nigrostriatal pathway, are not only associated with schizophrenia itself, but may also be related to the (genetic) risk of developing the disease. In addition this study shows that mechanical instrument measurement of movement disorders is more sensitive than assessment with clinical rating scales. Therefore, it may be used in screening programs for populations at risk for psychosis.
Policy of full disclosure: None.

S-11-003
Neuromotor abnormalities in first-episode psychosis patients: status at antipsychotic naïve state and response to anti-psychotic drugs

M. J. Cuesta (Pamplona, Spain)

Abstract: Primary neuromotor abnormalities are thought to be a manifestation of the brain pathology underlying the psychotic illness; however, their causes and consequences are poorly understood. This presentation has two aims. First, to study the prevalence and correlates of neuromotor abnormalities in neuroleptic-naive psychotic patients. And second, to examine whether antipsychotic drugs interact with or modify the disease-based motor disorders. Neuromotor abnormalities at the neuroleptic-naive state (Parkinsonism, catatonia, dyskinesia, and akathisia) were examined in a sample comprising one hundred psychotic inpatients were assessed. Patients received treatment with haloperidol ($n = 23$), risperidone ($n = 52$), or olanzapine ($n = 25$). Change scores in neuromotor ratings over the treatment period and rates of drug-responsive and drug-emergent neuromotor syndromes were examined. Neurological syndromes tended to co-vary, and 34 of the patients had at least one categorically defined neurological syndrome at naïve state. Antipsychotic drugs may both improve pre-existing abnormalities and cause "de novo" neurologic syndromes with a more favorable neuromotor profile for olanzapine regarding risperidone, which in turn has a more favorable profile than haloperidol Neuromotor abnormalities represent both an integral part of the disease process not influenced by chronicity or antipsychotic drugs and the relationship between antipsychotic drugs and neurologic abnormalities is more complex than previously acknowledged.
Policy of full disclosure: None.

S-11-004
Neurobiology and clinical correlates of quantitative motor activity in schizophrenia

S. Walther (University of Bern Psychiatry, Switzerland)

Objective: Motor symptoms are frequent in schizophrenia and comprise several aspects. Individuals with schizophrenia report less engagement in physical activity. We have investigated the association of objective motor activity with psychopathology, course and neurobiology in schizophrenia.
Methods: A series of studies was conducted with schizophrenia patients during acute episodes. All participants wore wrist actigraphs for 24 h. In two studies, we applied resting state perfusion MRI and diffusion tensor imaging. Furthermore, we were able to measure the longitudinal course of motor behavior in 17 patients.
Results: Objective motor activity differentiated schizophrenia subtypes and displayed minimal variation during the course of an episode or between episodes. We found a weak inverse correlation of activity data with the PANSS negative subscore. In contrast to controls, resting perfusion was not associated with motor activity in the basal ganglia in schizophrenia, but instead correlated with several cortical motor regions. In addition, a linear negative association was found between activity and white matter integrity underneath the right supplemental motor area (SMA) in patients. Probabalistic fiber tracking further indicated that motor activity was positively associated with the connectivity between left pre-SMA and SMA proper in patients. In contrast to controls, however, motor activity was not associated with the connectivity between pre-SMA and pallidum or between primary motor cortex and thalamus in patients.
Conclusion: Quantitative motor activity is altered in schizophrenia and related to subtypes. It helps to identify altered motor control in

schizophrenia. Results indicate that changes in resting perfusion and white matter organization may contribute to reduced motor activity in schizophrenia patients. The findings support the view that changes in the brain motor network seem to be a critical aspect of schizophrenia neurobiology.
Policy of full disclosure: None.

S-12 Negative symptoms of schizophrenia: assessment, domains and relationships with outcome

S-12-001
Assessment of negative symptoms in schizophrenia

B. Kirkpatrick (Department of Psychiatry, Texas A&M College of Medicine, Temple, USA)

Objective: To consider the best current methods for the assessment of negative symptoms.
Methods: A review of the recent literature.
Results: The distinction between primary and secondary symptoms is crucial, as primary negative symptoms have correlates that are not found for negative symptoms more broadly defined (i.e., including both primary and secondary symptoms). These include differences in associated symptoms, course of illness, risk factors, biological correlates, and treatment response. The Schedule for the Deficit Syndrome, which distinguishes patients with and without primary negative symptoms—i.e., deficit versus nondeficit groups—is appropriate for smaller studies, but requires careful attention to training. The Proxy for the Deficit Syndrome is a flexible approach that can be based on a variety of measures of emotionality and negative symptoms broadly defined, and is appropriate for use in larger datasets. Both of these methods require confirmation of the validity of the deficit/nondeficit categorizations, so that researchers can be sure that they are talking about similar patient groups. The National Institute of Mental Health's Consensus Statement on Negative Symptoms led to development of the Brief Negative Symptom Scale, which reflects the recommendations of the NIMH Consensus Development Meeting.
Conclusion: Methods that can be applied in a variety of settings are available for primary negative symptoms, and for negative symptoms broadly defined.
Policy of full disclosure: Disclosure (last 12 months): Abbott Laboratories, Boehringer Ingelheim, Sunovion.

S-12-002
Are abnormalities of reward processing a key component of negative symptoms in schizophrenia?

F. Schlagenhauf (Department of Psychiatry, Universitätsmedizin Berlin, Germany), G. Juckel, A. Heinz

Objective: A dysfunction of the dopaminergic reward system has been postulated in the pathophysiology of schizophrenia. A subcortical hyperdopaminergic state in unmedicated schizophrenia patients has been associated with the pathogenesis of positive symptoms and a prefrontal hypodopaminergic state with cognitive and negative symptoms. But negative symptoms like anhedonia have also been hypothesized to be associated with a dysfunction of the mesolimbic dopaminergic system. However, preclinical studies indicate that the mesolimbic dopaminergic system mediates motivation and incentive salience of reward-indicating stimuli rather than the ability to experience pleasure. Recent neuroimaging findings in schizophrenia patients confirmed dysfunctional activation during reinforcement learning.
Methods: We used functional magnetic resonance imaging (fMRI) to assess the BOLD response in the ventral striatum of unmedicated schizophrenia patients during presentation of reward-indicating stimuli and during reversal learning.
Results: Compared with healthy controls, unmedicated schizophrenics showed reduced ventral striatal activation during presentation of reward-indicating cues, which was negatively correlated with the severity of negative symptoms. During reversal learning unmedicated schizophrenia patients displayed behavioral impairments and reduced activation in the ventral striatum and the ventrolateral PFC.
Conclusion: In unmedicated schizophrenic patients, a high striatal dopamine turnover may interfere with neuronal processing of reward-indicating stimuli by phasic dopamine release, thus contributing to negative symptoms as such as loss of drive and motivation.
Policy of full disclosure: None.

S-12-003
The relationship between negative symptoms and neuropsychological impairment across psychotic disorders

A. Reichenberg (Department Psychosis Studies, King's College, London, UK), M. Russo

Objective: Negative symptoms and cognitive deficits in schizophrenia share many features and are correlated in their severity on a cross-sectional basis. However, two important questions regarding the specificity of the relationship remain unanswered. First, is the relationship general, evident across cognitive domains, or is it specific to certain functions? Second, is the relationship specific to schizophrenia or is it evident in other psychotic disorders?
Methods: Data from 500 first episode psychosis patients was used for an exploratory factor analysis of symptom dimensions. Next, the association between symptom dimensions and neuropsychological functioning was examined in a sub sample of 125 patients. Linear and non-linear regression models were used to analyse the relationship between symptoms and cognition.
Results: Negative symptoms, Mania, Disorganization, Depression, Hallucination and Delusions emerged as first-order factors that further grouped into 2 higher-order factors of Affective and Non-Affective psychosis. More severe negative symptoms were associated with greater memory impairment (8% of variance explained) and poorer premorbid IQ (10.4% of variance explained). Disorganization and depression were also associated with memory performance (7.5 and 7% of variance explained, respectively). Depression was also associated with processing speed and executive functions (10.6 and10.5% of variance explained, respectively) Mania was associated with verbal fluency (6.5–7.5% of variance explained). The affective psychosis higher-order factor showed a significant negative association with memory (9% variance explained) and a positive relationship with executive functions and verbal fluency (5 and 8% of variance explained).
Conclusion: Negative symptoms are associated with specific cognitive domains, but such specificity is also evident for other symptom dimensions. Cognitive impairment is not a dimension of symptomatology per se but it appears to be a transversal component present at different degrees of severity and specificity across symptom clusters.
Policy of full disclosure: None.

S-12-004
Persistent negative symptoms in first episode psychosis patients

S. Galderisi (University of Naples SUN Department of Psychiatry, Italy), A. Mucci

Objective: Negative symptoms that do not improve following antipsychotic treatment represent a real challenge for future development of effective treatments. It has been proposed that the identification of persistent negative symptoms in psychosis patients might foster research on new treatments development for negative symptoms of schizophrenia. Data on the prevalence of persistent negative symptoms in first episode psychosis patients and on their relevance to 1-year outcome are presented.
Methods: The study was carried out in first episode subjects from the EUFEST study. Psychopathology was assessed using PANSS at baseline and after 1 year of treatment. Remission of positive symptoms was assessed using Andreasen's criteria for clinical remission. Functional outcome was evaluated after 1-year of treatment using the Manchester Short Assessment of Quality of Life (MANSA) and the Camberwell Assessment of Need (CAN).
Results: Persistent negative symptoms were present in 11% of the study sample. After 1 year of treatment, subjects with persistent negative symptoms had poorer functional outcome and lower remission rates than those without persistent negative symptoms.
Conclusion: In first episode psychosis patients persistent negative symptoms are associated with poor response to treatment and low remission rate after 1 year of treatment.
Policy of full disclosure: None.

S-13 Antipsychotics in the elderly

S-13-001
Antipsychotics in treatment of behavioral and psychological symptoms in dementias

P. H. Robert (Centre Mémoire de Ressources et de Recherche, EA CoBTek, CHU de Nice, Université de Nice Sophia Antipolis, France), E. Mulin, R. David

Abstract: Alzheimer's disease (AD) is a complex progressive brain degenerative disorder that has effects on multiple cerebral systems. In addition to cognitive and functional decline, behavioural changes manifest with increasing severity over time, presenting significant management challenges for caregivers and health care professionals. Almost all patients with AD but also with other type of dementia are affected by neuropsychiatric symptoms at some point during their illness.
The most difficult neuropsychiatric symptoms to manage in dementia are agitation (aggressive and non-aggressive) and psychosis (delusions and hallucinations). Hallucinations may resolve over a few months, but delusions and agitation are more persistent. Non pharmacological approaches and caregiver training is the first line treatment however antipsychotics are often used to treat agitation and psychosis in people with dementia however their impact is unclear.

Overall, antipsychotics confer significant treatment benefit for the short-term (up to 12 weeks) treatment of aggression in people with AD, although the benefits must be weighed against the not insubstantial risk of serious adverse events. The evidence base is less robust for longer-term therapy, and for the treatment of psychosis, but the longer-term use of antipsychotics in people with AD is probably inadvisable, other than in exceptional clinical circumstances. In addition recent studies also suggest that further cognitive impairment is an additional risk of treatment with atypical antipsychotics that should be considered when treating patients with Alzheimer's disease.
Policy of full disclosure: In the past 5 years P Robert received honorarium and grants from the following pharmaceutical companies: Lundbeck, EISAI, Janssen, Novartis, GE, Mertz.

S-13-002
Pharmacotherapy of neuropsychiatric symptoms in dementia in nursing homes

M. Rapp (Department of Psychiatry and Psychotherapy, Charité Campus Mitte, Berlin, Germany; Geriatric Psychiatry Center, Psychiatric University Hospital St. Hedwig, Charité, Berlin, Germany), T. Majic, J.-P. Pluta, T. Mell, J. Kalbitzer, Y. Treusch, A. Heinz, H. Gutzmann

Objective: Neuropsychiatric symptoms of dementia like agitation, depression and apathy often result in increased prescriptions of psychotropics. In Germany, outpatient clinics at psychiatric hospitals play an important role in the treatment of neuropsychiatric symptoms in nursing homes. The aim of this study was to test whether the severity and pharmacotherapy differed in patients treated by outpatient clinics at psychiatric hospitals, as compared to primary care specialists.
Methods: A cross-sectional study of the prevalence of agitation, apathy, and depression, and the amount of psychotropics prescribed in defined daily dosages (DDD) in 304 residents with dementia in 18 Berlin nursing homes.
Results: Patients treated by outpatient clinics at psychiatric hospitals suffered from more severe neuropsychiatric symptoms ($P < 0.05$), were prescribed more antidepressants and antidementia agents ($P < 0.05$) and, when adjusting for the severity of agitation, less neuroleptics ($P < 0.05$) as compared to primary care specialists.
Conclusion: Psychiatric outpatient clinics at hospitals treat more severely demented patients who suffer from severe neuropsychiatric symptoms. The pharmacotherapy provided by these clinics displays a favourable profile according to established treatment guidelines.
Policy of full disclosure: None.

S-13-003
Vascular side effects of neuroleptics and their prevention

C. Turrina (Department of Psychiatry, University of Brescia, Brescia, Italy), E. Sacchetti

Abstract: One of the most feared vascular events associated with atypical and typical antipsychotics is the occurrence of cerebrovascular accidents. In fact, starting from 2002, post-hoc analyses of early, double-blind, placebo-controlled trials of risperidone and olanzapine in patients with dementia and behavioral and psychological symptoms demonstrated higher rates of cerebrovascular (CV) events in patients randomized to the active treatment versus individuals in the placebo group. As a consequence of these findings, specific warnings for increased risk of CV accidents in people with dementia treated with atypical antipsychotics were released. Since then, several pooled- and metha-analyses of existing controlled clinical studies of the atypicals and new double-blind trials of antipsychotics in this specific population have been carried on. Literature on CV risk in patients treated with antipsychotics has also been enriched by a number of large observational studies involving patients with dementia or mixed samples of elderly individuals with or without dementia. On the whole, this lecture supports some main conclusions: (1) People with

dementia are really at increased CV risk during treatment with antipsychotics, but the risk is probably less pronounced than initially supposed; patients with vascular dementia could be more susceptible to develop stroke or related accidents when treated with antipsychotics. (2) The relationship between use of antipsychotics and CV risk is reasonably not confined to patients with dementia, but more generally involves elderly patients treated with antipsychotics. (3) The abnormally high number of cases developing CV accidents while using antipsychotics involves all the classes of these medications and the typicals are reasonably at least equal to the atypicals as far as the CV risk. (4) CV accidents in elderly people treated with antipsychotics are overrepresented during the restricted time period corresponding to the earliest phases of treatment (5) Regardless of exposure to antipsychotics, elderly patients treated with these medications have a large number of relevant predispositions to CV accidents. (6) The contribution of antipsychotics and predisposing factors to the increased risk of CV accidents could be integrated within a comprehensive model that views stroke and related accidents during exposition to typicals or atypicals as a complex trait in which the therapy plays a fast permissive role when sufficient antecedent susceptibilities are also present.
Policy of full disclosure: Professor Emilio Sacchetti has received funding for consultancy, research, advisory board membership and sponsored lectures from Abbott, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Dainippon Sumitomo Pharma, Eli Lilly, Glaxo Smithkline, Innova Pharma, Italfarmaco, Janssen-Cilag, Lundbeck, Pfizer, Sanofi Aventis, Wyeth Lederle.

S-13-004
Use of antipsychotics in the elderly: regulatory aspects

K. Broich (Federal Institute for Drugs and Medical Devices, Bonn, Germany)

Abstract: Although individuals older than 60 years now account for more than 50% of drug prescriptions, they are often excluded from clinical and regulatory trials, particularly if they are older than 75, suffering from multiple co-morbidities or taking multiple medications. Instead of the limited data base the relative amount of psychotropic medications in the older population is still increasing over the recent years.
Therefore as regulators we try to foster clinical trials in the elderly providing better data for clinical use. Two options are emphasized: in disease entities like schizophrenia or major depression no separate trials in elderly populations might be necessary as long as a sufficient proportion of elderly is included in the pivotal trials and no signals for a separate side effect profile are evident (e.g. in the guidance for medicinal products for schizophrenia: "…the number of elderly patients included in the studies should suffice to generate this data. Safety data should be analysed separately with special attention to safety concerns relevant to this age group e.g. cardiovascular and stroke events …"). If a psychotropic medication is primarily developed for treatment in the elderly, e.g. behavioural abnormalities or psychotic symptoms in Alzheimer's disease, specifically designed trials in elderly patients are necessary to provide concise information for this group concerning dose recommendations and to allow a proper benefit-risk assessment.
In general older patients are more sensitive to side effects of antipsychotics and recently an increased mortality in elderly patients treated with antipsychotics has been confirmed. From a regulatory point of view we addressed this problem by adding warnings and contraindications to the SPCs of antipsychotics. When antipsychotics are used in the elderly careful monitoring of improvement in target symptoms, appearance of side effects, potential for drug interactions, and functional activities of daily living is indispensable.
On a national and European level regulators started a process to consult other regulatory bodies, learned societies, the pharmaceutical industry and patient representatives on how to improve the availability and quality of data produced from clinical trials involving older people, and how to improve the implementation of the guidelines on such trials.
Policy of full disclosure: None.

S-14 Glutamate dysfunction in schizophrenia and bipolar disorder: evidence from genetics and brain imaging

S-14-001
GWAS, sequencing, systems biology, gene-environment studies: how to navigate through the jungle of contemporary psychiatric genetics

T. Schulze (Department of Psychiatry and Psychotherapy, Georg August University, Goettingen, Germany)

Objective: Genomewide-association studies (GWAS) have robustly identified vulnerability genes for schizophrenia or bipolar disorder. They have taught us the following lessons: (1) Psychiatric disorders are polygenic disorders. The contribution of each locus to risk of disease is modest and disease risk increases substantially with the total burden of risk alleles carried. (2) The best findings from GWAS do not necessarily fall within those genes that have previously been widely studied. (3) Pursuing a "top-hits-only" strategy may prevent us from understanding the genetic complexity. (4) Allelic heterogeneity may be an important factor in psychiatric disorders. Allelic heterogeneity means that a phenotype can be caused by different alleles within a gene; this phenomenon has been extensively observed in monogenic disorders such as cystic fibrosis as well as in BRCA1/2-associated breast cancer. (5) Finally, as with other complex phenotypes, GWAS in psychiatric disorders demonstrate that the variants identified so far only account for a small fraction of genetic variability. Future research will need to embark on several complementary approaches in order to fill the yet "unexplained" part of the variance. These will among others include sequencing approaches, pharmacogenetic studies, detailed genotype-phenotype dissection approaches, systematic gene-environment studies, systems biology approaches, and the study of prospectively assessed phenotypes.
Methods: This presentation is meant to sketch out feasible approaches to combine all these methodologies in a meaningful and goal-directed way.
Results: Work from the National German Genome Research Network (http://www.ngfn.de), the US-GAIN consortium (http://www.genome.gov/19518664), the international Psychiatric GWAS Consortium (https://www.pgc.unc.edu) will be presented.
Policy of full disclosure: None.

S-14-002
Gamma oscillations, cognition and interaction of glutamatergic and GABAergic neurons

C. Mulert (University Hospital Hamburg, Germany)

Objective: Disturbed synchronization in the gamma-band range is a key mechanism of disturbed cognitive functions in schizophrenia. Since disturbed gamma oscillations have also been found in

unaffected siblings of patients with schizophrenia, a genetic background of disturbed oscillations in the gamma-band range can be assumed. One of the most often replicated risk genes for schizophrenia is neuregulin-1. Neuregulin-1 is necessary for inhibitory synapses of parvalbumin-positive interneurons on glutamatergic pyramidal cells. These inhibitory synapses are part of a feedback loop that is required for the synchronization within the gamma-band range. Here we present data demonstrating a close relationship between genetic polymorphisms in the neuregulin-1 gene and oscillations in the gamma-band range.
Methods: 80 individuals with schizophrenia (55 males and 25 females) and 266 control subjects (132 males and 134 females) were investigated. EEG was recorded with 27 electrodes referred to Cz. The paradigm was an auditory choice reaction task. Two different tones (800 and 1,200 Hz) were presented by earphones. The subject had to answer the stimulus with button press with the left hand following the higher tone or with the right hand following the lower tone. Analyses of gamma-band power were done using wavelet transformation. DNA extraction was done with the QIAamp Blood Maxi Kit. For the chromosomal region of interest in this analysis, SNPs were selected between the positions (Chr8: 31569311… 32756235) covering 160 SNPs.
Results: We present data demonstrating a close relationship between genetic different polymorphisms in the neuregulin-1 gene and oscillations in the gamma-band range.
Conclusion: Our findings suggest that neuregulin-1 is related to pathophysiological mechanisms underlying disturbed gamma oscillations and cognitive dysfunction in schizophrenia.
Policy of full disclosure: None.

S-14-003
Glutamatergic genes of schizophrenia and neuropsychological intermediate phenotypes

D. Rujescu (University of Munich, Germany)

Objective: We use complementary strategies to approach the pathobiology and genetics of schizophrenia including genetic association and family studies as well as animal and cell culture models. We aim to identify schizophrenia genes in a large case–control and family-based study. Over 1,000 patients, 200 first degree relatives and 2,420 community-based healthy volunteers entered the study. High-throughput genotyping was done and first results will be presented for glutamatergic genes.
Methods: Furthermore, we use endophenotypes as a complementary approach. These comprise, among others, electrophysiological (e.g. P50 suppression and eye movement) and neuropsychological (e.g. working memory, attention/vigilance, verbal/visual learning and memory, speed of processing, and problem solving) endophenotypes.
Results: Additionally, we use an NMDA-receptor antagonist animal model which mimics aspects of psychosis to identify candidate genes which can be used in human studies. In our model, chronic, low-dose treatment with MK801 alters the expression of NMDA receptor subunits in a pattern similar to schizophrenia. On a cellular level, the number of parvalbumin-positive interneurons was selectively decreased a finding which parallels observations in post mortem brains. On a functional level, recurrent inhibition of pyramidal cells was altered, as postulated from histological findings. Finally, on a behavioral level, these animals showed cognitive deficits, which again parallel findings in schizophrenia.
Conclusion: We used a functional genomic approach for the identification of glutamatergic candidate genes for psychosis-related traits and identified differentially expressed genes. In human genetic analyses, some of these genes were found to be strongly associated with schizophrenia and/or above-mentioned endophenotypes.
Policy of full disclosure: None.

S-14-004
Dysfunction of dopamine-glutamate interaction: evidence from multimodal imaging

J. Gallinat (Psychiatry & Psychotherapy, Charité Universitätsmedizin, Berlin, Germany), M. Schäfer, F. Schubert

Objective: A dysfunctional cerebral glutamate system in schizophrenia is a current hot spot of neurobiological research and several glutamate modulating therapeutics are in phase I and II trials. Improved proton magnetic resonance spectroscopy (H-MRS) with increasing field strength allows the assessment of biological effect of glutamate modulating agents during therapy.
Methods: In a RCT, 17 acute and 13 chronic schizophrenic patients (DSM-IV) on stable risperidone therapy were measured with H-MRS at baseline and after 6 weeks (T2) of add-on of memantine or placebo. Absolute glutamate concentrations were measured (left hippocampus, cingulate).
Results: At baseline, patients showed increased hippocampal glutamate concentrations (11.9 mmol/l vs. 10.7 mmol/l in healthy controls, $P = 0.007$). After therapy glutamate decreased in acute schizophrenics ($P = 0.023$), but remained unchanged in chronic patients ($P = 0.45$). The differential effects of memantine/placebo are not know due to blinding.
Conclusion: The study shows abnormal glutamate concentrations in a key region of schizophrenia pathophysiology. The normalization of glutamate during add on therapy may rely on modulation of the NMDA-receptors in response to memantine. The results indicate a different pathobiology between acute and chronic patients and favor H-MRS as an interesting in vivo tool for biological monitoring of glutamate functions.
Policy of full disclosure: None.

S-15 Cognition in schizophrenia: from neural mechanisms to psychological interventions

S-15-001
Brain circuits involved in thought and movement disorders

W. Strik (Univers. Hospital of Psychiatry, University of Bern, Switzerland), S. Walther

Abstract: The clinical features of psychotic disorders can be grouped into symptom domains to match functional brain modules. Namely, language related and motor symptoms of schizophrenia such as auditory verbal hallucinations, formal thought disorders and the motor symptoms of catatonia are apt to be studied in terms of dysregulations of the respective brain circuitries. A clinical study of 168 psychotic patients showed that the respective symptoms were not evenly distributed, but clustered in three major syndromes including language, motor and emotional symptoms. The respective symptom clusters showed a certain degree of independence, but were not mutually exclusive, which suggests a dimensional rather than categorical approach to these subgroups (Strik et al. 2010). Findings from a series of studies of our group support the relationship between language related symptoms with abnormalities in the language circuitry, and of motor symptoms and regions of the motor loop. În particular, the

severity of formal thought disorders was negatively correlated with the volume of the left superior posterior temporal gyrus (lSTG) (Wernicke's Area) and with a functional hyperactivity of the left fronto-temporal language system. On the other hand, metabolism and white matter integrity of the right supplementary motor areas (rSMA) was linked to quantitative movement parameters in schizophrenia. Structural and functional brain imaging studies support the hypothesis of an involvement of the language and the motor loop in the pathophysiology of specific schizophrenic core symptoms. The results indicate that there is a mild structural deficit in key regions for the regulation of the motor and the language loop. This may be the basis of a pathological excitation of the system and, at the behavioral level, inhibition or disinhibition of the respective functions including alogia or incoherence, and stereotypies or akinetic catatonia. An analogous pathophysiology has been proposed for the limbic system and emotional dysregulation in schizophrenia (Heinz and Schlagenhauf 2010; Heckers and Konradi 2011). The uneven distribution and individually different degrees of these neurobiological abnormalities in schizophrenia may account for the heterogeneity and variance of the findings.
Policy of full disclosure: None.

S-15-002
Brain-behavior relation of emotion in schizophrenia

F. Schneider (Dept. of Psychiatry, Psychotherapy and Psychosomatics, University Hospital, RWTH Aachen University, Germany)

Abstract: Emotional deficits are among the core symptoms of schizophrenia patients. Patients tend to misinterpret feelings in others or display inappropriate emotional reactions in their everyday life. It can be concluded that these impairments alone lead to social isolation and negative social support.
Furthermore the effects of emotion on cognitive processes, such as attention or memory, must not be underestimated—it should be assumed that at least some cognitive deficits in schizophrenia patients are closely connected to emotional deficits.
Modern brain imaging not only allows for the localisation of neuronal correlates of emotional functions and dysfunctions but also for the assessment of therapeutic interventions in psychiatric patients. New findings are to be expected especially from multimodal approaches (e.g. EEG-fMRI-studies) or more complex study designs, which can assess the effects of congruency in multimodal presentation of emotional stimuli.
These studies are a major step to improve the clinical relevance of imaging research and more importantly to improve the situation of schizophrenia patients significantly.
Policy of full disclosure: None.

S-15-003
New approaches to cognitive remediation

A. Medalia (Columbia University, New York, USA)

Objective: Marked cognitive impairment underlies much of the social and occupational dysfunction associated with schizophrenia. Cognitive remediation is a behavioral intervention consisting of training activities that aim to target a range of cognitive impairments, with the ultimate intent of improving functional outcome. While meta-analyses of cognitive remediation efficacy studies consistently report moderate effect sizes for improvement in cognitive and psychosocial functioning, there is a range of response. New approaches to cognitive remediation benefit by attending to the variables that have been found to moderate the effects of cognitive remediation on neurocognition and psychosocial outcome. This talk will consider empirical data suggesting an influential role of program setting, instructional techniques, and client factors on cognitive remediation outcomes and will discuss the implications of this data for new approaches to cognitive remediation.
Methods: 174 inpatients and outpatients with schizophrenia participated in several cognitive remediation trials that examined the role of client factors and instructional techniques on cognition and functional outcome. Methodology in these trials ranged from RCT to cross sectional.
Results: Instructional techniques that promote better outcomes include adequate session intensity, providing a learning context, combining drill and practice with strategy learning, and using motivationally enhancing strategies. Client factors that are associated with better outcome are enhanced intrinsic motivation and perceived competency to do the training tasks, and focal rather than global impairments.
Conclusion: Aspects of the treatment environment interact with certain client characteristics, to impact the impact of cognitive remediation. New approaches to cognitive remediation consider program setting, instructional techniques, and client factors in order to maximize therapeutic outcome.
Policy of full disclosure: Advisory Board: Eli Lilly Research funding: Sunovion Pharmaceuticals Inc., Eli Lilly.

S-15-004
Integrated cognitive therapies: update and perspective

V. Roder (University of Bern, Bern, Switzerland), S. J. Schmidt, D. R. Müller

Objective: Evidence suggests that several brain circuits are structurally deficient in schizophrenia. These neurobiological abnormalities contribute to the cognitive impairments that characterize schizophrenia and that act as rate-limiting factors for functional recovery and rehabilitation efforts. There is great interest in the treatment of cognitions in schizophrenia, called cognitive remediation therapy (CRT). Therefore, we developed the Integrated Neurocognitive Therapy (INT) designed for stabilized schizophrenia outpatients. This cognitive-behavioral group therapy approach targets all cognitive MATRICS domains. However, the neuronal mechanisms of change following CRT are not yet well understood and need further investigation.
Methods: INT was evaluated in an international randomized multicite study and was compared with treatment as usual (TAU). The sample comprised 169 schizophrenia outpatients. An assessment battery was applied before and after therapy and at a 1-year follow-up. Additionally, a literature search of studies using neuroimaging techniques was done to investigate whether such beneficial therapy effects by CRT were associated with neuronal changes.
Results: INT patients obtained significantly stronger effects in neurocognition, social cognition, negative symptoms, social functioning and coping than TAU group. These effects could be maintained at follow-up. The low drop-out rate of 10.3% of INT represents a high acceptance by the patients. The literature review identified five studies ($n = 99$) that evaluated the effects of CRT on cerebral activation during cognitive performance tests. Patients who received CRT demonstrated significantly increased activation in brain regions, which were generally activated in the respective cognitive tasks in healthy controls. Moreover, these activation patterns were correlated with cognitive performance changes following CRT.

Conclusion: These results suggest that INT is a comprehensive and effective cognitive rehabilitation approach for schizophrenia patients. CRT may provide enhancing and neuroprotective effects.
Policy of full disclosure: None.

S-16 EPA position statements concerning schizophrenia and beyond

S-16-001
Quality of mental health

W. Gaebel (Department of Psychiatry and Psychotherapy, Medical Faculty, LVR-Klinikum Düsseldorf, Heinrich-Heine-University, Duesseldorf, Germany)

Objective: To develop a European guidance on the structure of mental healthcare institutions based on the best available evidence in the framework of the European Guidance Initiative by the EPA.
Methods: A working group consisting of seven European mental healthcare experts was assembled. We performed a systematic literature review of the English and German literature pertaining to the structure of mental healthcare services, identified the evidence base for recommendations in this field, and formulated a set of guidances.
Results: The literature review resulted in few studies of high quality which dealt with the structural requirements of mental healthcare services. Most recommendations therefore had to be based on expert opinion mainly derived from non-evidence based recommendations for good clinical practice, derived, e.g., from accreditation procedures. The preliminary list consists of structural recommendations ($n = 14$: patient dignity and basic needs, integration of services, multiprofessionality of services, access to care, community based services, psychiatric workforce, community mental health teams, day hospitals, catchment areas, ethnic minorities, mental health education, mental health monitoring), process recommendations ($n = 6$; duration of hospital stays, access to special services wards, detained patients procedures, admission procedures, informed consent, physical illness) and recommendations at the interface of structures and processes ($n = 4$; safety issues, integration of in- and out-patient services, follow up care, availability of technologies).
Conclusion: The expert group agreed on 24 recommendations, but was faced with the challenge that very few controlled studies were available. Another issue was the transferability of evidence from one to another mental healthcare system or even to a hypothetical generalized European setting which formed the implicit framework of this project. Finally, the authors could not yet review the literature from all European countries and assess their usefulness for general European guidances because of language restrictions.
Policy of full disclosure: Personal financial relationship 2010 until now: Wolfgang Gaebel has received symposia support from Janssen-Cilag GmbH, Neuss, Lilly Deutschland GmbH, Bad Homburg and Servier, Munich. He is a member of the Scientific Advisory Board of Lundbeck International Neuroscience Foundation (LINF), Denmark.

S-16-002
Prevention of mental illnesses and promotion of mental health

D. Bhugra (The Royal College of Psychiatrists, London, UK)

Abstract: For a considerable period psychiatrists have shied away from dealing with prevention of mental illness and promoting good mental health. This has been due to a number of reasons even though these are core aspects of clinicians' clinical work load. Treatment of patients focuses on recovery and reducing secondary and tertiary complications. However, concepts of primary prevention are often not a part of training and service delivery due to insufficient resources and the volume of clinical work in some settings. Increasingly it has become apparent that there is considerable evidence which confirms that prevention can significantly reduce the onset of various forms of mental illness and resulting drop in quality of life and increasing burden on individuals, their families and society. Prevention of mental illness and promotion of good mental health often get confused. In addition sometimes there is a tension between various dimensions of mental health and mental illness. Acute psychiatric illnesses usually prevent positive mental health or wellbeing. However, those without mental illness can experience poor mental health and poor well-being mentally as well as socially.
Prevention of illness can be developed and delivered in multiple ways. Primary prevention addresses wider social, psychological and biological determinants across whole populations particularly related to health inequalities. Selective prevention should focus on special groups at higher risk of developing psychiatric disorders as well as general population. Secondary prevention focuses on early detection and early intervention and corresponds to indicated prevention. In this lecture these challenges and factors on the impact of mental illness will be described. There will be further discussion to build the case for prevention. The risks and protective factors, interventions across the life span and different psychiatric disorders will be discussed. The lecture will also describe the EPA Guidance on prevention of mental ill health and promotion of mental well being using the development of UK policy and strategy as examples. In European and global contexts these factors will be described and lessons across cultures discussed.
Policy of full disclosure: None.

S-16-003
Cardiovascular disease in people with severe mental illness

M. de Hert (UPC KUL Campus Kortenberg, Belgium)

Abstract: Metabolic syndrome, obesity, diabetes and other cardiovascular risk factors are highly prevalent in people with SMI. Patients are at risk for premature mortality and the mortality gap with the general population has increased over recent decades. In part these cardio-metabolic risk factors are attributable to unhealthy lifestyle, including poor diet, high rates of smoking, alcohol/substance use/abuse and sedentary behavior. But over recent years it has become apparent that antipsychotic agents and other psychotropic agents can have a negative impact on some of the modifiable risk factors. Also other somatic co-morbid disorders are also linked to antipsychotic treatment such as the consequences of hyperprolactinaemia, QTc-prolongation and constipation. Other somatic disorders such as poor dental care, HIV and other infectious diseases and some forms of cancer are also more prevalent in patients with schizophrenia. People with SMI also have limited access to effective screening and somatic care. The psychiatrist needs to be aware of the potential somatic side-effects of antipsychotic medication and to include them in the risk/benefit assessment when choosing a specific antipsychotic. He should also be responsible for the implementation of the necessary screening assessments and referral for treatment of any physical illness. Multidisciplinary assessment of psychiatric and medical conditions is needed. The somatic treatments offered to people with severe and enduring mental illness should be at par with general health care in the non-psychiatrically ill population.
Policy of full disclosure: None.

S-16-004
Value of antidepressants in the treatment of unipolar depression

H.-J. Möller (Department of Psychiatry,
Ludwig-Maximillians-University München, Munich, Germany)

Abstract: The lecture will start with some interesting results from our own observational study on short- and long-term treatment outcomes of depressive patients. Then it will highlight and discuss some of the important issues and controversies of current depression treatment like the efficacy of antidepressants, their effect on suicidality, their place in a complex psychiatric treatment strategy including psychotherapy and other psychosocial activities. The efficacy of antidepressants is clinically significant, but often monotherapy with one drug has to be followed by others or by comedication/augmentation therapy approaches. Psychosocial therapy, predominantly focused on psychotherapeutic strategies, can also contribute in a relevant way to the therapeutic success. Generally, antidepressants reduce suicidality, but under special conditions like young age or personality disorder, they can also be harmful in this respect. However, under the conditions of good clinical practice, the risk–benefit relationship of treatment with antidepressants can be judged as favourable. In addition, the lecture tries to analyse the question of how to reach individualised, evidence- and value-oriented decision-making in the complex treatment of depressive patients. The capacity of psychiatrists to individualise treatment decisions in terms of "the right drug/treatment for the right patient" is still restricted since there are currently not enough powerful clinical or biological predictors which help to achieve this goal. There is hope that in future pharmacogenetics will contribute significantly to a personalised treatment. The ideal that all steps of classical decision-making can be based on the strict rule of evidence-based medicine is far away from reality. Individualised decision-making is so complex that the rigorous expectations of evidence-based medicine can hardly be fulfilled. Finally, it should be considered that clinical decision-making is not only evidence—but also value-oriented.
Policy of full disclosure: None.

S-17 Social cognition and violent behavior in schizophrenia

S-17-001
Violent behavior among people with schizophrenia: a framework for investigations of causes, prevention and treatment

S. Hodgins (Department of Psychiatry, Heidelberg University;
Département de Psychiatrie, Université de Montreal; Institute
of Psychiatry King's College London)

Objective: The presentation will review the large body of evidence that has accumulated on violent behaviour among persons with schizophrenia.
Methods: A review of the literature.
Results: Many patients with schizophrenia engage in aggressive behavior towards others during an acute phase of illness when they are often forced onto psychiatric wards involuntarily. This aggressive behavior disappears within days as neuroleptic medications take effect. The most important predictor of violent behavior during an acute episode is the level of positive symptoms. By contrast, aggressive behavior that occurs at other stages of illness has distinct correlates and characterizes three sub-types of patients: (1) those who had Conduct Disorder prior to age 15 and who continue to engage in antisocial and aggressive behaviors after illness onset; (2) those with no childhood history of conduct problems who begin engaging in aggressive behavior as schizophrenia onsets; and (3) those with no history of previous aggressive behavior, with a chronic pattern of illness, who in the third or fourth decade of life engage in severe violence usually against a care-giver.
Conclusion: The characteristics of these three types of individuals with schizophrenia strongly suggest that they require different types of intervention to reduce their aggressive behavior. Presently, general psychiatric services do not provide such interventions and consequently some, but not all, of these antisocial and aggressive patients are transferred to forensic treatment.
Policy of full disclosure: None.

S-17-002
Social cognition and violence in schizophrenia: is there a link?

M. Brüne (Ruhr-Universität, Bochum, Germany), E. Brown

Objective: Social cognition concerns the processing of information that enables one to represent one's own and others' cognitive and affective mental states. Several studies have addressed the question whether social cognitive skills—or deficits thereof—are linked with violent behavior in schizophrenia.
Methods: Literature survey.
Results: Schizophrenia patients with a forensic background seem to be less impaired in their ability to appreciate the mental states of others as well as in their ability to recognise emotions compared to non-forensic patients, although deficits in empathising are evident in the former.
Conclusion: Partially preserved social cognitive skills in forensic patients with schizophrenia seem to be associated with several specific aspects of patients' psychopathology, including psychopathy, and excitement.
Policy of full disclosure: None.

S-17-003
Childhood disruptive behavior disorders: phenotypes, neuropsychiatric predictors, and genetic background effects

N. Kerekes (Sahlgrenska University Hospital, Gothenburg, Sweden),
S. Lundström, P. Jern, A. Tajnia, S. Brändström, M. Råstam,
P. Lichtenstein, H. Anckarsäter

Objective: To determine prevalences, patterns of overlaps and genetic background effects for Opposition Defiant Disorder (ODD) and Conduct Disorder (CD) in relation to Autism Spectrum Disorders (ASDs) and attention deficit hyperactivity disorder (ADHD).
Methods: In the Child and Adolescent Twin Study in Sweden (CATSS), parents of 17 220 twins aged 9 and 12 years were interviewed by the "Autism—Tics, ADHD and other Comorbidities" (A-TAC) inventory, including algorithms for ODD and CD. Main effects of predictors on the composite scores measuring disruptive behaviors were quantified by Generalized Estimating Equations and the relative importance of specific versus shared hereditary and environmental effects by quantitative genetic analyses.
Results: ODD symptoms were overall more common than CD symptoms (between 10–12% vs. 2–5%), and about twice as common in boys as in girls. The overlap between CD, ODD, and ADHD, which is a function of severity, ranges from being a rare feature in children with low-grade to moderate ADHD or with just one or two symptoms of ODD/CD to constituting the rule rather than the exception in severe cases. Two types of neurodevelopmental problems stood out as the

strongest predictors of the development of disruptive behaviors: hyperactivity/impulsivity from ADHD and social interaction problems from the ASDs. Substantial genetic effects were seen behind ODD and CD, to a large extent influencing not only disruptive behaviors but also ADHD and ASDs.
Conclusion: The overlaps between disruptive behavioral disorders are to a large extent due to the severity of problems. Interestingly, prediction and structural equation models suggested that ASD-related problems in social interaction are as important as hyperactivity/impulsivity dimension of ADHD for the development of disruptive behavior problems. Longitudinal follow-ups of the study cohort are currently carried out and the impact of the "ASD-Disruptive Behavior Disorders" complex on the etiology of violence will be explored.
Policy of full disclosure: The authors declare no conflicts of interest.

S-17-004
Disturbed social cognition as a treatment target in schizophrenia patients with a history of violence

N. Frommann (University of Düsseldorf, Duesseldorf, Germany), F. Lüneborg, S. Stroth, J. Brinkmeyer, C. Luckhaus, W. Wölwer

Objective: Impairments in facial affect recognition are well described for patients suffering from schizophrenia. It is suggested on a theoretical level that impaired processing of such social information may relate to violent behavior in schizophrenia. However, emotion perception is sparsely examined in violent schizophrenia patients yet. We investigated whether schizophrenia patients with a history of violence (defined as hands-on offences) show a larger or different impairment in emotion perception than matched schizophrenia patients without any history of violent acts. Moreover, we examined electrophysiological correlates of impaired emotion perception (EEG-ERP) and the effects of a cognitive remediation program (Treatment of Affect Recognition TAR, Frommann et al. 2003) on this impairment.
Methods: Affect recognition performance was assessed by a multiple choice labeling task in a sample of $n = 19$ with a history of violence and a comparison group of $n = 19$ without a history of violence. Concomitant ERPs were registered as neurobiological correlates of affect recognition performance. Participants were characterized with regard to psychopathological status, intelligence, anamnestic and demographic variables. Moreover, psychopathy (PCL: SV) and risk assessment (HCR-20) were assessed in the group of violent offenders. Groups were comparable regarding variables like age, IQ, additional addiction, psychopathological status, or medication. The forensic group was treated with TAR, treatment efficacy was evaluated using a waiting group design. Data were statistically analysed by t tests (M)ANOVAs and correlation coefficients.
Results: The results confirmed our hypothesis. The violent group was more impaired than the comparison group. TAR treatment improved affect recognition performance significantly for at least 2 months.
Conclusion: The results will be discussed in the context of disturbed emotion perception as a potential risk factor of violence in schizophrenia and as a worthy treatment target in forensic schizophrenia patients.
Policy of full disclosure: None.

S-18 Schizophrenia: a mild encephalitis?

S-18-001
The mild encephalitis hypothesis, specified for schizophrenia based on CSF investigation

K. Bechter (Guenzburg, Germany)

Objective: Immune and inflammatory mechanisms are detected in a subgroup of affective and schizophrenic spectrum disorder patients, defined as mild encephalitis (ME).
Methods: We analysed albumin, IgG, IgA, IgM, oligoclonal IgG and specific antibodies in paired cerebrospinal fluid (CSF) and serum samples. Numerical and graphical interpretation of CSF protein data was performed by Reibergrams with a new CSF statistics tool for nonlinear group analysis with reference to a large control group ($n = 4{,}100$).
Results: In 41% of the psychiatric patients ($n = 63$) we observed CSF pathologies: 14% displayed intrathecal humoral immune responses, 10% slightly increased CSF cell counts (5–8/lL), 29% moderate blood–CSF barrier dysfunctions. In the group of affective ($n = 24$) spectrum disorders 20% displayed a systemic immune reaction as detected by oligoclonal IgG. In 6% a virusspecific, bacterial or autoimmune associated ME was classified. Elevated CSF neopterin concentration in 34% of the patients was found. We also investigated the frequency of cells positive for the surface markers CD4, CD8, CD25, CD45, CD69, and CD127 by multiparameter flow cytometry and compared them with those from patients with non-inflammatory (NIND) or chronic inflammatory (CIND) neurological disorders, or acute meningitis (MEN). In MEN patients, CD4+ cell frequency in PB, but not in CSF, was significantly increased as compared to CIND and NIND. The frequency of CD4+ CD25+ cells in PB was significantly higher in MEN than in MPD or CIND. For CSF, the percentage of CD4 + CD127dim cells was significantly lower in MEN than in MPD. CD4 + CD127dim in PB and CSF showed overlapping characteristic clusters between MPD and CIND and MEN patients.
Conclusion: Overall, the hypothesis of low degree inflammation in a subgroup of schizophrenia is supported. The analysis of lymphocyte subsets in PB and CSF constitutes a novel promising tool to understand underlying pathomechanisms in psychiatric disorders. The low level intrathecal immune responses and barrier dysfunctions support the ME hypothesis in subgroups of schizophrenia.
Policy of full disclosure: None.

S-18-002
Inflammation in schizophrenia: results from neuropathological studies

B. Bogerts (Magdeburg, Germany)

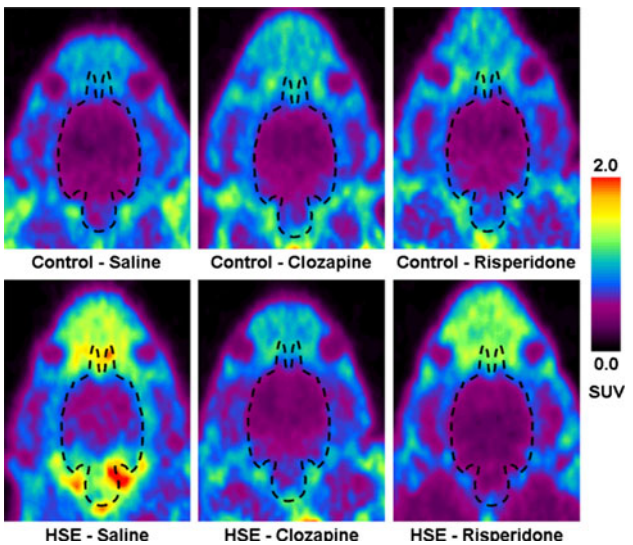
Abstract not received in due time.

S-18-003
Neuroinflammation in schizophrenia: a PET study

H. C. Klein (Groningen, Netherlands), J. Doorduin, R. Dierckx, I. Jonker, E. de Vries

Objective: The pathophysiological process that is responsible for exacerbations of psychoses in schizophrenia is unknown. There also remain questions about the working mechanism of antipsychotics. It is the aim of this study to trace potential viral activity (neurotropic herpes viruses) and neuroinflammatory activity (microglia activation) in the living brain of patients with "active psychoses". The effect of antipsychotics on inflammation by herpes simplex-1 infection (HSV-1) of the brain was an additional focus of investigation.
Methods: A PET (positron emission tomography) imaging design was used, both in an animal model of herpes encephalitis, and in patients with psychosis. In the HSV-1 infected animals, risperidone, clozapine or placebo were administered. In both the animal model and in human psychosis neuroinflammation was imaged with the tracer [11C] PK11195 for microglia activation. In 8 patients with psychosis the herpes virus activity was compared between severely affected patients and mildly affected (PANSS positive high vs. low) using the tracer [18F] FHBG.

Results: A significantly higher binding potential of [11C]-(R)-PK11195, indicative of neuroinflammation, was found in the hippocampus of 7 patients with psychosis, when compared to 8 healthy volunteers (2.07 ± 0.42 vs. 1.37 ± 0.30; $P = 0.004$). A significantly higher metabolic rate of [18F] FHBG was found in the temporal lobe of severely affected patients (5.9 ± 1.1 10E−4) as compared to less affected patients (3.8 ± 1.0 10E−4; $P = 0.035$). Clozapine and risperidone induced major reductions of microglia activation in HSE infected rat brains and prevented behavior abnormalities.
Conclusion: Neuroinflammation in the temporal lobe caused by local herpes virus replication is a powerful explanation for psychotic symptoms. Antipsychotic drugs risperidone and clozapine act by mitigating herpes related inflammation. Replication of HSV—being the only virus that characteristically infects the temporal lobe—may be an underestimated trigger of psychosis.
Policy of full disclosure: None.



S-18-004
Therapeutic consequences of inflammation in schizophrenia

N. Müller (Psychiatry and Psychotherapy, Ludwig-Maximilian-University, Munich, Germany)

Abstract: A persistent (chronic) infection as aetiological factor in schizophrenia is discussed since many years. Research points out that not one single pathogen but the immune response of the mother is related to the increased risk for schizophrenia. Several reports described increased serum IL-6 levels in schizophrenia. IL-6 is a product of activated monocytes and of the activation of the type-2 immune response. Moreover, several markers of the type-1 immune response are decreased in the majority of schizophrenic patients, while signs of activation of the type-2 immune response are described accordingly in schizophrenia. Mechanisms involved in the inflammatory process in schizophrenia will be outlined including the role of microglia cells, the macrophages of the brain. Cyclo-oxygenase-2 inhibitors have been evaluated in schizophrenia. A critical overview on results of these studies will be presented. In schizophrenia, the therapeutic effects of short-term studies (5–8 weeks) depend from the duration of disease, in our interpretation from the chronicity of the inflammatory process. Further therapeutic strategies based on immune-modulatory effects will be discussed, too.
Policy of full disclosure: None.

S-19 Psychomotor symptoms in schizophrenia

S-19-001
Neural correlates of psychomotor functioning in schizophrenia

L. Docx (University of Antwerp, Wilrijk, Belgium)

Objective: Psychomotor symptoms are a highly frequent phenomenon in schizophrenia. Theoretical models, such as the cognitive dysmetria hypothesis of Andreasen and colleagues (1998, 1999), assume that a disruption in the cortico-cerebellar-thalamic-cortical circuit (CCTC) is responsible for the occurrence of these symptoms. This study aims at addressing this hypothesis in vivo by means of Diffusion Kurtosis Imaging (DKI).
Methods: Twenty patients with a DSM-IV-TR diagnosis of 'schizophrenia' or 'schizoaffective disorder' (age 18–45 years) were studied. Psychomotor functioning was assessed by means of an extensive battery of neuropsychological tests (Finger Tapping Task, Pegboard Task, Pursuit Task, Symbol Digit Substitution Task and computerized writing tasks),psychiatric and neurological evaluation scales (Salpêtrière Retardation Raring Scale, St Hans Rating Scale, Neurological Evaluation Scale) and 24-h actigraphy. Besides DKI-scans were performed.
Results: The association between psychomotor functioning and fractional anisotropy (FA) in the CTCC-circuit will be investigated. We hypothesize a positive correlation between FA-values in this circuit and psychomotor functioning.
Conclusion: Implications of the results for the understanding of the neurobiological processes involved in psychomotor symptoms in schizophrenia will be discussed.
Policy of full disclosure: This research was supported by the Agency for Innovation by Science and Technology in Flanders (IWT).

S-19-002
The impact of negative and depressive symptoms on psychomotor functioning in schizophrenia

M. Morrens (University of Antwerp CAPRI, Wilrijk, Belgium)

Objective: Traditionally in schizophrenia three symptom clusters can be identified i.e. positive, negative and cognitive symptomatology. In addition to these symptom clusters, psychomotor slowing (PS) is another observable feature of schizophrenia characterized by the slowing of planning and initiation of movements. In addition, reduced levels of psychomotor activity have been reported in this illness as well. The relationship between these qualitative and quantitative psychomotor deficits on one hand and negative and depressive symptomatology on the other will be investigated.
Methods: Chronic, stabilized schizophrenic inpatients as well as a matched healthy control group completed a psychomotor test battery including the finger tapping test and a series of computerized writing tasks. The salpetriere retardation scale was administered to measure psychomotor slowing clinically. Quantitative psychomotor functioning was assessed by use of a 24-h actigraphy. In addition, clinical symptomatology was assessed by use of the Positive and negative syndrome scale (PANSS) and the Calgary depression scale (CDS).
Results: It was found that depressive and negative symptoms added independently to an already present slowing of psychomotor functioning in schizophrenic patients. Moreover, depressive and negative symptoms influenced different processes of psychomotor functioning.
Conclusion: We demonstrate that the subprocesses involved in the generation of psychomotor speed are affected differently by negative and depressive symptom clusters.

Policy of full disclosure: The presenter has received research fundings from Johnson & Johnson and Bristol Myers Squibb.

S-19-003
State and trait aspects of section monitoring in schizophrenia

E. De Bruijn (Radboud University Nijmegen, Netherlands)

Objective: Disturbed internal performance monitoring has been repeatedly demonstrated in schizophrenia and is considered an important trait marker of the disorder. However, along with internal monitoring, efficiently processing external task-relevant feedback is also crucial for adequate performance. It is unknown whether this form of external monitoring is disturbed in schizophrenia and whether it is trait or state dependent. The current study assessed the effects of treatment on both internal and external performance monitoring in schizophrenia.
Methods: Internal monitoring was investigated by means of the response-locked error-related negativity (Ne/ERN), an event-related potential (ERP) component elicited by erroneous responses. External monitoring was investigated by analyzing the feedback-locked P300 elicited by unexpected, but task-relevant external feedback. ERPs and behavioral parameters were measured in a group of schizophrenia patients and matched healthy controls, while performing a variant of an Eriksen Flankers Task. Both groups were assessed twice, with a six-week interval, during which the patients received treatment.
Results: Compared to healthy controls, the schizophrenia patients showed a diminished Ne/ERN amplitude, insensitive to treatment. On the other hand, P300 amplitudes were smaller in the schizophrenia patients at the start, but were normalized at the second assessment. This finding was also reflected in the behavioral results from the patients, showing an increased percentage of correct answers after unexpected task-relevant feedback.
Conclusion: This study thus demonstrates that diminished internal error processing reflects a 'trait' in schizophrenia, while the processing of externally offered feedback has a strong 'state' character in this disorder, susceptible to treatment.
Policy of full disclosure: None.

S-19-004
The effect of nicotine on cognitive and psychomotor functioning in smoking and non smoking schizophrenic patients

C. Quisenaerts (University of Antwerp, Wilrijk, Belgium)

Objective: The therapeutic agents currently used to treat schizophrenia effectively improve psychotic symptoms. However, they are limited by adverse effects and poor efficacy when cognitive symptoms are considered. For this reason the focus of research on treatment of the illness has shifted towards cognitive enhancement the last 10 years. In this light much attention has been given to the nicotinic receptor. Earlier trials suggest that nicotine ameliorates attention and working memory deficits seen in schizophrenia. The present study aims to replicate these earlier findings in a strict methodological design. Additionally we will assess the effects of nicotine on measures of social cognition and psychomotor functioning, domains that has never been investigated before in this research field. A second study has been conducted to investigate the effect of age in healthy volunteers in the same design.
Methods: In a three-way crossover double blinded randomized placebo-controlled trial, we investigate the effects of 1 and 2 mg nicotine on several cognitive domains in 16 smoking and 16 non-smoking schizophrenic patients. In the second study with similar design we compare 16 young with 16 old healthy volunteers. The battery consists of 16 tasks, including standard cognitive tasks (Continuous Performance Test, Letter Number Sequencing, Benton Visual Retention Test, Symbol Digit Substitution Test) psychomotor tasks (Pursuit tasks, Pointing Task, Stereotype Test Apparatus, Line Copying Task, Grooved Pegboard), electrophysiological tasks (Saccadic Eye Movements, Auditory Oddball, GoNoGo Tasks, P50 auditory Gating) and social cognitive tasks (Reading the mind in the eyes test, Emotion recognition matching, Ultimatum game).
Results: Results are not available at the moment of subscribing. Attention, processing speed, visual memory and P50 auditory gating are expected to be most responsive to nicotine in schizophrenic patients. Old could benefit more than young healthy volunteers from nicotine.
Conclusion: Clinical and scientific implications of the study will be discussed.
Policy of full disclosure: The study has been sponsored by Johnson & Johnson as well as by the agency of innovation by science and technology in Flanders.

S-20 Toxicity of relapse

S-20-001
Anatomy of relapse

M. Birchwood (University of Birmingham School of Psychology, Birmingham, UK)

Abstract: Relapse in psychosis, like the onset of psychosis takes place over a protracted period of time; however the modal time is between 2 and 4 weeks. Recent developments in the structure of psychotic symptoms and in the mode of onset, have confirmed that affective changes precede, accompany and outlive the emergence of the core psychosis symptoms. Studies of the process of relapse including our original work in 1989 show that: (1) Affective changes are part of the relapse process and frequently precede it (2) Even in individuals who have completely recovered on the Andreasen criteria show low-level symptoms (Upthegrove, Birchwood 2010) and I will argue that the emergence of positive symptoms in relapse builds on these symptoms (the 'roll back' hypothesis) (3) Each patient has a rather unique set of early signs of relapse which I coined the 'relapse signature'. I will argue that the individual us not a passive host of relapse but an active agent searching for meaning and control of a loss of well-being.
Policy of full disclosure: None.

S-20-002
Disorganisation and its association with progressive brain volume changes in schizophrenia

W. Cahn (UMC Utrecht Psychiatry, Utrecht, Netherlands), G. Collin, E. Derks, N. van Haren, H. Schnack, H. Hulshoff Pol, R. Kahn

Objective: There is general consensus on the presence of progressive brain volume changes in schizophrenia. However, heterogeneity in brain volume alterations within and between patient samples is large. This may be related to the vast clinical diversity that characterizes the disorder. To investigate the phenotypic heterogeneity, efforts are made to refine the phenotype by characterizing psychopathology in terms of quantitative symptom dimensions. This study examines the relationship between progressive brain volume changes and symptom dimensions in schizophrenia.

Methods: Global brain volumes measurements from 105 schizophrenia patients and 100 healthy comparison subjects, obtained at inclusion and 5-year follow-up, were used in this study. Symptom dimension scores (i.e. negative, positive, disorganization, mania and depression) were calculated for each subject by factor analysis of CASH lifetime rated items. In patients, linear regression analyses, with age, gender and intracranial volume as covariates, were performed to examine the relationship between symptom dimensions and progressive brain volume changes. Antipsychotic medication, outcome and IQ were examined as potential confounders.
Results: On average, total brain and cerebral grey matter volume decreased over time and ventricle volumes increased, patients exhibiting greater change than healthy comparison subjects. In patients, the disorganization dimension was associated with change in total brain ($\beta = -.295$, $P = 0.003$) and cerebellar ($\beta = -.349$, $P < 0.001$) volume. Furthermore, higher levels of disorganization were associated with lower IQ, irrespective of psychiatric status (i.e. patient or control).
Conclusion: Heterogeneity in progressive brain volume changes in schizophrenia is particularly associated with variation in disorganization. Schizophrenia patients with high levels of disorganization exhibit more progressive decrease of global brain volumes and have lower total IQ. We propose that these patients form a phenotypically and biologically more homogenous subgroup that may be useful for etiological (e.g. genetic) studies.
Policy of full disclosure: Dr. W. Cahn is or has been an unrestricted research grant holder with, or has received financial compensation as an independent symposium speaker or as an consultant from, Eli Lilly, BMS, Lundbeck, Sanofi-Aventis, Janssen-Cilag, AstraZeneca and Schering-Plough.

S-20-003
Relapses of schizophrenia and structural changes in the brain

N. van Haren (Rudolf Magnus Institute of Neuroscience, Department of Psychiatry, University Medical Centre Utrecht, The Netherlands)

Objective: Evidence is accumulating that schizophrenia is characterized by excessive loss of cerebral gray matter volume over time, both in the early and chronic stages of the disease. Since most gray matter tissue is found in the cortex, excessive cortical thinning may explain (part of) the (excessive) decreases in gray matter volume reported in this disease. Whether cortical thickness changes in schizophrenia patients over time are more pronounced relative to the changes that can be attributed to normal aging has not been studied.
Methods: This study examined change in cortical thickness over time by repeating magnetic resonance brain imaging (MRI) scans over a 5-year interval in 96 schizophrenia patients and 113 matched healthy participants in adulthood. In areas showing progressive decrease in cortical thickness, we investigated whether the cortical changes are modulated by clinical variables, such as stage and outcome of the illness and antipsychotic treatment during the scan-interval.
Results: At baseline, schizophrenia patients as compared to controls had thinner left orbitofrontal and right parahippocampal and superior temporal cortices and a thicker superior parietal lobule and occipital pole, while mean cortical thickness did not differ between the groups. Over time, excessive cortical thinning was found in widespread areas on the cortical mantle, most pronounced bilaterally in the temporal cortex and in the left frontal area. Poor outcome in patients was associated with more pronounced cortical thinning. Higher cumulative intake of typical antipsychotic medication during the scan-interval was associated with more pronounced cortical thinning whereas higher cumulative intake of atypical antipsychotic medication was associated with less pronounced cortical thinning.
Conclusion: In schizophrenia, the cortex shows excessive thinning over time in widespread areas of the brain, most pronounced in the frontal and temporal areas and progresses across the entire course of the illness. The excessive thinning of the cortex appears related to outcome and medication intake.
Policy of full disclosure: None.

S-20-004
ITAREPS: information technology aided relapse prevention programme in schizophrenia

F. Spaniel (Prague Psychiatric Center, 3rd Faculty of Medicine, Charles University Prague, Center of Neuropsychiatric Studies, Czech Republic)

Abstract: ITAREPS presents a mobile phone-based telemedicine solution for weekly remote patient monitoring and disease management in schizophrenia and psychotic disorders in general. The program provides health professionals with home telemonitoring via PC-to-phone SMS platform to identify prodromal symptoms of relapse and intervene early to prevent unnecessary hospitalizations. The web-based interface offers authorized physician a longitudinal analysis of the patient's dynamics and development of possible prodromes. A repeated mirror-design studies conducted since introduction into clinical practice in Czech Republic in 2005, confirmed 70% reduction in the number of hospitalizations in patients with schizophrenia enrolled into the program. The effectiveness of the ITAREPS, in conjunction with its low set-up and operating costs makes the program an attractive option in the long-term treatment and management of patients with schizophrenia and psychotic disorders in general.
Policy of full disclosure: None.

S-21 Co-morbidity of schizophrenia and physical illness

S-21-001
Review of evidence concerning co-morbidity of schizophrenia and physical illness

M. de Hert (UPC KUL Campus Kortenberg, Belgium)

Abstract: The lifespan of people with severe mental illness (SMI) is shorter compared to the general population. This excess mortality is mainly due to physical illness. We report prevalence rates of different physical illnesses as well as important individual lifestyle choices, side effects of psychotropic treatment and disparities in health care access, utilization and provision that contribute to these poor physical health outcomes. We searched MEDLINE (1966–August 2010) combining the MeSH terms of schizophrenia, bipolar disorder and major depressive disorder with the different MeSH terms of general physical disease categories to select pertinent reviews and additional relevant studies through cross-referencing to identify prevalence figures and relevant factors contributing to the excess morbidity and mortality rates. Nutritional and metabolic diseases, cardiovascular diseases, viral diseases, respiratory tract diseases, musculoskeletal diseases, sexual dysfunction, pregnancy complications, stomatognathic diseases, and possibly obesity-related cancers are, compared to the general population, more prevalent among people with SMI. It seems that lifestyle as well as treatment specific factors account for much of the increased risk for most of these physical diseases. Moreover, there is sufficient evidence that people with SMI are less likely to receive standard levels of care for most of these diseases.

Lifestyle factors, relatively easy to measure, are barely considered for screening; baseline testing of numerous important physical parameters is insufficiently performed. Besides modifiable lifestyle factors and side effects of psychotropic medications, access to and quality of health care remains to be improved for individuals with SMI.
Policy of full disclosure: None.

S-21-002
Excess mortality, causes of death and life expectancy in main groups of patients with recent onset of mental disorders in 2000–2006 in Denmark, Finland and Sweden

M. Nordentoft (Psychiatric Centre Copenhagen, University of Copenhagen, Faculty of Health Sciences, Copenhagen, Denmark; Nordic Research Academy in Mental Health, Nordic School of Public Health, Gothenburg, Sweden), K. Wahlbeck, M. Gissler, J. Westman, H. Alinaghizadeh, T. M. Laursen

Objective: To investigate the excess mortality in different diagnostic categories due to suicide and other external causes of death, and due to specific causes in connection with diseases and medical conditions.
Methods: In longitudinal national psychiatric case registers from Denmark, Sweden and Finland, a cohort of 277,210 recent-onset patients, who at least once during the period 2000 to 2006 were admitted due to a psychiatric disorder, were followed in national cause of death registers until death or the end of 2006. They were followed for 906,130 person years, and 27,500 deaths were analyzed. Life expectancy and standardized cause-specific mortality rates were estimated in each diagnostic group in all three countries.
Results: The life expectancy was generally approximately 15 years shorter for women and 20 years shorter for men, compared to the general population. The overall mortality figures were increased twofold to fivefold, and mortality due to every specific cause of death was at least doubled. The mortality due to diseases and medical conditions was increased two to three fold, while excess mortality from external causes ranged from three to 77-fold. Mortality due to diseases and medical conditions was generally lowest in patients with affective disorders and highest in patients with substance abuse and personality disorders, while mortality due to suicide was highest in patients with affective disorders and personality disorders, and mortality due to other external causes was highest in patients with substance abuse.
Conclusion: These alarming figures call for action in order to prevent the high mortality.
Policy of full disclosure: None.

S-21-003
Co-morbidity of schizophrenia and physical illness

H. Parmentier (Wonca, Global Family Doctor, Purley, UK)

Objective: Joint efforts between primary care and psychiatry in education, research, prevention, diagnosis and treatment will improve the care and outcomes of patients with mental health problems. Life expectancy of people with schizophrenia is approximately 20 years shorter than in the normal population and much of this excess mortality is due to co-morbid physical illness.
Methods: Primary Care covers the holistic care to people from conception till death and therefore General Practitioners/Family Doctors are well aware of the concept of managing co-morbidity. Therefore in theory Primary Care Clinicians are able to manage co-morbidity in the community but also within the psychiatric hospital setting with particular reference to the management of co-morbid diseases in both the adult and elderly population. Unfortunately due to lack of training the interest of dealing with patients with serious mental disorders in the primary acre setting is less then optimal and many patients are under-diagnosed and under-treated.
Results: Those diagnosed often present with complex needs that have long term consequences for themselves and their families. Although there may be well-developed secondary care systems to deal with such problems, because of the fear of stigma, many such patients prefer to be cared for by their general practitioners.
Conclusion: Examples will be explored how the care of people with a mental illness can improve.
Policy of full disclosure: None.

S-22 Advances in understanding the causes of schizophrenia

S-22-001
New genetic findings in schizophrenia

D. Rujescu (University of Munich, Germany)

Objective: A major challenge in medicine is to understand genetic, molecular and cellular mechanisms underlying common mental disorders.
Methods: The last few years have witnessed an explosion of interest in human genetics of complex diseases. The knowledge resulting from the availability of the complete sequence of the human genome, the systematic identification of single nucleotide polymorphisms (SNPs) throughout the genome, and the development of parallel genotyping technology (microarrays) established the conditions that brought about the current revolution in our ability to probe the genome for identifying disease genes. Genome-wide association (GWA) studies have opened a window into the biology of common complex diseases and have provided proof of principle and yielded several genes showing strong association with complex diseases or traits including Crohn's disease, diabetes and many others. These studies revealed genes involved in pathogenesis and identified entirely unexpected disease pathways. This is of utmost importance given that this knowledge can translate into the development of better treatment, a personalised medicine or even cure.
Results: The talk will especially focus on new found common and rare genetic variants presenting the newest and most promising results from large genome-wide efforts including tens of thousand of patients and controls. Structural chromosomal abnormalities are emerging as an important genomic cause of neuropsychiatric diseases. A significant fraction of individuals with neurodevelopmental diseases including schizophrenia carry CNVs and many will be defined as "genomic disorders" in the coming years. The question is if a substantial number of schizophrenia cases are caused by rare copy number variations and if we going to define a number of new diseases at the interface between mental retardation, autism and schizophrenia.
Conclusion: These new directions will be presented and critically discussed in this talk.
Policy of full disclosure: None.

S-22-002
The genetics of sensorimotor gating: a core endophenotyope of schizophrenia

B. Quednow (University of Zurich, Switzerland)

Abstract: Although schizophrenia is a strongly inherited disease with a heritability of 80% or more, the genetic basis of this disease is still elusive. One of the main challenges in the identification of biological markers or genetic factors arises from the fact that a diagnosis of schizophrenia is traditionally built on behavioural signs and symptoms as the biological basis was and is still unknown. Thus, the classical diagnosis of schizophrenia might be a melting pot for several syndromes with different aetiopathological pathways. To solve this problem, the endophenotype strategy was suggested to discover intermediate phenotypes that are more closely related to specific genes than the complex disease cluster schizophrenia. Sensorimotor gating—commonly operationalized by prepulse inhibition (PPI) of the acoustic startle response (ASR)—has been suggested as such a promising endophenotype of schizophrenia spectrum disorders. The discovery that PPI is heritable, that it is reduced in unaffected relatives of schizophrenia patients, that it is influenced by single nucleotide polymorphisms (SNP) within the dopamine, acetylcholine, and serotonin system, and that decreased PPI levels are already present during the prodromal stage of schizophrenia suggest that PPI might be an important and valid candidate as an intermediate or endophenotypic marker in genetic studies of schizophrenia. Most recently, it was demonstrated that a SNP within the transcription factor 4 (TCF4) gene, which plays an important role in the development of the mammalian cortex, was associated with schizophrenia as well as with sensorimotor gating. The implications of these findings for early intervention and further research will be discussed.
Policy of full disclosure: None.

S-22-003
Unraveling the pharmacogenomics of schizophrenia

R. Mössner (University of Bonn Dept. of Psychiatry, Germany)

Abstract: The aim of this talk is to present an overview of the robust pharmacogenetic findings on the response to antipsychotic medications. Novel replicated pharmacogenetic results on the response of positive symptoms will be presented. Moreover, an overview of established and replicated pharmacogenetic findings on negative symptoms will be shown. Thus, this presentation will provide a state-of-the-art of the pharmacogenetics of antipsychotics.
Policy of full disclosure: None.

S-22-004
Imaging genetics in schizophrenia

H. Walter (University of Berlin, Germany)

Abstract not received in due time.

S-23 PREVENT: A multidimensional study of people at risk to develop first episode psychosis—from the metabolic syndrome to the efficacy of CBT

S-23-001
Cortial excitability in people at risk of psychosis

T. Wobrock (Georg-August-Universität, Klinik für Psychiatrie und Psychotherapie, Goettingen, Germany), A. Hasan, B. Guse, M. Labusga, K. Levold, A. Bechdolf, J. Klosterkötter, C. Grefkes, J. Cordes, L. Kostorz, B. Janssen, W. Gaebel, P. Falkai

Objective: Disturbed cortical excitability towards dysfunctional inhibitory networks is a common finding in first-episode and chronic schizophrenia patients. Until now, there are no studies available concerning persons at risk of being prodromally symptomatic of psychosis (PAR). Transcranial magnetic stimulation (TMS) is a useful and well-established tool to evaluate inhibitory and facilitatory networks in the human motor cortex. The aim of the present study is to investigate if PAR display disturbances in cortical excitability as observed in schizophrenia patients and if this pattern of cortical excitability could be a neurobiological marker for the development psychosis.
Methods: 16 PAR (Ultra-High-Risk for Psychosis) and 18 healthy controls were investigated with TMS. Cortical excitability was accessed with single—and paired—pulse TMS to the left primary motor cortex. Resting motor thresholds, short-latency-intracortical-inhibition (GABAA-related), intracortical facilitation (NMDA-related) and the cortical silent period (GABAB-related) were tested according to previously published protocols.
Results: Parametric testing did not reveal a significant difference for the tested protocols between PAR and healthy controls at baseline. Compared to healthy controls, PAR showed a positive correlation between CSP and ICF.
Conclusion: This is the first study investigating PAR with TMS. PAR do not differ in motor-cortical excitability from healthy controls. The results of the present study indicate that the often observed cortical hyperexcitability in schizophrenia patients might develop after the onset of psychosis. However, these results are preliminary and further comparisons will be provided (sample divided into subgroups with those developing full-blown psychosis and with an independent sample of first-episode-patients).
Policy of full disclosure: None.

S-23-002
Stress experience and stress sensitivity in subjects at risk for psychosis

M. Wagner (University of Bonn, Germany), J. Drees, T. Lataster, A. Bechdolf, I. Myin-Germeys

Objective: Stressors in daily life affect mood and cognition, and an increased sensitivity to stress is probably part of the vulnerability for psychotic disorders. Previous studies with the Experience Sampling Method (ESM) have shown that patients with schizophrenia and also their non-affected relatives show a stronger increase of negative affect and mild psychotic symptoms in response to everyday stressors than healthy controls. We here examined whether this increased stress sensitivity would also be present in individuals at risk for psychosis.
Methods: 26 patients with an at risk mental state (attenuated psychotic symptoms or at least two cognitive basic symptoms) and 27 matched healthy control participants took part in an add-on study of the on-going randomized controlled trial PREVENT. Stress- and psychosis reactivity was measured with the ESM during six consecutive days. Subjects recorded Negative Affect, Subtle psychotic experiences (e.g., suspicion, feeling unreal), and the level of stress related to current activities, events, and social situation. Multilevel linear random regression analysis was used to investigate whether prodromal patients have a larger increase in (i) negative emotions or (ii) intensity of psychotic symptoms associated with daily life stress as compared to a control group.
Results: Results revealed a significant interaction effect for psychotic symptom intensity on the one hand and event-related ($B = -0.13$, 95% CI: -0.18 to -0.07, $P = 0.00$), activity-related stress (B = 0.23, 95% CI: 0.18–0.29, $P = 0.00$) and social stress ($B = 0.15$, 95% CI: 0.60–0.24, $P = 0.00$) on the other hand. Thus, the moment-to-moment stress reactivity associated with daily life stress was significantly different for the two groups. Stratified analyses revealed that activity-related

stress and social stress were positively associated with increasing psychotic symptom intensity. Analyses further revealed a significant interaction for negative affect on the one hand and event-related ($B = -0.06$, 95% CI: −0.12 to 0.00, $P = 0.07$), activity-related stress ($B = 0.17$, 95% CI: 0.12–0.24, $P = 0.00$) and social stress ($B = 0.15$, 95% CI: 0.60–0.24, $P = 0.00$) on the other hand.
Conclusion: Patients at clinical risk for psychosis show an increased emotional reactivity to minor stressor in daily life. Patients at risk also show variations in the intensity of psychotic symptoms associated with daily life stress. In other words, they seem to be behaviorally sensitized to stress in daily life. It remains to be seen whether high stress reactivity is related to transitions to psychosis. The present data support the rationale of interventions aimed at better stress management in everyday life for subjects with at risk mental states.
Policy of full disclosure: None.

S-23-003
Prevalence of the metabolic syndrome in men and women at risk of psychosis

J. Cordes (University of Duesseldorf, Germany), K. Kahl, M. Jänner, H. Müller, M. Wagner, W. Maier, M. Lautenschlager, A. Heinz, W. de Millas, B. Janssen, W. Gaebel, M. Michel, F. Schneider, M. Lambert, D. Naber, M. Brüne, S. Krüger-Özgürdal, T. Wobrock, M. Riedel, J. Klosterkötter, A. Bechdolf

Objective: We hypothesized drug naïve patients with an at risk mental state of psychosis to have an increased metabolic risk profile modulated by age and gender.
Methods: In the on-going randomized controlled trial PREVENT we surveyed the baseline data of the metabolic syndrome (IDF), baseline single risk factors and nicotine abuse in 162 drug naïve patients (men $n = 107$, woman $n = 55$) aged between 18 and 40 years with an at risk mental state of psychosis. The effects of age and gender on the prevalence of the single risk factors and the metabolic syndrome were determined.
Results: 107 male (mean age 23.59) and 55 female (mean age 24.67) drug naïve patients entered the analysis. The baseline data showed the following mean results: HbA1C 5.13%, fasting blood glucose 82.67 mg/dl, LDL 103.32 mg/dl, HDL 52.76 mg/dl, cholesterol 175.69 mg/dl, triglycerides 109.55 mg/dl, weight 75.25 kg, BMI 23.44, abdominal circumference 87.53 cm, systolic blood pressure 123.68. A high frequent nicotine abuse was found in 46.4% men and 44.2% woman. Significantly higher fasting triglycerides ($P = .02$), waist circumference ($P = .006$) and higher systolic blood pressure ($P < .001$) was found in men. The prevalence of the metabolic syndrome was 4.4% in the age range 18–23 years ($N = 90$), 6.8% in the age range 24–28 years ($N = 44$) and 13.8% in the age range 29–40 years ($N = 29$). We found a significantly age-related increase in LDL, cholesterol, triglycerides and BMI in both genders.
Conclusion: We found a high prevalence of nicotine abuse in drug naïve patients with an at risk mental state of psychosis. The risk for metabolic syndrome was influenced by age and gender. The age related increase of the metabolic syndrome in drug naïve patients suggest that the observed increase may be explained by adverse lifestyle changes or factors associated with schizophrenia itself.
Policy of full disclosure: None.

S-23-004
Dysfunctional cognitive and emotional empathy in the prodromal phase of schizophrenia

J. Gallinat (Psychiatry & Psychotherapy, Charité Universitätsmedizin, Berlin, Germany), C. Montag, Y. Gudlowski

Objective: Theory of Mind (ToM) deficits are well described in schizophrenic patients and important aspects of psychopathology may be mediated by an impaired capacity to infer one's own and other persons' mental states. However, possible ToM deficits in the prodromal phase of schizophrenia and their relationship to psychotic symptoms have been barely investigated.
Methods: In the framework of the PREVENT study, a large multicenter investigation of subjects at-risk for transition to schizophrenia, empathy and social cognition was assessed in large samples of patients and controls. The Multifaceted Empathy Test (MET), a well-established tool for the multidimensional measurement of empathy with separate assessment of emotional and cognitive aspects of empathy, was applied to at-risk patients and healthy controls matched according to age, gender and education.
Results: The talk will present first results assessed in this large sample and focus on the association between cognitive/emotional empathy and psychopathology as well as cognitive abilities.
Policy of full disclosure: None.

S-24 Strength based treatment in an early psychosis ACT team: engaging the troublesome avoiders

S-24-001
ACT and Recovery: a new perspective on treatment for early psychosis. The first 3 years: qualitative and quantitative data

M. Elfrink (Pro Persona, Nijmegen, Netherlands)

Objective: International research shows that Assertive Community Treatment (ACT) is effective in engaging patients with a first episode of psychosis. Nevertheless, recent reports show that initial effects of treatment do not last. Our hypothesis is that the lack of long lasting effect is due to the fact that in the first 2 years of treatment there is too much emphasis on response and remission of symptoms and too little on other aspects of recovery. We believe that the focus should be on personal and societal recovery ànd symptomatic recovery at the same time.
Methods: The ReACT (Recovery & ACT) team is part of a comprehensive mental health service which operates in a Dutch catchment area of 325,000 people, including the city of Nijmegen (161,000 inhabitants). Inclusion criteria: age between 16 and 65, never been treated for psychosis, difficult to engage, on average no motivation for treatment. We offer our patients any or all of our (social) interventions without any exception from day one. This helps to create a shared understanding, in which a free exchange of ideas and believes can take place in order to build a therapeutic alliance. Directed by the patients' needs and desires we use any social intervention in any order, or even at the same time.
Results: We have developed a collaborative approach in early psychosis that appears to be effective in creating a working alliance with both patient and family, in the remission of symptoms, in vocational recovery, and even remission of substance abuse.
Conclusion: In this presentation result of 3 years of treatment by the team will be presented.
Policy of full disclosure: None.

S-24-002
The daily teamwork: what, how, with whom and why

B. Jacobsen (Pro Persona Aurora GGZ Nijmegen, Netherlands)

Objective: I will try to give you insight how we work daily within an assertive community team with eight different disciplines sharing a caseload of 70 clients all together.
Methods: After intake we focus on wishes and desires our patients really want to have fullfilled. Therefore we go for a strong relationship and deep internal motivation. We look for the strengthes and possibilities there are instead of focussing on disease. We using eight terreins of interventions as feeling healthy, care for oneselve, work and education, sensegiving, social relationships, dealing with free time and housing, setting and receive own goals in all of these issues. Family interventions are one of our main focus.
Results: we see after time that people really realizing there own goals, getting control of there symptoms and are selfconfident.
Conclusion: Focus on recovery and own way of dealing with problems within an strong relationship works. There is a low drop out, symptoms are quite stable, people have stable housing, family is satisfied and a quite amount of our patient are back at work.
Policy of full disclosure: None.

S-24-003
ACT approach, substance abuse, psychosis and recovery

M. van Niekerk (Pro Persona, Nijmegen, Netherlands)

Objective: About 50% of our Assertive Community Treatment population uses drugs or used drugs until recently, mainly cannabis. During the 5 years that patients are in our ACT program, the frequency and dose of drug usage tends to decrease gradually, although follow-up data are not available yet.
Methods: As specific programs targeting on reducing drug use are not part of our standard therapy, we tried to identify which factors in the treatment do modulate this reduced usage. This was investigated through interviews with the patient, his closest relatives and most involved caregiver in the team and by studying the medical files.
Results: By combining the gathered data in a time schedule that showed the amount of used drugs over time, the presence of psychosis over time, together with the use of medication over time, being employed or otherwise socially active over time, proofed to be a helpful tool in providing insight to the patient about what is helpful to him and what is not.
Conclusion: Our program focuses on helping patients to find activities in 'normal life', which seems to be very helpful in finding a substitute for drug use and preventing relapse.
Policy of full disclosure: None.

S-24-004
Medication: on the road to shared decision making

B. Jacobsen (Pro Persona Aurora GGZ Nijmegen, Netherlands)

Objective: We will focus on the delivery of medical treatment using the principles of Strengths and Shared Decision Making with the troublesome avoiders in early psychosis.
Methods: Getting labeled as psychotic or even having schizophrenia and being forced to use medication is for quite a lot of our patients a reason to drop out or at least not to comply with the treatment. Of course when people become psychotic, there may be a phase when you have to intervene with medication. But as soon as a patient returns back to a more or less shared world, we start a dialogue in which the wishes of the patient are the basis of our interventions. Contrary to traditional ways in which patients are being seen as non-compliant, lacking insight and having problems in judgment, we see patients as individuals, with their own way to cope with a disease and a healthy desire to be autonomous. This also seems to have something to do with internal and external stigma. In traditional ways of treatment when people stop using medication, they often disappear until a next forced treatment brings them back to the hospital. In our approach when people want to stop medication we will experiment together. Unless, there is an acute danger. We believe that people have to learn to relate to their symptoms and to use medication in their own way, being informed and knowing about our guidelines. Even though patients in our team get relapses too, our results in social recovery and self-esteem are promising. This way of working and thinking is part of an integrated multidisciplinary approach in the treatment of early psychosis.
Results: Patients learn to use medication more in freedom when relationship at the same time get tightened. It needs some time but the effect are worth to tell about. Symptoms are low, people often regain work and forced treatment is minimised.
Conclusion: Real shared decision making from the very beginning of therapeutic contact and not waiting for a shared definition of the problems and remission help people to learn about themselves and the use of medication even if there is, in classical terms no insight.
Policy of full disclosure: None.

S-25 Psychotic symptoms in schizophrenia: biological correlates, clinical outcome and therapeutic consequences

S-25-001
Biological causes of psychotic symptoms such as auditory verbal hallucinations (AVH): DTI and EEG phase coherence results

C. Mulert (University Hospital Hamburg, Germany)

Objective: Auditory verbal hallucinations (AVH) are among the most common symptoms in schizophrenia. Earlier studies suggest changes in the structural connectivity of auditory areas involved in the pathophysiology of auditory hallucinations (Hubl et al. 2004; Whitford et al. 2010). Combining Diffusion Tensor Imaging (DTI) and fiber tractography provides a unique opportunity to visualize and to quantify entire fiber bundles. In addition, advanced EEG analysis based on both source localization and phase coherence analysis can be used to investigate functional relationships between brain regions.
Methods: Here, we used the combination of DTI and fiber tracking for different samples including patients with first episode of schizophrenia and patients with chronic schizophrenia in comparison to healthy controls. We also investigated phase synchrony of gamma oscillations between auditory areas.
Results: In patients with first episode schizophrenia, the subgroup of patients hearing conversing voices showed increased FA relative to patients without these symptoms ($P = 0.028$) and relative to healthy controls ($P = 0.038$). Gamma phase synchrony between auditory areas was reduced in schizophrenic patients and there was a positive correlation between auditory hallucination scales and interhemispheric phase coupling.
Conclusion: Our findings suggest that in addition to local deficits in the left auditory cortex and disturbed fronto-temporal connectivity, the interhemispheric auditory pathway might be an important factor in the pathogenesis of AVH.
Policy of full disclosure: None.

S-25-002
Different patterns of response to psychotic symptoms in schizophrenia patients: implications for clinical practice

M. Jäger (District Hospital Guenzburg, Günzburg, Germany)

Objective: The aim of the study was to describe the course of positive and negative symptoms during inpatient treatment and examine remission and response rates under routine clinical care conditions.
Methods: Two hundred and eighty inpatients with schizophrenia were assessed with the Positive and Negative Syndrome Scale (PANSS) at admission and at biweekly intervals until discharge from hospital. Remission was defined according to the symptom-severity component of the consensus criteria (Remission in Schizophrenia Working Group) as a rating of three or less in the relevant PANSS items at discharge, and response as a reduction of at least 20% in the PANSS total score from admission to discharge.
Results: The mean duration of inpatient treatment was 54.8 days. Of the total sample, 78.5% achieved the criteria for response and 44.6% those for remission. Mean PANSS total scores decreased from 72.4 at admission to 52.5 at discharge ($P < 0.001$). A reduction in PANSS total scores was found from visit to visit, up to week 8. The most pronounced decline was observed within the first 2 weeks of treatment. Logistic regression analysis revealed that the global functioning (GAF) in the year before admission, the total score of the Strauss-Carpenter Prognostic Scale and the PANSS negative subscore at admission were predictive for remission. The regression model showed a predictive value of about 70% and explained 36% of the observed variance.
Conclusion: A treatment under naturalistic conditions of "realworld" patients suffering from schizophrenia appears to be beneficial in terms of clinical effectiveness. The results might help to determine realistic expectations for the treatment of schizophrenic disorders.
Policy of full disclosure: Markus Jäger has received honoraria and travel payments from AstraZeneca, Janssen-Cilag and Lilly.

S-25-003
Occurence and treatment of residual symptoms in schizophrenia

R. Schennach-Wolff (Psychiatry and Psychotherapy, Ludwig-Maximilians-University, Munich, Germany), M. Riedel, M. Obermeier, F. Seemueller, M. Jäger, M. Schmauss, G. Laux, H. Pfeiffer, D. Naber, L. G. Schmidt, W. Gaebel, J. Klosterkötter, I. Heuser, W. Maier, M. R. Lemke, E. Rüther, S. Klingberg, M. Gastpar, H.-J. Moeller

Objective: To evaluate residual symptoms in patients achieving remission according to the consensus criteria and to analyse their potential influence on the patient's functioning at discharge and outcome 1 year after discharge.
Methods: 399 patients suffering from a schizophrenia spectrum disorder were evaluated within a naturalistic multicenter study within the Competence Network on Schizophrenia. Remission status was examined using the consensus criteria proposed by Andreasen et al. in 2005. Residual symptoms were defined as any symptom present at the time-point of remission following analogous analyses performed in depressed patients. Remitters with and without residual symptoms were compared regarding psychopathology, functioning and side effects.
Results: 236 patients (59%) were remitters at discharge with 94% of them suffering from at least one residual symptom. The most common residual symptoms were blunted affect (49%), conceptual disorganization (42%), social withdrawal (40%), emotional withdrawal (39%) and insight into illness (38%). The vast majority of residual symptoms were persistent baseline symptoms, which did not resolve during inpatient treatment. A significant association was found between the presence of residual symptoms and the severity of side effects ($P < 0.0001$) and functioning ($P = 0.0003$) at discharge as well as between residual symptoms and the risk of relapse and chance of remission 1 year after discharge. Despite these differences a decrease of residual symptoms from discharge to the follow-up assessment could be observed.
Conclusion: Residual symptoms were found to be highly prevalent in remitted schizophrenia patients. The fact that most residual symptoms were persistent baseline symptoms suggests an ongoing illness severity in remitted patients. This underlines on the one hand the need to examine and treat these symptoms. On the other hand the necessity to re-evaluate the consensus criteria questioning the status of remission in these patients is also pointed out.
Policy of full disclosure: None.

S-25-004
Metacognitive training: latest results on its efficacy in treating psychotic symptoms in schizophrenia patients

S. Moritz (University Hospital, Hamburg, Germany)

Objective: A number of studies implicate cognitive biases such as jumping to conclusions, attributional distortions, a bias against disconfirmatory evidence, theory of mind and overconfidence in the pathogenesis of paranoid schizophrenia. Many of these biases precede the psychotic episode and may represent cognitive traits.
Methods: Building upon this literature, we developed a metacognitive training program (MCT) that aims to convey scientific knowledge on cognitive biases to patients. The MCT provides corrective experiences in an engaging and supportive manner. The training is now available in 23 languages cost-free via http://www.uke.de/mkt.
Results: New studies are presented providing evidence for the feasibility and efficacy of the MCT approach (see Moritz et al. 2010, for a review). We have recently developed an individualized version, entitled MCT+, which is a hybrid of MCT, CBT and psychoeduation. A beta-version can be downloaded at no cost at http://www.uke.de/mkt_plus. A pilot study confirms its efficacy to reduce positive symptoms, delusion conviction and jumping to conclusions.
Conclusion: The last two decades have witnessed increasing support for psychological models of schizophrenia suggesting that cognitive impairments and biases as well as dysfunctional coping styles play an important role in formation and maintenance of the disorder. Psychological intervention should not only be recommended by guidelines but ultimately be integrated into standard care for schizophrenia, especially in view of tempered enthusiasm regarding the benefits of psychopharmacological mono-therapy.
References:
Moritz S, Veckenstedt R, Randjbar S, Vitzthum F, Woodward TS. (in press). Antipsychotic treatment beyond antipsychotics: metacognitive intervention for schizophrenia patients improves delusional symptoms. Psychological Medicine
Moritz S, Vitzthum F, Randjbar S, Veckenstedt R, Woodward TS. (2010). Detecting and defusing cognitive traps: metacognitive intervention in schizophrenia. Curr Opin Psychiatry, 23, 561–569.
Policy of full disclosure: None.

S-26 Psychosis: psychological therapies and their mechanisms of action

S-26-001
Time-series based analysis of integrative psychotherapy of psychosis

W. Tschacher (University of Bern Psychiatry University Hospital, Switzerland), F. Ramseyer

Objective: By definition, psychotherapy is a process with the purpose of changing behavior, emotion and cognition. Therefore, a complete picture of psychotherapy must include the longitudinal, temporal perspective, inherent to the meanings of 'process' and 'change'. We propose that methods be elaborated and applied that do justice to the processual nature of psychotherapy. We will present a methodology that can depict the process characteristics of psychotherapy in schizophrenia patients. Ultimately this will allow investigating the specific change mechanisms of psychotherapy of psychosis.
Methods: Time-series analysis (Time-Series Panel Analysis, TSPA) generates models of process patterns using fine-grained monitorings of different psychotherapy patients. The prototypical process model is obtained through aggregation of the sample of patients. Unbalanced longitudinal data with nested levels can be analyzed by TSPA; similar modeling is possible using mixed effects models or growth curve analysis. In an empirical dataset, trajectories of 90 schizophrenia patients were available. Patients were treated using integrative psychotherapy of psychosis in a group setting.
Results: Post-session questionnaires provided measures for change factors of this treatment approach for each session and patient. Based on this dataset, TSPA revealed how change factors interact in subsequent sessions: this pattern of interactions is called Granger-causal interactions. In systems-theoretical terms, this pattern may assume the shape of a negative or positive feedback loop, illustrating the mechanism by which therapy has proceeded.
Conclusion: TSPA can illuminate change mechanisms because TSPA approximates Granger-causal dynamical structures in non-experimental field data. TSPA is thus a promising tool for psychotherapy process research because it is capable of providing answers to a core concern, the question of change mechanisms and causal relationships.
Policy of full disclosure: None.

S-26-002
The role of cognitive behavioral therapy and cognitive remediation for the treatment of negative symptoms

S. Klingberg (Psychiatry and Psychotherapy, University of Tübingen, Tuebingen, Germany), W. Wölwer, C. Engel, A. Wittorf, J. Herrlich, C. Meisner, G. Buchkremer, G. Wiedemann

Objective: Cognitive Behavioral Therapy (CBT) is recommended in evidence based treatment guidelines for routine care of schizophrenia patients. However, the efficacy of CBT for the reduction of negative symptoms is unclear.
Methods: We conducted a multicenter randomized clinical trial comparing CBT and Cognitive Remediation (CR) regarding the reduction of negative symptoms. $N = 198$ schizophrenia patients were randomized and treated for 9 months (20 individual outpatient sessions). The study applied rigorous methodology. The primary endpoint was the negative syndrome assessed using PANSS.
Results: Patients in both groups improved with moderate effect sizes. We found no significant difference between the two study conditions. Additional analyses regarding secondary outcomes and differential treatment effects will be presented.
Conclusion: CBT as well CR might be helpful for patients suffering from negative symptoms. The specificity of treatment effects remains an open question.
Policy of full disclosure: The study was publicly funded by the "Deutsche Forschungsgemeinschaft" (grant KL1179/1-3).

S-26-003
What are the therapeutic ingredients of cognitive behavior therapy for psychosis? A systematic review

U. M. Junghan (Bern, Switzerland), M. Pfammatter

Objective: A series of meta-analyses points to the benefits of cognitive behaviour therapy for psychosis (CBTp). However, there are considerable differences in its controlled efficacy depending on the targeted treatment goals or the control conditions applied in the efficacy studies. Above all, the advantages compared to non-specific psychological therapies are moderate.
Methods: This brings up the question about the specific therapeutic ingredients of CBTp. Methods: Systematic electronic searches of clinical studies on CBTp with component control designs or process-outcome analyses were performed. The findings were integrated by calculating weighted mean correlation effect sizes of the relations between specific therapeutic components or processes to outcome. The statistical significance of the effect sizes was determined by computing 95% confidence intervals. In addition, homogeneity tests were applied to examine the consistency of the relations.
Results: The significant relations of specific therapeutic components such as cognitive restructuring by reality testing or the training of coping skills like focusing or distraction techniques to outcome indicate that they represent key therapeutic ingredients of CBTp. However, also so-called common factors such as the quality of the therapeutic alliance between the patient and the therapist are significantly associated with positive outcomes.
Conclusion: Compared to unspecific psychological support the benefits of CBTp are less distinctive. Therefore, there is an urgent need to dismantle and analyze its therapeutically active components and to promote the explicit and targeted implementation of empirically supported common factors such as the formation of a seminal therapeutic alliance or the systematic consideration of the patients' resources and motivation.
Policy of full disclosure: None.

S-26-004
CBT in persistent psychotic symptoms affects functioning and suffering

M. van der Gaag (VU University + EMGO Institute, Amsterdam, Netherlands)

Objective: CBT is not a pseudo-neuroleptic. It does not aim to reduce symptoms, but to change the appraisal of psychotic phenomena. Can these differential effects be demonstrated?
Methods: 216 patients were recurrent psychotic relapses were randomised into CBT versus TAU. The experimental period lasted 6 months and the patients were followed-up every 3 months up to 18 months. The demonstrated cost-effectiveness of this trial was reported in the Br. J of Psychiatry (in press). This study demonstrates the effects on objective (PANSS) and subjective measures (PSYRATS).

Results: The effects on the PANSS were minimal to absent, but subjective rating on the PSYRATS and normal social functioning (combined index based on SFS and PSYRATS) improved.
Conclusion: CBT changes appraisals of symptoms and illness. Despite persistent symptoms patients rate themselves as less suffering and functioning more normal. CBT is able to improve patients lives despite persistent symptoms.
Policy of full disclosure: None.

S-27 First-episode programmes: concepts and proven evidence

S-27-001
The EIS-concept in UK and recent findings from the youth-SPACE project

M. Birchwood (University of Birmingham School of Psychology, Birmingham, UK)

Abstract: It is now clear that long term recurring mental health problems begin mainly before the age of 25 and there are clear early signs of them developing in adolescence; there is also excellent epidemiological evidence concerning the link between social inequality and adverse health outcomes, including psychosis. The logic which provided the rationale for early intervention in psychosis is equally valid across the range of mental health problems. The UK government's mental health strategy places early intervention and prevention at the heart of its strategy. The Birmingham YouthSpace service (http://www.youthspace.me) is a growing program combining public youth mental health and services up to the age of 25. I will outline the evidence base for this wider focus, the policy drivers in the UK and sketch out the structure of YouthSpace in which resides our early intervention in psychosis services.
Policy of full disclosure: None.

S-27-002
Programma2000: concept and practical experiences

A. Meneghelli (AO Ospedale Niguarda Ca' Granda, Milan, Italy), A. Cocchi

Abstract: Programma 2000 is the first Italian Program in early intervention of psychosis, set up in 1999 in the Mental Health Department of Niguarda in Milan. It was organized since the beginning as a specific and comprehensive program addressed both to FEP and to high risk young people. The main goal was to prevent and/or moderate the onset and to promote and consolidate a multidimensional recovery providing also a focused intervention for families. Patients are recruited in a 200.000 inhab. catchment area, but is extended to other catchment areas of Milan, whenever active participation in the program seemed feasible. The battery of assessment includes ERIraos checklist, HoNOS; BPRS; DAS; CBA 2.O, SAT-P, CFI and a neurocognitive evaluation. The personalized treatment involves cognitive-behavioral psychotherapy, individual and group interventions, pharmacotherapy when necessary and a structured intervention with families. Besides strategies and initiatives to be linked with other department functions and with other involved agencies (CAHMS, General Practitioners, Schools, Families and Volunteers Associations) and to disseminate EI across Italy have been carried out. As for now 458 referrals were evaluated and 217 of them included in the multicomponent program. In the paper the symptomatological and social outcomes (3 and 5 years follow up on HonOS, BPRS and GAF) will be presented and the cost-effectiveness discussed.
Policy of full disclosure: None.

S-27-003
The TIPS-concept and recent findings

S. Friis (University of Oslo, Oslo, Norway), J. O. Johannessen, H. Barder, J. Evensen, U. Haahr, W. ten Velden Hegelstad, I. Joa, J. Langeveld, T. K. Larsen, I. Melle, S. Opjordsmoen Ilner, B. Rishovd Rund, J. I. Rossberg, E. Simonsen, K. Sundet, P. Vaglum, T. McGlashan

Objective: To try to shorten DUP and see if shortened DUP could improve outcome.
Methods: Two Early Detection (ED) sites ran comprehensive information campaigns and offered rapid evaluation and treatment. Two comparison (NoED) sites had no program to reduce DUP, but as soon as patients contacted in- or outpatient units, they were offered evaluation and treatment. All sites offered the same evidence based two-year treatment program: Antipsychotic medication, supportive psychotherapy and psychoeducational multi family groups. After 2 years the patients received the treatment their therapists considered necessary. All sites had total responsibility for their catchment areas. We recruited 281 consecutively admitted patients (age 18–65) with a first episode non-affective, non-organic psychosis (141 ED and 140 NoED). Eighty-nine patients declined participation (38 ED and 51 NoED). The refusers had significantly longer DUP (32 weeks vs. 10 weeks).
Results: The ED sites had significantly shorter DUP (median 5 weeks vs. 16 weeks) but with huge variability in all sites. On average the DUP of NoED patients was twice that of ED. ED patients had significantly lower symptom level and less suicidality at baseline. For positive symptoms the ED advantage disappeared at 3 months. For negative symptoms the ED advantage persisted at 1, 2 and 5 years. At 10 years the ED patients had a significantly higher percentage of recovery, but the percentage of non-remitted patients was not significantly different between ED and NoED. Both for ED and NoED the recovered patients had a significantly lower baseline level of negative symptoms than the non-recovered. For DUP there was no such difference.
Conclusion: An early intervention program can reduce DUP and seems to increase the chance for recovery by reducing the level of negative symptoms. However, the most severely ill patients seem to need more than reduced DUP and a standard treatment program.
Policy of full disclosure: None.

S-27-004
OPUS: concept and recent findings

M. Nordentoft (Psychiatric Centre Copenhagen, Copenhagen, Denmark; Faculty of Health Science, Copenhagen University, Copenhagen, Denmark), G. Secher, M. Bertelsen, A. Thorup, S. Austin, N. Albert, P. Jeppesen, G. Krarup, P. Jorgensen, L. Petersen

Objective: Intensive early treatment for first episode psychosis have shown to be effective. It is unknown if the positive effects are sustainable over time. The aim was to determine long term effects of specialised assertive early intervention programme (OPUS) for first episode psychotic patients.

Methods: 547 first-episode psychotic patients were enrolled in a single-blinded randomised clinical trial of 2 years of a specialised assertive early-intervention programme versus standard treatment. OPUS treatment consisted of ACT with family involvement and social skills training. Follow-up was 2, 5 and 10 years. 369 patients were interviewed after 2 years, 301 after 5 years and most likely approximately 310 after 10 years. All patients were followed for at least 5 years in the registers.
Results: At five-year follow-up, the effect of the treatment seen after 2 years (psychotic dimension: −0.32 95% CI −0.58 to −0.06, $P = 0.02$, negative dimension: −0.45 95% CI −0.67 to −0.22, $P = 0.001$) had equalized between treatment groups. A significantly smaller percentage of patients from the experimental group were living in supported housing (4% vs. 10%, OR 2.3, 95% CI 1.1–4.8, $P = 0.02$) and were hospitalized fewer days (mean days 149 vs. 193, mean difference 44, 95% CI 0.15–88.12, $P = 0.05$) during the five-year period. Results of the 10-year follow-up will be presented.
Conclusion: The OPUS treatment improved clinical outcome after 2 years, but the effects were not sustainable up to 5 years after. A difference on supported housing and use of bed days were found after 5 years in favor of the OPUS treatment.
Policy of full disclosure: None.

S-27-005
Specialised First Episode Psychosis services: are they worth it?

P. Power (St Patrick's University Hospital & Trinity College Dublin, Dublin, Ireland)

Abstract: It is now nearly 20 years since the first comprehensive first episode psychosis (FEP) service (EPPIC) began in Melbourne, Australia. Up until then, only a small number of specialist FEP research centres existed. Since then, there has been an unprecedented development of Early Intervention (EI) services, with national roll outs in several countries e.g. Canada, England, and New Zealand. There is now well established evidence that these new services are associated with relatively better clinical outcomes than standard services, with better rates of detection, engagement, recovery, and prevention of relapse. Qualitative outcomes e.g., quality of life and patient satisfaction are also better. Recent economic evaluations confirm the cost benefits of these services (saving the equivalent of €6,000 per patient per year). However, there are many variations of the EI service model. They vary from stand-alone specialist EI teams to standard generic teams with integrated EI workers, from fully comprehensive EI services (with prodrome teams, early detection teams, specialist FEP inpatient units, community follow-up teams) to individual professionals providing specific EI interventions e.g. early detection training. Whether one EI model is better than another remains unproven. Recent evidence is now emerging confirming the relative merits of each specialist component of EI.
Policy of full disclosure: None.

S-28 Dopaminergic and glutamatergic dysfunction in schizophrenia

S-28-001
The influence of risk genes on the glutamate system in schizophrenia: evidence from post-mortem studies

A. Schmitt (Department of Psychiatry and Psychotherapy, University of Göttingen, Goettingen, Germany), P. Falkai

Objective: Schizophrenia is a complex polygenetic disorder with an impact of risk genes of about 50-80%. A dysregulation of the glutamate system has been implicated in the pathophysiology of the disease. However, only little is known about the influence of risk genes of schizophrenia on glutamatergic neurotransmission. Neuregulin 1 activates a family of epidermal growth factor (ErbB) receptors, which are involved in processes such as neuronal signaling, neuroplasticity and activation of the glutamatergic N-methyl-D-aspartate (NMDA) receptor, stabilizing development of excitatory synapses.
Methods: Post-mortem studies of risk genes and their expression in schizophrenia patients and healthy individuals have been performed.
Results: In cerebellum of schizophrenia patients and controls, Individuals carrying at least one C allele of the neuregulin 1 rs35753505 (SNP8NRG221533) showed decreased expression of the NR2C subunit in the right cerebellum, compared to individuals homozygous for the T allele. Another important risk gene in schizophrenia is D-amino acid oxidase (DAAO). To establish if expression of DAAO is altered in cortical, hippocampal or thalamic regions of schizophrenia patients, we measured gene expression of DAAO in a post-mortem study of elderly patients with schizophrenia and non-affected controls. We found increased expression of DAAO-mRNA in the hippocampal CA4 of schizophrenic patients.
Conclusion: The increased DAAO expression could be responsible for a decrease in local D-serine levels leading to a NMDA-receptor hypofunction that is hypothesized to play a major role in the pathophysiology of schizophrenia. The schizophrenia neuregulin 1 risk haplotypes may result in a decrease in efficacy of glutamate—and GABA-mediated synaptic transmission with behavioral deficits in working memory or other cognitive or psychotic symptoms in schizophrenia. Further post-mortem studies with larger samples are needed to elucidate the influence of risk genes on the glutamate system.
Policy of full disclosure: The studies have been supported by the European Commission under the Sixth Framework Programme (BrainNet Europe II, LSHM-CT-2004-503039). Andrea Schmitt discloses the existence of any financial interest with a commercial supporter. Peter Falkai has held lectures for Janssen-Cilag, AstraZeneca, Lilly, BMS, Lundbeck, Pfizer, Bayer-Vital, SKB, Wyeth, Essex and is member of the advisory board of Janssen-Cilag, AstraZeneca, Lilly, Lundbeck.

S-28-002
Functional dysregulations in the language and limbic system as a basis for specific symptoms of schizophrenia

W. Strik (University Hospital of Psychiatry, University of Bern, Switzerland)

Objective: To present evidence that different brain systems are involved in the generation of different clusters of psychotic symptoms involving thought disorders and emotional dysregulation.
Methods: Review of the relevant literature and presentation of own empirical studies on patient groups with disorders in specific symptom dimensions, which are related to language or emotional functions. Investigations are based on structural and functional brain imaging methods.
Results: Both, the limbic and the language circuitries were found to be related to specific symptom dimensions. In particular, formal thought disorders show grey matter volume reduction in the left temporal lobe and hypermetabolism in the language system; acoustic verbal hallucinations are associated with hypermetabolism in the left temporal lobe which normalizes after successful treatment; and emotional dyregulation like delusions of threat or "Wahnstimmung" are related to structural increases in the right ventral striatum.

Conclusion: Different schizophrenia syndromes can be meaningfully mapped on different, well defined brain systems. The common denominator appears to be a mild structural deficit in a sensible key region (the left superior temporal lobe and the hippocampus, respectively) resulting in a disinhibition and an excitatory saturation of the respective system. This is proposed to be the pathophysiological basis of specific psychotic symptom dimensions.
Policy of full disclosure: None.

S-28-003
Dopamine dysfunction and alterations of reward-related learning in schizophrenia

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Abstract: Dysregulation of dopaminergic neurotransmission has been described in acutely psychotic, unmedicated schizophrenia patients. Phasic alterations in dopamine release represent a prediction error that indicates the difference between received and predicted reward. Stress-associated or chaotical dopamine release can induce aberrant attribution of incentive salience to otherwise irrelevant stimuli, which may explain delusional mood states when environmental stimuli appear to be "imbued" with meaning (Heinz, Eur Psychiatry 2002; Kapur, Am J Psychiatry 2003). Neuroimaging studies directly addressing this hypothesis suggest that neuronal activation associated with dopaminergic signaling, e.g. elicited by reward-predicting stimuli and the computation of prediction errors, is indeed altered in schizophrenia patients and directly correlated with delusion formation and motivational deficits such as apathy. High blockade of striatal D2 receptors with neuroleptic medication, on the other hand, also impaired neuronal signatures of reward anticipation and correlated with negative symptoms such as apathy.
References:
Heinz A (2002) Dopaminergic dysfunction in alcoholism and schizophrenia—psychopathological and behavioral correlates. Eur Psychiatry. 17(1):9–16.
Kapur S (2003) Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. Am J Psychiatry. 160(1):13–23
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S-28-004
Dopamine: the final common pathway to psychosis? - New data from the prodrome and chronic schizophrenia

O. Howes (MRC CSC, ICL and Institute of Psychiatry KCL, London, UK)

Background: Whilst a link between dopamine and schizophrenia has been apparent for many years, several streams of new evidence have substantially refined understanding of dopamine's role in the pathoaetiology of schizophrenia. This evidence derives from in vivo neurochemical imaging studies, findings on the impact of environmental risk factors, and research into people at clinical risk of schizophrenia and animal models. However, it is not known when dopaminergic dysfunction first occurs in the development of psychotic disorders such as schizophrenia, how it changes with the development of psychosis, or how it relates to treatment resistance. We have addressed these questions using PET and functional MR imaging of individuals from the prodrome to the first frank psychotic episode.
Methods: The following age-matched groups have received longitudinal [18F]-DOPA PET imaging: (a) two cohorts of individuals with at risk mental states (ARMS, $n = 30$ and $n = 28$) who show prodromal signs of developing psychosis; (b) healthy controls ($n = 40$); (c) treatment resistant patients. The ARMS subjects received follow-up to determine who developed psychosis and repeat PET scans to determine change in [18F]-DOPA influx constants (Ki) values. The ROIs were the whole striatum (S), and limbic (LS), associative (AST) and sensorimotor (SMST) striatal subdivisions.
Results: There was a significant group effect on Ki values at baseline for the whole striatum ($F = 3.7$, $df = 2.42$, $P = 0.035$), and the AST striatal subdivision ($F = 6.5$, $df = 2.42$, $P = 0.004$), which was confirmed in a second independent cohort scanned using a different scanner. The elevation in the ARMS group was seen in the ARMS subjects who developed psychosis, who also showed an increase in dopaminergic function over time ($t = 3.01$, $df = 7$, $P = 0.020$). Treatment resistant patients did not show the same pattern of dopaminergic dysfunction.
Conclusion: These findings indicate that elevated dopamine synthesis capacity (i) predates the onset of psychosis in people with prodromal symptoms, (ii) increases further over time with the development of psychosis; (iii) there may be another mechanism in treatment resistance.
Policy of full disclosure: None.

S-29 Understanding minds: a conceptual framework in the research and clinical features of schizophrenia

S-29-001
Theory of mind in at-risk stages of schizophrenia

M. Brüne (Ruhr-Universität, Bochum, Germany)

Objective: Research into social cognition—the ability to appreciate own and others' mental states—have consistently revealed that patients with schizophrenia perform poorly, relative to controls, in a broad variety of tasks examining mental state attribution. A few studies using functional magnetic resonance imaging (fMRI) were also able to demonstrate that patients with schizophrenia display underactivations in those brain regions involved in mental state attribution or mentalising, although comparability of these studies is limited due to differences in design and sample characteristics. There is evidence that impaired social cognition is intimately linked with poor social functioning in schizophrenia. Conversely, deterioration of social functioning is often already a sign of subjects at high risk for developing psychosis, such that it is conceivable that there might be deficits in social cognition already in early stages of psychosis including at-risk stages of schizophrenia.
Methods: Ten subjects with at-risk ("prodromal") states of psychosis, 22 schizophrenia patients and 26 healthy controls were recruited. During fMRI scanning, participants were shown a series of cartoons. The task was to infer the mental states of the cartoon characters in terms of beliefs, states of knowledge and intentions.
Results: Subjects at risk of psychosis activated the ToM neural network comprising the prefrontal cortex, the posterior cingulate cortex,

and the temporoparietal cortex more strongly than patients with manifest schizophrenia, and, in part, also more strongly than healthy controls. Manifest schizophrenia patients and controls activated the ToM neural network differently with little overlap of activated regions, where overall, controls showed stronger activations than schizophrenia patients.
Conclusion: Findings suggest a compensatory overactivation of brain regions critical for empathic responses during mental state attribution in at-risk subjects for schizophrenia.
Policy of full disclosure: None.

S-29-002
Vulnerable self, poor understanding of others' mind, threat anticipation and cognitive biases as triggers for delusional experience in schizophrenia: a theoretical model

G. Salvatore (Terzo centro Psicoterapia Cogn, Rome, Italy), P. H. Lysaker, R. Popolo, M. Procacci, A. Carcione, G. Dimaggio

Objective: It remains unclear what processes lead to the establishment of persecutory delusions in acute phases of schizophrenia. Recently it has been argued that persecutory delusions arise from an interaction among a range of emotional, cognitive and social factors. In this work we systematically explore this possibility.
Methods: We first discuss the relevant aspects of recent theories explaining the path to persecutory delusions. Then we offer a critical analysis of the literature, illustrated with clinical observations.
Results: We suggest that persecutory delusions are triggered during stressful inter-subjective transactions by the interactions of: (a) an alteration in empathetic perspective-taking and in the pragmatic understanding of others' minds; (b) a perception/representation of the self as vulnerable and inadequate and of the other as dominant and threatening; and (c) a hyper-functioning of the threat/self-protection system when faced with perceived danger. Implications for future research and treatment of people suffering from this symptom are discussed.
Conclusion: Relative to existent models of persecutory delusion we suggest that the our model provides a potentially richer understanding of the role played by interpersonal stress. For instance, it allows that specific stressors may increase a subject's difficulties in pragmatically comprehending others' minds, so previously understood communicational signals are opaque. The model also provides a testable hypothesis about the neurobiological bases of dysfunctional empathetic perspective taking and its relationship to disturbances in self experience in schizophrenia as described by phenomenologists. Our model also introduces a potentially key role played by a hyperactive threat system. On the basis of a perception of a threat to the self, an overactive threat system could produce aggressive defensive behavior which leads to a cycle in which selective attention and cognitive biases reinforce a persecutory delusion.
Policy of full disclosure: The authors declare that there does not exist any significant financial interest or other affiliations with a funding organisation or with a commercial supporter of the session and/or provider of commercial services.

S-29-003
Associations of mastery with daily function in schizophrenia

P. H. Lysaker (roudebush VA med center, Indianapolis, USA), M. Procacci, A. Carcione, G. Salvatore, R. Popolo, G. Dimaggio

Objective: Deficits in metacognition, or the ability to think about thinking, are common in schizophrenia and represent a barrier to recovery of healthy function on their own. Unknown are what elements of function are affected by what aspects of metacognition. To examine this issue we conducted a study in which we explored whether participants with differing capacities for Mastery, a domain of metacognition that reflects the ability to use knowledge about mental states to respond to psychological challenges, had difficulties in different elements of daily function.
Methods: Participants were 98 adults with a schizophrenia spectrum disorder in a non-acute phase who were participating in active treatment. All were classified into three groups on the basis of ratings of their capacity for metacognitive Mastery using the Metacognitive Assessment Scale. The first group Low Mastery included participants unable to plausibly represent psychological challenges. The second group, Intermediate Mastery included those able to plausibly represent psychological problems but cope primarily through passive measures or avoidance. The third group High Mastery included those able to cope with plausible problems through cognitive means. Participants in all three groups completed assessments of coping preference, insight, self-esteem, anxiety and neurocognition.
Results: MANOVA and ANOVA revealed that the High Mastery group had a greater preference for coping with stressors by thinking and talking about them, and greater insight than all other groups, and higher levels of feeling accepted by peers than the intermediate Mastery group. The intermediate Mastery group reported higher levels of resignation when facing stressors and more social phobia than the other two groups. The group with Low Mastery had the greatest level of deficits in executive functioning while the High Mastery group had the best functioning in terms of neurocognitive processing speed. These findings of Mastery group differences in self-esteem and anxiety persisted when neurocognition was controlled for in an ANCOVA.
Conclusion: One possible conclusion is that the Mastery domain of metacogntion appears linked to coping preference, insight, self-esteem and anxiety in a generally non-linear manner.
Policy of full disclosure: The authors declare that there does not exist any significant financial interest or other affiliations with a funding organisation or with a commercial supporter of the session and/or provider of commercial services.

S-29-004
Functional neuroimaging of Theory of Mind (ToM) abilities in patients with schizophrenia

K. Koelkebeck (Department of Psychiatry, University of Muenster, Muenster, Germany), A. Pedersen, J. Bauer, M. Brandt, P. Ohrmann

Objective: The ability to have a Theory of Mind (ToM), an aspect of social cognition, has been shown to be reduced in patients with schizophrenia. A "social brain" network encompassing e.g. the superior temporal gyrus (STS) and the anterior cingulate cortex (ACC) has been suggested by functional neuroimaging studies in healthy controls. In this study we used the "moving shapes" paradigm (Abell et al. 2000), which successfully activated the neural ToM network in previous imaging studies. Impaired clinical performance and differential activation patterns in ToM regions of the brain in patients with schizophrenia as compared to controls were hypothesized.
Methods: 14 patients with schizophrenia and 15 healthy controls participated in the study. 9 silent animated movies depicting moving triangles displaying ToM sequences as well as an intentional movement and a baseline condition were presented in the functional magnetic resonace imaging (fMRI) scanner. Imaging data were processed using SPM5. Statistical significance was set at $P < 0.001$,

uncorrected. After the scan, descriptions of the movies were recorded and evaluated according to standardized rating criteria.
Results: Behavioral data revealed a significantly reduced use of ToM-related vocabulary in schizophrenia patients as compared to healthy controls. Group comparisons of functional activation patterns related to ToM versus Baseline sequences did not show any group differences. However, schizophrenia patients activated ToM-related brain areas more than healthy controls during performance of lower-level ToM abilities sequences.
Conclusion: Behavioral ToM performance deficits in schizophrenia patients as compared to healthy controls are replicated in our study. As well, hyper-activation of ToM-related brain areas was found in schizophrenia patients. These findings are in line with those of previous neuroimaging studies that suppose hyper-mentalizing and compensatory mechanisms. Results are discussed taking into account recent neuroimaging studies in schizophrenia.
Policy of full disclosure: The authors declare that there does not exist any significant financial interest or other affiliations with a funding organisation or with a commercial supporter of the session and/or provider of commercial services.

S-30 Early recognition and early intervention: facts and visions

S-30-001
Prediction of psychosis: current state and future directions

S. Ruhrmann (Department of Psychiatry and Psychotherapy, University of Cologne, Cologne, Germany), J. Klosterkötter

Objective: During the last 15 years, prediction of psychosis has become a highly dynamic and successful area of research. However, available prediction models have still to be refined.
Methods: The initially observed high transition rates were not confirmed in recent investigations, demonstrating a broader predictive variance of the employed 'ultra-high risk' (UHR) criteria. Narrowing the criteria became no convincing strategy to generate risk enriched samples as required for prevention trials: a higher specificity was achieved only at the cost of a considerable loss of sensitivity. As a possible solution, the European Prediction of Psychosis Study introduced the stratification of risk by a prognostic index (PI) based on individual risk scores. Furthermore, the basic symptoms (BS) criterion 'Cognitive Disturbances' (COGDIS) showed to enhance the predictive value of UHR criteria. Thus, combining risk detection by UHR/COGDIS and risk stratification by a PI is suggested.
Results: UHR criteria may not detect the onset of the deterioration of social and role functioning as it seems to emerge before the onset of (attenuated) psychotic symptoms. The German Research Network on Schizophrenia introduced a two-stage model: A criterion based on perceptive-cognitive BS ('COPER') primarily defined an 'early', attenuated and transient psychotic symptoms defined a 'late' at-risk state. Meanwhile, a retrospective study supported this sequence.
Conclusion: Future tasks relate to the still under-investigated sensitivity of at-risk criteria in help-seeking samples and beyond. First neurocognitive and neurobiological studies employing appropriate statistics are promising, yet their contribution to existing prediction models has to be further evaluated. Furthermore, data regarding the long-term (life-time) risk associated with current criteria are still sparse: characterization in follow-up studies spanning several years is required. Finally, considering the clinical course of negative symptoms and social/role functioning in non-converters, transition to psychosis is not the only worse outcome in high-risk groups, an important issue for further intervention studies.
Policy of full disclosure: None.

S-30-002
Predicting psychosis in those at genetic or cognitive high risk

S. Lawrie (Division of Psychiatry, University of Edinburgh, Edinburgh, Scotland), A. Stanfield, B. Moorhead, A. McIntosh, D. Owens, E. Johnstone

Objective: Several studies demonstrate structural imaging deficits in patients with schizophrenia and that these are partly evident in 'at risk' populations. Therefore, those with the greatest deficits at baseline are most likely to develop psychosis and/or there are additional changes nearer to the time of onset. Low IQ (<70) increases the risk for schizophrenia and may include a sub-population of people with early onset schizophrenia which manifests as low IQ.
Methods: In the Edinburgh High Risk Study (EHRS), we have followed up 162 people from multiply affected families with schizophrenia, initially aged 15–25, over 10 years, during which time 21 developed schizophrenia. In the Edinburgh Study of Co-morbidity (ECS), 137 participants aged 13–22 years, receiving additional learning support, were recruited. All underwent detailed clinical evaluation and structural magnetic resonance imaging (MRI) at baseline, as did 36 and 40 controls respectively, and the majority had repeated examinations at approximately 18 month intervals.
Results: In the EHRS, memory deficits at baseline predicted psychosis, an average of 2.5 years later, without any apparent change over time. Under-activations on fMRI in medial temporal lobe/superior temporal gyrus, anterior cingulate, lingual gyrus and cerebellum predicted the onset of schizophrenia 1–15 months later. Baseline volumetric reductions in medial temporal lobes and thalamus were weak predictors. Baseline sMRI cortical folding (increases in rPFC) was however a moderately powerful predictor of psychosis; while there were more pronounced reductions in medial and lateral temporal lobe (and cerebellum) grey matter density (GMD) over time in those who went on to develop schizophrenia. Anxiety/depression, stressful major (independent) life-events, cannabis use and isolated/transient psychotic symptoms all apparently preceded these sMRI changes. In the ECS, low birthweight and preterm birth ($\sim$13% of cases) were associated with enlargement of subarachnoid cisterns and callosal thinning, as well as reduced GMD in the temporal cortex. Individuals with intellectual disability had smaller total white matter and total brain tissue volumes than controls, as well as regionally reduced grey and white matter density. Increased white matter density was detected in the left temporal lobe of subjects scoring above the threshold for autism as compared to subjects below the threshold. We found significant correlations between anxiety and GMD in the right thalamus and left temporal lobe. Those who scored above a schizotypy cut-off had more psychotic symptoms, greater cognitive impairment, higher right prefrontal lobe gyral folding, and greater reductions in temporal lobe GMD compared to those below.
Conclusion: These findings suggest both common and differential mechanisms in those at genetic and cognitive high risk of schizophrenia. If baseline Schizotypal cognitions, Memory impairment and Increased pre-frontal cortex folding, and temporal lobe GMD loss over time, predict schizophrenia in those at increased risk both for genetic and for cognitive reasons, we may have found a final common pathway leading to schizophrenia. Maximal power in early detection of psychosis will come from focussing on these changes in the years before transition and, critically, on their pathophysiological underpinnings. Other risk factors and 'pathways to psychosis' could be distinguished by different imaging modalities.
Policy of full disclosure: None.

S-30-003
Neurophysiological paradigms in patients at ultra high risk for developing psychosis

D. Nieman (Department of Psychiatry, Academic Medical Center, Amsterdam, The Netherlands), S. Dragt, M. van Tricht, J. Koelman, L. Bour, E. Velthorst, D. Linszen, L. de Haan

Objective: Subjects at ultra high risk (UHR) for psychosis show dysfunctions in several neurophysiological paradigms. To our knowledge, studies reporting on several neurophysiological paradigms in the same UHR subjects are scarce.
Methods: Eye movements (antisaccades, smooth pursuit eye movements) and event-related potentials (N100, N200 N200b, P200, and P300 amplitudes) were assessed in 61 UHR subjects, of whom 18 subjects (30%) made a transition to psychosis over a 3-year follow-up period (UHR + T) and 43 did not (UHR + NT) and 28 age—and intelligence matched healthy control subjects.
Results: The UHR subjects showed increased antisaccadic errorrate and higher corrective ($t = 2.62$, $P = .011$) and non-corrective saccadic rates ($t = 2.19$, $P = .023$) during smooth pursuit eye movements compared to controls. In addition, UHR + T subjects showed smaller parietal P300 amplitudes, compared with controls ($t = 6.73$, $P < .0001$) and UHR + NT subjects ($t = 4.16$, $P < .001$). N2b difference was larger in controls compared with both UHR + T ($t = 2.32$, $P = .025$) and UHR + NT ($t = 2.44$, $P = .017$) subjects. Reduced P300 amplitudes were the best predictor for subsequent psychosis in the UHR group (Wald = 10.4, $P = .001$, HR = 1.37).
Conclusion: UHR subjects showed reduced antisaccade and smooth pursuit eye movement performance indicating prefrontal lobe dysfunction. In addition, P300 amplitude was reduced in UHR + T subjects. Reduced P300 amplitude was the best predictor of transition to psychosis. Our results can be used to create a neurophysiological profile for subjects most at risk for transition to psychosis.
Policy of full disclosure: None.

S-30-004
Indicated prevention in people at-risk of psychosis: recent findings

A. Bechdolf (Department of Psychiatry, University of Cologne, Cologne, Germany)

Objective: In recent years, criteria based on sub-threshold levels of psychotic symptoms or self-perceived cognitive deficits have been found to predict psychosis onset within 12 months in 20–30% of the cases.
Methods: These findings have provided the opportunity of indicated prevention efforts in order to reduce or prevent the devastating effects of schizophrenia. It has been argued that cognitive behaviour therapy (CBT) may have some advantages compared with antipsychotics (AN): (a) more acceptable, tolerable and less stigmatizing to (b) no risk of exposing false positives to pharmacological side effects, (c) effective treatment for false positives (depression, anxiety disorders). Six randomized controlled trials (RCTs) in the at-risk population have been completed so far. They have included evaluations of low dose risperidone and cognitive behavioural therapy (CBT) combined, CBT or an integrated psychological intervention, olanzapine and omega-3 fatty acids.
Results: The results of the treatment phase indicated advantages on a descriptive level or significant results in favour of the respective experimental condition. However, due to a number of methodological limitations the empirical evidence of the superiority of psychological interventions or antipsychotics to unspecific control conditions in the at-risk population is preliminary.
Conclusion: Therefore there is a need for methodological sound collaborative large scale RCT involving CBT and antipsychotics as preventive strategies. Such trials are on the way at present.
Policy of full disclosure: None.

S-31 Animal models of schizophrenia: between genotype, endophenotype, nongenetic second hit and the disease

S-31-001
Schizophrenia-related behavioral and hippocampal morphological alterations after prenatal kainic acid lesions

M. von Wilmsdorff (Universität Düsseldorf, Duesseldorf, Germany), M.-L. Bouvier, A. Schmitt, W. Gaebel

Objective: Although schizophrenia affects both sexes in humans, there are sex-dependent differences with respect to the age of onset, clinical characteristics, course and prognosis of the disease.
Methods: To investigate sex-dependent differences in motor coordination and activity as well as in cognitive and social behavior, we repeatedly tested female ($n = 14$) and male ($n = 12$) Fisher rats (postnatal days, PD 56–174) that had received intracerebroventricular injections of kainic acid as well as female ($n = 15$) and male ($n = 16$) control animals. The hippocampus was examined histologically.
Results: Both female controls and female animals with prenatal intervention spent less time in a dark box before entering an unknown illuminated area in the alcove test than male controls. Compared to controls, animals that received prenatal injection (particularly females) committed a higher number of perseveration errors in the T-maze alternation task. Female rats exhibited a higher degree of activity than males, suggesting that these effects are sex-dependent. Animals that received prenatal intervention engaged in a longer duration of social contacts. Histological analysis showed that pyramidal cells in hippocampal area CA3 (in both hemispheres) of control animals were longer than those found in treated animals. Sex-dependent differences were found in left hippocampi of control animals and animals after prenatal intervention.
Conclusion: These results demonstrate important differences between males and females in terms of weight gain, response to fear, working memory and social behavior. We also found sex-dependent differences in the lengths of hippocampal neurons. Further studies on larger sample sets with more detailed analyses of morphological changes are required to confirm our data. KEYWORDS: Psychiatric disease; Neurodevelopment; CA3 region; Working memory; Social contact.
Policy of full disclosure: None.

S-31-002
The reeler mouse model of schizophrenia: from behavior to proteomics

A. Schmitt (Department of Psychiatry and Psychotherapy, University of Göttingen, Goettingen, Germany), P. Pilz, D. Martins-de-Souza, M. von Wilmsdorff, P. Falkai

Objective: Like schizophrenia patients, heterozygote reeler mice have a partial reduction of reelin protein. Heterozygous reeler mice show cognitive disturbances and a deficit of prepulse inhibition of the

acoustic startle response (PPI), a pre-attentional paradigm, which has also been found in schizophrenia patients, however results are not consistent. Proteome analysis is a valuable approach for the discovery of potential biomarker candidates as well as to reveal biochemical mechanisms through the differentially expressed proteins that may be involved in disease pathogenesis.
Methods: Mice were offspring from two pairs of hybrid mice B6C3Fe a/a-Relnrl/J (reeler mouse) from Jackson Laboratories (Wilmington, USA). We investigated PPI in heterozygote reeler and wildtype mice. Here we present the results of the proteome analysis of four brain regions [the two hippocampal subregions dentate gyrus and CA3; the anterior cingulate cortex and cerebellum] from a pool of 10 heterozygote reeler mice compared to 10 wildtype mice using the most traditional approach for proteome studies, two-dimensional gel electrophoresis (2DE) for protein separation, MALDI-TOF/TOF mass spectrometry for protein identification, and Western blot analysis for validation of some differentially expressed proteins.
Results: Heterozygote reeler mice had a PPI deficit compared to wildtype mice ($P = 0.032$). Detailed analysis showed a stronger effect of genotype in male compared to female mice. The average PPI-deficit was significant only in male mice if averaged over PNDs 28-112 ($P = 0.034$), while it was not significant in females. Most of differentially expressed proteins are involved in energy metabolism pathway, as also shown in the proteome of tissues from schizophrenia patients, except in ACC, where most of the differentially expressed proteins are related to cell growth and cytoskeletal proteins.
Conclusion: The male heterozygous reeler mouse may represent a valid animal model for schizophrenia and several deficits in energy metabolism and structural proteins may be caused by a reelin deficit in schizophrenia patients.
Policy of full disclosure: None.

S-31-003
Region-specific alteration of GABAergic markers in the brain of heterozygous reeler mice

S. Nullmeier (Otto-von-Guericke Universität, Magdeburg, Germany), P. Panther, H. Dobrowolny, H. Schwegler, R. Wolf

Objective: Heterozygous reeler mice (HRM), haploinsufficient for reelin, have been proposed to be a genetic mouse model of schizophrenia. Beside behavioral similarities, HRM also demonstrate several neuroanatomical traits similar to patients suffering from schizophrenia.
Methods: Using immunocytochemical procedures, we investigated HRM and wildtype mice (WT) for differences in the numbers and densities of tyrosine hydroxylase (TH)-immunoreactive neurons in the ventral tegmental area and substantia nigra, serotonin transporter (5-HT-T)-immunoreactive neurons of the raphe nuclei, glutamic acid decarboxylase (GAD) 67 and parvalbumin (PARV)-immunoreactive neurons in the hippocampus.
Results: HRM, when compared to WT, showed a significant decrease of GAD67-immunoreactive neurons in hippocampal subregion CA1 (stratum pyramidale), CA2 (stratum oriens, stratum pyramidale, stratum radiatum) and dentate gyrus (granule cell layer) and also a significant decrease of PARV-containing neurons in CA1 (stratum oriens, stratum pyramidale) and CA2 (stratum pyramidale). However, no morphological differences were found for dopaminergic markers in the substantia nigra/ventral tegmental area or serotonergic markers in the raphe nuclei.
Conclusion: These results support a hippocampal GABAergic dysfunction in HRM as previously described by other authors and may be based on a downregulation of GAD67 and PARV expressions. In summary, the reelin haploinsufficient mouse may provide a useful model for studying the interaction between reelin and hippocampal GABAergic system, its effect on dendritic spine maturation and plasticity related to schizophrenia.
Policy of full disclosure: None.

S-31-004
Neurodevelopmental disorder in Srgap3−/− mice leads to lethal hydrocephalus or 'schizophrenia-related' behaviours

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Objective: SRGAP3 regulates the RHO protein RAC1. RHO proteins are involved in actin cytoskeleton dynamics during brain development, in synaptic plasticity and in neurodevelopmental disorders. SRGAP3 is located on chromosomal region 3p25 and was attributed to severe mental deterioration. In genome-wide association studies, the locus was found at risk for schizophrenia and childhood-onset schizophrenia.
Methods: To investigate the role of SRGAP3 in aberrant neurodevelopment, we generated Srgap3−/− knockout mice.
Results: Ten percent of these Srgap3−/− mice develop a hydrocephalus and die before adult age. The remaining animals express neuroanatomical changes: lateral ventricles, white matter tracts and dendritic spines are enlarged. RAC1 basal activity is increased in Srgap3−/− mice. In behaviour, they exhibit a complex phenotype: locomotor activity is lower, animals have tics. Spontaneous alternation and social behaviour are impaired, long-term memory is normal. Srgap3−/− mice show increased methylphenidate stimulation, prepulse inhibition is impaired.
Conclusion: Together, the results show neurodevelopmental deterioration in Srgap3−/− mice leading either into lethal hydrocephalus or a complex syndrome related to schizophrenia endophenotypes. These findings provide novel insights into the neurodevelopmental hypothesis of schizophrenia.
Policy of full disclosure: None.

S-32 Classification of different long-term outcomes of psychosis in the schizophrenia spectrum: a need for re-conceptualization

S-32-001
Biological and social predictors of clinical outcome after the first psychotic episode: findings from the AESOP 10-year follow up study

P. Dazzan (Institute of Psychiatry, London, UK)

Objective: AESOP is a large epidemiological study that evaluated social and biological risk factors in individuals with a first psychotic episode. The study is now completing a 10-year follow up of the original cohort, and aims to evaluate clinical and functional outcome, and factors that can predict these outcomes.
Methods: The original cohort comprised 357 patients. To date, we have attempted to follow up 327 of these. Approximately 88% of patients have been traced, and invited to undergo a second evaluation. Social deprivation, neurological function, and brain structure were

evaluated at first presentation and again at follow up (7 years for MRI and 10 years for all other factors). At follow up we have assessed clinical and functional outcomes through subject interview, case-note review, informant interview, recorded using the WHO Life Chart and the Global Assessment of Function (GAF). To assess functional outcomes we included: time employed; independent accommodation; global function score; marital and parental status.
Results: At follow up, approximately 30% of the sample had a continuous illness course, 30% an episodic illness course, and 40% an illness course intermediate between the two. Most patients had been admitted to hospital at least once during follow up. Patients who suffered more brain changes over time (grey matter reduction, ventricular volume enlargement, $P < 0.001$), and more neurological dysfunction ($P < 0.001$), had a poorer outcome (no remission of at least 6 months, more time spent in hospital, amore exposure to antipsychotics). The role of social factors is also being investigated.
Conclusion: There are many possible outcomes following a first psychotic episode, and these may be predicted at the time of illness onset by using a combination of social and biological factors.
Policy of full disclosure: None.

S-32-002
Quality of life and recovery in psychotic disorders: ten-years follow-up of the TIPS study

I. Melle (Oslo university hospital Psychosis research unit, Norway), J. Evensen, W. Hegelstad, U. Haahr, J. I. Rossberg, J. O. Johannessen, I. Joa, T. K. Larsen, S. Opjordsmoen, E. Simonsen, K. Sundet, P. Vaglum, S. Friis

Objective: Subjective quality of life (sQoL) is increasingly recognized as a valid outcome measure in psychotic disorders. The purpose of the current study is to investigate the relationship between sQoL and other outcome measures after 10 years in treatment.
Methods: The results are based on a prospective longitudinal study of patients with broad schizophrenia spectrum psychotic disorders ($N = 301$), followed from their first week in treatment and reexamined after 1, 2, 5 and 10 years. Of the original 301 patients, 185 participated in the 10 year follow-up. Patients that did not participate in the 10 year follow-up were significantly less satisfied with their life at start of treatment compared to those who did.
Results: There was a small—but statistically significant and stable—improvement in sQoL from start of treatment throughout the 5 year follow-up, but with a subsequent fall from 5 to 10 years. There were also different patterns of change on the individual level. While sQoL at baseline mainly was determined by depressive symptoms and pre-treatment factors such as poor premorbid functioning and longer duration of untreated psychosis, sQoL at the 10-year follow-up was—as previously found at the 2-year follow-up—independently influenced by current affective symptoms, suicidal symptoms, global functioning and social relations in addition to alcohol use. Levels of positive and negative symptoms did not influence sQoL after correction for differences in affective symptoms. Patients meeting recovery criteria had higher sQoL in bivariate analyses. The difference in sQoL between groups was no longer statistically significant after correcting for affective and suicidal symptoms, the presence of alcohol misuse and social relations.
Conclusion: This implies that sQoL also taps other aspects than those covered by symptomatic and functional indices of recovery, and that an assessment of patients' experience of their own lives is an important addition to these recovery measures in evaluating treatment outcomes.
Policy of full disclosure: None.

S-32-003
The clinical relevance of the different criteria of "outcome" in psychosis: a critical analysis from the Cantabria First Episode Study

J. L. Vazquez Barquero (Janssen Cilag Psychiatry, Madrid, Spain), B. Crespo-Facorro, R. Pérez-Iglesias, J. Vázquez-Bourgon

Abstract: During the last few decades, different operational criteria for the definition of "outcome" in psychosis have been proposed. Based on them different concepts such as response, remission and recovery are currently used to evaluate treatment effectiveness and clinical course in clinical trials and first episode studies. In general these concepts have been defined combining scores of core psychopathological and functional manifestations of illness, with a time criterion of persistence or absence of these clinical manifestations. Clinical experience has demonstrated that these criteria appear to be practicable and useful in clinical practice for a significant proportion of psychotic patients. They, in general, are related to a better overall symptomatic status and to certain extend also to functional outcome, but they tend to be poorly associated to a better quality of life and cognitive performance. This is very relevant as achieving symptomatic remission is not automatically concurrent with an adequate status in other key outcome dimensions. Thus, the general consensus is that although these concepts have been progressively refined and have at present a clear utility for clinical practice, they are still imprecise for adequately measuring the real outcome of the illness. They also lack adequate levels of consistency in the different studies. Thus, there is still a need to develop more precise and valid operational criteria of "outcome" for the evaluation of the different key dimensions of the illness clinical course. The objective of this presentation is to describe, using data from the Cantabria's First Episode Psychosis Clinical Program (PAFIP), the clinical relevance and implications of applying each of the different criteria of "outcome" in the definition of the 3 years clinical course of this series of first episode patients. Based, on these findings we will also try to formulate recommendations for elaborating a more reliable and valid consensus definition of global recovery for patients with psychosis.
Policy of full disclosure: See affiliation.

S-32-004
Differences in course of illness and predictors of bad outcome and recovery in the OPUS I cohort after 5 and 10 years

R. G. Secher (Psychiatric Centre Copenhagen Research Unit, Bispebjerg, Denmark), S. Austin, N. Albert, M. Nordentoft

Objective: This investigates the predictors of good outcome after first-episode psychosis and the clinical.
Methods: A cohort of 547 patients with first-episode psychosis was sought interviewed 5 and 10 years after first diagnosis. Recovery was defined as working or studying, having a GAF-function score of 60 or above, having remission of negative and psychotic symptoms, and not living in a supported housing facility or being hospitalized during the last 2 years before the interview.
Results: After 5 years a total of 40 (15.7%) were found to be recovered, and 76 (29.8%) had a job or were studying. Of those working 20 still had psychotic symptoms. Out of the 40 recovered, less than half were recovered after 2 years. Recovery after 5 years was predicted by female sex (OR 2.4, 95% CI 1.0–5.8), higher age (OR 0.91, 95% CI 0.83–0.99), premorbid social adaptation (OR 0.72, 95% CI 0.56–0.93), growing up with both parents (OR 2.6, 95% CI 1.0–6.8) and low level of negative symptoms (OR 0.51, 95% CI 0.33–0.77) at baseline.

Conclusion: Our findings suggest that a stable social life with normal social functioning has a predictive value for good outcome. These measures might be influenced by negative symptoms, but in the multivariate analysis with negative symptoms included they have an independent effect. Also our findings suggest that, after first-episode psychosis, some patients can still experience psychotic symptoms, but have a job and a fairly stable life. The results above are based on the 5-year follow-up of the OPUS cohort. The interviews for the ten-year follow-up of the same cohort were just finished. Results regarding course of illness, including bad outcome and recovery will be presented.
Policy of full disclosure: None.

S-33 Molecular linkage between energy metabolism and oligodendrocyte pathology in schizophrenia

S-33-001
Neurobiology of feeding and energy expenditure

T. L. Horvath (University of Magdeburg, Germany)

Objective: Empirical evidence points to the hypothalamus as a critical regulator of the adaptation of the CNS to the changing environment in support of survival.
Methods: This information, when analyzed didactically, leads to the conclusion that specific subsets of hypothalamic neurons are critical and mandatory upstream regulators of brain regions classically considered as master determinants of CNS function, such as the cortex and hippocampus.
Results: The regulatory role of the hypothalamus in cortical and hippocampal functions is asserted via classical neuronal pathways, and by the regulation of peripheral tissue output in the form of hormones and nutrients. When the hierarchical relationship between various brain regions and peripheral tissues are reconsidered, a new viewpoint on the brain, its functions and relationship to integrative physiology and disease becomes apparent.
Conclusion: I argue that the approach to physiological and pathological aspects of brain and whole body functions from this new perspective will offer previously unsuspected possibilities to better understand the etiologies of various brain disorders, specifically schizophrenia.
Policy of full disclosure: None.

S-33-002
Postmortem and PET studies are indicating impaired cerebal glucose metabolism in schizophrenia

J. Steiner (University of Magdeburg Department of Psychiatry, Germany), H.-G. Bernstein, B. Bogerts

Objective: Apart from "peripheral" glucose metabolism, cerebral insulin signaling and glucose utilization seem to be likewise affected in schizophrenia.
Methods: This talk is presenting a summary of previous human postmortem and PET studies on this topic.
Results: There is evidence for a reduced expression of insulin receptors in the dorsolateral prefrontal cortex of schizophrenia cases, along with a reduced insulin signal transduction (via AKT). Moreover, a reduced activity of insulin-degrading enzyme (IDE) may contribute to the pathogenesis of cerebral insulin resistance in diseased brains. These observations are reflected by fluorodeoxyglucose positron emission tomography (FDG-PET) findings of disease state-dependent alterations in cerebral glucose-metabolism and functional disconnection in brain regions which are involved in the pathophysiology of schizophrenia (e.g., of the prefrontal cortex, thalamus and mediotemporal lobe).
Conclusion: Disturbances in neural glucose uptake and utilization may contribute to the pathophysiology of schizophrenia.
Policy of full disclosure: None.

S-33-003
Histological studies of oligodendrocytes in psychiatric diseases

A. Schmitt (Department of Psychiatry and Psychotherapy, University of Göttingen, Goettingen, Germany), C. Steyskal, S. Strocka, F. Frank, K. Wetzestein, H.-G. Bernstein, J. Steiner, B. Bogerts, P. Falkai

Objective: Structural magnetic resonance imaging and post-mortem studies showed volume loss in the hippocampus in psychiatric disorders like schizophrenia, depression and bipolar disorder. The noted tissue reduction in the posterior section suggests that some cellular subfractions within this structure might be reduced.
Methods: To address this, we investigated numbers and densities of neurons, oligodendrocytes and astrocytes in the posterior and anterior hippocampal subregions in postmortem brains from 10 patients with schizophrenia, 8 patients with bipolar disorder, 8 patients with major depression and 10 normal controls using design-based stereology performed on Nissl-stained sections.
Results: Compared to normal controls, patients with schizophrenia showed a decrease in the mean number and mean density of oligodendrocytes in the left and right CA4 ($P < 0.05$). Multivariate analysis revealed an effect of gender ($P = 0.03$) and age or duration of the disease (patients) on the number of astrocytes ($P = 0.000$) as well an effect of age on the density of astrocytes ($P = 0.000$), but no effects of diagnosis. In patients with bipolar disorder, an increased number of neurons has been observed in CA1 ($P = 0.022$) and subiculm ($P = 0.026$), whereas patients with major depression showed increased oligodendrocytes in CA4.
Conclusion: These are the first findings of reduced numbers of oligodendrocytes in the CA4 subregion of the posterior hippocampus in schizophrenia. Results from anterior hippocampus will be presented. Compared with other major psychiatric disorders, results seem to be specific for schizophrenia. Our results may indicate disturbed connectivity of the hippocampus and, thus, contribute to the growing number of studies showing the involvement of posterior hippocampal pathology in the pathophysiology of psychiatric disorders. Increased cell numbers in bipolar patients point to a decreased neuropil, these are axons and dendrites. The present findings may contribute to the literature about hippocampal pathology leading to disturbances in connectivity in neuronal networks.
Policy of full disclosure: None.

S-33-004
Impaired biochemical pathways in schizophrenia: a proteomic overview

D. Martins-de-Souza (University of Cambridge, UK)

Objective: Considering that schizophrenia is a consequence of serial alterations of a number of genes and proteins that, together with environmental factors, will lead to the establishment of the illness, proteomic analysis of post-mortem schizophrenia brain tissue and

peripheral fluids may lead to the identification of schizophrenia-related proteins that will ensure the comprehension of this pathogenesis as well as indicate potential biomarkers.
Methods: We used a shotgun mass spectrometry approach combining isoelectrofocusing and RP-HPLC prior MALDI-TOF/TOF powered by isotope coded protein labeling (ICPL) for proteome quantitation as well as two-dimensional gel electrophoresis/mass spectrometry-based proteome analysis.
Results: We have found the most often alterations in energy metabolism, oligodendrocyte-function and myelinization, calcium homeostasis and cytoskeleton. Several protein biomarker candidates related to those pathways were also found differentially expressed.
Conclusion: The recurrent identification and validation of inter-related protein clusters, determined in different samples by different proteomic approaches reinforces the putative involvement of certain pathways in SCZ and reveal new potential biomarkers to schizophrenia.
Policy of full disclosure: None.

S-34 Heterogeneity and functional significance of white matter changes in schizophrenia

S-34-001
Heterogeneity of diffusion tensor imaging findings in schizophrenia

M. Kyriakopoulos (King's College London, UK)

Objective: Several lines of evidence are suggestive of aberrant cerebral integration in schizophrenia, with white matter (WM) abnormalities, underlying the interconnections of brain regions into functional networks, being considered integral to its pathophysiology. Diffusion Tensor Imaging (DTI) is a magnetic resonance imaging technique which quantifies the structural and orientational characteristics of WM. Although WM integrity, as inferred by DTI, appears to be compromised in schizophrenia, the pattern of identified abnormalities is not totally consistent across all studies. Our aim was to explore factors affecting this apparent heterogeneity of DTI findings.
Methods: Systematic qualitative review of DTI studies in schizophrenia between 1998 and 2011. Meta-analysis of studies reporting on the effects of antipsychotics on fractional anisotropy (FA).
Results: There is significant heterogeneity of DTI findings in schizophrenia. DTI mostly points towards abnormalities in callosal, fronto-temporal, fronto-parietal and temporo-occipital WM tracts as well as projection fibers and cerebellar WM. Younger age and earlier age at onset of schizophrenia are possibly associated with differential pattern of WM abnormalities. Antipsychotic medication treatment also seems to have an effect on WM FA.
Conclusion: Sample characteristics, including age, age at onset, duration of illness and antipsychotic medication treatment may explain to an extent the heterogeneity of DTI findings in schizophrenia. Our current knowledge is limited by the lack of longitudinal studies of patients at different stages of the illness.
Policy of full disclosure: No conflict of interest.

S-34-002
Methods of white matter tracts integrity investigation

R. Mandl (University Medical Centrum, Utrecht, Netherlands)

Abstract: Diffusion tensor imaging (DTI) [1] is a magnetic resonance imaging (MRI) technique that measures the diffusion profile of water molecules in brain tissue allowing us to non-invasively probe the microstructure of the human brain in vivo. This information can be used to reconstruct the major white matter fiber bundles but is also considered an index of fiber integrity when studying diseases like schizophrenia. Different methods are used to analyze DTI data—each with their own (dis)advantages [2]. Frequently used methods include manually defined region of interest (ROI) methods, voxel-based analysis and tract-based analysis. These methods basically differ in at what level (i.e. ROIs, voxels, reconstructed fiber tracts) groups (patients/controls) are compared. However, they have in common that they do not take relations between different brain regions into account. Network-based analysis is a method that does take these relations into account [3]. It represents the relations by graphs and then uses measures from graph theory to study these relations. DTI can also be combined with other MRI techniques (e.g. magnetization transfer imaging, MR spectroscopy) or even other imaging modalities (e.g. Positron Emission Tomography, Single Photon Emission Tomography) [4]. Such combinations provide complementary information that can help us to better understand the mechanisms that underpin schizophrenia. In this presentation I will give an overview of the various methods and discuss their possibilities.
References:
[1] Bihan DL, ed (1995) Diffusion and Perfusion Magnetic Resonance Imaging.
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[3] van den Heuvel MP, et al. (2010) Aberrant frontal and temporal complex network structure in schizophrenia: a graph theoretical analysis. J Neurosci 30:15915–15926.
[4] Mandl RCW, et al. (2010) Tract-based analysis of magnetization transfer ratio and diffusion tensor imaging of the frontal and fronto-temporal connections in schizophrenia. Schizophr Bull 36:778–787.
Policy of full disclosure: None.

S-34-003
Microstructural alterations of the acurate fasciculus are associated with auditory verbal hallucinations in psychotic and in non-psychotic individuals

A. de Weijer (University Medical Center Utrecht, Neuroimaging Research Group, Utrecht, Netherlands)

Objective: The pathophysiology of auditory verbal hallucinations (AVH) is still unclear. Cognitive as well as electrophysiological studies indicate that a defect in sensory feedback (corollary discharge) may contribute to the experience of AVH. This could result from disruption of the arcuate fasciculus, the major tract connecting frontal and temporo-parietal language areas. Previous diffusion tensor imaging studies indeed demonstrated abnormalities of this tract in schizophrenia patients with AVH. It is, however, difficult to disentangle specific associations with AVH in this patient group as many other factors, such as other positive and negative symptoms, medication or halted education could likewise have affected tract integrity. We therefore investigated AVH in relative isolation and studied a group of non-psychotic individuals with AVH as well as patients with AVH and non-hallucinating matched controls.
Methods: We compared tract integrity of the arcuate fasiculus and of three other control fibertracts, between 35 non-psychotic individuals with AVH, 35 schizophrenia patients with AVH and 36 controls using diffusion tensor imaging and magnetic transfer imaging.
Results: Both groups with AVH showed an increase in magnetic transfer ratio (MTR) in the arcuate fasciculus, but not in the other control tracts. In addition, a general decrease in fractional anisotropy

(FA) was observed for almost all bundles in the patient group, but not in the non-psychotic individuals with AVH.
Conclusion: As increased MTR in the arcuate fasciculus was present in both groups with hallucinations, a specific association with AVH seems plausible. Decreases in FA, on the other hand, seem to be related to other disease processes of schizophrenia.
Policy of full disclosure: None.

S-34-004
Multimodal analysis (DTI, fMRI) neurobiological substrates of neurological soft signs in schizophrenia

T. Kasparek (University Hospital Brno Psychiatry, Czech Republic), J. Rehulová, M. Kerkovský, P. Bednarík

Objective: To assess if the neurological signs (NS), such as inadequate capacity to sequence movements correctly, result from abnormal integration of brain function and connectivity.
Methods: 27 schizophrenia patients (SCH) and 27 age and sex matched healthy subjects (HS) were examined using functional magnetic resonance (fMRI) and diffusion tensor imaging (DTI). Functional integration during modified sequential finger tapping and finger opposition tasks was analyzed using Independent Component Analysis. Brain connectivity analysis was performed by Tract-based Spatial Statistics of fractional anisotropy images. The neurological signs were assessed using Neurological Examination Scale. Group differences between SCH and HS and between patients with and without neurological signs were analyzed using nonparametric statistics.
Results: Schizophrenia patients expressed significantly more NS than HS, the most frequent abnormalities were movement sequencing impairments (in 63% of patients). Sensory-motor network was activated during sequencing of movements. There were no group differences in the network activation between SCH and HS. However, patients with movement sequencing abnormalities activated the network significantly less than patients without neurological signs. The TBSS analysis showed reduced fractional anisotropy in many white matter tracts in schizophrenia, including white matter within precentral and postcentral gyrus, and corticospinal tract.
Conclusion: Movement sequencing abnormalities are the most frequent neurological signs in schizophrenia, they are linked to lesser activation of sensory-motor network. Abnormal white matter integrity was seen also in areas that connect individual nodes of the sensory-motor network. Therefore, movement sequencing abnormalities may result from abnormal connectivity of relevant cortical areas.
Policy of full disclosure: Supported by a research grant of the Czech Ministry of Health No. NS9855-4.

W-01 MedicaWiki: a webbased independent evidence based psychopharmacological prescription decision system: decide & prescribe

W-01-001
MedicaWiki: a webbased independent evidence based psychopharmacological prescription decision system "decide & prescribe"

W. Broekema (Symfora groep, Clinical Pharmacy, Amersfoort, The Netherlands)

Objective: Participants in this workshop will

- learn about the motive, history, background and actual developments of MedicaWiki.eu
- learn about the basic principles of a wiki
- learn about more sophisticated wiki plug in applications like Flagged Revisions
- learn about caution areas
- learn about quantifying psychotropic drugs in special caution areas
- learn about calculating drug doses, tapering speeds and switches
- learn about internet regarding MedicaWiki.eu
- actively contribute their opinion in how MedicaWiki.eu should further development

Methods: The whole workshop will be an interactive session. The founder and editor-in-chief of the MedicaWiki.eu (= MW) will start with presenting an introduction about the motive, history and background of the MW. Then the participant gets a view of the front and the backside of the MW. Special topics will be presented and discussed like

- the outcome of requests from participants regarding profiling specific patients with the assistance of the MW. For example which antidepressant do you choose to treat a 33 year old female who is vulnerable for diabetes, who has a prolonged QTc-syndrome and who wants continuing driving her car?
- which definition should cover a specific Caution Area?
- how to cope with the incidence and severity of drug reactions in relation to comorbidity?
- how to calculate drug dosing?
- how to calculate drug switches?
- how to handle the problem of liability?
- how to grow and keep the quality on a high level?
- how to improve usability?
- what benefits the patients? Is this medication safety, efficiency, a sound second opinion and empowerment & adherence?

Finally the future of MW will be discussed.
Results: The participant of the workshop has a good insight in the features, developments and pitfalls of MedicaWiki.eu.
Conclusion: The participant probably will conclude that MedicaWiki.eu is an useful tool that improves medication safety and efficiency on the long run.
Policy of full disclosure: None.

W-02 Past, current and future European Schizophrenia Research Projects

W-02-001
Transition and beyond: findings of the European prediction of psychosis study (EPOS)

S. Ruhrmann (Department of Psychiatry and Psychotherapy, University of Cologne, Cologne, Germany), F. Schultze-Lutter, R. K. Salokangas, D. Linszen, M. Birchwood, G. Juckel, A. Heinz, S. Lewis, A. Morrison, J. Klosterkötter and the EPOS group

Objective: Prevention of psychosis has been identified as one of the most important challenges for psychiatry. Furthermore, it has become clear that prevention should be tailored to the needs of the patients, thus making further progress from a general to an individualized intervention strategy. To achieve this aim, sophisticated multivariate prediction models are required.
Methods: The European Prediction of Psychosis Study (EPOS) was designed as a prospective, naturalistic multicenter project. Funded by the European Commission, the six participating centers (Cologne, Amsterdam, Berlin, Birmingham, Manchester, Turku) followed a

sample of $n = 245$ subjects for 18 months, thereby employing a broad range of parameters related to psychopathology, personality and biographical features, social/vocational functioning, neuropsychology and neurobiology. Furthermore, EPOS was the first study, which investigated both the ultra-high risk (UHR) and the basic symptom (BS) approach simultaneously.
Results: The general 18-month transition rate was 19%; simultaneous appearance of UHR and BS resulted in the highest transition rate. Based on clinical and demographical variables, a prognostic index was developed, which enable a further stratification of risk. The resulting 18-month transition rates ranged from 3.5 to 85.1%. The course of non-converters (NC) is of also of major interest, particularly with regard to preventive interventions and treatment. A detailed analysis revealed that a considerable part of the NC showed no improvement or even worsened, thereby still fulfilling the risk criteria at the end of the study.
Conclusion: The European multicenter approach made it possible that EPOS became one of the worldwide leading studies in this field. The large sample size enabled an innovative approach to estimate the risk of psychosis, combining risk detection and risk stratification. Beyond transition, the course of the at-risk state ranged from (clinical) remissions (at least during the 18-month period) as well as prolonged at-risk states, calling for longer follow-up periods.
Policy of full disclosure: None.

W-02-002
Novel methods leading to new medications in depression and schizophrenia (NEWMEDS)

A. Reichenberg (King's College London, Department Psychosis Studies, London, UK)

Abstract not received in due time.

W-02-003
European Twin Study Network on Schizophrenia (EUTwinsS)

I. Nenadic (Klinik für Psychiatrie und Psychotherapie, Jena, Germany), H. Sauer

Objective: The European Twin Study Network on Schizophrenia (EUTwinsS) is a collaborative, EU-funded project involving 9 partners in 6 European countries (London, Utrecht, Amsterdam, Barcelona, Bonn, Heidelberg, Szeged, Zurich, and Jena). It focuses on twin research as a unique opportunity to assess genetic versus non-genetic contributions to schizophrenia. In this presentation, we will outline the rationale and implementation of the project, as well as initial results.
Methods: EUTwinsS has focused on five major methodological branches: neuroimaging, genetics, neuropsychology, neurophysiology, and twin research methodology/statistical modelling. As part of the EU's FP6, it was implemented as a research training network (RTN), including a strong educational component for junior researchers recruited as Marie Curie fellows of this RTN.
Results: EUTwinsS has made use of recruitment of twins in four of its centres, and together with data from previous collaborations this has formed the largest European database of twins with schizophrenia. From this, several studies and novel findings have emerged. This includes neuroimaging analyses on the regionally differences of genetic contributions on cortical thickness and gyrification. Neuropsychological projects have identified specific cognitive functions to share common genetic bases with schizophrenia and IQ, resp. Genetic approaches include differences in the expression profiles of genes in discordant monozygotic twins.
Conclusion: EUTwinsS has built on and strengthened intra-European collaboration on twin research in schizophrenia. Similar models might serve as platforms to establish co-operations making use of the resources within the European Research Area.
Policy of full disclosure: Work relating to this project has been funded by the European Union (FP6, EUTwinsS RTN).

W-02-004
Genomic variations underlying common behavior diseases and cognition trait in human populations (ADAMS)

A. Papassotiropoulos (University of Basel, Basel, Switzerland)

Abstract: The subject of the project is the search and analysis of genomic variations related to Alzheimer's disease (AD), alcoholism and schizophrenia—wide-spread diseases in human populations. Though a number of genomic variations possibly associated with AD, alcoholism and schizophrenia have been described for European populations, The significance of the putatively associated alleles, genetic background as well as the role of environmental factors is still poorly understood. Within the framework of this project we extend the studies of genomic variations underlying these diseases by performing genome-wide association analyses in cohorts of patients and healthy individuals from several ethnic populations of Europe and Russia. Genetic factors related to cognitive endophenotypes are also studied. Candidate regions, both newly found and reported previously for these diseases will be additionally analyzed by sequencing. Such large scale population studies combined with deep analysis of particular genes and genomic regions will allow us to uncover some biological underpinnings of these multifactorial diseases. The comparison of several ethnic cohorts (different populations from Russia and Central/Western and Southern Europe) will also help to elucidate the influence of genetic background and environmental factors on the etiology of neuropsychiatric diseases.
Policy of full disclosure: None.

W-03 Writing manuscripts for publication in English language scientific journals

W-03-001
Writing manuscripts for publication in English language scientific journals

S. Hodgins (Department of Psychiatry, Heidelberg University, Germany; Département de Psychiatrie, Université de Montreal, Canada; Institute of Psychiatry King's College, London, UK)

Abstract: The final phase of any research project is having the results published in one or more peer-reviewed journals. The higher the impact factor is, the greater the challenge to the researchers. Publishing in English adds to the challenge for researchers with another first language. The skills for successful publishing differ from those necessary in other phases of a research project. This brief (3 h) workshop will describe the steps and the skills necessary to publish in a high impact, English language scientific journal. The workshop assumes that the research project is methodologically rigorous, advances knowledge, and has been conducted ethically. The workshop will cover the following topics: (1) factors to consider when dividing up results to be reported in different papers; (2) specifying the goal and objectives of the paper; (3) the structure of a scientific paper; (4) the content of each section of the paper; (5) writing style

and terms to use and not use; (6) criteria to use when selecting a journal for submission; (7) criteria for authorship and order of authors; (8) using a rejection to improve the manuscript; and (9) responding to reviewers' comments and revising a manuscript.
Policy of full disclosure: None.

W-04 European practice guidelines: a need for harmonisation?

W-04-001
ADAPTE: a systematic approach to cross-cultural and cross-organisational guideline adaptation

J. A. Swinkels (University of Amsterdam, Amsterdam, The Netherlands)

Objective: When to use ADAPTE or when to do it all over again? ADAPTE is a systematic approach to the endorsement and/or modification of a guideline(s) produced in one cultural and organizational setting for application in a different context. Adaptation may be used as an alternative to de novo guideline development (see http://www.adapte.org).
Methods: Experiences from adapting the schizophrenia guidelines from NICE.
Results: It's not an easy task using ADAPTE. Even for the pharmacology of the disorder it's usefull to be a GIN member, an international organisation representing 48 countries of guideline developpers to promote cooperation i.e. exchange of databases.
Conclusion: It's possible to adapte with ADAPTE but an international accreditation of the evidence based guideline development method and being a member of GIN for the database exchange can help. A European systematic cooperation with the Cochrane collaboration could help to standardize more the interpretation of the data from the search of the literature for evidence based guideline development. More standardisation will help!
Policy of full disclosure: None.

W-04-002
Recommendations on pharmacological treatment: recent updates

W. Gaebel (Department of Psychiatry and Psychotherapy, LVR-Klinikum Düsseldorf, Medical Faculty, Heinrich-Heine-University, Duesseldorf, Germany)

Objective: Evidence-based guidelines are a major tool for quality improvement and assurance in health care. With respect to existing disparities in quality of mental health care between countries in Europe as well, pan-European guidelines might also contribute to overcome qualitative inadequacies. Since different national and international guidelines for schizophrenia exist, it should be examined to benefit from available evidence-based recommendations. However, guideline quality itself varies and needs to be considered.
Methods: Based on a former review on guidelines for schizophrenia (Gaebel et al. 2005) qualitatively sound guidelines were examined for recent updates and analyzed regarding methodological quality with the AGREE-instrument. In addition, clinical content was compared regarding seven core topics in schizophrenia treatment decisions.
Results: Five guidelines have been identified and quality on average is good, with highest AGREE-scores for the updated NICE guideline. Revision of the German guideline resulted in noticeable quality improvements. Regarding content, recommendations largely correspond in five areas across guidelines (drug dose, drug application, non-response/treatment resistance, long-term drug treatment strategies, psychosocial interventions). However, discrepancies or vagueness exist in two areas due to newly emerging (drug choice) or still restricted evidence (duration of antipsychotic treatment).
Conclusion: There are increasing efforts to develop guidelines with improved and sound quality, as recently again emphasized and elaborated by the US institute of Medicine (IOM 2011). Also, there is a need to harmonize and improve health care quality across countries. Since many formal and content-related issues are 'universal', development of trans-national guidelines seems indicated. Nevertheless, core recommendations should be adapted to regional conditions using available tools for adaptation.
References:
Gaebel et al. (2005): Schizophrenia practice guidelines: international survey and comparison. BJP, 248-55 Gaebel et al. (in press): Schizophrenia guidelines across the world: a selective review and comparison. Int Rev Psychiatry.
IOM (2011) Clinical Practice Guidelines We Can Trust. NAP
Policy of full disclosure: Personal financial relationship 2010 until now: Wolfgang Gaebel has received symposia support from Janssen-Cilag GmbH, Neuss, Lilly Deutschland GmbH, Bad Homburg and Servier, Munich. He is a member of the Scientific Advisory Board of Lundbeck International Neuroscience Foundation (LINF), Denmark.

W-04-003
NICE recommendations on psychological treatments: recent updates

E. Kuipers (Department of Psychology, King's College London, Institute of Psychiatry, London, UK)

Abstract: I was Chair of the NICE Guideline for Schizophrenia Update Group (2009). The evidence base of randomised controlled trials (RCTs) for psychological treatments continues to show that both Cognitive Behavioural Therapy (CBTp) and Family Intervention for psychosis (FIp) change outcomes, and both remain recommended. In a pilot piece of work in the South London & Maudsley (SLAM) NHS Foundation Trust, UK, Professor Philippa Garety, Dr Suzanne Jolley and myself have looked at how to begin to offer increased access to these therapies.
This work has revealed a number of challenges. For instance—a misunderstanding of who can be offered therapy, what therapy consists of, and then of how to identify, to train and supervise appropriate therapists. The suggestion is put forward that we need an IAPT (Improving Access to Psychological Therapies) for psychosis. The solutions we are using in SLAM will be noted, as well as the difficulties we are still facing.
Reference: NCCMH Schizophrenia—The NICE Guideline on core interventions in the treatment and management of schizophrenia in adults in primary and secondary care. Updated Edition 2010. Published by The British Psychological Society and The Royal College of Psychiatrists. Professor Elizabeth Kuipers, Chair, Guideline Development Group.
Policy of full disclosure: None.

W-04-004
How much pan: European consensus is necessary?

K. Wahlbeck (National Institute for Health and Welfare (THL), Helsinki, Finland)

Abstract: Service users, policy makers and the general public increasingly demand that mental health care should provide good "value for money". When developing accessible, affordable and effective mental health services, exchange of data between countries is an important moving force towards better mental health care.
Nowadays each European national psychiatric association tries to produce its own guidelines. In an assessment of European psychiatric guidelines ($n = 61$), the general quality of the guidelines was medium grade (Stiegler et al. 2005). The recommendations of only about half of the assessed guidelines could be considered to be evidence-based. The methodological quality of many schizophrenia guidelines was at best moderate (Gaebel et al. 2005).
National particularities were very rarely considered by European psychiatric guidelines (18%), and then only very vaguely (Stiegler et al. 2005). This is not surprising, since the evidence available for guidelines is almost always of an international nature.
The need for valid and comparable mental health services benchmarking is today addressed only by single initiatives, such as the OECD work to establish quality indicators for mental health care. Also the five Nordic countries have established a common set of mental health care quality indicators. Real leadership in developing harmonized mental health guidelines and quality criteria across Europe is lacking. Given the enormous expenditure of time and money that is necessary to develop a methodologically sound guideline, a European Guidelines Centre should be established. It could then be the task of the national associations to adapt guidelines to the specific conditions of their own countries. Such a procedure could improve the quality of most national guidelines and foster the ongoing standardisation of European medical care.
Mental health issues, which often are neglected and forgotten due to lack of awareness and stigma, need strong European institutions. A European Centre for Mental Health Care Guidelines could be such a strong institution and a flagship for promoting awareness about the importance of mental health and mental health care.
References:
Gaebel, W., Weinmann, S., Sartorius, N., et al. Schizophrenia practice guidelines: international survey and comparison. Br J Psychiatry 187:248–55, 2005.
Stiegler M, Rummel C, Wahlbeck K, Kissling W, Leucht S. European psychiatric treatment guidelines: is the glass half full or half empty? Eur Psychiatry. 20(8):554–8, 2005.
Policy of full disclosure: None.

O-01 Comorbidity

O-01-001
Is it time to consider comorbid substance abuse in schizophrenia as a dimension and indication for new antipsychotic drug development

A. G. Awad (University of Toronto Department of Psychiatry, Canada)

Objective: To present evidence for considering co-morbid substance abuse in schizophrenia as possibly a dimension of the disease process itself and as such as an indication for development of new antipsychotics or add-on medications to antipsychotics Comorbid drug abuse in schizophrenia has been consistently reported as high with estimates ranging between 10 and 70%. The development of comorbid addictive state in schizophrenia is possibly multifactorial in origin, yet recent research assigned a significant neurobiological role in its genesis and which includes abnormalities in hippocampal/cortical functioning which mediate reward and reinforcement behavior.
Methods: Review of the recent neurobiology literature about addictive states in schizophrenia as well as author's research and expertise in the area.
Results: Recent preliminary data suggest that the vulnerability of patients with schizophrenia to substance use disorders may be a primary disease symptom. Historically the management of comorbid substance abuse in schizophrenia relies on the use of antipsychotic medications. Recent data raises the concern about whether first generation antipsychotic in long term use can conversely lead to enhancement of the substance's reinforcing properties. Recent reports have assigned a favorable outcome to Clozapine and second generation antipsychotics pointing to a possible differential role for various antipsychotics.
Conclusion: In view of the high prevalence of comorbid drug abuse in schizophrenia, its impact on outcome and the recent emerging neurobiological information, it is our contention that comorbid drug abuse possibly constitutes a dimension by itself and deserves to receive an indication in the development of new antipsychotics similar to negative symptoms or cognitive deficits.
Policy of full disclosure: None.

O-01-002
Cardiovascular risk factors in patients treated with antipsychotics: A follow-up study

P. Steylen (Vincent van Gogh Institute Clinical Research, Venray, Netherlands), F. van der Heijden, W. Verhoeven

Objective: Patients with severe mental illnesses (SMI) have a reduced life expectancy compared to the general population. Most common causes of death are cardiovascular diseases. Patients with SMI are more likely to be overweight and to have hypertension, dyslipidemia, hyperglycemia and diabetes mellitus. Antipsychotic medication is known to induce or worsen such risk factors. The aim of this study was to assess the treatment regiments for metabolic cardiovascular risk factors at baseline and after 1 year in patients treated with antipsychotics.
Methods: A health monitor was introduced as a screening instrument in a schizophrenia outpatient treatment and recovery program (F-ACT). Patients were screened at least once yearly. Assessment included physical examination and laboratory tests, demographics, DSM-IV diagnoses, remission-criteria, social functioning, use of medication, and substance abuse.
Results: Over a period of 30 months (2008–2010) 515 patients treated with antipsychotics were included. From this group, 180 patients were screened at baseline and after 1 year. Percentages of cardiovascular risk factors at baseline versus follow-up were: abdominal obesity 62% versus 65%, hypertension 63% versus 54%, dyslipidemia 83% versus 89%, hyperglycemia 24% versus 17% and diabetes mellitus 11% versus 12%. Rates of non-treatment for metabolic cardiovascular comorbidity at baseline versus follow-up were: 86% versus 81% for dyslipidemia, 81% versus 76% for hypertension and 50% versus 50% for diabetes mellitus.
Conclusion: Metabolic cardiovascular risk factors are highly prevalent in patients treated with antipsychotics and a substantial number of patients is not treated adequately for cardiovascular comorbidity. Therefore, close collaboration between psychiatrists and general practicioner and/or somatic medical specialists is warranted.
Policy of full disclosure: None.

O-01-003
Relationship between functionality and metabolic syndrome in schizophrenia

J. M. Pelayo Teran (CSM Arriondas Psychiatryf, Madrid, Spain), Y. Zapico-Merayo, P. Trabajo-Vega, M. M. Martínez-Pérez, J. Martínez-Diez, C. Fernández-Borregan, M. J. Castelao-Lorenzo, P. Álverez-Tejeiro

Objective: The objective was to investigate the relationship between functionality and metabolic risk factors. The hypothesis was that patients with a lower function would present a higher degree of metabolic risk.
Methods: The study was part of a longitudinal research focused in physical health of patients treated with antipsychotic medication, performed in the outpatient clinics of El Bierzo (150,000 inhabitants) and Arriondas (50,000 inhabitants), Spain. 65 patients (42 males and 23 females) with a DSM-IV diagnosis of schizophrenia ($n = 47$), schizoaffective disorder ($n = 7$) or related psychoses ($n = 9$) were included. The Global Impression—severity scale (CGI) and the Personal and Social Performance Scale (PSP), Height, weight, abdominal perimeter and blood pressure were assessed. Fasting blood samples were extracted to evaluate glucose, LDL and HDL Cholesterol and Triglycerides. Metabolic syndrome was defined according to NCEP criteria. Relationships between PSP dimensions and metabolic risk factors were assessed by partial correlations, adjusted by gender and age.
Results: 37.7% of the patients fulfill metabolic syndrome criteria. 73.0% showed incremented abdominal perimeters, 15.9% increased blood pressures, 26.7% hyperglycemia, 47.5% hypertriglyceridemia and 46.7% low HDL-c levels. Glycemia was associated to Selfcare ($r = 0.390$; $P = 0.006$) Social Activity ($r = 0.322$; $P = 0.024$), Disturbing Behaviours ($r = 0.468$; $P = 0.001$) dimensions and total PSP ($r = -0.332$; $P = 0.020$). Triglyceridemia was associated to Social Activity ($r = 0.320$; $P = 0.025$), Personal Relationship ($r = 0.304$; $P = 0.034$) dimensions and total PSP ($r = -0.344$; $P = 0.015$). Abdominal Perimeter was related to Social Activity ($r = 0.326$; $P = 0.022$). Selfcare dimension was related to the number of altered factors ($r = 0.324$; $P = 0.017$). ICG score was not related to any factor (Fig. 1).
Conclusion: Metabolic syndrome is highly frequent in patients with schizophrenia and other psychosis. Metabolic factors were associated with functionality dimensions. Evaluation and treatment of functionality deficits may lead to a better treatment and prevention of metabolic risk.
Policy of full disclosure: None.

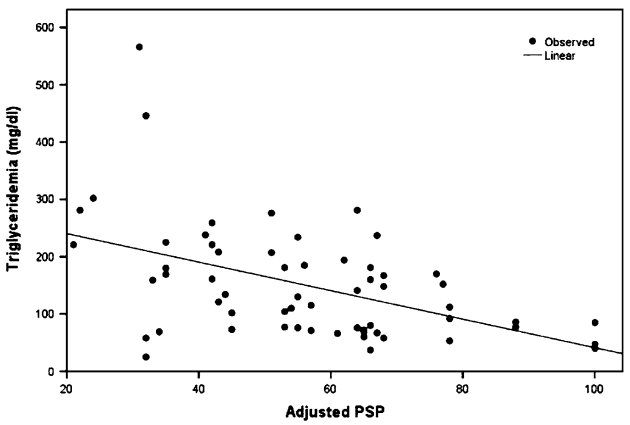


Fig. 1 Relationship between PSP total score (adjusted PSP) and fasting triglyceridemia

O-01-004
Long term maintenance of weight loss in patients with severe mental illness through a behavioral programme in the UK. Results at 10 years of follow up

J. Pendlebury (Ramsgate House, Manchester, UK), R. Holt, H. Wildgust, C. Bushe

Objective: The prevalence of obesity is approximately two-fold higher in people with severe mental illness (SMI) than in the general population. Many patients treated with antipsychotics have reported clinically significant weight gain.
Methods: A weight management clinic started 10 years ago (2000) and accepted self-referred patients only. The clinic is staffed by a community mental health nurse and an occupational therapist. The programme runs an 8-week rotational topic cycle with weekly 1-h group sessions.
Results: Since May 2000, 120 patients (52 men, 68 women) have enrolled providing a total of 153 patient episodes. Mean (±standard error) baseline weight was 90.5 ± 1.6 kg (BMI 32.1 ± 0.5 kg/m2). Mean number of sessions attended was 67 (median 45; range 1–402). 80% of patients attended continuously for >8 weeks and 58% for >6 months. There was a progressive statistically significant reduction in mean weight and BMI throughout attendance at the clinic with no suggestion of a plateau. Weight loss occurred in 93% of patients, weight maintenance 4%, and weight increase 3% at final visit. Mean final weight loss was 7.6 ± 0.6 kg (range −43.7 to +17.0 kg). Percentage weight change was similar for men and women. Weight loss was correlated only with the number of sessions attended ($r = 0.44$, $P < 0.0001$). On average, patients lost 0.43 ± 0.08 kg per session. Of patients attending for >2 years ($n = 45$), 73% had lost >7% body weight or had BMI < 25 kg/m^2. The prevalence of obesity (≥30 kg/m^2) fell from 61% at baseline to 39% at final visit.
*Conclusion: T*he sole significant predictor of weight loss was the number of sessions attended. Patients continuing to attend the weight clinic lost weight incrementally with clinically significant shifts in BMI over time. Interpretation is limited to naturalistic data from a well-motivated cohort.
Policy of full disclosure: CB is an employee of Eli Lilly. This study has received no funding from Eli Lilly and no author has received any payment. Attendance of JP has been funded by Eli Lilly.

O-01-005
Cancer co-mortality profile in schizophrenia and psychotic disorders

V. Ajdacic-Gross (Psychiatric University Hospital Social Psychiatry, Zurich, Switzerland), A. Tschopp, M. Bopp, F. Gutzwiller, W. Rössler

Objective: This study explored the co-mortality pattern of cancer and schizophrenia/psychotic disorders. It investigated whether their cancer profile diverges from the profile of cancer deaths in the general population.
Methods: The analysis covered Swiss mortality data from a 39-year period (1969–2007). Due to the registration priority system, schizophrenia and other psychotic disorders have been typically recorded as additional causes of death and cancer as the main cause of death. The comparisons were confined to the most frequent cancers. We developed a two-step analysis design, thereby applying a case–control approach within a bootstrapping procedure. The case–control approach served to account for the demographic factors, which interfere differently in each cause of death. In the second step we reweighted the figures in order to account for the co-registration

practice in specific cancers. Odds-ratios (OR) were used as statistical measures.
Results: Cancers with deviant ORs included stomach cancer (1.6; 2.15 after reweighing), lung cancer (0.81; 0.51 after reweighing), skin cancer (1.38; 1.7 after reweighing) and breast cancer (1.56; 1.46 after reweighing).
Conclusion: The cancer profile in schizophrenia patients diverges from the profile in the general population. Particularly in lung cancer, the results are paradoxical in view of the smoking habits of schizophrenia patients—an issue, which has been often debated but never satisfactorily explained.
Policy of full disclosure: None.

O-01-006
Panic attacks, alexithymia and hallucinations in schizophrenia

S. Vanheule (Gent University FPPW, Gent, Belgium), R. Kessels, P. Naert, S. Van Geert

Objective: Panic attacks occur frequently in schizophrenic patients. Evidence indicates that comorbid panic symptoms may be related to positive symptoms (Ulas et al. 2007). Previous studies on alexithymia in schizophrenia indicate problems with identifying feelings (van't Wout et al. 2007). However, it still remains unclear how alexithymia interacts with specific symptoms of schizophrenia. In this study, we examine the relationship between panic attacks, the emotion-regulation factor alexithymia and different aspects of hallucinations as measured with Beliefs About Voices Questionnaire (BAVQ-R; Chadwick, Lees, & Birchwood 2000; subscales: malevolence, benevolence, omnipotence, resistance, engagement) and Psychotic Rating Scales (PSYRATS; Haddock 1994).
Methods: 47 inpatients diagnosed with schizophrenia and experiencing auditory hallucinations were interviewed with PSYRATS. Patients filled in BAVQ-R and Toronto Alexithymia Scale (TAS-20; Bagby, Taylor, & Parker 1994). Panic attacks were measured according to DSM-IV-criteria. Analyses of variance with recent panic attacks as independent variable and subscales of BAVQ-R and PSYRATS auditory hallucination rating scale (AHRS), and a logistic regression were performed.
Results: Patients with panic attacks have significant higher scores on TAS difficulties identifying feelings subscale ($P = 0.005$) and total TAS-score ($P = 0.03$), on several PSYRATS AHRS items and on BAVQ-R resistance ($P = 0.04$). Patients without panic attacks have significant higher scores on BAVQ-R engagement ($P = 0.04$). There is no significant relationship between TAS-subscales and gender. Binary logistic regression revealed a significant relationship between PSYRATS AHRS items and panic attacks.
Conclusion: This study supports hypotheses about links between panic attacks and alexithymia, and between panic attacks and different aspects of hallucinations. These links with panic attacks relate for both alexithymia and hallucinations to the same aspects.
Policy of full disclosure: None.

O-02 Epidemiology and clincal phenotypes

O-02-001
COMT genotype and poor cognition is associated with a negative/disorganised schizophrenia subtype

M. Green (University of New South Wales School of Psychiatry, Faculty of Medicine, Darlinghurst, Australia), M. Dragovic, A. Jablensky, M. Cairns, P. Tooney, R. Scott, C. Loughland, V. J. Carr

Objective: Progress in the genetics of schizophrenia has been limited by a poorly defined phenotype. We sought to delineate valid clinical subtypes using Grade of Membership analyses, and to investigate the role of candidate genotype and cognitive performance in predicting clinical subgroup membership.
Methods: Grade of Membership (GoM) analysis was applied to lifetime clinical symptom data derived from the Diagnostic Interview for Psychosis (DIP) for 617 patients diagnosed with schizophrenia ($N = 526$) or schizoaffective disorder ($N = 91$) within the Australian Schizophrenia Research Bank. Prediction of group membership in each clinical phenotype was subsequently examined using the Val158Met common variant of the catechol-O-methyl transferase (COMT) gene, and cognitive performance on the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).
Results: The most parsimonious GoM solution yielded 3 Pure Types: Type I ($N = 162$; 26.3%) comprised individuals with a predominance of Schneiderian First Rank Symptoms with florid psychotic symptoms, including auditory hallucinations; Type II ($N = 338$; 54.8%) comprised the majority of the sample, with persecutory phenomena including delusions and hallucinations; Type III ($N = 117$; 19%) comprised individuals with negative and disorganised symptoms. The three GoM-derived phenotypes did not differ significantly from each other in cognitive performance alone, but were all significantly impaired compared to healthy controls ($N = 659$). However, using multinomial logistic regression, a combination of Val (homozygous or carrier) genotypes and poor cognitive performance significantly predicted membership of the Negative/Disorganised subtype III.
Conclusion: The power of genetic investigations in schizophrenia may be increased with the application of novel statistical procedures to derive naturally occurring clinical phenotypes.
Policy of full disclosure: This research was supported by NHMRC Enabling Grant 386500 (CI Carr) and NHMRC Project Grant 630471 (CI Green). MJG is supported by the Australian Research Council Future Fellowship FT0991511. All authors declare no conflicts of interest.

O-02-002
Psychosis dimensions and corollary scales in young and middle-aged adults in Zurich

V. Ajdacic-Gross (Psychiatric University Hospital Social Psychiatry, Zurich, Switzerland), M. P. Hengartner, K. Landolt, S. A. Rodgers, M. Müller, I. Warnke, W. Kawohl, W. Rössler

Objective: There are three corollary approaches in epidemiological surveys to disentangle different psychosis dimensions: comorbidity, corollary scales and risk factors. This study examines the figurations of associations between psychotic symptoms and corollary scales such as the Scale for Assessing Interpersonal Ambiguity (SIA), the Structured Interview for Assessing Perceptual Anomalies (SIAPA), the Creative Experiences Questionnaire (CEQ), the Brief Core Schema Scale (BCSS) by means of factor analysis and co-occurence network analysis.
Methods: The data is derived from the ongoing epidemiologic survey of the Zurich Program for Sustainable Development of Mental Health Services (ZInEP). The survey is geared to the longitudinal Zurich Study and includes adults aged 20–40 years. The participants completed a screening interview, a personal interview and series of questionnaires presented as checklists. Psychotic symptoms were assessed by two subscales of the Symptom Checklist 90-R (SCL-90-R), the brief version of the Schizotypal Personality Questionnaire (SPQ-B), the Paranoia Checklist (PC), and by subscales of the Assessment of DSM-IV Personality Disorders (ADP-IV) questionnaire. Factor analysis was used to derive the basic dimensions in the

data, while co-occurrence network analysis deserved to exploit the multitude of association patterns within and beyond the factors.
Results: The preliminary results from the factor analyses indicate two major psychosis dimensions, one related to social perceptions and the other related to other perceptions. In co-occurence network analysis the BCSS are mainly configured with the former dimension, whereas SIA, SIAPA and CEQ are typically configured with the latter dimension.
Conclusion: Corollary scales provide an interesting supplementary approach to better understand the heterogeneity of psychosis.
Policy of full disclosure: None.

O-02-003
Neurocognitive features in subgroups of bipolar disorder

S. R. Aminoff (Psychosis Research Unit (TOP) OUS, Oslo, Norway), T. Hellvin, T. V. Lagerberg, A. O. Berg, O. A. Andreassen, I. Melle

Objective: To: (1) Examine the overlap for clinically important subgroups of DSM-IV bipolar disorders (BD): BD type I or II, history of psychosis, presenting polarity and age at onset, and (2) examine which of these subgroups differentiate best regarding neurocognitive measures.
Methods: A total of 199 patients with BD type I (BDI) (64%) or BD type II (BDII) (36%) were characterized by clinical and neurocognitive features. We used multivariate regression analyses to assess relationships between neurocognitive variables and subgroups.
Results: The distribution of subgroups were as follows: History of psychosis 64%; depression as presenting polarity 59%; early—61%, mid—25%, and late—onset 14%. There were significant overlaps between having a BDI diagnosis and history of psychosis, and between having a depressive presenting episode and early onset. The BDI diagnosis, history of psychosis and elevated presenting polarity appear to capture some common aspects of an underlying phenomenon related to impairments in verbal memory, where elevated presenting polarity explains most of the variance. History of psychosis and BDI are related to impairment in semantic fluency, with history of psychosis explaining most of the variance.
Conclusion: Poor performance in primarily verbal memory seems associated with an elevated presenting polarity and poor performance in primarily semantic fluency with a history of psychosis.
Policy of full disclosure: None.

O-02-004
Schizophrenia and autism: overlap and difference

M. Fitzgerald (Dept of Psychiatry, Trinity College, Dublin, Ireland)

Objective: This paper aims to examine the overlap and differences between Schizophrenia and Autistic conditions which were seen in the past as separate categories.
Methods: The method of this paper will include clinical features, developmental histories, genetic findings, brain findings and treatment approaches.
Results: Results will show considerable overlap including Bleuler's four key symptoms of Schizophrenia, as well as language, social interactions, non-verbal deficits, genetic overlaps, some overlap in neuro-imaging and treatment. Unique features also occur in the clinical area—more bizarre delusions in Schizophrenia and less severe Theory of Mind Difficulties in Schizophrenia, Neuro-Imaging Differences, Age of Onset Differences. Common and different aetiologies will also be discussed.
Policy of full disclosure: None.

O-02-005
Midlife progression and its clinical correlates in schizophrenia: a 43-year follow-up in the Northern Finland 1966 Birth Cohort

M. Isohanni (University of Oulu Psychiatry, Finland), E. Jääskeläinen, A. Alaräisänen, I. Isohanni, J. Miettunen

Objective: Schizophrenia usually progresses in midlife from age 30 to 50 years Population based studies have provided important insights into these developmental trajectories. We analyzed this progression and its translational correlates in key areas: brain structure and function, cognition, education, comorbidity and clinical outcomes.
Methods: Northern Finland 1966 Birth Cohort ($N = 12058$) were followed serially from mid-pregnancy until age 34 and 43, with register data on 120 schizophrenic psychoses at age 34 and 194 (1.8% of the total sample) at age 43. Structural and functional MRI, cognitive, and clinical analyses were performed in field survey at ages 34 (73 schizophrenic psychoses and 104 controls) and at ages 43 (60 schizophrenic psychoses and 170 controls); 44 cases and 77 controls participated in both surveys.
Results: During the midlife, brain matter deficits, cognitive decline, excess somatic comorbidity and mortality were found. Gray and white matter deficits were associated with duration of illness, suggesting progressive brain abnormalities. Recovery is uncommon and outcomes relatively poor.
Conclusion: A deteriorating course is common in midlife. Enduring adverse consequences during midlife reduce adult well-being and creativity typical to this epoch. The main clinical conclusions were: schizophrenia diagnosis is often delayed and not accurate; unwanted pregnancy is more common among parents with psychosis and prevention of unwanted pregnancy is important in such families; metabolic problems start at age 30s but adverse clinical manifestations later and there exist a window for intervention; excess mortality mainly due to suicide is clinical reality in schizophrenia and high premorbid intellectual performance elevates suicide risk.
Policy of full disclosure: None.

O-02-006
What is the standard of living among clients in community early intervention programs? Data from the Matryoshka Project

C. Cheng (First Place Clinic, Thunder Bay, Canada), C. S. Dewa, L. Trojanowski, D. Loong

Objective: This presentation considers the standard of living of early intervention psychosis (EIP) program clients and the opportunities such as employment and education to raise their standard of living. Can early intervention services help to improve their standard of living?
Methods: In 2004/2005, the government of the province of Ontario in Canada invested new funds in community mental health, including early intervention for psychosis programs. The Matryoshka Project was a 4-year multi-site project looking at specialized community mental health programs, examining the effect of the Government's new investments on the continuity of care experienced by clients of the mental health system. The Project's sites were in rural and community settings. Quantitative interviews were completed of clients and case managers in three waves, each winter between 2005 and 2008.
Results: 29% of clients are unattached and 76% are living in low income. The median proportion of income spent on shelter is 48%. Nearly a quarter of the clients indicated they felt distressed about staying in their current residence long-term. Clients living in low income are forced to make choices among shelter, food, clothing and

transportation. Unemployment rates are 31%. 31% do not have a high school diploma and 80% are not continuing their education.
Conclusion: A large proportion of clients are at risk of living in low income. A key risk factors was being unattached. Clients living in low income have a low standard of living and quality of life. This presentation will discuss the implication that few clients living in low income have opportunities to raise their standard of living. Further, this presentation will discuss whether early intervention services change their clients' standard of living or improve their continuity of care?
Policy of full disclosure: None.

O-03 Early Stages of Schizophrenia

O-03-001
The period of prodromal symptoms to acute phase of illness: untreated schizophrenia

G. Bogojevic (Special Prison Hospital Acute psychiatry, Belgrade, Serbia), L. Žiravac

Objective: Schizophrenia occurs over a long period of time, and to the appearance of the typical clinical manifestation passes many years. In the period of gradual development of symptoms person and its surroundings are hoping a gradual recovery. They feel some discomfort at the thought of contact with a psychiatrist. Recent studies show that the prodrome phase is preferred time frame to modify the course of the disease and prevent chronicity.
Methods: This retrospective study included 102 patients with diagnosis of schizophrenia who committed criminal offense, and were sentenced to security measure of compulsory psychiatric treatment in the period from 2006 to 2010. The research is related to patients and family members in order to determine the time when they first noticed changes in patients. On the other hand, we wanted to know why they did not treat, despite the onset of symptoms. During research, additional parameters were used: (1) age of the patient's at the time of crime, (2) sex, (3) marital status, (4) alcohol or drugs abuse, (5) attempt of suicide, and (6) heredity.
Results: The first changes in behavior were observed on average 11 months (range 6–34 months) prior to any initiatives to help. The patients have a negative self-evaluation, insecurity and low self-esteem, and often experience that people don't understand them. The family is difficult to accept the existence of mental disorders, especially schizophrenia, and therefore it shows greater tolerance for unusual behavior, especially if in the family already existed psychiatric disorders.
Conclusion: Education of the wider population significantly shortens the period to the initiation of treatment. Untreated schizophrenia increases the risk of suicide, substance abuse, aggressive behavior, professional stagnation and problems in the family and society, and a prolonged period without therapy is clearly associated with poorer outcome.
Policy of full disclosure: None.

O-03-002
Duration of untreated psychosis and its relation to outcome in schizophrenia within the Northern Finland 1966 Birth Cohort

M. Penttilä (University of Oulu Psychiatry, Finland), J. Miettunen, H. Koponen, J. Veijola, M. Isohanni, E. Jääskeläinen

Objective: A long duration of untreated psychosis (DUP) seems to relate to poor outcome in schizophrenia especially in the first years of illness. The association between DUP and later course of illness remains unclear. Our aim was to define associations between length of DUP and several dimensions of short- and long-term outcomes in longitudinal sample.
Methods: 89 subjects with schizophrenia from the population based Northern Finland 1966 Birth Cohort were analysed. DUP (mean 200 days. median 89 days) was assessed from medical records. Outcome was measured utilizing variables describing short (under 2 years) and long-term (over 2 years) outcome. Onset age of illness and sex were used as covariates.
Results: Longer DUP predicted longer length of first hospitalization ($P = 0.004$) and increased risk of rehospitalization or relapse ($P = 0.011$) during 2 years. Occupational and symptomatic outcome did not associate with DUP in short- or long-term follow up. Longer DUP associated with occupational recovery in short-term ($P = 0.016$) and decreased probability of disability pension ($P = 0.048$) in long-term follow-up.
Conclusion: Only few outcome variables describing short-term outcome associated to DUP and DUP did not correlate with poor long-term clinical and social outcome at all. Regarding early outcome long DUP may be a modest marker of severe clinical phenotype supporting early intervention, although the long-term benefits of early intervention remain unclear. Long DUP and somewhat poorer outcome in short-term might mediate through brain morphological changes especially in the hippocampus (Penttilä et al. Sch Research 2010;123:145–52) which plays a critical role in cognitive functioning.
Policy of full disclosure: None.

O-03-003
How does childhood adversity impact on schizophrenia? Findings from the Australian Schizophrenia Research Bank (ASRB)

K. McCabe (Schizophrenia Research Inst, Darlinghurst, Australia), E. Maloney, H. Stain, C. Loughland, V. Carr

Objective: Research exploring the aetiology of psychotic disorders increasingly shows a complex interaction between genetic and environmental factors. There is evidence that rates of childhood adversity are greater for people with schizophrenia compared to controls and non-affected relatives (Read et al. 2005). The aims of this study was to compare the rate of childhood adversity in schizophrenia relative to a healthy control group and to examine associations between adverse childhood experiences, illness course as well as personality characteristics and intellectual functioning.
Methods: Data from the Australian Schizophrenia Research Bank (ASRB) (Loughland et al. 2010) were used to examine the rates of childhood adversity of $N = 408$ (mean age = 40.72) people with a confirmed diagnosis of schizophrenia and $N = 267$ (mean age = 39.27) healthy controls. All volunteers completed the Childhood Adversity Questionnaire. In addition, socio-demographic and clinical data was collected including symptom ratings (SANS), personality (IPDE) and IQ tests.
Results: Schizophrenia participants were significantly more likely than controls to report experiencing any childhood adversity (86.8% vs. 69.5%, OR 2.87, 95% CI 1.95–4.23, $P < 0.001$). In addition, schizophrenia participants reported more childhood adversities compared to controls (mean 5.4 vs. 2.3; $t(671) = -10.31$, $P < 0.001$). Endorsement of more cluster A,B personality traits were significantly associated with increased rate of childhood adversity, and premorbid and current IQ were found to be associated with different childhood adversity groupings.
Conclusion: Consistent with previous findings, people with schizophrenia reported the experience of more childhood adversities compared to a control group. Further, several measures of clinical and neurocognitive functioning were found to be associated with specific

childhood adversity groupings. Furthermore personality traits were associated with increased rates of childhood adversity which may have implications for treatment in this group.
Policy of full disclosure: None.

O-03-004
Severe social anxiety in early psychosis is associated with poor premorbid functioning, depression and reduced quality of life

K. L. Romm (Oslo University Hospital Psychosis Research Unit, Norway), I. Melle, C. Thoresen, O. A. Andreassen, J. I. Rossberg

Objective: The main aims of the present study were to test whether first episode psychosis patients with severe social anxiety shows poorer premorbid and current functioning, higher level of current clinical symptoms and better insight. Furthermore, to explore whether social anxiety was associated with reduced quality of life (QoL).
Methods: A sample of 144 individuals was divided into three groups depending upon current level of social anxiety symptoms measured by the Liebowitz social anxiety scale, self-rated version; (1) no social anxiety (no-SaD), (2) clinically relevant symptoms of social anxiety (SaD) and (3) generalized social anxiety symptoms (G-SaD). Analysis of variance was performed including measures of demographic and clinical characteristics. Furthermore, a hierarchical regression analysis was performed to explore possible predictors of QoL.
Results: Seventy-nine per cent had some clinical symptoms of social anxiety, and 68 (47%) met the criteria for G-SaD. There were no significant differences between the three groups on age, education or primary diagnosis. Being in the G-SaD group was associated with poorer premorbid adjustment, lower social functioning, lower self-esteem and higher levels of depression, while there were no group differences in level of psychotic symptoms. Furthermore, the G-SaD group revealed a higher awareness of mental illness (more related to depression and low self-esteem, than to psychotic symptoms), and experienced reduced QoL. The final regression model revealed that higher level of social anxiety predicted poorer QoL even when adjusted for psychotic symptoms and depression.
Conclusion: The current study indicates that those mostly impaired by social anxiety, exhibit distinct clinical patterns and are more impaired on several measures as; poorer premorbid functioning, higher levels of depression and lower self-esteem, despite the fact that there were no significant differences between the groups on measures of psychotic symptoms. Furthermore, social anxiety is an important factor associated with poorer QoL.
Policy of full disclosure: This study was directly supported by Oslo University Hospital and Josef and Haldis Andresens Grant. The TOP study framework is additionally supported by grants from the Norwegian Research Council and South Eastern Norway Health Authority. The funding sources had no further role in study design, in the collection, analysis and interpretation of data, in the writing of the report, or the decision to submit the paper for publication.

O-03-005
Fullness of life reduces risk of psychosis in high-risk patients

R. K. R Salokangas (University of Turku Department of Psychiatry, Finland), M. Heinimaa, S. Luutonen, J. Klosterkötter, S. Ruhrmann, H. Graf von Reventlow, D. Linszen, M. Birchwood

Objective: Follow-up studies have shown that previous successfulness in various areas of life, fullness of life, associates with good outcome in schizophrenia. We hypothesised that fullness of life associates with reduced risk of transition to psychosis (TTP) in patients at high risk of psychosis.
Methods: In the EPOS (European Prediction of Psychosis Study) project, six European outpatient centres in four countries examined 245 young help-seeking patients, who fulfilled the inclusion criteria for clinical risk of psychosis according to the Structured Interview for Prodromal Syndromes (SIPS 3.0) or Bonn Scale for the Assessment of Basic Symptoms—Prediction List basic symptoms (BASBS-P). The baseline interview included an assessment of FoL from the Prognostic Scale (Strauss and Carpenter Schizophr Bull 1977;3:209–13). Patients were followed for 18 month and TTP was identified. Association between TTP and fullness of life was analysed in Cox-regression analysis.
Results: During the previous year before baseline assessment, 23.8% of the patients had spent relatively empty, 47.5% moderately full, 23.8% full and 4.9% very full life. During the follow-up period, 37 patients experienced TTP. Patients' background did not associate with TTP. Of the patients with relatively empty life, 29.3% experienced TTP, while the corresponding figure for the rest of patients was 10.8%. In Cox regression analysis, the patients with relatively empty life experienced TTP more often ($P = 0.001$, RR 2.981, CL 95% 1.561–5694) than other patients.
Conclusion: Fullness of life seems to be a protective factor against full-blown psychosis in high-risk patients. In addition to clinical symptoms, when making treatment plan for high-risk patients, it is also important to assess how they have managed in their life in general.
Policy of full disclosure: None.

O-03-006
Indicated prevention with Omega-3 fatty acids in young people with 'at-risk-mental-state' for psychosis: design of a 5-year follow-up

K. Papageorgiou (Medical University of Vienna Psychiatry and Psychotherapy, Austria), M. R. Schäfer, M. Schlögelhofer, N. Mossaheb, G. P. Amminger

Objective: In the first randomized, placebo-controlled trial (RCT) in help-seeking young people with 'At-Risk-Mental-State' for psychosis that tested the efficacy of long-chain polyunsaturated omega-3 fatty acids (PUFA) in a preventive role, we found that 1.2 g/day of omega-3 PUFA, provided for 12 weeks, were effective in reducing the transition rate to first-episode psychosis in UHR individuals over the entire study period of 12 months.
Methods: The study was conducted between 2004 and 2007 and included 81 randomized participants, 76 of which (93.8%) completed the trial. We now aim to follow up this cohort 5 years since they were last assessed. Psychiatric diagnoses, psychiatric symptoms and psychosocial functioning will be evaluated.
Results: At 12-month follow-up, 4.9% (2/41) individuals in the omega-3 group and 27.5% (11/40) in the placebo group made a transition to psychosis ($P = 0.007$). The difference between the groups in the cumulative risk of progression to psychosis was 22.6% (95% CI 4.8–40.4).
Conclusion: Although these findings suggest a preventive, disease progression modifying treatment effect, the efficacy of omega-3 PUFA beyond 12 months remains unclear. We hypothesize that the initial 12-week intervention with omega-3 PUFA would continue to show significant reductions in the transition-to-psychosis rate compared to the placebo group, about 5 years since their last assessment.
Policy of full disclosure: None.

O-04 Drug and Other Somatic Treatments

O-04-001
Comparative assessment of haloperidol and risperidone effect on neuromarkers and endothelium dysfunction indices in patients with the first psychotic episode

N. Govorin (Department of Psychiatry, Chita State Medical Academy, Russia), A. Vasilyeva

Objective: Haloperidol and risperidone effect on productive, negative, neurocognitive disorder and neurodestruction—neuroreparation processes has been studied.
Methods: Clinical psychopathologic condition, neuromarker levels and endothelium dysfunction indices such as BDNF, GFAP, NSE, antibodies to NR2 subunit of NMDA receptors, NO, endothelium-1 have been determined at 23 subjects with the first psychotic event.
Results: Before the therapy the biomarkers levels didn't differ in the both groups but values in the control group were lower. After 8 weeks' psychotropic therapy the continued tendency of growth BDNF and NO levels, decrease in the GFAP, NSE, antibodies to NR2 subunit of NMDA receptors, endothelium-1 levels has been noted both in group of the patients receiving risperidone and in group where the haloperidol was given. Correlations between the examined biological parameters are determined in patients with acute schizophrenia treated with risperidone: the higher levels of GFAP and antibodies to NR2 subunit of NMDA receptors, increased value of BDNF and NO. Association of changes of the examined signs with psychopathological disorders on scale PANSS has been determined in patient with schizophrenia. Patients receiving treated by a haloperidol didn't reveal the described laws of dynamics of biological parameters.
Conclusion: Risperidone has been estimated to press high therapeutic effect on productive, negative, and cognitive disorders, and ability to reduce brain neurodestruction markers as well as to improve protective compensation processes directed on neuroplasticity restoration.
Policy of full disclosure: None.

O-04-002
Dopamine D2 receptor occupancy with risperidone or olanzapine needed for the maintenance treatment of schizophrenia: A cross-sectional study

Y. Mizuno (Department of Psychiatry, Kawasaki Municipal Hospital, Japan), R. R. Bies, G. Remington, D. C. Mamo, T. Suzuki, B. G. Pollock, T. Tsuboi, H. Takeuchi, M. Mimura, H. Uchida

Objective: In the acute phase treatment of schizophrenia, a therapeutic window of 65-80% occupancy of dopamine D2 receptors is suggested to achieve optimal therapeutic effect while minimizing risks for side effects. However, it remains unexplored as to whether maintaining such a degree of D2 receptor occupancy is necessary for the maintenance treatment.
Methods: Daily peak and trough D2 receptor occupancy levels were estimated in clinically stable patients with schizophrenia (DSM-IV) who were receiving risperidone or olanzapine. Using two plasma samples collected at two different given time points, plasma antipsychotic concentrations at peak and trough were estimated with population pharmacokinetic techniques. Corresponding dopamine D2 receptor occupancy levels were then estimated, using our recently developed model (Fig. 1).
Results: 35 subjects with stable schizophrenia completed the study (mean ± SD age, 48.8 ± 13.8 years; 14 men; 23 Asians and 12 Caucasians; 20 for risperidone at 3.2 ± 2.3 mg/day, and 15 for olanzapine at 9.2 ± 4.9 mg/day) between September and December 2010. 48.6% ($N = 17$) did not achieve continuous blockade at ≥65%. Moreover, 11.4% ($N = 4$) did not hit the 65% threshold even at the estimated peak concentrations.

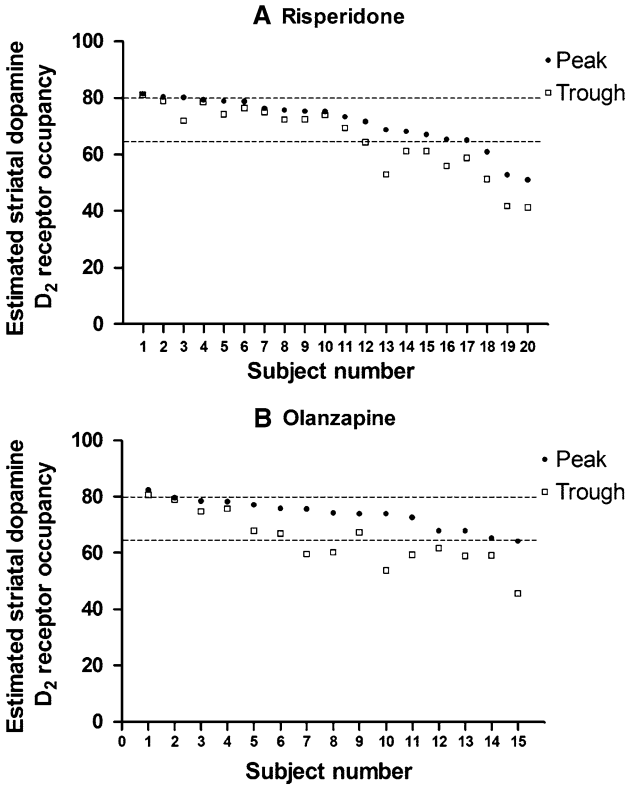


Fig. 1 Estimated striatal dopamine D_2 receptor occupancy in clinically stable subjects with schizophrenia who were receiving risperidone or olanzapine

Conclusion: Approximately half the subjects with stable schizophrenia did not achieve estimated continuous blockade of D2 receptor occupancy at ≥65%. Although a causal attribution cannot be made due to the cross-sectional study design, these findings suggest that lower levels of D2 receptor occupancy may be sufficient in the maintenance treatment of schizophrenia, compared to acute phase treatment.
Policy of full disclosure: This work was funded by Grant-in-Aid for Young Scientists-B from the Ministry of Education, Culture, Sports, Science and Technology (HU) and Japan Research Foundation for Clinical Pharmacology (HU).

O-04-003
Mentalizing skills deficits in schizophrenia as a cue for drug choice? Clozapine versus other antipsychotic profiles on keeping outpatients stable

R. Duñó (Parc Tauli Hospital Psychiatry, Barcelona, Spain), K. Langohr, D. Palao, A. Tobeña

Objective: The study attempts to determine wether Theory of Mind (ToM) deficits are linked with resistance to antipsychotic treatment in patients with schizophrenia. Given that abnormalities on mentalizing are particularly severe in patients with poor premorbid adjustment, and poor premorbid adjustment is described as a factor of

refractoriness to treatment, we expected to find a connection between ToM deficits and increased rates of antipsychotic drug resistance.
Methods: Design: Descriptive and comparative study between fifty-seven schizophrenic patients and forty-eight patients with no psychiatric diagnosis, matched by sex, age and educational level. Assessment: Premorbid Adjustment Scale (PAS), Theory of Mind Tasks: First order "The cigarettes", "Sally and Anne". Second order: "The burglar", "The Ice Cream Van".
Results: Ordinal regression analysis revealed a main association between deficits in first-order and second-order ToM tasks respectively and poor social premorbid adjustment (social isolation). Concerning first order ToM tasks, deficits also were related to a poor performance on the Trail Making Test B and males. In contrast, the test showed the highest significant association between second order ToM tasks with block design, males and clozapine treatment. R-square values amounted to 0.300 and 0.657, respectively.
Conclusion: The ordinal regression showed that poor premorbid adjustment, males block design, and clozapine treatment (predictors of unfavourable response to treatment) were linked with deficits in second order ToM tasks in stabilized schizophrenic outpatients. Some refractory responses to drug treatment might derive from nuclear anomalies in social cognition.
Policy of full disclosure: None.

O-04-004
Neuroleptic-induced movement disorders: a cross-cultural perspective

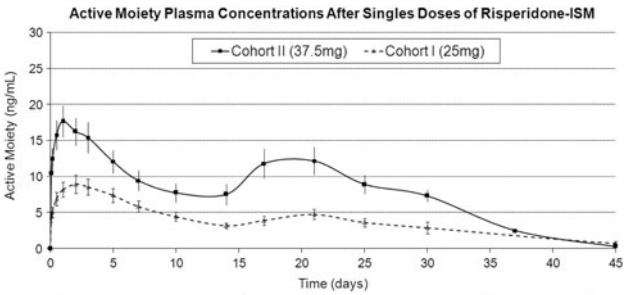
E. Pi (USC School of Medicine Psychiatry, Los Angeles, CA, USA),

Objective: Present a cross-cultural perspective of the implications and management of neuroleptic-induced movement disorders.
Methods: This presentation is a comprehensive review of classification, diagnostic assessment, and ethnic variation in the risk of developing neuroleptic-induced movement disorders.
Results: All the typical neuroleptics are essentially the same in antipsychotic efficacy and different in some of their side effects. They produce a range of unwanted extrapyramidal side effects (EPS), including dystonia, akathisia, Parkinsonism, and tardive dyskinesia (TD). These movement disorders may be confounded with negative symptoms of schizophrenia, which can further interfere with patients' psychosocial function and medication compliance, subsequently increase risks of relapse of psychoses and adversely affect the prognosis.
Conclusion: The recent introduction of a few atypical neuroleptics, although they are still far from "perfect" in relation to their efficacy and side effect profiles, which are considered therapeutically superior as these agents induce no or less EPS then typical neuroleptics. Thus, perhaps related to the favorable EPS profiles, there has been noted an improvement in negative as well as positive symptoms of schizophrenia.
Policy of full disclosure: None.

O-04-005
A clinical trial to evaluate the pharmacokinetics, safety and tolerability of single doses of risperidone with the novel long-acting injectable technology ISM® in healthy subjects

M. Farré (Imim-psmar Pharmacology Unit, Barcelona, Spain), J. Martinez-Gonzalez, P. Cordero, F. Martinez-Rodriguez, I. Ayani, F. Fonseca, L. Ochoa, J. L. Pedraz, I. Gutierro

Objective: The novel ISM® (In Situ Microparticle) technology is intended for use with risperidone in order to improve its pharmacological profile allowing a monthly administration without needing initial oral supplementation and storage in refrigerator. This is the first study in humans using the ISM® technology with an antipsychotic drug aimed to evaluate its pharmacokinetics, safety and tolerability.
Methods: This is a single-centre, open-label, single-dose, dose-escalation study in 2 cohorts of healthy male volunteers, aged 18–38. Each subject from the first cohort (9 subjects) and afterwards, from the second cohort (8 subjects), received one intramuscular injection in gluteus of Risperidone-ISM® 25 and 37.5 mg, respectively. Blood samples for PK measurements were obtained at baseline and then at several time points from 2 h up to 45 or 59 days. Usual PK parameters were calculated from plasma concentrations of risperidone, 9-OH-risperidone and its active moiety (risperidone + 9-OH-risperidone). Safety and tolerability were assessed by ECG, vital signs, chemistry, hematologic and urine parameters, prolactin values and recording adverse events.
Results: Mean active moiety plasma concentrations at 2 h and day 30 post-administration were 4.37 and 2.90 ng/ml respectively after the 25 mg injection, and 10.43 and 7.34 ng/mL after the 37.5 mg injection. Mean (SD) of the main PK parameters and the curves from active moiety plasma concentrations are shown in the figure. No serious unexpected adverse events were reported during the study. All volunteers showed hyperprolactinemia, as it has been previously described on subjects receiving risperidone.
Conclusion: It was shown that the ISM® technology provides a sustained release of the drug since the first day after single intramuscular doses of risperidone 25 and 37.5 mg which may be suitable for a one-monthly administration in schizophrenic patients and consequently might improve patients' compliance.
Policy of full disclosure: This study has been supported by Rovi. JM, FM, IA, LO and IG are employees of Rovi. The study has been registered in ClinicalTrials.gov (NCT#01320410).



Dose	T_{max} (h)	C_{max} (ng/mL)	AUC_{0-t} (ng·h/mL)	AUC_{ext} (%)
25mg	104.00 (152.74)	9.60 (3.53)	4284.12 (1407.36)	1.90 (1.63)
37.5mg	93.00 (131.73)	18.28 (6.39)	8598.97 (2872.75)	0.44 (0.24)

O-04-006
Effect of cardiovascular exercise on global brain volumes in patients with schizophrenia and matched healthy controls

T. Scheewe (UMCUtrecht Psychiatry, Utrecht, Netherlands), N. van Haren, G. Sarkisyan, T. Takken, H. Hulshoff Pol, F. Backx, R. Kahn, W. Cahn

Objective: In schizophrenia brain volume reductions have been consistently found [1]. These brain volume reductions appear to be progressive and under the influence of genetic and environmental factors. Cardiovascular exercise training appears to increase hippocampal volume in schizophrenia, but the effect of physical exercise on global brain volumes has not yet been reported.

Methods: 15 patients with schizophrenia and 43 matched healthy controls whose compliance percentage was at least 85% were included in a single blind randomized controlled trial. Cardiovascular fitness (VO2max and WATTmax), was determined and all subjects underwent MRI scanning on a Philips 3-Tesla. After assessment of baseline measurements subjects were randomly assigned to either cardiovascular exercise or occupational therapy (patients)/life as usual (healthy controls). Repeated measures general linear models were used to investigate the effect of physical exercise on the progressive brain volume change. Linear regression analyses investigated the association between cardiovascular fitness and brain volume changes.
Results: Progressive whole brain volume change in patients was diminished through physical exercise (time*randomization $F = .711$, $P = .403$; time*group $F = 1.636$, $P = .207$; time*group*randomization $F = 3.883$, $P = .054$). Progressive change in third ventricle volume occurred in the occupational therapy group (Time*randomization $F = 3.623$, $P = .063$; time*group $F = 4.381$, $P = .041$; time*group*randomization $F = 7.544$, $P = .008$). A trend was found for gray matter reduction in the occupational therapy/life as usual group (Time*randomization $F = 2.859$, $P = .097$). No significant changes were found for white matter, cerebellum and lateral ventricles. In patients change in WATTmax was associated with lateral ($B = -.05$, $t = -3.006$, $P = .011$) and third ($B = -.004$, $t = -4.704$, $P = .000$) ventricle volume. VO2max was associated with gray matter volume change ($B = 3.371$, $t = 3.247$, $P = .006$).
Conclusion: These findings suggest that, through an increase of cardiovascular fitness, the progressive brain volume changes in schizophrenia will diminish with physical exercise.
Policy of full disclosure: W. Cahn is or has been an unrestricted research grant holder with, or has received financial compensation as an independent symposium speaker or as an consultant from, Eli Lilly, BMS, Lundbeck, Sanofi-Aventis, Janssen-Cilag, AstraZeneca and Schering-Plough.

O-05 Psychosocial treatment

O-05-001
Is social cognitive remediation therapy effective in the treatment of schizophrenia patients?

D. R. Mueller (University of Bern Univ. Hospital of Psychiatry, Switzerland), S. J. Schmidt, V. Roder

Objective: On the background of an increased interest by clinicians and researchers in social cognition as a treatment objective for schizophrenia patient, several new Social Cognitive Remediation Therapy (SCRT) approaches were developed during the last decade. SCRT directly intervene in individual or multiple social cognitive domains like emotion or social perception, theory of mind, social schema or attribution. Some of these approaches integrate SCRT with therapeutic components intending to ameliorate neurocognitive and social skills or with work rehabilitation. Until today no quantitative review to evaluate the efficacy of SCRT has been presented.
Methods: After an extended literature search 23 randomized-controlled trials (RCTs) with a total of 1,088 participants could be identified and were finally included in a meta-analytical procedure. Based on the outcome variables from each study, effect sizes (d) between SCRT and control groups were calculated.
Results: Over an average length of 22.2 weeks of therapy (48 sessions) a significant effect in proximal outcome addressing general social cognition was evident favoring SCRT compared to controls ($d = .57$). The effects in social cognition could be maintained during a mean follow-up period of 8.6 months ($d = .48$). Significant therapy effects were found in all social cognitive domains with the exception of social attribution ($d = .26$). Additionally, the neurocognitive domains of speed, attention, verbal memory, working memory and problem solving showed significant evidence of amelioration compared with the control groups during therapy (mean score: $d = .34$) and at follow-up ($d = .38$). More distal effects were found in social functioning during therapy ($d = .52$) and at follow-up ($d = .34$), but not in positive and negative symptoms ($d < .12$).
Conclusion: The results support strong empirical evidence for the efficacy of SCRT in schizophrenia patients. SCRT approaches should be included within the multimodal psychiatric standard care to optimize psychiatric rehabilitation in schizophrenia.
Policy of full disclosure: None.

O-05-002
Mechanisms of functional recovery in cognitive remediation therapy for schizophrenia patients

S. J. Schmidt (University Hospital Psychiatry, Bern, Switzerland), D. R. Mueller, V. Roder

Objective: Functional impairments in living, work and leisure are an essential diagnostic feature of schizophrenia. They often persist after symptom remission and despite novel treatments for schizophrenia patients. Empirical evidence supports the relevance of social cognition, negative symptoms and functional capacity as mediators between neurocognition and functional recovery in schizophrenia. However, no study has assessed these variables at different measurement points in order to infer the temporal order postulated by the mediator model. Moreover, comparing resulting models of the treatment and control group could shed light on potential change mechanisms.
Methods: Data were collected in the context of an international RCT evaluating the Integrated Neurocognitive Therapy (INT) in comparison to treatment as usual (TAU). 169 outpatients with a diagnosis of schizophrenia according to DSM-IV-TR participated in the study. The sample was analyzed separately for INT ($n = 86$) and TAU group ($n = 83$). We adopted a longitudinal design with three measurement points (baseline: neurocognition; after 3 months/after therapy: social cognition, negative symptoms and functional capacity) and after 1 year (functional recovery). Based on prior research, path analysis was first performed linking all variables in the model. Post hoc modifications were subsequently formed based on theory, model fit statistics and the statistical significance of each path.
Results: Social cognition, negative symptoms and functional capacity served as mediators between neurocognition and functional recovery in the INT group. All indirect paths were significant and resulted in a good model fit. This mediator model could not be confirmed in the TAU group: Social cognition and negative symptoms were not significantly associated with functional recovery.
Conclusion: The results of this study provide further evidence for integrated treatments. Social cognition, negative symptoms as well as functional capacity seem to be viable targets to optimize current cognitive remediation therapy approaches.
Policy of full disclosure: None.

O-05-003
Remediation of social cognition deficits in schizophrenia: a proof of concept pilot study using biofeedback

K. McCabe (Schizophrenia Research Inst, Darlinghurst, Australia), C. Loughland, T. Lewin, M. Hunter, V. Carr

Objective: Social cognition has a strong relationship with functional outcome in schizophrenia. Within the social cognition domain, one of the most consistent and widely explored deficits in schizophrenia is face emotion processing. To date, remediation strategies for this deficit have adopted a largely top-down approach. This is despite evidence of visual sensory processing abnormalities that may impact the accurate recognition of faces. The rationale for the present study was that in order for the brain to assign meaning to face emotion stimuli it must first generate reliable neurological responses relating to the location and sampling of sensory information.
Methods: Utilizing a novel remediation strategy derived from the neurosciences, we predicted that visual scanpath performance would be altered (with patients recording a less restricted viewing strategy and increased fixations) with a downstream improvement in emotion recognition. Twenty-five participants with schizophrenia were randomly allocated to a emotion recognition treatment program (METT/SETT) or a biofeedback based treatment. Participants completed training weekly for 6 weeks. At baseline, post treatment participants completed a battery of tasks assessing face emotion and complex stimuli recognition while their eye movements were recorded.
Results: Post treatment improvement was observed ($P = 0.001$) with both remediation groups showing improvement in emotion recognition. Further, paired sample t test revealed a significant increase in raw scanpath length for the biofeedback group only post treatment ($P < 0.05$).
Conclusion: Training targeting low level visual processes results in gains in emotion recognition, a process highly relevant to psychosocial functioning in schizophrenia. Further, these gains were observed at a psychophysiological level via the normalisation of some visual scanpath parameters for the bottom-up based remediation alone suggesting that treatments targeted at low level functions have significant downstream effects.
Policy of full disclosure: None.

O-05-004
Cognitive psychotherapy in early psychosis: metacognition and disorders remission

R. Popolo (Terzo centro Psicoterapia Cogn, Rome, Italy), M. Procacci, G. Salvatore, G. Dimaggio

Objective: The cognitive behavioural psychotherapy in psychosis has the role of reducing sufferings produced by positive and negative symptoms. In early psychosis the psychological intervention has to enhance the cognitive functioning and the patient ability to reflect upon his own mental states. A solid therapeutic relationship is a prerequisite of effectiveness in the therapy for psychosis. There are several obstacles to the therapeutic relationship; among these, we underline that psychotic patient isn't aware of its own pathology, of having his own mental activity and of using it for his goals and purposes. These psychological malfunctions often go with poor interpersonal and social skills. First of all in this work we analyze the difficulties of building a solid therapeutic alliance with psychotic patients. We describe also how the enhancement of metacognitive functioning (self reflectivity and decentralization) encourages the process of remission and stabilization of symptoms in early psychosis. We present some clinical samples from sessions of cognitive behavioural psychotherapy in early psychosis.
Policy of full disclosure: The authors declare that there does not exist any significant financial interest or other affiliations with a funding organisation or with a commercial supporter of the session and/or provider of commercial services.

O-05-005
The Opus-trial: Intensive, early, psycho-social intervention versus treatment as usual for first-episode psychosis patients. Results from the 10-year follow-up

R. G. Secher (Psychiatric Centre Copenhagen Research Unit, Bispebjerg, Denmark), S. F. Austin, N. P. Ole Mors, M. Nordentoft

Objective: This study is the 10-year follow up of the OPUS-trial. In the OPUS-trial, 547 patients with a first diagnosis within the schizophrenic spectrum were randomized to either 2 years of OPUS-treatment or treatment as usual (TAU). The OPUS-treatment was an intensive, individually tailored, psychosocial intervention. TAU usually offered treatment at a community mental health centre, generally with none of the individually tailored psychosocial interventions offered by the OPUS-treatment. After 1 year and after 2 years, the levels both of positive and of negative symptoms were significantly lower in the OPUS-group. After 5 years there was no longer any significant effect in the symptom-level of the OPUS-group, but significantly fewer were living in supported housing. *Objectives*: (1) To investigate whether the positive effects of the OPUS-treatment which were shown at 1-, 2-, and 5-year follow-up, will be present at ten-year follow-up, (2) To describe the clinical and social ten-years course of illness in the hitherto largest representative cohort of first episode psychotic patients in the world.
Methods: At the time of inclusion, 10 years ago, the patients were between 18 and 45 years, had a diagnosis within the schizophrenia spectrum and none of them had received antipsychotic medication for more than 12 continuous weeks. The primary outcome measures will be psychotic and negative symptoms (SANS and SAPS) and Social functioning (GAF (f) and PSP). Secondary outcomes include second diagnosis of substance abuse, medication and service use, depressive symptoms, suicidal behaviour, housing situation, vocational situation, the ability to cope with everyday life and symptoms and more.
Results: The data collection was terminated by March 2011. Results will be presented.
Policy of full disclosure: None.

O-05-006
Day clinic treatment and recovery in patients with schizophrenia

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Objective: More recently, recovery in schizophrenia has become a major issue. The specialized empowerment and recovery oriented program of the day clinic might improve the recovery process in people with schizophrenia. The aim of the study is to evaluate the effect of day clinic treatment on recovery.
Methods: Data from two groups of patients are collected twice, at baseline and after 5 weeks. The experimental group attends the day clinic treatment (20 patients) and the control group waits for the day clinic treatment (20 patients). At both times measures of recovery, hope and quality of life are obtained. Moreover, sociodemographic and clinical data including psychopathology are collected. T test and general linear model will be conducted to analyze longitudinal data.
Results: Changes in recovery during the 5 weeks within both groups as well as differences between the two groups will be presented. Moreover, results on other outcome variables such as hope, quality of life and psychopathology will be demonstrated.
Conclusion: The findings of this pilot study will help to calculate the sample size for a randomized controlled study assessing the effectiveness of day clinic treatment on recovery.
Policy of full disclosure: None.

O-06 Genetics and Neurobiology

O-06-001
Rare variants in the schizophrenia-associated microdeletion region on 1q21.1

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Objective: A rare recurrent microdeletion on chromosome 1q21.1 spanning several genes was previously identified as a strong genetic risk factor for schizophrenia. However it is unknown whether the region harbours other rare variants of high penetrance. Also none of the genes in the region were identified as the underlying risk gene/genes. We aimed to investigate the presence of such rare variants and pinpoint the schizophrenia risk gene/genes lying in the region.
Methods: We performed exon-targeted Sanger resequencing in 94 DSM-IV-diagnosed schizophrenia patients and 94 controls. 28.4 kb of genomic sequence per individual was generated. The identified variants were filtered for rarity (minor allele frequency, MAF $< 1\%$) and classified as potentially functional or non-functional by use of bioinformatical tools. 4 of the 7 genes were resequenced in an additional 96 patients to enrich our pool of promising variants for further genotyping. Genotyping in 2,000 patients and 2,000 controls is being performed by iPlex Gold Sequenom MassARRAY system.
Results: Resequencing in 7 genes revealed a total of 18 potentially functional rare variants in patients and controls. Majority were not listed in dbSNP and 1,000 Genomes Project. In 4 of the genes there was an overrepresentation of variants in patients. Additional resequencing in patients revealed other novel promising variants. All the variants observed necessarily in patients, located in 1 of the 4 genes and with a MAF $< 1\%$ in controls were selected for the ongoing genotyping step. Preliminary results suggest an overrepresentation of 2 of the 15 genotyped variants in patients.
Conclusion: As a preliminary conclusion, we hypothesize that small rare variants contribute to the disease allele spectrum at this particular locus. Ongoing genotyping suggests that 1 of the 7 genes in the region might be a schizophrenia risk gene. However more definite conclusions will be made after completion of the genotyping. F. B. Basmanav and A. J. Forstner contributed equally to this work.
Policy of full disclosure: None.

O-06-002
Gene expression and schizophrenia phenotype in the course of antipsychotic pharmacotherapy

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Objective: To assess medication effects on gene expression and candidate gene association with schizophrenia phenotype.
Methods: We collected clinical, neurocognitive, peripheral lymphocyte gene expression and high-resolution magnetic resonance brain imaging data from 19 initially treatment-naïve schizophrenia patients from the National Institute of Mental Health in Angoda (Sri Lanka) and 19 closely matched healthy community control subjects.

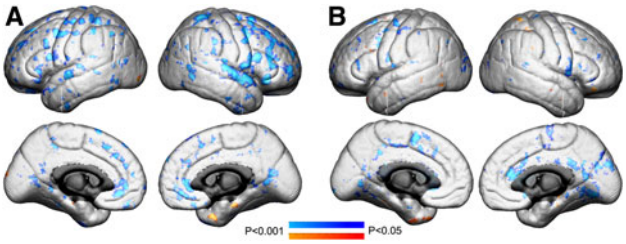

Fig. 1 Results (see text for detailed description)

Results: We found predominantly right-hemispheric grey matter reduction in frontal, temporal and parietal cortical regions thereby significantly affecting 19 Brodmann areas in the patient group ($P = 0.03$–0.007; Fig. 1a). This grey matter reduction was also highly inter-correlated and accounted for 74% of grey matter variance in patients but not in the control group. There was also some preliminary evidence in the patient group for associations of regional grey matter deficits with symptom expression (Fig. 1b) and cognitive impairment (i.e., semantic fluency [$r = 0.57$] and figure copying performance [$r = 0.64$] with left inferior temporal gyrus and digit span performance [$r = 0.64$] with right dorsolateral prefrontal cortex [$P < 0.05$]). The genetic analysis was conducted for gene expression before and after commencing antipsychotic drug treatment. Of the 10,207 genes expressed in peripheral lymphocytes, 219 were identified as up regulated and 426 as down-regulated prior to antipsychotic treatment when compared to matched control subjects. This included schizophrenia-associated genes, such as AKT1, DISC1, and DGCR6. When comparing pre versus post pharmacotherapy, no gene was found to be down-regulated. By contrast, 7 genes were up-regulated, with an additional 18 genes showing a trend towards up-regulation. DISC1 emerged as the strongest candidate gene in a multiple regression analysis explaining 57.9% of the grey matter variance in right anterior cingulate cortex ($P = 0.001$). DISC1 expression also normalised with pharmacotherapy along with improving symptoms ($P < 0.05$).
Conclusion: These findings suggest diagnostic specificity and potentially a common genetic determination in schizophrenia.
Policy of full disclosure: Funded by the Schizophrenia Research Institute, Sydney, Australia and the World Health Organisation.

O-06-003
Gene expression of HERG1, HERG2 and HERG3 isoforms in peripheral blood mononuclear cells of schizophrenia patients

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Objective: One of the recently identified risk gene in schizophrenia (SCH) is human ether-a-go-go related (HERG) gene. A leading adverse effect of the antipsychotic treatment is the acquired long QT syndrome, which results from the blockade of ERG channel subtypes,HERG1, HERG2 and HERG3 (KCNH2, Kv11.1; KCNH6, Kv11.2 and KCNH7, Kv11.3, respectively) mainly expressed in brain and heart, and they all exhibit a tetrameric composition of one main alpha-subunit, which comprises six transmembrane-spanning domains, and one auxiliary beta-subunit. To determine if alterations of HERG1, HERG2 and HERG3 are present in SCH, we studied the gene expression of 8 known isoforms in total and the impact of genetic variation of HERG1 in peripheral blood mononuclear cells(PBMCs).

Methods: 84 SCH patients and 74 healthy controls were included in the study after the exclusion of individuals having prolonged or shortened QT interval on electrocardiogram. We performed gene expression of HERG1(isoform a,b,c,and d),HERG2 (isoform1 and 2) and HERG3 (isoform 1 and 2) by quantitative real-time PCR. We also genotyped the HERG1 polymorphism rs1805123,which is within the risk haplotype that we have previously published (Atalar et al. 2010).
Results: Our analysis revealed that the expression of HERG1c and HERG1d isoforms were significantly higher in SCH patients than controls(200-fold and 2.3-fold respectively) ($P = 0.000$), though HERG1a and HERG1b isoforms were found higher in controls compared to SCH patients.The mRNA levels of HERG2 and HERG3 isoforms did not differ in between groups.There was no association between HERG1 polymorphism rs1805123 and the expression of HERG1 isoforms in SCH patients.
Conclusion: Our results particularly indicate that the potassium channel gene HERG1 is related to schizophrenia and implicate the contribution of HERG1c and HERG1d isoforms to its pathobiology. Our findings might also imply the involvement of HERG channels in the pathogenesis of psychosis and its treatment.
Policy of full disclosure: None.

O-06-004
BDNF and S100B as biomarkers in schizophrenia spectrum disorders?

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Objective: In patients with psychotic disorders, antipsychotics exert their effect mainly on positive symptoms and treatment response cannot be predicted. The neurotrophic proteins Brain Derived Neurotrophic Factor (BDNF) and S100B are involved in brain plasticity processes. Alterations in serum levels of the proteins and relationships with symptomatology and outcome have been established in patients with schizophrenia. In this study, the relationship between neurotrophic proteins BDNF and S100B and psychopathological syndrome prior to and after 6 weeks of treatment with antipsychotics was investigated.
Methods: 80 patients with acute and chronic schizophrenia spectrum disorders were evaluated during 6 weeks of treatment with various antipsychotics. Symptomatology was evaluated with the CASH, PANSS and CGI, both at baseline and after 6 weeks. At the same time points, serum levels of neurotrophic proteins were measured. Symptom profile and treatment response were related to biochemical parameters.
Results: Patients were divided into groups according to their baseline serum levels of BDNF and S100B (mean, ± 1 SD). No significant differences in PANSS total scores were present between the three groups. With respect to BDNF, however, a significant difference was found at baseline on the items "poor insight" and "unusual thought content" between the groups with higher and lower values. Concerning S100B, significant differences were found between the higher and the lower group on the item "suspicion" (baseline as well as 6 weeks) and on the PANSS positive scale at week 6. Moreover, lower values of neurotrophic proteins were associated with higher symptom severity scores.
Conclusion: Serum levels of BDNF and S100B are related to symptom intensity in patients with schizophrenia spectrum disorder. BDNF and S100B can be hypothesized to serve as state and trait biomarkers respectively.
Policy of full disclosure: None.

O-06-005
Impaired long-term potentiation and long-term depression in schizophrenia: new insights towards reduced neuroplasticity

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Objective: Neural plasticity involves reorganization of synaptic connections and represents the ability of the brain to reorganize its function in response to a challenge. Plasticity implies changing synaptic activity and connectivity and the underlying mechanisms are long-term potentiation (LTP) and long-term depression (LTD). Disturbed neuronal plasticity is considered to be part of the pathophysiology of schizophrenia and has been linked to the different clinical features of this severe illness. The aims of the two present studies were to investigate LTP-like and LTD-like cortical plasticity in schizophrenia patients.
Methods: Using excitability-enhancing anodal and excitability-diminishing cathodal transcranial direct current stimulation (tDCS), we performed the first in vivo assessment of glutamate-dependent LTP-like and LTD-like cortical plasticity in 29 schizophrenia patients and 50 control subjects. Animal and human research indicates that tDCS can induce LTP-like and LTD-like plasticity in the human motor cortex. To determine the physiological basis of possible plasticity changes, GABAA, GABAB and glutamate-dependent intracortical neuronal circuits were tested with well-characterized transcranial magnetic stimulation protocols (TMS).
Results: Multi-episode schizophrenia patients showed significantly reduced LTP-like plasticity compared to recent-onset schizophrenia patients and healthy controls. All schizophrenia patients presented abolished LTD-like plasticity, which was accompanied by a GABAergic dysfunction (GABAB). Schizophrenia patients showed a dysfunctional plasticity spread (LTD) across hemispheres. Furthermore, a cortical disinhibition was revealed in all schizophrenia patients.
Conclusion: The pattern of our results provides evidence for a specific plasticity deficit in schizophrenia patients which might be associated with a hyperglutamatergic state and dysfunctional *N*-methyl-D-aspartate-receptors. The disturbed LTP-like plasticity seems to be related to the disease course. An increased GABAB-dependent neurotransmission might compensate for the reduced LTD-like plasticity. The dysfunctional plasticity spread might reflect altered hemisphereic connectivity in schizophrenia patients. These findings may reflect a reduced signal-to-noise ratio, a disturbed filter function and dysfunctional information processing in schizophrenia patients.
Policy of full disclosure: Alkomiet Hasan has been invited to scientific congresses by Astra Zeneca, Lundbeck and Janssen Cilag. Alkomeit Hasan has received funding from the Deutsche Forschungsgemeinschaft (DFG) and the Guarantors of "Brain".

O-06-006
Association of candidate genes with neuroimaging phenotypes: results from the Homburg Multidiagnosis Study (HMS)

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Objective: Genomic imaging has become a very important tool of current research in the field of clinical neurosciences and particularly in biological psychiatry. Multiple genes such as DTNBP1, DISC1 and NRG1 have been linked to the risk for major psychosis. The aim of this study was to investigate the effects of selected single nucleotide

polymorphisms (SNPs) in these candidate genes on cognition, regional brain volumes and MRS parameters in human subjects.
Methods: Overall 232 subjects participated in the study. Subjects were genotyped with respect to selected SNPs of candidate genes conferring risk for major psychosis and other relevant functional polymorphisms, and underwent magnetic resonance imaging (MRI) and spectroscopy (MRS). MRI data were analyzed using both manual volumetric assessment of regions of interest and voxel-based morphometry (VBM) as implemented in SPM5.
Results: We found significant effects of the DTNBP1-SNP rs2619522 on regional brain volumes bilaterally in the hippocampus as well as in the anterior middle frontal gyrus and the intraparietal cortex. T/T homozygotes showed significantly lower grey matter volumes in these brain regions than carriers of the G allele. Furthermore, manual volumetric assessment revealed a significant effect of the DISC1-SNP rs821616 on hippocampus volume with Ser homozygotes having lower relative right hippocampal volume compared with Cys carriers. VBM showed significant effects bilaterally in the middle frontal gyrus as well as in right parietal cortex with Ser homozygotes having lower gray matter volumes in these cortical regions. Significant effects of the NRG1-SNP rs4733263 on regional brain volumes were found in several medial and lateral frontal brain regions.
Conclusion: This study shows effects of DTNBP1, NRG1, DISC1 and G72 on volumes of brain regions implicated in the pathogenesis of schizophrenia and other major psychoses. Further investigations are necessary in order to elucidate the pathophysiological pathways that connect these variations in susceptibility genes with macroscopic changes of regional brain volumes.
Policy of full disclosure: None.

O-07 Neuropsychology and Neuroimaging

O-07-001
Verbal memory in first episode schizophrenia: a 5-year follow-up (TIPS study)

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Objective: Cognitive impairments in patients with schizophrenia are well documented. Less is known about the change over time. In a previous study (Rund et al. 2007) we reported significant improvements from baseline to the 2-year follow-up on tests of working memory and verbal learning in patients with first episode psychosis (FEP). The present study examines the development over an extended time period of 5 years. Based on recent literature we expect that the positive trend in performance slow down and possibly level off.
Methods: Sixty-four patients (52% male, age 28 $\pm$ 9 years) with FEP were examined on a test of verbal learning and memory, the California Verbal Learning Test (CVLT), at baseline, and at 1-, 2- and 5-year follow-ups.
Results: No significant main effect of time on verbal memory was found over the time course of 5 years. An increase in performance from baseline to 2 years was confirmed at trend level, followed by a decrease to baseline from 2 to 5 years. The same pattern applied for both learning and memory scores.
Conclusion: The results revealed a non-significant change in verbal memory functioning over a time period of 5 years. Previously reported increase in performance over the first 2 years was followed by a decrease to baseline from 2 to 5 year assessments. These findings indicate overall stable memory functioning over a period of 5 years. Extended follow-ups are needed to investigate whether the pattern of initial increase followed by later stage decrease suggests a neurodegenerative pattern, and if so, for which subgroup this pattern applies.
Policy of full disclosure: None.

O-07-002
Specificity and relevance of planning deficits in schizophrenia

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Objective: Planning competence is essential for behavior in complex environments. Planning deficits have been repeatedly described in patients with schizophrenia. However, their specificity and impact on patient-relevant outcome measures are still unclear. In two related studies we addressed the following research questions: (1) Does planning ability differentiate patients with schizophrenia from patients with depression and healthy controls? (2) Is an ecologically valid assessment of planning useful for predicting functional outcome?
Methods: In study 1 we recruited 26 patients with schizophrenia and 26 patients with major depression from the outpatient clinic of a general psychiatric hospital. In addition, 26 healthy controls were recruited. All participants performed Tower of London, Zoo-Map and the newly developed Plan-a-Day task for ecological assessment of planning in addition to a neuropsychological test battery. In study 2 we assessed 80 patients with schizophrenia with a comprehensive neuropsychological test battery including the three above mentioned planning tasks. Global assessment of functioning and a measure of functional capacity were included as outcome measures.
Results: In study 1 patients with schizophrenia and depression performed worse than controls on attention, working memory and planning. Importantly, patients with schizophrenia performed worse than patients with depression on the planning summary score. This differential impairment was evident in the Tower of London and Zoo-map tasks, but not in the Plan-a-Day task. In study 2 Plan-a-Day showed incremental validity for prediction of global assessment of functioning, but this was not the case for the other planning tasks.
Conclusion: Planning deficits seem to be more prominent in patients with schizophrenia than in those with major depression. Ecologically valid tests of planning might improve prediction of functional outcome beyond other neurocognitive variables. Overall, we conclude that depending on the goal of neuropsychological assessment—specificity or functional relevance—different approaches to the assessment of planning might be required.
Policy of full disclosure: None.

O-07-003
Cognitive identity: a dimensional cognition model for schizophrenia

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Objective: The scientific comprehension of schizophrenia (SZ) lacks sufficient understanding of progression and etiology of the disease. Cognitive deficits associated with aberrations of the visual system could serve as disease progression markers from the SZ prodrome to the chronic, stabilized syndrome.
Methods: In an extensive literature review, we derived that disturbed oculomotor and visuo-spatial abilities impact higher order cognitive functions leading to the phenotypic expression of symptoms. We

tested different hypotheses of this model with a series of oculomotor, visuo-cognitive, and visuo-spatial experiments.
Results: Patients showed specific vision-related deficits indicating that visual strategic inflexibility might underlie cognitive deficits. Specifically, the results empirically support a dimensional cognitive disturbance model, which emphasizes that visuo-cognitive aberrations are linked to a cognitive identity deficit reflecting symptomatology.
Conclusion: These results stress the importance that progression and etiological models of schizophrenia require the assessment of visual information acquisition and processing disturbances, which could serve as dimensional markers. Results can be put into context with current models of disease progression, as well as with current research and treatment targets.
Policy of full disclosure: None.

O-07-004
Slowed response initiation in schizophrenia: evidence from lateralized movement-related and attention-related brain potentials

B. Reuter (Humboldt-Universitaet Berlin Institut fuer Psychologie, Germany), D. Möllers, N. Kathmann

Objective: Slowed reaction time in schizophrenia patients have been documented for more than 100 years. However, the underlying cognitive mechanisms are still not fully understood. Here we follow the hypothesis that the slowing reflects a deficit in volitional response initiation, including the activation of simple manual responses. Recent findings of increased onset latencies of the lateralized readiness potential (LRP) in schizophrenia patients might indicate a slowing of response initiation but could also be due to delayed allocation of attention to imperative stimuli.
Methods: In the present study with 20 schizophrenia patients and 20 matched healthy control subjects, we used a Simon-type spatial compatibility task for combined assessment of onset latencies of the LRP and the N2pc of the event-related potential—an electrophysiological correlate of the focusing of attention.
Results: The results confirmed increased onset latencies of the LRP in schizophrenia patients. There were also deviances in the waveforms of the N2pc of SZ patients, possibly indicating a slowing during the focusing of attention. However, experimental effects on reaction time showed that a putative slowing of attentional processes cannot fully explain increased LRP latencies.
Conclusion: In sum, the results corroborate the assumption of slowed volitional response initiation in schizophrenia.
Policy of full disclosure: None.

O-07-005
Egocentric spatial navigation in schizophrenia. Differentiated impairment and challenge-dependent activation of mesiotemporal, retrosplenial and parietal regions

J. Siemerkus (Psychiatric Univers. Hospital Clin. f. Social a. Gen. Psych., Zurich, Switzerland), E. Irle, C. Schmidt-Samoa, M. Mehlitz, J. Baudewig, P. Dechent, G. Weniger

Objective: Egocentric spatial navigation is modeled as being independent of landmarks. A recent study of our own group could show an unimpaired egocentric spatial navigation in schizophrenia. An fMRI-study of our own group revealed the involvement of parahippocampal, retrosplenial and parietal regions. This study aimed to investigate possible functional alterations in egocentric navigation in patients with schizophrenia.
Methods: 16 patients with schizophrenia (SZ) and 16 healthy controls (HC) performed an egocentric spatial navigation task during fMRI. The navigation task was a three dimensional virtual maze lacking any landmarks. Subjects were to find a goal in the maze and to remember its position. The assessment included 5 trials of a given time period in the same maze. Navigational capacity was quantified by counting the visit of cul-de-sacs or intersections not lying within the direct way to the goal.
Results: The SZ showed a worse performance in trials 4 and 5. The general pattern of activation was similar and comprised parahippocampal cortex, retrosplenial and posterior cingulate cortex and the Precuneus. Good navigation skills correlated with a lower degree of activation in the HC, but with a higher degree of activation in the SZ. Region-of-interest-analyzes showed a correlation of navigation skills and right hippocampal and right and left parahippocampal cortex in the HC and with right and left retrosplenial activation in the SZ.
Conclusion: To our knowledge this is the first study to investigate egocentric navigation during fMRI in schizophrenia. Whereas egocentric navigation in the HC seems to be dependent on mesiotemporal regions and in particular the right parahippocampal cortex, in the SZ the retrosplenial and posterior cingulate cortex is of importance for successful egocentric navigation. The different challenge-dependent activation points to an altered neuronal network or compensational mechanisms for implicit memory in schizophrenia.
Policy of full disclosure: None.

O-07-006
Trust versus paranoia: investigating the neural mechanisms of social reward learning in health and psychosis

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Objective: Psychosis is characterised by an elementary lack of trust in others. Recent studies in 'neuroeconomics' have shown that trust is an essential and inherently rewarding aspect of successful social interactions. The purpose of our study was to investigate the lack of trust manifest in psychosis, both at a behavioural and neural level. The hypotheses were: Psychosis is associated with (i) lower investments and reduced responsiveness to cooperation; and (ii) reduced activation of the brain reward system and the social brain.
Methods: Functional magnetic resonance imaging data was acquired on 20 patients with non-affective psychosis and 20 healthy controls, while they were participating in a multiple-round trust game. Subjects performed the role of the first player (i.e. the investor) during the whole session. The second player consisted of a computer algorithm programmed to appear either cooperative or deceptive.
Results: Compared to controls, patients invested significantly less during the first round of the trust game, and responded significantly less to a cooperatively playing counterpart, suggesting a behavioural index of reduced trust in patients. At a neural level, we found reduced activation in patients in the caudate, inferior frontal cortex, insula, and cingulate cortex, in response to cooperation.
Conclusion: Reduced sensitivity to rewarding social interactions might underlie the basic loss of trust in psychosis. This sensitivity to social reward seems to be mediated by cortical regions traditionally associated with both reward and social cognition.
Policy of full disclosure: None.

P-01 Drug treatment I: clinical

P-01-001
Comparative effect of typical and atypical antipsychotic medication on cognitive functions in schizophrenia: cross-sectional study on patients admitted in a psychiatric unit in Bucharest in a 3 months period

A. I. Mihailescu (UMF Carol Davila Medical Psychology, Bl27, Ap67, Bucharest, Romania), T. Donisan, B. Caval, M. Ilie, O. Dumitru

Objective: Cognitive functions are typically impaired in patients with schizophrenia. As cognitive deficits can occur even from the first episode of the disease and they can affect on a long run quality of life, they are important targets for pharmacological interventions. There is an ongoing debate whether typical or atypical antipsychotics should be used. In Romania, there are still few studies that investigated this effect. The aim of this study was to evaluate the comparative effect on cognitive function of typical or atypical antipsychotics in a group of Romanian patients with stable schizophrenia.
Methods: This transversal non-interventional study comprised patients diagnosed with schizophrenia admitted consecutively in March–June 2010 at Psychiatry Hospital „Al. Obregia"—Bucharest. Duration of treatment was at least 1 month. Cognitive performance was evaluated by tests from the Brief Assessment of Cognition battery (BAC) and Raven test for non-verbal intelligence. Severity of the disease was assessed with PANSS. Subsequently, multiple analysis of variance was done to evaluate the amount of differences between the two study groups.
Results: 41 patients were included, 14.6% males, 85.4% females, mean age 41.6 years old, SD = 9.42. 15 patients were treated with typical and 26 with atypical antipsychotics. While controlling for intelligence quotient and severity of the disease, we have found that patients treated with atypical antipsychotics preserved better working memory and processing speed ($F = 6.89$, $P < .01$), but for other cognitive abilities the differences to typical antipsychotics were not significant.
Conclusion: Our study found that, within our study groups, cognitive effects of atypical and typical antipsychotics were generally similar. An exception is represented by the positive impact of atypical antipsychotics on working memory and processing speed, however prospective studies are necessary, in order to assess in detail these effects and the global effect of atypical antipsychotics on neurocognition.
Policy of full disclosure: None.

P-01-002
Impact on creativity of typical versus atypical antipsychotic medication in schizophrenia: cross-sectional study on patients admitted in a psychiatric unit in Bucharest in a 3 months period

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Objective: Literature data suggest the conservation or even the enhancement of creative abilities in schizophrenia. This phenomenon is contingent, however, not only to the form of schizophrenia, but also to the type of medication used, with patients receiving new antipsychotics (e.g. amisulpride, clozapine, olanzapine, and risperidone) being reported to have a higher creativity. In Romania this is the first study that investigated the effect of medication on creativity, by using specific instruments. The aim of the study was to determine the effect of typical and atypical antipsychotics on creativity, in a group of Romanian patients diagnosed with schizophrenia.
Methods: Design of the study was transversal. Study group consisted of 41 patients with mean age 41.6 years (SD = 9.42), of which 15 (13.3% males, 15.4% females) were treated with typical antipsychotics, and 26 (86.7% males, 84.6% females) with atypical antipsychotics. Duration of treatment was at least 1 month in all cases. Creativity and intelligence were assessed by administering Guilford-Alternative task test and Raven non-verbal intelligence test. Subsequently, multiple analysis of variance was done to evaluate the amount of differences between the two study groups.
Results: Although patients treated with typical antipsychotics obtained higher scores at most components of creativity (originality, fluency, flexibility), this effect was not statistically significant. When controlled for intelligence and duration of studies score differences remained significant only for fluency ($F = 4.58$, $P < .04$).
Conclusion: Similar effects on creativity were found for typical and atypical antipsychotics, which is consistent to recent findings of their effects on cognition at schizophrenic patients.
Policy of full disclosure: None.

P-01-003
Comparative assessment of haloperidol and risperidone effect on neuromarkers and endothelium dysfunction indices in patients with the first psychotic episode

A. Vasilyeva (Department of Psychiatry, Chita State Medical Academy, Russia), N. Govorin

Objective: Haloperidol and risperidone effect on productive, negative, neurocognitive disorder and neurodestruction—neuroreparation processes has been studied.
Methods: Clinical psychopathologic condition, neuromarker levels and endothelium dysfunction indices such as BDNF, GFAP, NSE, antibodies to NR2 subunit of NMDA receptors, NO, endothelium-1 have been determined at 23 subjects with the first psychotic event.
Results: Before the therapy the biomarkers levels didn't differ in the both groups but values in the control group were lower. After 8 weeks' psychotropic therapy the continued tendency of growth BDNF and NO levels, decrease in the GFAP, NSE, antibodies to NR2 subunit of NMDA receptors, endothelium-1 levels has been noted both in group of the patients receiving risperidone and in group where the haloperidol was given. Correlations between the examined biological parameters are determined in patients with acute schizophrenia treated with risperidone: the higher levels of GFAP and antibodies to NR2 subunit of NMDA receptors, increased value of BDNF and NO. Association of changes of the examined signs with psychopathological disorders on scale PANSS has been determined in patient with schizophrenia. Patients receiving treated by a haloperidol didn't reveal the described laws of dynamics of biological parameters (Table 1).
Conclusion: Risperidone has been estimated to press high therapeutic effect on productive, negative, and cognitive disorders, and ability to reduce brain neurodestruction markers as well as to improve protective compensation processes directed on neuroplasticity restoration.
Policy of full disclosure: None.

Table 1 Endothelial dysfunction and neuromarkers indices in serum of healthy and sick of acute schizophrenia

Index (unit)	Control (n=10)	Before treatment (n=23)	After treatment (n=23)
BDNF (pg/mL)	395 (25th—321; 75th—946)	24,230 (25th—20,570; 75th—7,110)	30,960 (25th—25,640; 75th—38,320)
GFAP (ng/mL)	0025 (25th—0.022; 75th—0.040)	0.65 (25th—0.54; 75th—0.83)	0.45 (25th—0.32; 75th—0.63)
NR2 (ng/mL)	0.57 (25th—0.53; 75th—0.93)	1.92 (25th—1.41; 75th—2.19)	1.263 (25th—0.93825; 75th—1.407)
End (Fmol/ml)	0.56 (25th—0.48; 75th—0.80)	1.46 (25th—1.03; 75th—2.02)	1.30 (25th—1.11; 75th—1.41)
NO total (umol/L)	31.54 (25th—27.21; 75th—43.47)	86.66 (25th—76.68; 75th—101.02)	109.64 (25th—94.72; 75th—38.52)
NO_2 (umol/L)	12.82 (25th—10.96; 75th—18.48)	23.04 (25th—19.22; 75th—25.32)	28.18 (25th—23.92; 75th—35.8)
NO_3 (umol/L)	18.91 (25th—16.15; 75th—24.99)	64.94 (25th—57.46: 75th—75.7)	84.24 (25th—70.98; 75th—107.03)

Reliability in groups as comparison to control and reliability in groups before and after treatment $P < 0.005$

P-01-004
Predicting dopamine D2 receptor occupancy following antipsychotic dose reduction: a Pilot PET study

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Objective: Population pharmacokinetics can predict antipsychotic plasma concentration at a given time point prior to an actual dosage change. This in turn can be used to estimate a corresponding dopamine D2 receptor occupancy, using a close link between peripheral and central pharmacokinetics. However, this two-step prediction has never been tested.
Methods: Eight subjects with schizophrenia (DSM-IV) (mean ± SD age = 58 ± 8 years) participated in the study. Two plasma samples for the measurement of risperidone and 9-hydroxyrisperidone concentrations were collected at separate given time points. Following a dose reduction of risperidone, subjects received a [11C]raclopride positron emission tomography scan for the calculation of D2 receptor occupancy. A plasma concentration associated with the dosage change was predicted, using the two samples with a population pharmacokinetic model, using NONMEM. D2 occupancy level was then estimated, by incorporating the predicted plasma concentration into a hyperbole saturation model. Accuracy of the predictions was then evaluated.
Results: The mean (95% CI) prediction error and root squared prediction error (%) for the prediction of D2 receptor occupancy were as low as −4.6 (−13.5–4.4) and 9.9 (3.9–15.8), respectively. The observed and predicted dopamine D2 receptor occupancy levels were highly correlated ($r = 0.71$, $P = 0.047$).
Conclusion: Our preliminary data suggest that D2 occupancy at a given time, following a dosage change, can be predicted from plasma concentrations collected at different time points in advance. In turn, these results may be used to predict the oral dose to achieve the target D2 receptor occupancy in the treatment of schizophrenia.
Policy of full disclosure: This work was funded by Grant-in-Aid for Young Scientists-B from the Ministry of Education, Culture, Sports, Science and Technology (HU) and Japan Research Foundation for Clinical Pharmacology (HU).

P-01-005
Pharmacological daily dose and cognitive impairment in patients with schizophrenia spectrum disorders

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Objective: Most patients with schizophrenia spectrum disorders suffer from cognitive impairment. Recent research showed that exceeding certain Antipsychotic Daily Doses (ADD) can lead to impairment in cognitive performance. Parallel to the D2-receptor antagonism, many antipsychotics show a significant binding affinity to cholinergic receptors. There is evidence showing a significant impairment in complex attention and memory with treatment with high anticholinergic daily doses (CDD). Aim is to examine the association between individual cognitive performance and increasing antipsychotic and anticholinergic daily doses.
Methods: We analyzed a sample of 129 inpatients with schizophrenia spectrum disorder diagnoses. All patients received a thorough neuropsychological test battery. For calculation of the individual ADD and CDD, the medication at the time of testing was converted using currently available equivalent-models. After extracting 4 cognitive components (Verbal Memory, Information Processing Speed (IPS), Set Shifting and Attention) we examined the impact of ADD and CDD on cognitive performances via multiple regression analysis.
Results: ADD showed a significant moderate effect on verbal memory ($B = -0.284$; $P < 0.05$) and a trend effect on IPS ($B = 0.268$; $P < 0.1$). In respect to CDD there was a moderate effect on IPS at trend level only ($B = 0.298$; $P < 0.1$). Finally, complex model estimators were applied. Results showed that verbal memory performances decreased and dropped below its sample mean by exceeding 4.53 mg/day RIS-Eq (Risperidon Equivalents). IPS reaction times on the other hand increased rapidly by exceeding 4.26 mg/day Ris-Eq, whereby escalating antipsychotic load lead to consecutively worse reaction times. Regarding memory performances and CDD showed a stable tendency around the sample mean, whereas IPS increased under escalating daily doses.
Conclusion: While a higher initial dose of antipsychotic medication is necessary to break florid psychotic symptoms in schizophrenia spectrum disorders, medication for relapse prevention should be chosen carefully accounting for the ADD and CDD due to their potential impact on cognition.
Policy of full disclosure: None.

P-01-007
Treatment with haloperidol and changes in glucose values in patient with schizophrenia

O. Kozumplik (Clinic for Psychiatry Vrapce, Zagreb, Croatia), S. Uzun, N. Mimica, M. Jakovljevic

Objective: To report a case of a patient with schizophrenia whose glucose value was above reference range during treatment with haloperidol depot.
Methods: Follow up of a patient with schizophrenia whose glucose value was above reference range during treatment with haloperidol depot.

Results: Patient, 39 years old, with diagnosis of schizophrenia, was in psychiatric treatment for the past 20 years. The patient's compliance with previous oral antipsychotic therapy was poor and for that reason she was treated with haloperidol depot during period of 5 years. The patient occasionally had ideas of reference, but with such treatment she was able to function in her social activities and at work. At control examination, the patient reported often being thirsty and also reported frequent urination. The laboratory examination and examination of specialist of internal medicine were advised. Results of laboratory examination showed glucose value above the reference range. In the same time, there was no change in patient's body weight. Also, there was no change in patient's diet. Treatment with haloperidol was discontinued and treatment with fluphenazine was initiated, again as depot injection, because of poor compliance with oral antipsychotic therapy. The patient responded well to such therapy, she was able to function in her social activities and at work, and values of glucose gradually returned to previous values (within reference range).
Conclusion: Laboratory examination showed glucose value above the reference range in the patient who was treated with haloperidol depot; after switching to fluphenazine depot values of glucose gradually returned to previous values (within reference range).
Policy of full disclosure: None.

P-01-008
Lamotrigine withdrawal associated worsening of positive symptoms in patients with schizophrenia

T. Szafranski (IPiN III Department of Psychiatry, Warszawa, Poland)

Objective: There is some evidence from controlled clinical studies suggesting that lamotrigine (LTG) augmentation may be an effective strategy for patients with treatment resistant schizophrenia although the evidence is not robust. LTG is generally safe and well tolerated. Objective of the study is to report exacerbation of psychotic symptoms related to LTG discontinuation in patients with schizophrenia.
Methods: A case series study. Five patients with schizophrenia who were stabilized on clozapine (CLZ) dose 500–650 mg but were only partially responsive and had LTG added to their ongoing CLZ treatment. LTG was titrated up to a final dosage of 100–150 mg/day over 6–8 weeks. After 8–24 weeks of treatment LTG augmentation was judged to be ineffective. LTG was tapered off slowly over a period of 2–3 weeks. CLZ dose remained stable.
Results: After 2–7 days following LTG discontinuation the patients experienced increase in anxiety, tension, and the exacerbation of positive symptoms. The symptoms returned to baseline level over a period of next 7–21 days.
Conclusion: Our patients experienced possible withdrawal symptoms although LTG dose reduction was not rapid. Mechanisms of LTG action in schizophrenia remain unclear. It is possible that the effect on glutamate release may explain observed rebound phenomena. LTG in general does not affect the plasma level of CLZ, but elevation of CLZ levels was described in some patients. We cannot exclude the possibility of lowering of CLZ blood levels after LTG discontinuation because we did not measured CLZ levels in our patients. We propose that this symptoms are associated with LTG withdrawal because time relationship of their occurrence but of course we cannot exclude that the time relationship was purely by chance. We think that physicians should be alerted that exacerbation of anxiety and psychotic symptoms may occur after discontinuation of LTG in patients with schizophrenia even after no evident clinical effect of add-on LTG treatment on target schizophrenia symptoms.
Policy of full disclosure: None.

P-01-009
Post-hoc analysis from two randomised studies: efficacy, tolerability and dose–response of quetiapine XR 400/600/800MG/day in acute schizophrenia

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Objective: Evaluate extended-release quetiapine fumarate (QTP-XR) in acute schizophrenia and existence of QTP-XR efficacy dose–response.
Methods: Post-hoc analysis of pooled data from patients receiving QTP-XR 400, 600, 800 mg/day, or placebo in two, identically designed, randomised, double-blind studies (D1444C00132 + D1444C00133). In both studies, primary endpoint: LSM change at Day 42 in PANSS total score (LOCF); secondary endpoints: PANSS positive and negative subscale scores. Jonckheere-Terpstra analysis assessed if PANSS total change at Day 42 increased with increasing QTP-XR dose (not adjusted for study; no corrections for multiplicity). AEs were recorded.
Results: 914 patients included; efficacy assessed in the modified ITT population ($n = 889$). LSM change from baseline in PANSS total diverged significantly from placebo at: Day 14 for QTP-XR 800 mg/day (-15.3 vs. -12.1 for placebo, $P = 0.018$); Day 21 for 600 mg/day (-17.3 vs. -14.2, $P = 0.039$); Day 42 for 400 mg/day (-19.2 vs. -15.4, $P = 0.033$). Jonckheere–Terpstra analysis showed a significant QTP-XR dose–response ($P = 0.0196$; $P < 0.0001$ with placebo). PANSS positive diverged by Day 21 for QTP-XR 800 (-5.7 vs. -4.8, $P = 0.049$) and 600 mg/day (-5.8 vs. -4.8, $P = 0.046$). PANSS negative diverged by Day 21 (-4.0 vs. -3.2, $P = 0.040$) and 42 (-4.8 vs. -3.6, $P = 0.009$) for QTP-XR 800 and 600 mg/day, respectively. AEs occurred in 59.4, 66.5, 62.1 and 56.2% patients receiving QTP-XR 800, 600, 400 mg/day and placebo, respectively. Most common AEs: somnolence, dry mouth, sedation, insomnia, dizziness, headache, constipation and nausea.
Conclusion: QTP-XR was efficacious in acute schizophrenia with a tolerability profile consistent with previous studies. Higher doses appeared to confer an earlier improvement. Jonckheere–Terpstra analysis showed a significant QTP-XR dose–response. Financial support: AstraZeneca.
Policy of full disclosure: Consultant to AstraZeneca.

P-01-010
Norquetiapine and depressive symptoms in schizophrenia

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Objective: Recently quetiapine has been approved for treatment of bipolar depression and it has now been recommended as first-line treatment. Quetiapine produces an active metabolite, norquetiapine. In contrast to its parent compound, norquetiapine inhibts the norepinephrine transporter (NET) Since NET inhibition is a known mechanism of action of conventional antidepressants e.g. serotonin–norepinephrine reuptake inhibitors (SNRIs) norquetiapine may explain the antidepressant effect of quetiapine observed in clinical trials. Here we explore pharmacokinetic properties of norquetiapine and its clinical effect on depressive symptoms in first-episode initially antipsychotic-naïve schizophrenia patients before and after treatment of 6 months quetiapine therapy.
Methods: Fifteen initially antipsychotic-naïve first-episode patients participated. Symptom severity was assessed by trained raters using the PANSS-D depression cluster.

Results: Significant reductions in both PANSS positive symptoms and the PANSS-D cluster score were found following the 6 months quetiapine treatment. The reductions in PANSS negative, general and total scores were non-significant. Plasma concentrations of quetiapine or norquetiapine did not correlate significantly with treatment effect on the PANSS-D.
Conclusion: Following a 6 months quetiapine treatment period patients with first episode schizophrenia showed a significantly reduced PANSS-D score, however, this effect was not correlated with quetiapine or norquetiapine plasma concentration. This finding is inconsistent with the theory that quetiapine improves depressive symptoms in schizophrenia through NET-inhibition by its first metabolite, norquetiapine.
Policy of full disclosure: None.

P-01-011
Treatment with ziprasidone and changes in ECG in patient with schizophrenia

S. Uzun (Clinic for Psychiatry Vrapce, Zagreb, Croatia), O. Kozumplik, N. Mimica, M. Jakovljevic

Objective: To present a case of prolongation of QTc interval in a patient with schizophrenia during treatment with ziprasidone.
Methods: Follow up of a patient with schizophrenia, who had prolongation of QTc interval during treatment with ziprasidone.
Results: Patient, 34 years old, with diagnose of schizophrenia, according to DSM-IV TR criteria, was in psychiatric treatment for the past 10 years. She was treated with different antipsychotics, and with different treatment results. Treatment with some antipsychotics was discontinued because of side effects (leucopenia, extrapyramidal symptoms, changes in value of glucose). Treatment with ziprasidone was initiated during hospital treatment that was initiated after worsening in patient's mental condition—ideas of reference and auditory hallucinations dominated in clinical presentation. Before initiation of treatment with ziprasidone values of laboratory parameters were within reference range, and ECG was normal. Treatment with ziprasidone was initiated in daily dosage of 80 mg and daily dosage of ziprasidone was gradually increased to 160 mg. Also, patient was taking lorazepam and zolpidem in the evening as concomitant therapy. On the seventh day of treatment with ziprasidone the patient reported the feeling of pressure on her chest. She was examined by the specialist of internal medicine, and ECG was performed showing prolongation of QTc interval. The specialist of internal medicine found this result to be significant and related it to antipsychotic therapy. The treatment with ziprasidone was discontinued and control ECG performed several weeks after that showed normal value of QTc interval.
Conclusion: Prolongation of QTc interval may occur during treatment with ziprasidone.
Policy of full disclosure: None.

P-01-012
Evolution of function and sleep in a sample of schizophrenics patients during 1 year of treatment with extended-release paliperidone

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Objective: To assess the evolution of function and sleep in a sample of patients diagnosed with schizophrenia during 1 year of treatment with paliperidone.
Methods: Poorer function in schizophrenia is related to poorer quality of sleep and to an increased prevalence of sleep disturbances and insomnia of all types in schizophrenic patients. Drugs such as paliperidone extended-release have been shown to be effective in improving both function and sleep. Schizophrenic patients from three Mental Health units in the province of Toledo (Spain) were recruited. The inclusion criteria were an age over 18 years, a diagnosis of schizophrenia (based on the ICD-10 criteria), the start of treatment with oral paliperidone, and the non-utilization of any drugs such as hypnotics or sleep correcting agents. A series of demographic variables were recorded and the PSP (Personal and Social Performance) scale was used to assess function, while the COS (Sleep Oviedo Questionnaire) scale was used to evaluate subjective sleep quality and the severity of insomnia (categorical and dimensional variables of the scale). The scales were again applied 3, 6 and 12 months after the start of treatment.
Results: $N = 97$ patients (73 males and 24 females), with a mean age of 38 years. The predominant diagnosis was paranoid schizophrenia (62%). There were 7 dropouts during the year of follow-up. The results showed an improvement in PSP score during the 12 months, manifesting from the third month (ANOVA, $P < 0.05$). Likewise, statistically significant differences (ANOVA, $P < 0.05$) were observed with the COS scale for both severity of insomnia and subjective sleep quality; these results persisted over the year of follow-up and were manifest from the third month.
Conclusion: Oral paliperidone improved function and sleep in our sample of patients diagnosed with schizophrenia during 1 year of treatment, improving subjective sleep quality and reducing the severity of insomnia.
Policy of full disclosure: None.

P-02 Comorbidity

P-02-001
Alcohol abuse and schizophrenia: possible predictors and consequences

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Objective: The purpose of study was to compare group of schizophrenic patients with and without comorbidity of alcohol abuse according to the possible predictors, as well as consequences of alcohol abuse comorbidity.
Methods: The study was prospective and conducted in the Special Hospital For Psychiatric Disorders „Kovin"Serbia, and included population of a 50 patients. The experimental group consisted of patients with two diagnoses (schizophrenia and alcohol abuse), while in the control group were patients with a diagnosis of schizophrenia only. We observed them 2 years. All data were tested using logistic regression, correlation, Krascal–Wollis test.
Results: We found statistically significant difference when heredity of alcoholism was observed (experimental group 77.78 and 4.35% control group). Frequency of early neurotic disorders was found in 44.44% of experimental and 56.52 of control group. Maladaptive behavior forms during the adolescence were found in 82.61% of experimental and 44.44%. Suicide attempts were more frequent in experimental group (55.56%) comparing to control (17.39%). Organicity had significantly higher rates in group with comorbidity as expected, but general rate was unexpectedly low—below 15% in both compared subgroups.
Conclusion: Findings indicate that behavioral disorders in adolescence have impact on the prediction of comorbidity of alcohol abuse

in schizophrenic patients, while early neurotic symptoms have the effect of „paradoxical protection factor". Based on this research, specific predictor of comorbidity could be positive family history of alcohol. When it comes to the consequences of comorbidity should be highlighted attempted suicide, while the organic decay was significantly expressed in subpopulations schizophrenic patients with comorbidity of harmful use of alcohol, as expected.
Policy of full disclosure: None.

P-02-002
The relationship between baseline prepulse inhibition levels and ethanol withdrawal severity in rats

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Objective: Prepulse inhibition (PPI) of the acoustic startle reflex is thought to reflect the functioning of the sensorimotor gating system in the brain. The current literature indicates that similar neurotransmitter systems may play roles both in the regulation of PPI and in the development of ethanol withdrawal syndrome (EWS). The aim of the present study was to test if individual baseline PPI levels have any relationship to the behavioral and neurochemical consequences of EWS in rats.
Methods: A batch of rats ($n = 30$) was sorted according to baseline PPI levels and classified as either high-inhibitory (HI) or low-inhibitory (LI) rats ($n = 10$ in each group). Ethanol was administered in a liquid diet for 21 days. On the 22nd day, ethanol was removed from the diet, and EWS was induced. At the 2nd, 4th, and 6th hours of EWS, locomotor activity and behavioral symptoms were evaluated. Brain tissue concentrations of dopamine, serotonin and noradrenaline in hippocampus, cortex, and striatum were measured after the 6th hour of EWS testing. Another batch of rats ($n = 30$) was classified using the same procedure and fed with regular diet. On the 22nd day, rats were decapitated and neurochemical measurements were repeated.
Results: HI and LI rats consumed similar amounts of ethanol. However, EWS signs such as stereotyped behaviors, wet-dog shakes, and tremor were more intense in LI rats compared to their HI counterparts. Audiogenic seizures occurred in both groups in a similar manner. Although the catecholamine concentrations in the brains of both groups were parallel under baseline conditions, after the 6th hour of EWS dopamine levels increased in the cortex of LI and in the striatum of HI rats, whereas striatum serotonin levels decreased only in LI rats.
Conclusion: The present data suggest that the behavioral symptoms and neurochemical changes observed in EWS may be predicted by baseline PPI levels.
Policy of full disclosure: *This study has been published in PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY (2010;34:1507–1514). This study was supported by the Scientific and Technological Research Council of Turkey (TUBITAK) (Grant No: 105S387, SBAG 3194).

P-02-003
Relationship between smoking cessation and gender in first psychotic patients after long-term follow-up

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Objective: Patients with schizophrenia and bipolar disorder appear to have more difficulties with smoking cessation than the general population. Moreover, gender and unsuccessful smoking cessation are associated with depression and negative emotional experience. Less attention has been given to the association of cigarette smoking in women and the use of other substances. The aim of this study is to determine the influence of gender and substance abuse on smoking cessation in a long-term follow up after a first psychotic episode.
Methods: Patients were evaluated at years 1, 3, and 5 obtaining information about functional outcome, positive and negative symptoms and substance use. At 8th year, functional outcome and use of substance were recorded. Patients were classified in two groups: those who stopped smoking during follow-up, and those who did not stop.
Results: At baseline, rates of tobacco smoking were high with no differences between genders. Difficulty with smoking cessation was associated with female ($P = 0.017$) and typical antipsychotics ($P = 0.032$). Those who used alcohol continuously were less likely to stop smoking ($P = 0.050$) controlling for typical antipsychotics. The interaction with gender was not significant. Continuous cannabis use was not associated with smoking cessation, but women who use cannabis continuously were less able to stop smoking than men (adjusted $P = 0.036$).
Conclusion: Women are less prone to quit smoking than men during long-term follow-up after the development of psychosis. Different treatments should be considered for men and women in relation to tobacco dependence in patients with psychotic disorder. Treatment for women smokers should probably be more supportive and intensive.
Policy of full disclosure: None.

P-02-004
The increasing comorbidities in schizophrenic patients

A. Dangellia (QSU Psychiatry, Tirana, Albania)

Objective: Although the treatment of schizophrenia has improved in recent years, we stil encounter in our clinical practice an increasing number of schizophrenic patients with somatic and mental pathologies which require specialised diagnostication and qualified treatment. Maser and Cloninger (1990) definite comorbidity as: "When a patient has particular index disorder there may be a relatively greater or lesser risk of other disorders being diagnosed or other symptoms observed."
Methods: We investigated 85 schizophrenics with comorbidities that have been discharged from our university clinic of psychiatry during the period from 2000 to 2010. This group of patients has been compared with a group of 85 schizophrenics that have been discharged from the years 1990 till 2000. The comparison consisted about the frequency of comorbidities that we have diagnosticated in the two groups of the discharged patients. It's an empirical clinical comparison of two groups of patients diagnosticated with schizophrenic disorder according to the DSM-4. The majority of patients were paranoid schizophrenics. Some of them had a chronic course of the disorder with frequent admissions to our clinic.
Results: In the decade 2000–2010 the patients had an increase of the frequence of the lung disease (cancer due to heavy smoking), of alcohol and drug abuse and also of gambling. We analysed a number of admitted patients who developed depression symptoms, perhaps due to the chronic course of schizophrenic disorder or due to the more frequent use of the old neuroleptics during the period 1990–2000 probably. The improvement of the standard of living of our patients changed their life style with an increasing of the consume of food, alcohol and nicotine. A new comorbidity is for the decade 2000–2010 the gambling through the fortune plays that are widespread in our society.

Conclusion: It's our duty to diagnose early the somatic or other comorbidities like depression in schizophrenic patients, and in particular in those with a chronic course of the disease.
Policy of full disclosure: None.

P-02-006
Alexithymia and psychopathology in schizophrenia

S. Van Geert (FPPW PP08, Gent, Belgium), S. Vanheule, R. Kessels, P. Naert

Objective: Emotions play an important role in schizophrenia. The occurrence of negative affects is associated with poorer recovery. Alexithymia, a measure for affect regulation, appears to be an important factor in understanding psychopathology. In this study, we investigate the relationship between alexithymia and overall psychopathology in schizophrenia.
Methods: 65 inpatients diagnosed with schizophrenia were interviewed with Positive and Negative Syndrome Scale (PANSS; Kay, Opler, & Fiszbein 1987). Patients filled in Toronto Alexithymia Scale (TAS-20; Bagby, Taylor, & Parker 1994), Beck Depression Inventory (BDI-II, Beck 1994), and Symptom Cecklist (SCL-90-R; Derogatis 1975). Regression analyses between subscales of the TAS-20 (subscales: difficulties identifying feelings (TASdif), difficulties describing feelings (TASddf) and external oriented thinking (TASeot)), BDI-II (subscales: cognitive, affective, and somatic), and SCL-90-R were performed. Construct validity between depression subscales of those instruments is investigated.
Results: All TAS-20 subscales are significant explanatory factors for BDI-II subscales, except TASeot, which is only a significant predictor for BDI-II affective subscale. All TAS-20 subscales have a significant predictive value for the SCL-90-R subscales, except for the sleeping problems subscale. TASdif and TASddf are significant predictors for PANSS depression and general pathology subscales. TASddf is also a predictor for PANSS anergia subscale. Significant correlations are found between SCL depression subscale and all BDI subscales given a 5% significance level. PANSS depression subscale is significantly correlated with BDI total score, BDI cognitive and affective subscales.
Conclusion: There is a strong relationship between self-reported alexithymia and overall psychopathology in schizophrenia. As in other disorders, affect regulation is an important factor in understanding psychopathology. Construct validity between the different depression scales is established as shown through multivariate correlation analyses.
Policy of full disclosure: None.

P-02-007
Suicidality level correlated with borderline personality traits in patients with depressive disorder and schizophrenia

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Objective: The authors have researched correlation between primary illness (schizophrenia and depressive disorder—axis I) and underlying borderline personality traits (axis II) compared with expressed suicidality level in patients.
Methods: We have included 15 patients with schizophrenia and 19 patients with depressive disorder according to diagnostic criteria of International Classification of Diseases (ICD-10). The sample had been collected for 3 months during hospital treatment, when achieved stabilization phase of illness. The patients were treated with psychopharmacologic therapy indicated for specific disease: second generation antipsychotics for schizophrenia and selective serotonine reuptake inhibitors for depressive disorder. We have used several scales in order to conduct our research: "Hamilton Depression Scale" (depressive patients), "Positive and Negative Symptom Scale" (schizophrenic patients), "Suicidal Behaviour Questionnaire Revised" (for estimation of suicidality level) and "Borderline Symptom List—23" (self-assessment scale for determination of borderline personality traits). Statistical analysis was conducted with Statistical Package for the Social Sciences (SPSS) programme.
Results: Generally, all patients with high suicidal risk have shown significantly higher "Borderline Symptom List 23" score ($P = 0{,}007$; Kruskal–Wallis test). Sample of patients with schizophrenia had significant positive correlation, using Pearson correlation coefficient, of "Suicidal Behaviour Questionnaire Revised" and "Borderline Symptom List 23" ($P = 0{,}007$; $r = 0{,}662$). Depressive patient sample had resulted in positive correlation of "Hamilton Depression Scale" score and "Suicidal Behaviour Questionnaire Revised" score.
Conclusion: Interestingly, we have found strong link between borderline personality traits and suicidality level than with primary illness in patients with schizophrenia. However, the depressive patients have shown positive correlation of depressive symptoms and suicidality level but with not so strong correlation towards borderline personality traits. Also, due to relatively simple use of scales for suicidality and borderline personality traits we have implemented them in our routine approach towards severe patients.
Policy of full disclosure: None.

P-02-008
Suicidal ideation among schizophrenic patients

T. Rahim (College of Medicine Psychiatry, Erbil, Iraq), B. Saeed

Objective: Suicide is an increasing risk in schizophrenia patients. We aimed to study the demographic as well as clinical risk factors for suicide thoughts among schizophrenic patients.
Methods: 100 schizophrenic patients with mean age of 32.96 year, who did visit the psychiatry unit of Hawler Teaching Hospital, between the periods of August 2009 to February 2010, were assessed for the risk of suicidal ideation by adopting standardized diagnostic and symptoms rating scales.
Results: 23% of the sample shows moderate-high suicidal ideation. No particular demographic variable was significant predictor for current suicidal ideation. However, past history of suicide (OR = 0.095; P value = 0.001), concurrent depression (OR = 0.079; P value = 0.001), and positive psychotic symptoms (OR = 1.102; P value = 0.068) were more predictive for current suicidal ideation.
Conclusion: Suicide is an essential element in schizophrenia assessment; clinicians have to pay great attention to the history of previous suicide attempts, concurrent depressive disorders, and positive symptoms, particularly hallucinatory behaviors. Also clinicians have to be aware not to misinterpret depressive symptoms as negative symptoms of schizophrenia.
Policy of full disclosure: None.

P-02-009
Metabolic syndrome in patients treated with antipsychotics: a follow-up study

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Objective: Patients with severe mental illnesses (SMI) have a reduced life expectancy compared to the general population. Cardiovascular disease is the most common cause of death. In 2001 the Adult Treatment Panel III described a definition of the metabolic syndrome comprising the cardiovascular risk factors abdominal obesity, hyperglycemia, hypertension, elevated triglycerides and low HDL-cholesterol. Antipsychotic medication may induce or worsen these cardiovascular risk factors. The aim of this study was to assess the prevalence of metabolic syndrome and its individual components at baseline and follow-up in patients treated with antipsychotic medication.
Methods: A health monitor was introduced as screening instrument in a schizophrenia treatment and recovery program (so called F-ACT) at the outpatient departments. Apart from physical examination and laboratory analysis (including metabolic parameters), an ECG was made and motor disturbances were assessed. In addition, information about demographics, DSM-IV diagnoses, remission-criteria, social functioning, use of medication and drugs was documented.
Results: Over a period of 30 months (2008–2010) 515 patients treated with antipsychotic medication were evaluated at baseline. According to ATP-III, metabolic syndrome was present in 52% of patients (61% abdominal obesity, 54% hypertension, 22% hyperglycemia, 55% high triglycerides, 48% low HDL-cholesterol). At baseline, metabolic syndrome was significantly associated with concomitant use of antidepressant medication. A total of 180 patients were screened at follow-up 1 year after baseline assessments. Metabolic syndrome was present in 52% of patients (65% abdominal obesity, 54% hypertension, 18% hyperglycemia, 55% high triglycerides, 57% low HDL-cholesterol).
Conclusion: Metabolic syndrome and its individual components are highly prevalent in patients treated with antipsychotic medication at baseline and follow-up assessments. Concomitant use of antidepressant medication increases the risk for development of metabolic syndrome.
Policy of full disclosure: None.

P-02-011
Cardiovascular risk factors in patients with schizophrenia; do we detect and treat it?

A. Pose Cabarcos (Hospital de Mostoles Psiquiatría, Madrid, Spain), J. J. De Frutos Guijarro, F. García Sánchez

Objective: The prevalence of cardiovascular risk factors has been assessed in a sample of chronic psychotic patients, studying if treatment has been established.
Methods: 54 patients that had been diagnosed of chronic psychotic disease who were admitted in the psychiatric acute ward of Mostoles University Hospital in 2009 were studied. Gender, age, weight, height, blood pressure, fasting plasma glucose, fasting cholesterol, smoking habit, and the presence or absence of their treatment datum was compiled. Statistical analyses were performed using PASWStatistics 18.
Results: A high prevalence of obesity, dyslipidemia and smoking habit was observed. One-third of the participants showed impaired fasting glucose. Many patients did not received any treatment despite these parameters were checked by routine. A high number of primary care referrals were detected.
Conclusion: Although several studies demonstrated the correlation between the prevalence of metabolic syndrome and chronic antipsychotic treatment, little is known about how and how many of these patients are assessed. All results of this study were similar to previously done studies. Psychiatrist tends to focus only on patient's psychopathology. Cardiovascular risks factors are not properly assessed despite all parameters are well checked. In addition some studies showed that severe mental ill patients find more difficult to access to primary care services. An integrated approach by psychiatrics should improve the quality of life and longer survival of these patients.
Policy of full disclosure: None.

P-02-012
Dental hygiene in schizophrenia: a large-scale cross-sectional survey

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Objective: Clinical significance of dental hygiene in schizophrenia is often overlooked. The objective of this study was to examine their dental conditions and to identify clinical and demographic variables associated with poor oral hygiene in a large number of patients with schizophrenia.
Methods: Inpatients with schizophrenia in one of the participating hospitals in Tokyo, Japan between October and November, 2010 were asked to receive an assessment of their dental conditions, using the decayed-missing-filled teeth (DMFT) index. A univariate general linear model was used to examine the effects of the following variables on the DMFT score: age, sex, smoking status, daily intake of sweets, dry mouth, frequency of daily teeth brushing, tremor, and the Clinical Global Impression-Schizophrenia Overall severity score.
Results: 523 inpatients were enrolled (mean $\pm$ SD age $=$ 55.6 ± 13.4 years; duration of illness $= 29.8 \pm 13.9$ years; DMFT $=$ 19.7 ± 7.8; 297 men; 172 smokers). Older age, smoking, tremor burden, and less frequent teeth brushing were significantly associated with a greater DMFT score (all P's < 0.05). In addition, schizophrenia patients showed a greater degree of DMFT score when they were compared to the reference data of healthy people, especially in middle age.
Conclusion: Given that poor dental hygiene has been related with an increased risk of physical co-morbidities, physicians should be aware of patients' dental status, especially for aged smoking patients with schizophrenia. Furthermore, for schizophrenia patients who do not regularly brush their teeth or who exhibit tremor, it may be advisable for caregivers to encourage and help them to perform teeth brushing more frequently.
Policy of full disclosure: None.

P-02-013
Thyroid abnormalities in schizophrenia

S. C. Nova Bethania (St Johns Medical College Psychiatry, Bangalore, India)

Objective: To look at associations between thyroid abnormalities in acutely ill inpatients of schizophrenia.
Methods: In a retrospective case–control design we examined the association between T3, T4 & TSH abnormalities in Schizophrenia.
Results: The relevance of our findings and that of the association of thyroid abnormalities in Schizophrenia is discussed.
Conclusion: Thyroid dysfunction is relatively common in patients with schizophrenia. Research on co-morbidity has the potential to advance understanding of pathogenesis of both psychiatric and autoimmune disorders.
Policy of full disclosure: None.

P-03 Neuroimaging

P-03-001
Alterations of the brain reward system in antipsychotic naïve schizophrenic patients

M. Nielsen (University of Copenhagen Psychiatric Center Glostrup, Denmark), E. Rostrup, S. Wulff, S. Kapur, B. Glenthoj

Objective: Core schizophrenic symptoms have been suggested to be caused by a dysfunction of the brain reward system. Several studies have found alterations of the reward processing during the anticipation of salient events and during the evaluation of outcome, while it is still unclear if there are any alterations during the anticipation of valence. So far, there have been no studies on antipsychotic naïve patients.
Methods: 26 antipsychotic naïve schizophrenic patients and 26 age and gender matched healthy controls have been examined with functional Magnetic Resonance Imaging while playing a variant of the Monetary Incentive Delay task in a 3 Tesla Philips scanner. The psychopathology of the patients was rated with Calgary depression scale, subjective wellness-scale, PANSS and GAF.
Results: During the anticipation of salient events, the patients showed a pronounced decrease in the BOLD response in several reward related areas, such as ventral tegmentum, ventral striatum (VS) and cingulate gyrus. We found a negative correlation between the BOLD response in striatum and the PANSS positive score. There were no significant group differences in the BOLD response evoked by the anticipation of valence or during the gain of a monetary reward, but we found an altered activation pattern in the schizophrenic patients during the omission of a reward.
Conclusion: Our results are in line with earlier studies on medication free schizophrenic patients, finding an attenuated response to salient cues in VS. The decreased activation in VS of the patients might be the result of an increased dopamine turnover, which increases the noise and thereby eliminates the BOLD signal. The negative correlation between VS BOLD response and the PANSS positive score supports this interpretation and support the salience hypothesis.
Policy of full disclosure: None.

P-03-002
Dopamine disturbances in relation to reward processing in schizophrenia

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Objective: We plan to examine how reward processing abnormalities are related to striatal dopamine D2/D3 binding potentials (BP) and psychopathology in antipsychotic-naïve first-episode schizophrenia patients. Furthermore, we will explore how these disturbances are modulated by interventions with the D2/D3 antagonist amisulpride.
Methods: The study is designed as a 6 week case–control follow-up study of 30 antipsychotic-naïve patients with schizophrenia and 30 matched healthy controls. The participants are examined at baseline and at 6 weeks follow up with an extensive battery of assessments, including Single Photon Emission Computed Tomography (SPECT), structural and functional Magnetic Resonance Imaging (fMRI), neurocognitive- and psychophysiological testing and clinical rating scales. After baseline examinations the patients are treated with flexible doses of amisulpride according to their clinical condition. In order to examine the reward disturbances, fMRI is performed with a variant of the monetary incentive delay task. We use SPECT and 123IBZM (123 labeled iodbenzamid) as radioligand to examine the BP of dopamine D2/D3 receptors in the striatum. Matlab is used for the co-registration between MRI and SPECT images.
Results: Data collecting and analysis are ongoing. Currently we have fMRI and SPECT data from 13 patients at baseline, 9 at follow-up and 9 healthy controls. We find a decrease in the PANSS score and a decrease in the BP of dopamine D2/D3 receptors after treatment. Preliminary data will be presented.
Conclusion: We expect that blockade of striatal D2/D3 receptors with amisulpride has a positive correlation with treatment effect on positive psychotic symptoms and decrease in salience abnormality. We further expect to find an individual narrow therapeutic window of D2/D3 blockade, within which there is a therapeutic effect on the positive symptoms without addition of negative symptoms. Our data are limited, but they seem to support our hypothesis.
Policy of full disclosure: None.

P-03-003
Association of serum BDNF levels with hippocampal volumes in first psychotic episode drug-naive schizophrenic patients

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Objective: Evidence suggests that hippocampus contains the highest brain levels of neurotrophic factors, which are major determinants of neuronal plasticity. A smaller hippocampal volume in first episode patients with schizophrenia is thought to be associated to the pathophysiology of schizophrenic disorder.
Methods: In the present study we investigated the correlation between serum BDNF levels and hippocampal volumes in a sample of first episode drug-naïve patients with schizophrenia (FEP) ($n = 20$, M/F 8/12, mean age 30.75 ± 10.52) and healthy controls ($n = 21$, M/F 11/10 mean age 34 ± 4.70). Region of interest analysis was conducted on the images acquired via MRI.
Results: We found that hippocampal volume (HV) was decreased in FEP patients. Corrected right HV of FEP patients were significantly smaller compared to corrected right HVs of healthy subjects (patients vs. healthy controls 3526.51 ± 167.32 vs. 3757.18 ± 285.97, $P = 0.003$). The serum BDNF levels in the sample of FEP patients was significantly reduced compared to the healthy subjects (patients vs. healthy controls 9.76 ± 4.61 ng/ml vs. 15.33 ± 6.34 ng/ml, $P = 0.003$). A significant positive association was found between serum BDNF and the corrected right HV in the group of patients (Pearson $r = 0.452$, $P = 0.045$).
Conclusion: Our findings indicate that low serum BDNF levels are associated to reduction in hippocampal volume at the onset of schizophrenia and may further support the theory of neurodegenerative reaction associated with the onset of psychosis.
Policy of full disclosure: None.

P-03-004
Against an unitary view of schizophrenia: commonalities and differences of two phenotypes using connectivity fMRI

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Objective: The ICD/DSM schizophrenia diagnosis is an ill-defined phenotype. The Wernicke-Kleist-Leonhard school distinguish 35

major phenotypes in the psychotic spectrum. Among them, the cycloid psychoses (CP, remitting forms) and affect laden paraphrenia (ALP, the core of paranoid schizophrenia) appear promising. We used a resting state functional connectivity analysis to find commonalities and differences between these 2 groups.
Methods: Seventeen patients with CP and 17 with ALP all fulfilling DSM-IV defined schizophrenia were recruited together with 57 controls. Participants took part to a 20 min resting state fMRI scan keeping eyes closed but remaining awake. The signal from the 78 Brodman areas was averaged and a correlation coefficient was the metric for functional connectivity between them. Groups were compared using permutation test corrected for multiple testing.
Results: CP and ALP commonly differed from controls by a disconnection of their temporal regions (internal temporal, the temporal pole, the inferior temporal—in black). But CP had an increase of connectivity between the same temporal regions relative to both ALP and controls. Conversely ALP had a much larger disconnectivity pattern relative to both CP and controls including the cingulate and the orbito-frontal regions as a whole (in white).
Conclusion: CP and ALP share temporal disconnectivity which could be correlated with psychosis proneness. However the reasons for it appear different in the two groups: an excess of intra-temporal connectivity in CP, a more global and widespread decrease of connectivity in ALP which correlate with the type of residual symptoms observed in this group.
Policy of full disclosure: None.

P-03-005
Dysfunctional neural networks of time perception in schizophrenia

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Objective: With the double objective of searching for a physiological brain circuit concerned with time estimation and establishing whether this circuit is dysfunctional in schizophrenia patients, we carried out an activation likelihood estimate (ALE) meta-analysis of published functional neuroimaging studies.
Methods: ISI Web of Science and Medline databases were searched up to March 2010 using the keywords positron emission tomography* and functional magnetic resonance imaging* cross-referenced with time estimation*, timing* OR time perception*, where * indicates a wild-card. For the second meta analysis, a further search was conducted in which positron emission tomography* and functional magnetic resonance imaging* were crossreferenced with schizophrenia*. Tailarach coordinate space data from the studies were imported into ALE software developed at the Research Imaging Center (online at http://www.brainmap.org/ale).
Results: The normal-case meta-analysis confirmed the neurophysiological finding that time perception significantly activates the frontal, parietal, and temporal regions and the putamen, thalamus and cerebellum. Analysis of those results that related to explicit time estimation alone identified similar activation clusters to those found when implicit task results were included. The meta-analysis of results with schizophrenic subjects showed, relative to healthy subjects, significantly lower activation of the right frontal regions: the right precentral gyrus, the superior and middle frontal gyrus; left anterior cingulate the right parietal cortex; and the right putamen and the thalamus ($P < 0.05$).
Conclusion: Our results suggest that there is a failure of interhemispheric cooperation in response to timing tasks in schizophrenia and that the right hemisphere is predominantly involved. Thus, a dysfunctional time estimation network may be linked with other critically impaired functions in schizophrenia.
Policy of full disclosure: None.

P-03-006
Task positive and task negative network in schizophrenia: Decreased deactivation is related to structural deficits

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Objective: Previous studies have revealed that patients with schizophrenia show reduced deactivation in task-positive (TPN) and task-negative networks (TNN) during working memory task. However, it remains unclear how these alterations in functional connectivity are related to structural deficits.
Methods: We applied multimodal imaging to 15 patients with schizophrenia and 16 healthy controls: independent component analysis (ICA) during N-back (0b-2b) task and rest conditions, voxel-based morphometry (VBM) and diffusion tensor imaging (DTI).
Results: ICA revealed that patients with SQZ shown decreased modulation of the TPN (fronto-parietal network) and default mode network (DMN) during working memory task and rest. In patients, TPN and DMN activation correlated positively with reduced volume in anterior cingulate and right parietal lobe; and decreased Fractional Anisotropy in right anterior thalamic radiation (all results at threshold of $P = 0.05$ corrected).
Conclusion: In patients with schizophrenia, working memory impairments may be related to reduced deactivation of TPN and DMN. Alteration in functional connectivity are related to white and grey matter deficits.
Policy of full disclosure: None.

P-03-007
Contribution of the mirror neuron system to joint action perception

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Objective: Aim of this study is to further characterize the neural networks involved in the perception of cooperative behaviour between humans during object manipulations using functional magnetic resonance imaging (fMRI). We suppose that the putative mirror neuron system (MNS, e.g. Gazzola et al. 2007; NeuroImage 35, 1674–1684) play a fundamental role. We expect an altered brain activation pattern in associated regions in schizophrenic patients who show reduced social-cognitive skills.
Methods: Schizophrenia patients and matched healthy controls performed two fMRI-experiments. A functional localizer task for mirror neurons was conducted to mask individual brain areas, which are active during both action production and action observation. In the main paradigm subjects watched short videos with two actors manipulating objects, either with or without cooperation. FMRI data were acquired during these tasks. The intersection of brain activity in the first experiment (conjunction analysis) was applied as regions of interest on data of the second experiment.
Results: In healthy subjects the functional localizer consists of areas, which are often found in literature during MNS-tasks, such as the inferior parietal lobe and medial temporal gyrus. The activation contrast between object manipulation with cooperation versus no cooperation reveals higher activation in parts of the temporal, inferior

parietal and frontal lobe. However, the activation pattern in patients differs moderately.
Conclusion: The results suggest that MNS related areas are involved in the perception of cooperative behaviour between humans during object manipulations. These areas have been reported before in the context of cooperative behaviour tasks and stimuli with social relevance [Oberman et al. 2007; Soc Cogn Affect Neurosci 2, 62–66]. The different functioning of these networks in patients, shown during perception of joint action, is discussed as a possible cause of social impairment in schizophrenics.
Policy of full disclosure: None.

P-03-008
Auditory oddball P300 and 1H-magnetic resonance spectroscopy of the dorsolateral prefrontal cortex in young male patients with schizophrenia

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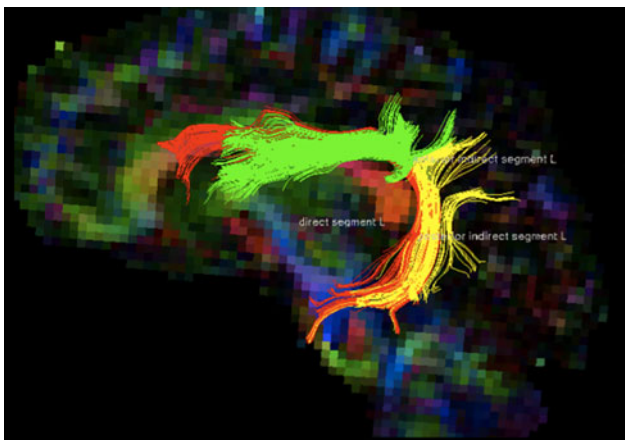
Objective: The study was aimed to the analysis of neurophysiological markers of information processing and some biochemical characteristics of the dorsolateral prefrontal cortex (DLPC) in schizophrenia. The brain area was chosen due to its key role in pathogenesis of the disease.
Methods: 18 young (17–28 years) male patients with schizophrenia (F20, ICD-10) were examined. Averaged PANSS summarized score was 60.5 ± 7.9, positive subscale score—10.9 ± 2.5. 16 age and sex matched mentally healthy subjects comprised the control group. Auditory ERPs in the standard auditory oddball paradigm (60 dB, 80% non-targets (1,000 Hz), 20% targets (2,000 Hz) tones) were recorded and analyzed on BrainWin (Russia) mapping system. Peak amplitudes and latencies of P300 in F7, F3, F4, F8, Pz were taken into analysis. 1H magnetic resonance spectroscopy (MRS) was conducted on 3T Phillips Achieva (Holland) scanner (sequence PRESS, TE = 35, TR = 2,000). The voxel ($20 \times 15 \times 10$ mm^3) was placed in the middle part of the middle frontal gyrus. The ratio NAA/H_2O was analyzed. The statistical analysis was done by SPSS10.0.
Results: There were no intergroup difference by NAA level, however in patients the statistically significant ($P < 0.05$) P300 reduction and prolongation were found in the frontal and frontal-temporal leads, while in Pz the difference by amplitude was revealed. In patients, NAA didn't correlate with PANSS scores and P300 characteristics.
Conclusion: An insignificance of intergroup differences by NAA probably reflects either the "normalization" of DLPC brain functions after the treatment or non-involvement of this brain area in pathological processes. However, neurophysiological parameters remain still impaired seemingly due to deficiency of the other structures which also support the executive functions and selective attention.
Policy of full disclosure: The work was supported in part by RGNF 10-06-00714a grant.

P-03-009
Auditory hallucinations in first episode psychotic subjects: adiffusion tensor imaging study of the arcuate fasciculus

F. Marques-Teixeira (Institute of Psychiatry Psychiatric Research, Porto, Portugal), T. Reis Marques

Objective: Several studies have been using DTI to study the role of the arcuate fasciculus in auditory hallucinations in psychotic patients. All former studies have just analyzed FA and MD as metrics and the arcuate fasciculus as a whole, not considering the contribution of its different segments to the findings reported. This study is the first one using streamline tractography to analyse the different segments of the arcuate fasciculus separately using all the diffusion metrics in auditory hallucinations in psychotic patients.
Methods: 50 patients with psychosis and 45 healthy controls were enrolled in this study. From the former group, 22 patients have auditory hallucinations (AH group) and 28 did not (Non-AH group). Using a three ROI approach, we compared FA, MD, axial and radial diffusivity and MODE, in all of the three segments of the bilateral arcuate fasciculus, between psychotic patients and healthy controls, and hallucinated and non-hallucinated patients.
Results: We found increased MODE in the direct segment right in psychotic patients compared to healthy controls ($P = 0.027$). We found increased axial diffusivity in the right posterior indirect segment in the AH group compared to the Non-AH group ($P = 0.038$). We also found a significant positive correlation between severity scores of auditory hallucinations (P3 subscale score of PANSS) and axial diffusivity in the posterior indirect segment right in hallucinated patients ($P = 0.020$).
Conclusion: This study found significant increased axial diffusivity on the right direct segment of the arcuate fasciculus in patients with auditory hallucinations. The involvement of the right arcuate fasciculus in auditory hallucinations, supports the hyperconnectivity hypothesis of auditory hallucinations. This can provide the basis by which frontal speech-production areas can influence the misidentified inner speech as an auditory input.
Policy of full disclosure: None.

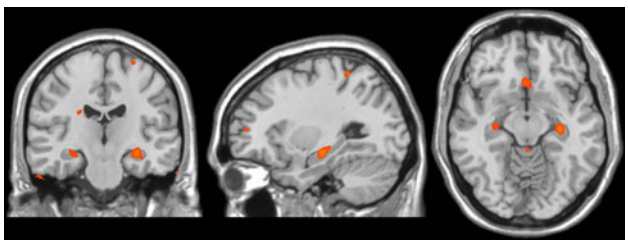


P-03-010
Hippocampal gray matter density correlates with disorganized symptoms in schizophrenia

J. Siemerkus (Psychiatric Univers. Hospital Clin. f. Social a. Gen. Psych., Zurich, Switzerland), I. Eva, R. Mirjana, L. Claudia, W. Godehard

Objective: Several studies revealed an altered hippocampal volume or gray matter density in schizophrenia. However, nonuniform findings in different samples with volume or density reduction or increase and a volumetric study of our own group raise the question, whether a different psychopathology may relate to a structural alteration of the hippocampus. We aimed to investigate the possible effect of disorganized symptoms on hippocampal gray matter density.
Methods: T1-data of 63 patients (19 female) with schizophrenia were analyzed using SPM5. A DARTEL-algorhythm was used for alignment. Psychopathology was measured using SAPS and SANS. We

calculated a score for disorganized symptoms with the sum of the items bizarre behavior, positive thought disorder and attention divided by the number of items. The score was used to calculate a *t* test with the preprocessed MRI-data. Imaging results were accepted as significant with $P < 0.002$ (unc.).
Results: The mean [±SD] of the disorganized symptom score was 1.87 [±1.21]. Regions which showed significant clusters comprised orbitofrontal and frontal cortex, anterior cingulate gyrus, left parietal cortex, right caudate, and right and left hippocampus. The left hippocampal body contained a cluster with 188 suprathreshold voxels and a maximum [mean] value of $t = 3.91$ [3.31]. The right hippocampal body contained a cluster with 80 suprathreshold voxels and a maximum [mean] value of $t = 3.42$ [3.16].
Conclusion: The present data suggests preserved hippocampal integrity in disorganized patients. In contrast to our previous findings voxel based morphometry did reveal an effect for the disorganized symptom score. Our data support the hypothesis of psychopathologically defined endophenotypes. This is of interest with regard to the upcoming revisions of DSM and ICD. Volume alteration of the hippocmapus and its effects on clinical and neuropsychological variables needs further interpretation.
Policy of full disclosure: None.



P-03-011
Increased midline noise power in the gamma band in schizophrenia related to negative symptoms, working memory deficit and insular activity

V. Suazo (Neuroscience Institute of Castilla y León, Salamanca, Spain), V. Molina, A. Diez, C. Martín, A. Ballesteros, P. Casado, M. Martin loeches, P. Tamayo, C. Montes

Objective: There is an increasing support for a disorganized cerebral activity in schizophrenia, perhaps in relation to a decreased deactivation of the default mode-network and/or to an inhibitory deficit in that illness. We aimed to explore the possibilities of noise power (scalp-recorded EEG activity unlocked to stimuli) to assess those possibilities.
Methods: 50 schizophrenia patients (of which 23 were acute drug-free and 27 stable treated patients) and 28 healthy controls underwent clinical and cognitive assessments and an EEG recording during a P300 paradigm to calculate noise power magnitudes in the theta and gamma bands. Besides, regional activity was simultaneously assessed with perfusion SPECT in the treated patients and controls.
Results: A significant increase of gamma noise power common to acute, and stable patients in comparison to controls was found over Fz, P3 and, at trend level, over P4. That increase was positively correlated to negative symptoms severity and negatively correlated to working memory scores. In the patients, Fz noise power was positively related to right insular perfusion. Gamma Fz noise discriminated significantly between patients and controls. No differences were found in theta noise power.
Conclusion: Gamma noise power may represent a useful and non-invasive tool to investigate brain dysfunction in psychotic illness. These results suggest an inefficient activation pattern common to early, acute and stable stages of schizophrenia.
Policy of full disclosure: None.

P-03-012
Combination of morphological features for recognition analysis of first-episode schizophrenia patients.

T. Kasparek (University Hospital Brno Psychiatry, Czech Republic), D. Schwarz, E. Janoušová, R. Přikryl, E. Češková

Objective: to recognize first-episode schizophrenia (FES) and healthy subjects (HS) with the use of classification analysis based on the combination of brain morphological features extracted from MR images.
Methods: 52 FES and 52 age and sex matched HS were examined using whole brain magnetic resonance imaging (high-resolution T1 scans). We performed voxel-based and deformation-based morphometric analyses to obtain voxel-wise information on gray matter density and local brain volume. These morphological features entered the classification analysis based on k-nearest neighbors (k-NN). Leave-one-out cross validation was performed to assess the accuracy of the results.
Results: The accuracy of the classification analysis based on the combination of morphological features reached 87.5%, with 88.5% sensitivity and 86.5% specificity. The accuracy of classification analyses based on either gray matter density, or local brain volume was lower: 77.9 and 84.6% respectively.
Conclusion: We were able to recognize a significant percentage of first episode schizophrenia patients and healthy subjects based solely on the information on brain morphological features. The combination of morphological features led to more successful recognition. These results indicate that using different imaging modalities representing different aspects of the neurobiology of schizophrenia may lead to clinically meaningful diagnostic results.
Policy of full disclosure: Supported by a research grant of the Czech Ministry of Health No. NS9893-4.

P-03-013
Neural correlates of cognitive behavioral therapy effects in schizophrenia

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Objective: The use of cognitive behavioral therapy (CBT) in treatment of schizophrenic disorders is scarcely implemented in routine care. By now there is a good evidence for its effectiveness. However, the topic "neural correlates of CBT effects in treatment of psychotic disorders" has only been investigated for very small sample sizes. The results of a multicentre fMRI study on the neural basis of CBT effects in patients with psychosis will be presented.
Methods: In this study ninety-eight schizophrenia patients from the POSITIVE clinical trial and eighty-nine healthy subjects were recruited at six German university hospitals (Bonn, Duisburg-Essen, Düsseldorf, Frankfurt, Cologne, Tübingen). After 9 months of therapy (either with CBT or Supportive Therapy), patients and controls were re-examined enabling the study correlates of cerebral reorganization processes. Differences in brain activation relating to phenomena of decision-making under uncertainty (Jumping-To-Conclusions-Task, JTC) and biased attribution (self- vs. external reference of emotional events, Attributional-Bias-Task, AB) were analyzed.

Results: The JTC-task showed activations in key areas for decision making (prefrontal and inferior parietal networks). Activation in these areas diminished significantly in patients with chronified psychosis. The comparison of brain regions of both groups in the AB-task also revealed significant decreased activation in the medial superior prefrontal cortex and middle temporal gyrus of patients with schizophrenia compared with healthy subjects.
Conclusion: We found reliable activations in task-relevant brain areas. Diminished activations in these brain regions increased significantly in patients after 9 months of psychotherapy. These results suggest that there are neuroplastic changes present due to relearning strategies in psychotic patients with schizophrenia. This is an encouraging finding, hopefully giving rise to a more widespread application of CBT in schizophrenia.
Policy of full disclosure: None.

P-03-014
Structural brain correlates of sensorimotor gating in first-episode antipsychotic-naïve schizophrenia patients

T. B. Hammer (Copenhagen University Hospital, Denmark), B. Oranje, A. Skimminge, B. Ebdrup, H. Bro, H. R. Siebner, B. Fagerlund, B. Glenthoj, W. Baare

Objective: Prepulse inhibition (PPI) of the startle reflex, a cross-species measure of early information processing, is modulated by a complex neural network extending from the brainstem to higher order cortical areas. PPI has consistently been found to be impaired at all stages of schizophrenia. Previous studies investigating the relationship between PPI and MR-Imaging found brain correlates of PPI to differ between schizophrenia patients and healthy controls. However, these studies only included chronically ill and medicated patients. Aim Here we examined structural brain correlates of PPI in antipsychotic-naïve first-episode schizophrenia patients and healthy controls.
Methods: Twenty-eight antipsychotic-naïve schizophrenia patients and 40 matched healthy subjects (all male) were included in the study. Women were excluded since PPI fluctuates through the menstrual cycle. Acoustic PPI assessment and structural MR-imaging (1.5 or 3 Tesla) were performed in separate sessions at baseline. Voxel-based-morphometry was used to investigate the relationship between PPI and regional grey matter volumes (GMV).
Results: Patients had significant lower PPI than healthy controls ($t = 2.03$; $P < 0.05$). Patients and healthy controls did not differ significantly with respect to brain areas, in which PPI and GMV were correlated. The amount of grey matter in the right superior parietal gyrus (SPG; $P = 0.007$, FWE corrected) and right pre-supplementary motor areas (pre-SMA), superior medial frontal gyrus (SMFG) and left supplementary motor area (SMA) correlated positively with the level of PPI ($P < 0.001$, uncorrected; $k = 89$ voxels). For details please see Table 1. However the correlations within the frontal areas were driven by correlations within the control group. The frontal areas could not be found in single group analysis of the patients; not even with post-hoc analysis specifically searching for them.
Conclusion: Cortical areas involved in planning, inhibition and cognition seem to be involved in the regulation of PPI both in healthy controls and antipsychotic-naïve first-episode patients. In spite of the fact that patients showed significantly lower PPI than healthy controls, we found no significant group interactions with regard to PPI-GMV correlations in any brain regions. This could indicate that there are quantitative but not qualitative differences in the regulation of PPI between healthy controls and antipsychotic-naïve schizophrenia patients. However the PPI-GMV correlations we found in the frontal areas were restricted to the healthy controls indicating a kind of hypofrontality in the regulation of PPI in patients.
Policy of full disclosure: None.

P-04 Epidemiology, diagnosis

P-04-001
The epidemiology of schizophrenia and other psychotic disorders among Finnish prisoners

M. Joukamaa (Finland School of Health Sciences, University of Tampere, Finland), J. Aarnio, S. Hakamäki, T. Lintonen, A. Mattila, H. Vartiainen, P. Viitanen, T. Wuolijoki

Objective: Penrose's Law states that as the number of psychiatric inpatients declines, the number of prisoners increases. Several studies have proposed that after deinstitutionalization the prevalence of psychotic disorders among prison populations has grown up. We wanted to study if this is true also in Finland where the number of psychiatric beds nowadays is one quarter of that 25 years ago.

Table 1

Anatomical area	Lobe	Side	Controls and patients[a]					Healthy controls ($n = 38$ men)[b]					Patients ($n = 27$ men)				
			MNI coordinates			*t* value	Cluster size	MNI coordinates			*t* value	Cluster size	MNI coordinates			*t* value	Cluster size
			X	Z	Y			X	Z	Y			X	Z	Y		
Pre-SMA	Frontal	R	4	23	61	3.9	321	4	24	64	5.11	508					
SMA		L	−21	2	72	4.3	237	−21	3	67	3.77	110					
Sup. medial		R/L	0	52	15	3.9	122										
Superior (7A)	Parietal	R	33	−66	58	5.8*	589	33	−60	57	4.9	140	30	−66	60	5.6	220
			9	−67	51	3.8	116										

Correlation maps were thresholded at $p < 0.001$ with an extended threshold of $k = 89$ voxels. Three separate maps were made: One included patients and controls, one included only controls, and one included only patients. Only positive correlations were found

[a]Corrected for diagnosis, scanner-type, age, and scanner drift

[b]Corrected for scanner-type, age, and scanner-drift

*$p = 0.007$, FWE-corrected

Methods: This study forms a part of a large health survey of Finnish prisoners in 2006. The study received approval from the ethical council and from the Ministry of Justice. Participation was voluntary and a written informed consent was obtained from all participants. The material ($N = 610$) consisted of male and female prisoners, life sentence offenders and fine defaulters and represents all Finnish prisoners. Structured clinical interview for DSM-IV disorders was the psychiatric diagnostic tool.
Results: The life time prevalences of schizophrenia, schizoaffective psychoses and delusional disorders were 0.7, 0.6 and 1.0% without any significant differences between the subsamples. The life time prevalence of the whole schizophrenia group disorders was 7.0% consisting mainly of psychotic disorders NOS (3.8%).
Conclusion: When compared with the results of similar earlier prison health survey before the deinstitutionalization in Finland started, no rise in the prevalence of schizophrenia, schizoaffective psychoses and delusional disorders was found. Similarly the prevalence figures now obtained were essentially at the same level as in a recent epidemiological study, with a sample representative to the whole Finnish adult population. So the deinstitutionalisation process in Finland has not led to an accumulation of psychotic criminal offenders (mostly with no responsibility for the crime accused "not guilty by reason of insanity") to prison.
Policy of full disclosure: None.

P-04-002
Temperament in individuals with psychotic disorders before and after the onset of illness

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Objective: The Temperament and Character Inventory (TCI) is used to measure novelty seeking (NS), harm avoidance (HA), reward dependence RD), and persistence (P). There are not many longitudinal studies of temperament among individuals with psychosis. We were able to study 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 onset of illness before ($n = 17$) or after ($n = 18$) the 31-year follow-up, and healthy controls ($n = 100$) filled in these scales again at age of 43. We studied also association between psychotic symptoms (measured with Positive and Negative Syndrome Scale, PANSS) and temperament (at 43 years).
Results: The 31- and 43-year temperament scores correlated strongly among controls (Pearson's r: NS 0.69, HA 0.65, RD 0.56, P 0.57), whereas correlations among psychotic individuals with onset before first follow-up were weaker (NS 0.38, HA 0.51, RD 0.30, P 0.51). Individuals who had their onset of psychosis after the first follow-up had significant increase from age 31 to 43-years in HA when compared to controls. At age of 43 years, HA correlated highly positively with total PANSS score, especially among those with more recent onset ($r = 0.83$), but also among those with onset before age 31 years ($r = 0.40$). Other temperament dimensions were quite independent from psychotic symptoms.
Conclusion: Temperament was stable among controls, and more unstable in individuals with psychoses. In psychoses, increase in harm avoidance associated with getting ill, and it had very strong positive association to amount and severity of symptoms. When studying temperament in psychoses, duration of illness and symptom severity should be taken into account.
Policy of full disclosure: None.

P-04-003
A new epidemiological survey on stress, mental health and psychotic symptoms in young and middle-aged adults in Zurich

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Objective: The Zurich Program for Sustainable Development of Mental Health Services (ZInEP) was designed in order to enhance the development of psychiatry in the canton of Zurich. This presentation introduces one of the six subprojects, the Epidemiologic Survey. The major aim of the cross-sectional survey is to generate comprehensive data about mental health in the general population of adults aged 20–40 years. The design of the Survey is geared to the longitudinal Zurich Study (Angst et al. 2005).
Methods: The Survey consists of three components. (1) Approximately 10,000 subjects representative of the canton of Zurich will be screened with a computer assisted telephone interview (CATI) using the SCL-27. (2) Applying a stratified sampling procedure, 1,800 participants will be selected for a comprehensive face-to-face-interview using the Mini-SPIKE (a short form of the SPIKE used in the Zurich Study) covering psychiatric syndromes and their social consequences. Additional self-reporting instruments will cover issues such as psychotic symptoms (SPQ-B, PC, BCSS, CEQ, SIAPA) and personality disorders (ADP-IV). (3) Furthermore, 200 participants of the interview-sample will be selected for a longitudinal survey. These subjects will initially perform a series of neurophysiological tests including biological markers and will be interviewed in detail with regard to psychotic and depressive symptoms (e.g. PANSS). Subsequently they will be interviewed in 2-month intervals over a period of 1 year.
Results: Combined with the Zurich study the Epidemiologic Survey will provide information on: (a) the change of prevalence rates of mental disorders and subthreshold syndromes over the past 30 years; (b) the modification of use of health services, professional and alternative help; (c) the provision of information on attitudes towards psychiatric disorders; (d) the differentiation of subthreshold psychotic syndromes and (e) information on the influence of stress-related effects and life-events on depressive and psychotic symptoms.
Policy of full disclosure: None.

P-04-004
Concordance rates and early risk factors in schizophrenia; a set-up for a twin study, including preliminary data on concordance rates from linking the Danish Twin Register and the Danish Psychiatric Central Register

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Objective: Background: From early twin studies the concordance rates for schizophrenia have been found ranging from 33 to 78% in monozygotic (MZ) twins and 8–28% in dizygotic (DZ). More recent studies have estimated rates of 41–65% in MZ twins and 0–28% in DZ. There is empirical evidence for methodological procedures being systematically associated with different concordance rates, such that

register based sample selection and zygosity determination by genetic testing significantly lower concordance rates. Furthermore studies indicate that a refinement of concordance rates based on whether the twins share a placenta (mono-chorionic vs. di-chorionic) may be plausible. Pre- and postnatal environmental factors have been shown to increase the risk of developing schizophrenia, including perinatal events, CNS infections in childhood, adverse childhood experiences, and drug abuse. Objectives: There are 2 specific aims of the present part of the twin study: (1) To establish concordance rates in the included twins after a validation of diagnosis (SCAN), zygosity (blood sample) and chorion-placental status (birth records), which, to our knowledge, has not been done before. (2) To identify early risk factors for schizophrenia and examine whether there is a synergistic effect of several risk factors towards developing schizophrenia, and to identify environmental predictors of discordance in twins.
Methods: We want to examine clinical endophenotypes and early risk factors in a twin study design. Twins, concordant and discordant for schizophrenia will be included from the Danish Twin Register. We plan to include min. 40 MZ pairs matched with 40 DZ twin pairs and 80 healthy twin pairs. Data on risk factors from the Danish registers of known high quality will be linked and combined with the most recent neurobiological examination methods.
Results: The linkage between the Danish Twin Register and the Danish Psychiatric Central Register is on-going, and preliminary data on concordance rates from the baseline twin data will be presented.
Policy of full disclosure: None.

P-04-005
Does reduced facial affect bias clinicians to overrate depression in patients with schizophrenia? Prevalence and explanatory factors of disconcordance between self-and observer rated depression in schizophrenia

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Objective: Schizophrenia patients with comorbid depression report less subjective quality of life and show an increased risk of relapse and suicide. A precise assessment of depressive symptoms in these patients is therefore relevant to treatment and prognosis. Observer-rated symptom scales are widely used to estimate schizophrenia symptoms. Self-rated questionnaires are more common in the assessment of depression. The aim of this investigation is to analyze the concordance between self-and observer-ratings of depression in schizophrenia and to detect factors that explain discrepancies between observer and patient ratings.
Methods: In- and outpatients with schizophrenia ($n = 118$) were assessed with regard to depression, psychotic symptoms and socio-demographic variables. We applied two observer-rated interview-based scales to identify symptoms of depression: CDSS and PANSS Item G6. Furthermore, we applied two self-rated questionnaires: BDI and the subscale Depression of the SCL-90-R. To assess differences between persons with higher or lower self-and observer-ratings we used univariate between-subjects analyses of variance (ANOVA).
Results: Twenty-four percent of the schizophrenia patients fulfilled the DSM-IV-criteria of depression. In 49%, the patients' ratings of depression were comparable to those conducted by the clinicians. Approximately 25% of the patients' ratings were higher and these patients were characterized by higher general psychopathology indicated by scores on the SCL-90 ($F(2, 114) = 10.3$; $P \leq 0.01$). In another 25%, the clinicians rated depression symptoms higher than the patients. These patients were significantly more impaired by negative symptoms such as blunted affect ($F(2, 114) = 10.3$; $P \leq 0.01$) and poor affective rapport ($F(2, 114) = 4.5$; $P \leq 0.05$).
Conclusion: Our findings show reasonable concordance between the estimation of the patients and the observers (49%). However, clinicians should be aware that negative symptoms such as blunted affect might bias them towards overvalued ratings of depression in patients with schizophrenia.
Policy of full disclosure: None.

P-04-006
Cycloid psychoses: where are they in ICD-10 and DSM-IV?

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Objective: Leonhard described the cycloid psychoses (CP) and delineated three subtypes (anxiety-happiness, confusion and motility psychosis). CP are characterised by acute onset, intraphasic bipolarity and good prognosis. The original work gave rise to a set of criteria formulated by Perris and Brockington (P&B, 1981), including onset and symptomatology, but not outcome and intraphasic bipolarity. The P&B criteria are integrated in ICD-10 acute polymorphic psychosis (APP). The DSM-IV brief psychotic disorder (BPD) requires good outcome, but comprises non-specific symptomatology only. This study aimed to determine the prevalence of Leonhard CP in patients with psychotic disorders. Moreover, the overlap with DSM-IV and ICD-10 categories was established. Finally, clinical characteristics of CP were elaborated.
Methods: 80 patients with psychotic disorders (acute episode or exacerbation) were assessed at baseline and after 6 weeks of anti-psychotic treatment. CASH, PANSS and CGI were used to evaluate symptomatology. Furthermore, Leonhard and P&B criteria for CP were applied. During consensus meetings with experienced psychiatrists, patients were classified according to DSM-IV, ICD-10, Leonhard and P&B.
Results: In 12 patients, a diagnosis of Leonhard CP was present. Overlap between Leonhard and P&B CP was significant but rather small. Classification according to ICD-10 and DSM-IV showed considerable diagnostic heterogeneity. CP patients were mostly diagnosed with DSM-IV BPD and ICD-10 APP. There was a significant but modest categorical overlap. As could be expected, Leonhard CP patients showed, compared to non-CP patients, significantly more key symptoms like perplexity, motility disturbances and pananxiety.
Conclusion: The estimated prevalence of CP is 15% in patients with psychotic disorders. CP appears to be by no means identical to BPD or APP. Although identification of CP is of heuristic value, this can not be asserted by current classification systems. Thus, extensive and detailed clinical evaluation is mandatory, especially in patients presenting with perplexity, psychomotor disturbances or severe anxieties.
Policy of full disclosure: None.

P-04-007
Klinefelter syndrome in a male identical twin and chronic schizophrenia-like psychosis

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Objective: Klinefelter syndrome (KS) or 47, XXY is a common chromosomal disorder characterized by tall stature, reduced fertility and cognitive, emotional and language dysfunctions, especially the

production of expressive language. Intellectual impairment is infrequent. In addition, high levels of autistic and schizotypal personality traits are present. Over the past decades, several reports have been published suggesting an increase in psychiatric disorders in KS patients, particularly psychoses from the schizophrenia spectrum.
Methods: A 51-year-old male with KS was referred to the outpatient clinic for re-evaluation of long lasting psychotic symptoms that had lead to severe occupational problems. Detailed neuropsychiatric and neuropsychological assessment was performed including genetic work-up and MRI of the brain. His identical twin brother who had no psychiatric problems, was also extensively investigated.
Results: With respect to psychopathology, most pronounced symptoms were paranoid ideation, bizarre delusions of influence and broadcasting (convinced of implantation of active electronic devices in his feet), ideas of reference, associative thinking and religious preoccupations as well as lack of insight. Neuropsychological assessment disclosed a total IQ of 86 (KAIT), dysfunctions in attention, and fragmented perception. His personality showed marked traits of extraversion and impulsivity. Karyotyping confirmed 47, XXY; SNP micro array analysis as well as MRI scanning of the brain showed no abnormalities. In his identical twin brother with also 47, XXY karyotype, no formal psychiatric disturbances could be detected. His total IQ was 92 (KAIT). There were mild problems in attention and memory. His personality was typified by extraversion and distinct positive attitude towards daily life.
Conclusion: In the patient with psychotic symptoms, a diagnosis of chronic paranoid schizophrenia-like psychosis was made. He refused treatment with antipsychotics. This case report is suggestive for an association between Klinefelter syndrome and increased risk for psychotic disorders, possibly related to its psychological vulnerability profile.
Policy of full disclosure: None.

P-04-008
Psychiatric disorders in children with cerebral palsy

C. Bertoncelli (Paediatric Neurology, Lenval Hospital, Nice, France), D. Bertoncelli

Objective: A high degree of psychiatric disorders has repeatedly been described among children with brain disorders (Goodman R et al. 1997, Craven C. et al. 2002). However few systematic studies of psychiatric comorbidities in children and adolescents with CP have been conducted, as main focus has been so far on the physical disabilities (Foster T et al. 2010). The objective of this research was to identify the presence of psychiatric disorders in a population of children with cerebral palsy.
Methods: The sample consists of 45 patients with Cerebral Palsy observed at the Department of Neurodevelopment Disorders (EEAP) at the University Paediatric Hospital Lenval of Nice between January 2005 and June 2008 (42 months). We took note of their neurological illness and their psychiatric pathologies. All patients underwent a structured battery of neurological and psychomotor tests. Therefore we utilized observable behaviours in structured and non-structured situations, questionnaires and diagnostic interviews, together with the history of specific target symptoms. When possible we interviewed them using the Structured Clinical Interview for DSM-IV (SCID).
Results: Children with cerebral palsy showed clinical disorders (coded on axis I of DSM IV-TR), diseases usually first diagnosed in infancy, childhood, or adolescent. All of them observed generic psychopathological disorders as learning, motor skills, communication, attention-deficit, elimination disorders and mental retardation (coded on axis II). In addition of these generic diseases we established personal clinical characteristics as: cognitive disorders, mental disorders due to a catatonic type condition, psychotic, anxiety and mood disorders, sexual disorders not otherwise specified.
Conclusion: Children with cerebral palsy have a higher-than-expected rate of psychiatric disorders. This study underlines the presence of psychiatric disorders in a population of children with cerebral palsy. This may help us to develop a personalized and integrated programme of rehabilitation specified to these kinds of patients.
Policy of full disclosure: None.

P-04-009
Influence of child and adolescent psychiatric disorders on neurological development pathologies

C. Bertoncelli (Paediatric Neurology, Lenval Hospital, Nice, France), M. Bertoncelli

Objective: This study is intended to analyse the relation between comorbid psychiatric disorders with some kinds of neurological diseases. Subjects with neurological development pathologies may show in addition to core symptoms some kinds of psychiatric diseases which are relevant for the treatment and the course of the disease.
Methods: Analysis was conducted on a sample of 56 children showing some very particular kinds of neurological disorders diagnosed at the Department of Neurodevelopment Disorders (EEAP) at the University Paediatric Hospital Lenval of Nice between January 2005 and June 2008 (42 months). Neurological pathologies (cerebral palsy, encephalopathy, epilepsy, quadriplegia), were observed to be related with a variety of psychiatric disorders.A structured battery of neurological and psychomotor tests was performed on all children under analysis. We collected our data from different type of sources: observable behaviours in structured and non-structured situations, questionnaires and diagnostic interviews, together with the history of specific target symptoms. We interviewed the children able to answer the test using the Structured Clinical Interview for DSM-IV (SCID).
Results: The four most significant psychiatric profiles we found were: (1) Mental retardation in 37.5% of the patients, (2) Psychotic disorders (14.3%), (3) Pervasive development disorders (autistic disorder, Rett's disorders) (12.5%), (4) Mental disorders due to a catatonic type condition (8.9%). The above profiles covered about 73% of the psychiatric profiles we found, while the remaining 27% were difficult to be classified due to extremely critical patients clinical condition.
Conclusion: Subjects with neurological development pathologies may show in addition to core symptoms some kinds of psychiatric disorders. On our sample of study we classified the most relevant types of psychiatric outcomes we observed. The above results should be helpful in order to improve both prognosis and rehabilitation of the patients.
Policy of full disclosure: None.

P-04-010
Psychosis in herpes Encephalitis

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Objective: Herpes encephalitis is the most common cause of viral encephalitis worldwide. Psychiatric symptoms often appear before any obvious brain damage, and it is easy to confuse them with primary psychotic disorders, as there is sometimes no increase in temperature or any other physical sign permitting diagnosis. At present the diagnostic test is the detection of the DNA of the simple herpes virus by PCR in the cephalorachidian fluid, a highly sensitive

(98%) and specific (94–100%) test that is rapidly carried out. We review the scientific literature on neuropsychiatric manifestations found in patients with viral encephalitis and present a case recently studied in liaison psychiatry.
Methods: We report the case of a 69-year-old man referred to the Emergency Department for behavioural disturbances with paranoid delusional ideation accompanied by visual and auditory hallucinations whose symptoms had evolved over a period of days, and who displayed intense psychomotor agitation on admission. The observation of attention and orientation disturbances led to the diagnosis of delusion and he was transferred to internal medicine.
Results: The most frequent psychiatric manifestations during the acute phase of viral encephalitis are, in order, psychomotor agitation, drowsiness, disorientation, visual hallucinations, delusional ideas and sleeplessness. The development of psychotic and contusional symptoms is usually intermittent and changeable. Interepisodic periods of symptom remission are frequent and there are residual mnesic disturbances after the patient's recovery.
Conclusion: A review of the medical literature reveals little information on the presence of psychiatric symptoms in subjects with herpes encephalitis, delusion and psychosis being those most frequently described during the acute phase of the infection. Many cases of encephalitis begin with psychiatric symptoms with no other features of organicity. High temperature, though frequent, is not absolutely necessary for diagnosis and focal neurological symptoms do not always appear. As in our case, agitation, disturbances of consciousness and visual hallucinations are the most frequent psychiatric symptoms in the initial phase of herpes encephalitis.
Policy of full disclosure: See affiliation.

P-05 Genetics, neurotransmission

P-05-001
The Australian Schizophrenia Research Bank (ASRB): The first 650 sample profile

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Objective: The Australian Schizophrenia Research Bank (ASRB) is a national resource aiming to achieve a sample of 2,000 cases with schizophrenia and 2,000 healthy controls comprehensively assessed using a structured clinical diagnostic interview and symptom ratings, together with neuropsychological evaluations, structural MRI scans, and genetic (DNA) analyses of blood samples.
Methods: Participants were assessed using a comprehensive assessment battery that consists of socio-demographic questions including medical and family history, neurological evaluation (NES), neuropsychological assessment and cognitive performance measures (WTAR,WASI, RBANS, LNS, COWAT), a diagnostic interview that includes drug and alcohol history (DIP, Castle et al. 2006) to confirm diagnosis, ratings for negative symptoms (SANS), general functioning (GAF), and questionnaires of childhood adversity, personality disorder (IPDE) and psychosis proneness (SPQ).
Results: A sample of 657 people with schizophrenia (mean age = 39.62 years; SD = 10.91) and 636 healthy controls (mean age = 42.20 years; SD = 13.60) were compared across measures. The schizophrenia sample had a higher proportion of males (cases 66.20%; controls 44.80%), fewer living in married or de facto relationships (cases 14.80%; controls 56.90%) and fewer years of education (cases 12.95, SD = 2.90; controls 14.98, SD = 3.11). Schizophrenia participants also had lower premorbid IQ (cases 103.34, SD = 12.79; controls 110.39, SD = 9.33), current IQ (cases 102.44, SD = 15.23; controls 116.46, SD = 10.65) and RBANS total score (cases 80.33, SD = 14.21; controls 101.14, SD = 12.22), consistent with performance reported previously for Australian samples (Loughland et al. 2007).
Conclusion: These findings are consistent with those reported previously in the Australian Low Prevalence Disorders Study (Castle 1999), suggesting the ASRB sample is broadly representative of people with schizophrenia living in Australia. The ASRB is a unique schizophrenia resource that is accessible to approved Australian researchers and to international scientists in 2011.
Policy of full disclosure: None.

P-05-002
Association of dystrobrevin-binding protein 1 gene with cognitive functioning in schizophrenic patients

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Abstract: Despite extensive research in past decades, the influence of genetics in the regulation of cognitive functions in schizophrenia remains unclear. Dystrobrevin-binding protein 1 (DTNBP1) is one of the most promising candidate genes of schizophrenia. An association of DTNBP1 with cognitive dysfunction, particularly memory impairment, has been reported by a number of studies. However, the results remain inconsistent. The aim of the study was to measure the association between DTNBP1 polymorphism and cognitive functioning, thereby focusing on careful selection and homogenizing the measurements of cognitive functions. 93 clinically stable outpatients had been tested with a wide battery of cognitive tests, and six single nucleotide polymorphisms (SNPs) of DTNBP1 were genotyped in all participants. Factor analysis revealed three factors which correspond to distinct cognitive domains, namely attention, memory and executive functioning. We found a significant association of SNP rs909706 with attention and executive functioning. No other SNP predicted any cognitive functions. Unlike the majority of studies in this field, we did not find any significant association of DTNBP1 with memory. However, a trend was detected on one of the memory tests. The present study supports the involvement of DTNBP1 in the regulation of cognitive processes, particularly attention and executive functioning in schizophrenic patients. The replication of this finding in a larger sample is needed in order to confirm the importance of this particular SNP in the genetics of schizophrenia. Also, further studies concerning the functional impact of this SNP or an associated genetic variation have to be performed.
Policy of full disclosure: None.

P-05-004
Genome-wide significant association with negative mood delusions in 3q26.1

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Objective: Genome-wide association studies have successfully identified susceptibility variants in psychiatric disorders. Taking into account consideration the heterogeneity of these disorders, testing clinical symptoms dimensions seems feasible. Therefore this concept

has here been applied to data from genome-wide association studies (GWAS) of BD.
Methods: We performed a GWAS of factor dimensions in 637 clinically well-characterized BD patients of German ancestry. In subsequent follow-up studies of our top GWAS results, an additional 290 BD patients, 977 SCZ patients and 554 MDD patients were included, all of German descent.
Results: Rs9875793, which is located in an intergenic region of 3q26.1 located near to solute carrier family 2 (facilitated glucose transporter), member 2 gene (SLC2A2), was significantly associated with the factor dimension "Negative Mood Delusions" in the combined BD sample ($n = 927$; $P = 4.65 \times 10^{-8}$, OR = 2.66). In a subsequent case–control analysis, the G allele of rs9875793 was overrepresented in patients with "Negative Mood Delusions" symptoms ($P = 0.0007$, OR = 1.74). This association finding we are currently replicating in an independent BD sample. Further the association between rs9875793 and "Negative Mood Delusions" could be extended to patients with schizophrenia (SCZ) ($n = 977$) and major depressive disorder (MDD) ($n = 554$). We observed a trend for association of rs9875793 with "Negative Mood Delusions" in MDD patients, and allele frequencies of rs9875793 differentiated schizoaffective patients of depressive subtype from other SCZ patients (PSCZ = 0.023, OR = 1.65).
Conclusion: In our factor analytic study we could identify a genome-wide significant variant close to SLC2A2, which is associated with "Negative Mood Delusions". Further we could show that this association is not specific to a given diagnosis, but extends across bipolar BD, SCZ and MDD.
Policy of full disclosure: None.

P-05-005
Early visual processing measured with backward masking: the new endophenotype of schizophrenia?

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Objective: Over the last years, endophenotypes have become of primary interest in schizophrenia research. Endophenotypes are stable, easily measurable markers of a phenotype which are assumed to be related to a small number of genes involved in a specific pathway of phenotype pathophysiology. Among other cognitive or electrophysiological measures, visual backward masking (VBM) as a measure of early information processing proved to be one of the promising candidate endophenotypes of schizophrenia. In a series of studies, the key features required for a reliable endophenotype have been studied for VBM. Performance appears to be impaired in schizophrenic patients compared to controls, displaying nearly 90% sensitivity and specificity. First degree relatives exhibit an impaired performance compared to controls. The impairment on VBM performance appears to be time and state independent. Therefore, we concluded a strong genetic component and have further studied the genetic background of VBM. An exploratory pilot study was conducted that investigated several schizophrenia candidate genes such as DTNBP1, COMT, CHRNA7 and GRM3, and ZNF804A. A significant relationship between VBM performance and CHRNA7 has been shown, other results are pending. The results of the present study clearly outline the genetic background of early visual processing measured by VBM, and supporting its role as a reliable endophenotype for schizophrenia.
Policy of full disclosure: None.

P-05-006
Association of polymorphisms rs2055314, rs2272522 and rs331894 in close homologue of L1 gene with schizophrenia in State of Qatar

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Objective: Single nucleotide polymorphisms (SNPs) in the CHL1 (close homologue of L1) gene on chromosome 3p26 are associated with schizophrenia among different populations. The aim is to investigate the associations of the of theses SNPs of CHL1 gene locus; rs2055314(C/T), rs2272522 (C/T) and rs331894 (A/G) and its haplotypes in schizophrenic patients in Qatari populations.
Methods: A case control association study was carried out on 48 Qatari schizophrenic patients and 47 Qatari unrelated, healthy, control subjects. Schizophrenia was diagnosed according to the Fourth Edition (DSM-IV) by two independent psychiatrists. Genotyping of these SNP was carried out by the 5′ nuclease assay using TaqMan MGB probe by means of an ABI 7500.
Results: All SNPs are within the Hardy–Weinberg Equilibrium. The minor allele frequency [MAF], T allele for rs2055314 was 0.361 in all subjects, with Odds Ratio [OR] = 0.84 and 95% CI (0.36–1.91) and P value = 0.672 between cases and controls. The [MAF], T allele for rs2272522 was 0.170 in all subjects, with OR = 1.41 and 95% CI (0.46–4.34) and P value = 0.545 between cases and controls. The [MAF], G allele for rs331894 was 0.407 with OR = 0.28 and 95% CI (0.12–0.64) and P value = 0.002 between cases and controls. Using the genetic recessive model revealed that rs331894 had OR = 0.044 with 95% CI (0.004–0.406) and Chi-Squared Bonf. P value = 0.0008 between cases and controls. Haplotype analysis revealed one haplotype (CGC) spanning CHL1 was significant (Chi-Squared Bonf. $P = 0.006$) with OR = 2.23 and 95% CI (1.12–5.14).
Conclusion: Of all SNPs studied, only rs331894 has a significant association with schizophrenia. Our findings strengthen the association between the studied CHL1 gene SNPs haplotypes with schizophrenia.
Policy of full disclosure: None.

P-05-007
Association of the CTLA-4 gene with schizophrenia in Coimbatore, South Indian population

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Objective: Cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) is important for down-regulation of T-cell activation, and CTLA-4 gene polymorphisms have been implicated as risk factors for schizophrenia patients.
Methods: Previous studies of the association between the exon 49 polymorphism of the CTLA-4 gene in schizophrenia have provided conflicting results. In order to determine association of the CTLA-4 gene with schizophrenia in schizophrenia population, we used denaturing gradient gel electrophoresis (DGGE) to genotype polymorphisms of four SNPs of the CTLA-4 gene in 67 schizophrenia patients and 67 healthy controls. Furthermore, meta-analysis of all available studies relating polymorphism to the risk of schizophrenia was performed to confirm the disease association.
Results: Among the SNPs examined, the genotype frequencies of CTLA-4 þ49 and CT60 in RA patients differed significantly from controls. In addition, the distribution of four haplotypes constructed by these two SNPs was significantly different between patients and controls. The meta-analysis also revealed that in schizophrenia

populations, the CLTA-4 þ49 G allele was associated with the risk of schizophrenia.
Conclusion: These results suggested that the CTLA-4 gene might be involved in the susceptibility to schizophrenia in the Coimbatore, south Indian population and both þ49 and CT60 of CTLA-4 gene might be the causal variants in schizophrenia disease.
Policy of full disclosure: None.

P-05-008
DTNBP1, HSPs and TAAR6 variations influence schizophrenic phenotype and treatment response

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Objective: A pharmacogenetic approach is used to challenge the hypothesis that DTNBP1, HSP-70 and TAAR6 mutations may impact the clinical presentation or treatment outcome in a sample of 240 Schizophrenic in patients.
Methods: A sample of 240 Schizophrenic Korean in patients was enrolled in the study. Patients were administered the PANSS test at the moment of admission and at the moment of discharge, 45 days after on average. Patients were treated with typical and atypical antipsychotics with low benzodiazepine doses as the only other treatment allowed. Sociodemographic, clinical and treatment related variables entered the analysis as covariates. For power analysis on average, we had a power of 0.8 to detect a minimum difference of about 2% in the PANSS scores.
Results: DTNBP1 haplotype A-A (rs3213207, rs1011313) haplotype was associated with lower PANSS total and positive scores at baseline ($P = 0.01$; $P = 0.005$) and at discharge ($P = 0.008$; $P = 0.005$). HSPs haplotypes A-C-G-G and G-C–C–C (rs2075799, rs1043618, rs562047, rs539689) were found to be associated with worse baseline PANSS negative scores ($P = 0.0001$) and clinical improvement ($P = 0.04$ and $P = 0.03$ respectively). TAAR6 rs8192625 G/G genotype was found to be associated with worse clinical presentation ($P = 0.01$), whilst no significant associations were found after haplotype analyses.
Conclusion: Variations within the DTNBP1, HSPs and TAAR6 genes seem to be associated with the psychotic symptoms' severity at the beginning of treatment. DTNBP1, HSPs variations seem to impact the antipsychotic treatment response too.
Policy of full disclosure: None.

P-05-009
Protein of metabotropic glutamate receptor has been detected in plasma of blood in schizophrenia

L. Smirnova (Mental Health Research Institute, Tomsk, Russia), L. Loginova

Objective: Pathogenesis of schizophrenia is still unclear but disturbances of protein metabolism in schizophrenia are known. Nevertheless, protein—marker, inherent in only this illness, still has not been detected. Use of mass-spectrometric methods in proteomics allows analyzing high-molecular proteins.Objective is proteomic analysis of blood plasma in patients with schizophrenia.
Methods: Object of investigation was blood of 8 healthy persons and 10 patients with schizophrenia and 5 patients with neurotic disorders. Diagnosis was conducted according to current classification ICD-10. We have carried MALDI-TOF analysis of blood plasma on mass-spectrometer Autoflex III (Bruker Daltonics, Germany) with software flexControl 2.4. Processing of obtained spectra and formation on their basis of peak list was conducted with use of program kit flexAnalysis 2.4 of firm Bruker Daltonics (Germany). Identification of proteins was conducted with use of program Mascot—Matrix Science.
Results: In result of investigations, it has been revealed that in plasma of blood of patients with schizophrenia we have detected protein of metabotropic glutamate receptor (mGluR6). Long activation of metabotropic glutamate receptors results in reinforcement of NMDA-dependent generation of active forms of oxygen what entails damage of receptors.
Conclusion: Research on microchips has revealed decrease of expression of regulator of transmission of signal in synapses of G–protein–4 (RGS4) in schizophrenia. RGS4 is a negative regulator of receptors connected with G–proteins, including metabotropic glutamate receptors and plays an important role in development of nervous system. In prevailing pathogenetic model, schizophrenia is a result of developmental disturbances of nervous system. Thus, obtained results allow supposition that glutamatergic synapses are the basic place of action in pathogenesis of schizophrenia.
Policy of full disclosure: None.

P-05-010
CB2 cannabinoid receptor is involved in schizophrenia-like behaviors

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Objective: The present study evaluated the role of the cannabinoid CB2 receptors in the regulation of schizophrenia-like behaviours. Mice lacking the CB2 receptor (CB2KO) were challenged with different types of experimental paradigms to evaluate their response in terms of schizophrenia-like behaviours.
Methods: Male CB2KO and wildtype (WT) mice were used. In order to determine the behavioural profile, we analysed motor activity, anxiety-like behaviour, depression-like behaviour, memory and prepulse inhibition. The effects of acute cocaine in motor activity and chronic risperidone in prepulse inhibition were tested. Using real time PCR, molecular differences and the effect of chronic risperidone treatment on receptor gene expression between CB2KO and WT mice were evaluated by measuring dopamine D2, adrenergic Alpha2C, and serotonergic 5-HT2A and 5-HT2C receptors gene expressions in prefrontal cortex, locus coeruleus and dorsal raphe nucleus.
Results: CB2KO mice presented anxiogenic-like and depressogenic-like responses and decreased spontaneous motor activity. In contrast, the acute administration of cocaine increased significantly motor activity in CB2KO compared with WT mice. In addition, CB2KO mice displayed disrupted short- and long-term memory consolidation in the SDIA. Baseline prepulse inhibition in CB2KO mice was significantly lower than WT mice. Chronic oral treatment with risperidone (15, 30, 60 μg/kg) markedly attenuated prepulse inhibition deficits in CB2KO mice whereas impaired prepulse inhibition in WT mice. CB2KO mice showed different gene expression levels in comparison with WT and chronic risperidone treatment tended to "normalize" toward WT gene expression values.
Conclusion: Taken together, these results suggest that mice lacking CB2 receptor display behavioural alterations commonly expressed in preclinical animal models of schizophrenia. These behavioural alterations may be related to the changes found in receptor gene expression that are "normalized" after treatment with treatment with risperidone. In conclusion, the CB2 receptor may be considered a new potential therapeutic target for schizophrenia-related disorders.
Policy of full disclosure: None.

P-05-011
Ketamine affects gene expression of key brain molecules at crossroads of glucose metabolism and neurotoxicity: possible implications in psychosis

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Objective: Dysfunctions in glucose metabolism have been reported in distinct brain regions of schizophrenic patients. Functional genomics studies demonstrated specific impairment of transcripts playing key roles in glycolysis, glycogen synthesis and glycogenolysis in brain areas involved in the pathophysiology of schizophrenia. Recent evidence reported a direct implication of glucose-related signaling molecules, such as GSK3β, in both psychosis pathophysiology and the mechanisms of action of antipsychotics. Here we investigated the impact of ketamine, a NMDA receptor antagonist widely used to mimic psychosis in rats, on specific genes involved in glucose metabolism and cell survival, hexokinase I (Hk1) and glucose transporter 3 (GLUT3), in distinct areas of the rat brain correlated to psychotic symptoms in animal models.
Methods: Sprague–Dawley rats were acutely administered with ketamine 12 mg/kg (KET12) and 50 mg/kg (KET50) and killed 3 h after injection. Quantitative in situ hybridization was performed to evaluate changes in Hk1 and GLUT3 transcripts in: Prefrontal Cortex, Striatum, Nucleus Accumbens, Retrosplenial, Visual and Auditory Cortices, Hippocampus, Ventrotegmental Area, and Substantia Nigra. Statistical analysis was carried out by ANOVA.
Results: HKI expression was increased in motor, auditory and visual cortices by KET50, which also up-regulated Hk1 in retrosplenial cortex. Both KET12 and KET50 increased Hk1 transcript in CA1 and CA3 regions of hippocampus. Finally, HKI signal was heightened in all striatal subregions by KET50. GLUT3 expression showed a reduction trend in cortical and subcortical regions.
Conclusion: In agreement with human studies, here we report the direct evidence that acute ketamine administration in rats may impact the expression of genes directly involved in glucose metabolism and cell survival in distinct areas of the brain that have been implicated in the etio-pathogenesis of schizophrenia. These effects occur after ketamine acute administration, suggesting a fast impairment of neuronal functions in response to systemic NMDA receptor blockade.
Policy of full disclosure: None.

P-06 Neurobiology

P-06-001
White blood cell count in first episode non smoking patients

C. Garcia-Rizo (Hospital Clinic Psychiatry, Barcelona, Spain), E. Fernandez-Egea, C. Olivera, M. Bernardo, B. Kirkpatrick

Objective: Epidemiological evidence suggests that white blood cell count (WBC) correlates with coronary heart disease factors and atherosclerosis. Higher WBC has been described to be increased in chronic schizophrenic patients and correlated with more severe pathology. A higher WBC has been described in regular smoking population and also correlated with an increased risk of metabolic syndrome. Schizophrenic patients show a marked increase in mortality mainly due to cardiovascular diseases. The aim of the study is to examine whether WBC is increased in first episode non-smoking psychosis patients and is correlated with symptomatology.
Methods: Fasting values of WBC were obtained in non-smoking patients with a first episode psychosis ($N = 42$) and age matched controls ($N = 51$). Psychopathological evaluation was obtained in patients thorough the positive and negative scale in schizophrenia (PANSS).
Results: Patients showed an increased mean value WBC [SD] 6.97×10^9/L [2.2] compared with age matched controls 5.93×10^9/L [1.4] ($P < 0.01$). Log-transformed WBC was used due to non normal distribution. No correlation was found in the psychosis group between WBC value (log-transformed) and PANSS items.
Conclusion: WBC count is increased in first episode psychosis patients before the introduction of antipsychotic treatment. This finding may contribute to the metabolic side-effect of antipsychotic treatment.
Policy of full disclosure: Drs. Garcia-Rizo, Fernandez-Egea and Oliveira have nothing to disclose. Dr. Bernardo received consultant fees from Bristol-Meyer-Squibb and Wyeth. He also received honoraria from Janssen–Cilag, Eli Lilly Company, Pfizer, Synthelabo, Glaxo Smith Kline and Astra-Zeneca. Dr. Kirkpatrick received consulting fees from Eli Lilly, Cephalon, Abbott, Boehringer Ingelheim, and Sunovion.

P-06-002
Influence of acute psychosis on breathing regulation and its impact on heart rate variability

T. Rachow (Psychiatry and Psychotherapy, University Hospital, Jena, Germany), S. Berger, A. K. Israel, K. Bär

Objective: Many studies could show that patients suffering from schizophrenia do have an increased risk for cardiac mortality. A reduced vagal modulation might play an important role. The discharges of the nervus vagus are coupled to the breathing-phase-associated discharges of neurons in the brainstem. We aimed to investigate alterations of breathing parameters and their impact on heart rate variability in acute schizophrenia.
Methods: We included 25 unmedicated patients suffering from acute paranoid schizophrenia and 25 matched healthy controls. Respiratory induction-plethysmography (RIP) was performed during 30 min of resting. Additionally a high-resolution electrocardiogram was recorded. Psychotic symptoms were quantified using PANSS (Positive and Negative Syndrome Scale).
Results: Patients showed a significantly increased heart rate and decreased respiratory sinus arrhythmia (RSA). Besides breathing rate and the ratio of inspiration-time to expiration- time were increased in the patient group. Breathing minute volume did not differ between groups.
Conclusion: Patients showed increased values of heart rate and breathing rate. The respiratory sinus arrhythmia and the expiration time were reduced in patients, whereby the breathing minute volume did not differ between groups. Because the activity of cardio-inhibitory neurons near the nucleus of the nervus vagus is coupled to the expiration-time this could explain the reduced RSA.
Policy of full disclosure: None.

P-06-003
Peripheral endothelial dysfunction in patients suffering from acute schizophrenia: a potential marker for cardiovascular morbidity?

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Objective: Patients suffering from schizophrenia have an increased standardized ratio for cardiovascular mortality compared to the

general population. Endothelial function was identified as a prominent parameter for cardiac risk stratification in patients with heart disease. Here, we aimed to analyze the reactivity of the microcirculation applying the post-occlusive reactive hyperemia (PORH) test and spectral analysis of skin vasomotion as markers of endothelial function.
Methods: We investigated 21 unmedicated patients suffering from paranoid schizophrenia as well as 21 matched controls. The capillary blood flow was assessed on the right forearm after compression of the brachial artery. Parameters of PORH such as time to peak (TP) or PORH index were calculated. In addition, spectral analysis of skin vasomotion was performed and five frequency bands (endothelial, sympathetic, vascular myogenic, respiratory and heart beat activity) were studied. Psychotic symptoms were quantified using the Positive and Negative Syndrome Scale (PANSS) and correlated to the parameters obtained.
Results: We report a blunted hyperemic response in patients after occlusion of the brachial artery indicated by significantly increased TP and decreased PORH indices. In contrast, vasomotion as investigated by spectral analysis of skin flow was rather sparsely altered showing differences at rest for the sympathetic and cardiac components only.
Conclusion: Our results are suggestive of peripheral endothelial dysfunction in unmedicated patients suffering from schizophrenia. Future, prospective studies should address the relation of endothelial dysfunction to cardiac morbidity in patients with schizophrenia.
Policy of full disclosure: None.

P-06-004
Catalytic activity of abzyms in patients with schizophrenia with movement disorders was increased

L. Smirnova (Mental Health Research Institute, Tomsk, Russia), N. Fattahov

Objective: Recently the catalytic activity of immunoglobulins has been studied carefully. Investigations of antibodies catalytic properties in schizophrenic patients were not carried out so far. Objective is studying DNase activity of IgG allocated from the serum of schizophrenic patients.
Methods: Antibodies of G group were isolated from the blood serum. The control group included 15 healthy persons. Schizophrenic patients have been divided into 2 groups: 6 patients with tardive dyskinesia (TD) and 15 patients without TD. All patients were treated in the department of endogenous disorders of Mental Health Research Institute, Tomsk. The diagnosis of schizophrenia was based on ICD-10 criteria. The severity of TD has been assessed using the abnormal involuntary movement scale (AIMS). DNase activity has been defined using the hydrolysis level of DNA plasmid pBluescript, proteolytic activity has been tested using the level of hydrolysis of myelin basic protein and its peptides.
Results: It has been established the higher specific DNase activity of IgG in schizophrenic patients in comparison with healthy persons (0.029 ± 0.006 pÌDNA/mgG/h). It has been shown that specific DNase activity of antibodies in patients with TD 2 times higher (0.74 ± 0.3 pÌDNA/mgG/h), than in group without TD (0.3 ± 0.13 pÌDNA/mgG/h). It has been demonstrated that specific DNase activity was the inner property of antibodies. The hydrolysis of myelin basic protein by antibodies in group of the patients with TD was also high 58.6%, unlike patients without TD 12.7%. In control group the hydrolysis level was 1.5%.
Conclusion: It is supposed that DNA-hydrolyzing IgG carry out function of DNase in an organism of the patient in connection with prospective increase in quantity of extracellular DNA at patients of a schizophrenia.
Policy of full disclosure: None.

P-06-005
Oxidative and inflammatory status in first-episode psychoses and its relationship with cognitive impairment

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Objective: Both oxidative stress and the inflammatory chemokine MCP-1 have been linked to the pathophysiology of certain mental illnesses such as psychosis. There are previous studies in rats and dogs suggesting that oxidative stress can cause cognitive impairment. The study objective is to correlate oxidative stress and the chemokine MCP-1 levels with cognitive impairment and functioning in first episode psychosis.
Methods: 28 patients with first episode psychosis and 28 healthy controls matched by sex and age were included in the study, who were given a battery of neurocognitive tests and we determined their blood levels of lipid peroxidation (TBARS), nitric oxide, total antioxidant status (TAS), glutathione, activity of enzymes catalase (CAT), glutathione peroxidase (cGPx) and superoxide dismutase (SOD) and the inflammatory chemokine MCP-1. We evaluated patient functioning using the Strauss-Carpenter scale.
Results: Healthy controls had better TAS than patients and increased activity of enzymes cGPx and CAT. We found a statistically significant negative relationship between levels of MCP-1 and working memory, attention and verbal memory. At higher levels of chemokines, worse cognitive functioning in these areas. Verbal memory was also negatively related, in a meaningful way, with nitric oxide levels in blood. Likewise, we found that higher levels of glutathione correlated with better scores on the 3 tests performed of verbal fluency. Using regression models we observed that the relation between cognition and functioning was mediated by oxidative stress/inflammation parameters.
Conclusion: In patients with a PEP, levels of certain markers of oxidative stress and inflammation are associated with poorer cognitive functioning and worse functioning.
Policy of full disclosure: None.

P-06-006
Methods and composition for modulation of activity of voltage gated ion channels

A. Elayyan (Amman, Jordan)

Objective: This research is directed to find out chemical structure of modulator of activity of voltage gated ion channels which are positively charged molecules attached to S4 (voltage sensing segment) in voltage gated ion channels. And impact of partial or total release of these molecules from S4 (voltage sensing segments) on modulation of activity of voltage gated ion channels and conditions associated with this release.
Results: Here we show, that chromium chloride (CrCl3) is modulator of activity of voltage gated ion channels with contribution of S4 (voltage sensing segments). It is attached to S4(voltage sensing segments) in all voltage gated ions channels. Finally, we show that when chromium chloride is partially or totally released from voltage sensing segments due to breakage of hydrogen bonds, ability of these

segments to change their conformation to closed or opened states of ion channel according to changes to membrane potential will be affected, thus ion channel will malfunction and many conditions will occur including but not limited to: schizophrenia, epilepsy, depression, bipolar disorder, ADHD, migraine, cardiac arrhythmia, glaucoma, diabetes type2, asthma and essential hypertension. Our explanation of schizophrenia is, when chromium chloride is totally released from voltage gated calcium channels in terminal buttons in dopaminergic neurons in limbic system in brain, a continuous influx of calcium ions flows into these cells leading to continuous secretion of dopamine neurotransmitter from synaptic vesicles into the synaptic cleft through exocytosis process thus, schizophrenia will occur.
Conclusion: We suggest that medication of conditions associated with this malfunction is by administering sufficient amount of chromium compounds preferably chromium polynicotinate for a limited period of time to restore ion channel functionality. Dose is 200 mcg daily for 3 months.
Policy of full disclosure: None.

P-06-007
The synesthetic phenomenology in the schizophrenic organization

E. Venga (Naples, Italy), D. Venga

Objective: Synesthesia is defined as the blending of perceptions relevant to two or more senses.
Methods: It was also investigated whether synaesthesia is genuine. We are a bit 'perplexed in regard this as we believe that the physiopathological representation is what is perceived to become symptomatic. It is also clear that the same symptoms as a representation of synesthesia, to correlate symptomatic, may or may not be decisive, for structural purposes, for which the "true" and "false"are not differentiable. We must also make clear that the structural research is not addressed to the physiology or pathophysiology—there is no dichotomy-the 'organ or system, but the biological structure-individual. The study of synaesthesia research were also addressed to understand the neurobiological factors. Indeed, it was analyzed the mechanism by which the brain processes visual information in conjunction with other brain areas such as area V4—fusiform gyrus of the temporal lobe—and the cortical region located in an area called TPO (acronym for the junction of the temporal lobe, parietal and occipital). In this sense, we can represent, with different areas, a single-phenomenological interpretation.
Results: In our view, the study aimed to detect or to elect a brain structure to represent the phenomenology of synesthesia and useful but not necessary, since it is involved in the biological structure and determine any minimum threshold of perception.
Conclusion: In this regard we find solace in the single-cell origin from which we will differentiate ourselves also and especially in polygenesis functional. This suggests to us that the same structure can be organized differently. The study of synesthesia has given us also an interesting starting point for the study of all diagnostic nosographic. It is the same diagnostic research to enlighten targeted to be addressed in the study of synesthetic representation, regardless of the ratio-etiopathogenetic interpretation.
Policy of full disclosure: None.

P-06-008
Alterations in hippocampal function in a maternal immune activation animal model of schizophrenia

A. Wolff (Psychology, University of Otago, Dunedin, New Zealand), D. Dickerson, D. Bilkey

Objective: Reduced hippocampal volume and cytoarchitectural alterations are thought to underscore a range of symptomotology in schizophrenia. The maternal immune activation (MIA) animal model of schizophrenia reproduces reduced hippocampal volume and altered cytoarchitecture in adult animals, and therefore, provides an ideal platform for examining these effects at the single-cell level. Here we examine the effects of MIA on the basic firing properties of pyramidal cells in the dorsal hippocampus of adult animals. We also examined the relationship between single-unit activity and the phase of local field potentials (LFPs).
Methods: Female Sprague–Dawley rats ($\sim$3 months old) were mated with the day after copulation considered gestational day (GD) 1. On GD15, dams were briefly anesthetized with halothane and injected with the cytokine inducer polyriboinosinic–polyribocytidylic acid (poly I:C; 4 mg/kg, i.v.) or a saline injection equivalent. Litters were culled to give a maximum of 6 males, and left undisturbed until testing (3 months). Animals were implanted with moveable tetrode microdrives in dorsal CA1 for recording hippocampal single-unit activity and LFPs while animals foraged freely in an open-field.
Results: Cells recorded from MIA animals were found to have lower average firing rates, and reduced information content, and sparsity relative to control cells (all $P < 0.05$). The relationship between single-unit firing to the phase of the LFPs was significantly different between the treatment groups in both the low (38–40 Hz; control: 114°, MIA: 298°; $P < 0.001$) and high gamma frequency bands (52–100 Hz; control: 338°, MIA: 100°; $P < 0.001$).
Conclusion: A single MIA intervention produces changes in the firing of hippocampal cells in adult animals. The alteration in preferred firing phase of hippocampal neurons to local gamma frequency oscillations in MIA animals suggests that altered spike-phase relationships may also be a factor in schizophrenia.
Policy of full disclosure: None.

P-06-009
Clozapine administration ameliorates disrupted prefrontal-hippocampal synchrony in an animal model of schizophrenia

D. Dickerson (Department of Psychology, University of Otago, Dunedin, New Zealand), A. Restieaux, D. Bilkey

Objective: Synchronization of neural activity appears to underlie the integration of information in the brain. Abnormal synchrony is thought to underlie core symptoms in schizophrenia. We have previously described disrupted synchronization between the medial prefrontal cortex (mPFC) and the dorsal hippocampus, two regions implicated in schizophrenia pathology, in the maternal immune activation (MIA) model of schizophrenia. This model is based on epidemiological evidence of increased risk of schizophrenia in adulthood following prenatal exposure to infection and is induced through a single injection of the synthetic immune system activator polyriboinosinic-polyribocytidylic acid in pregnant rat dams. The current study sought to determine the specificity of the synchrony deficits and the impact of clozapine (CLZ) administration.
Methods: A baseline measure of EEG coherence between the mPFC, dorsal (dHPC) and ventral HPC (vHPC) was obtained in MIA ($n = 8$, from 8 l) and control ($n = 9$, from 8 l) animals in open field and resting state environments. MIA and control animals were then pseudo-randomly exposed to the clozapine manipulation (vehicle, 1, and 5 mg/kg; i.p.).
Results: In both environments, the MIA intervention produced a significant reduction in baseline theta frequency (4–12 Hz) coherence, specific to dHPC-mPFC coupling ($P < .05$), while vHPC-mPFC coherence was unaffected. CLZ administration during resting state produced a significant dose-dependent increase in theta coherence ($P < .0005$) in both control and MIA groups. Theta power in the

mPFC showed a dose-dependent increase ($P = .004$), which correlated with mPFC-dHPC coherence ($P < .0005$). Theta power in the dHPC was not dose-dependently increased ($P = .397$) and did not correlate with coherence ($p = .51$).
Conclusion: These findings indicate that the MIA derived disruption to synchrony in the mPFC-dHPC does not represent a global deficit, and is present even at rest. Furthermore, CLZ ameliorates the synchrony deficits in MIA and appears to act via the mPFC providing a putative mechanism by which this medication exerts its therapeutic effect.
Policy of full disclosure: This research was supported by the New Zealand Health Research Council and Marsden Fund.

P-06-010
Impaired cortical excitability in schizophrenia is related to the disease course: a cross-sectional study

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Objective: Abnormalities in cortical inhibition are a common, but controversially discussed finding in schizophrenia patient. Especially GABAA and GABAB related intracortical circuits seem to be affected, whereas antipsychotic treatment is a prominent confounding factor. However, there is only limited knowledge about the effect of the disease course on cortical inhibition in schizophrenia.
Methods: 35 first-episode-schizophrenia patients (FE-SZ), 37 chronically ill schizophrenia patients (CH-SZ) and 50 healthy controls were investigated with transcranial magnetic stimulation (TMS). Several measures of cortical inhibition were tested with single—and paired—pulse TMS to the left primary motor cortex. In detail the GABAB-dependent cortical silent period (CSP) and the GABAA-dependent short-latency-intracortical inhibition (SICI) were investigated.
Results: All schizophrenia patients showed a reduced SICI compared to healthy controls, whereas a difference between FE-SZ and CH-SZ could not be detected. For CSP, analysis revealed a significant effect between the three study groups: FE-SZ and CH-SZ had prolonged CSP compared to healthy controls and FE-SZ had longer CSP compared to CH-SZ. Antipsychotic medication had an impact on cortical inhibition with differences between different second-generation antipsychotics.
Conclusion: This is the first cross-sectional TMS study investigating schizophrenia patients. Our results suggest an impaired GABAA-mediated cortical inhibition in FE-SZ and CH-SZ compared to healthy controls. The prolonged GABAB-dependent CSP might reflect a compensatory mechanism in FE-SZ, which is altered in CH-SZ. This might be related to a neurodegenerative process during the disease course. Antipsychotic medication is associated with GABAA and GABAB mediated intracortical inhibition.
Policy of full disclosure: Alkomiet Hasan has been invited to scientific congresses by Astra Zeneca, Lundbeck and Janssen Cilag. Alkomiet Hasan was founded by the Deutsche Forschungsgemeinschaft and the Guarantors of "Brain".

P-07 Drug Treatment II: Basic

P-07-001
In vivo pharmacological evaluation of novel olanzapine analogues in rat: potential novel antipsychotic drugs with lower obesogenic effect

S. Jafari (University of Wollongong School of Health Sciences, Australia), F. Fernandez, X.-F. Huang

Objective: Olanzapine is an atypical antipsychotic drug with high clinical efficacy but causing severe weight gain and metabolic syndromes. It has been reported that blockade of the H1 receptors plays a key part in olanzapine inducing weight gain while its therapeutic profiles is mainly attributed to its favourable 5HT2A/D2 receptor binding affinity ratios. A new antipsychotic agent with similar 5HT2A/D2 receptor binding affinity ratios to olanzapine but with lower affinity for H1 receptor may represent a significant advancement in schizophrenia treatment. We have previously reported the design, synthesis and in vitro pharmacological evaluation of novel olanzapine derivatives (Olz-1 and Olz-2) with thienobenzodiazepine structure [Jafari et al. in preparation]. Now we are aiming to test the weight gain and therapeutic effects of these compounds in animal model.
Methods: In an in vivo study, female Sprague–Dawley rats were treated orally, three times daily with olanzapine, Olz-1 and Olz-2 (3 mg/kg/day) self-administered in a sweet cookie dough pellet at eight-hourly intervals) or vehicle ($n = 8$/group) for 5 weeks. Body weight, food intake and water intake were monitored every 48-h.
Results: Our animal study revealed a significant effect of olanzapine on total body weight gain ($F(2,48) = 19.008$, $P < 0.01$) compared to controls after 5 weeks of drug treatment. Weight gain effect of Olz-1 (-27%, $P < 0.01$) and Olz-2 (-35%, $P < 0.01$) was significantly lower than olanzapine groups. There was no significant effect of drug treatment on total food intake and total water intake.
Conclusion: Conclusion: The novel analogues with lower affinity to the H1 receptors turn up as promising antipsychotic agents, which induced lower weight gain than olanzapine in rats. Our previous study also showed similar pKi 5HT2A/D2 receptor binding affinity ratio of these compounds and olanzapine (value = 1.17). We suggested these novel analogues are potential antipsychotics for schizophrenia treatment.
Policy of full disclosure: None.

P-07-002
Neurobehavioural adaptations to steady state dose of haloperidol associated to treatment efficacy and failure

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Objective: Antipsychotics improve psychosis symptoms, but their long term efficacy is inconsistence. A previous approach have delineated a time-course when the effect of relevant antipsychotics doses shift from efficacy to failure in representative animal models. We described the adaptive neurobehavioural dynamics responses to stimuli during antipsychotic efficacy and failure in rats.
Methods: We performed a microdialysis study in freely moving rats after 6 (drug efficacy) and 14 (drug failure) days treatment with haloperidol (HAL) or vehicle using osmotic mini-pumps. Extracellular dopamine, noradrenaline and serotonin levels were recorded before and after exposing rats to novelty, preferred-food and a mild aversive tail pinch in the medial prefrontal cortex (mPFC), caudate-putamen (CPu) and nucleus accumbens (NAcc), using HPLC-EC. The behavioural activity was, also, recorded.
Results: HAL decreased dopamine levels in the PFC, but not in the NAcc and CPu after 6 days treatment, and in all three brain areas after 14 days. Noradrenaline baseline levels were reduced after 6 and 14 days treatment while serotonin levels were substantially preserved. HAL 6 days treatment inhibited NAcc dopamine response to tail pinch and novelty, but not to preferred-food. HAL 14 days treatment lost efficacy in inhibiting NAcc dopamine response to tail pinch while gained efficacy in inhibiting NAcc dopamine response to preferred-food. Finally, HAL preserved its ability to inhibit NAcc dopamine response to novelty. The inhibition of locomotor activity induced by

tail pinch observed during 6 days haloperidol treatment was reversed after 14 days. Similar results were obtained during exposure with preferred-food while the inhibition of the locomotor activity induced by novelty was preserved during the 2-week treatment.
Conclusion: The neurochemical dynamics responses to stimuli occurred during HAL failure were associated to decreased catecholamine basal levels. The reduced basal tone of catecholamine may be responsible for the maladaptive responses to stimuli.
Policy of full disclosure: None.

P-07-003
Comparative study on animal model of neuroprotection and cardioprotection for long-acting antipsychotics

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Objective: The comparative evaluation of the neuroprotective and cardioprotective effect of long-term action antipsychotics on animal model. The efficacy of treatment with long action antipsychotics can be limited by decrease of neuroprotection and cardiovascular adverse effects.
Methods: We using in our study on animal model (Common Wistar rats) 4 antipsychotics with long-term action (haloperidole decanoate, flupentixol decanoate, rispolept consta and olanzapine powder and solvent for prolonged release suspension for injection). We formed 4 study lots and a control lot each constituted of 5 male adults rats, weighting 200-250 g, held in temperature, humidity, food and ambient stressless conditions. The substances were administered intramuscular, in the 0- and 7-day, the equivalent to: N1—haloperidole decanoate (0.50 mg/kg/week), N2—flupentixole decanoate (0.50 mg/kg/week), N3—olanzapine long-acting injection (5 mg/kg/week) and N4—14 days before study risperidone oral solution (0.05 mg/kg/day) and rispolept consta (0.50 mg/kg/week) in the 0- and 7-day. The study animals were sacrificed on the 15th day. We monitorized EPS and sudden death. The sample brain was histopathologically processed through specific colouring and fixation techniques. We evaluated the neuroprotection and cardioprotection comparing the cytoarchitectural changes in frontal cortex, hippocamp and cardiac tissue.
Results: Important changes of the cytoarchitecture at the frontal cortex and the hippocampic zone (vacuolizations and pinocytosis), important vascular changes (neoformation vessels, blood extravasation and microhaemorrhage), at cardiac tissue level were observed edema and vessels changes in N1 lot (haloperidole decanoate) and N2 lot (flupentixol decanoate). The cytoarchitectural and vascular changes decrease in a significant way for the N3 lot (olanzapine long-acting injection) and N4 lot (rispolept consta).
Conclusion: Neuroprotection and cardioprotection is better for olanzapine powder and solvent for prolonged release suspension for injection and rispolept consta compaired to first generation antipsychotics (haloperidole and flupentixol decanoate).
Policy of full disclosure: None.

P-07-004
The effect of cannabidiol in a MK-801-induced rat model of aspects of schizophrenia

A. Gururajan (Monash Institute of Pharmaceut Medicinal Chemistry & Drug Act, Melbourne, Australia), D. Taylor, D. Malone

Objective: Cannabidiol, the non-psychoactive phytocannabinoid, is purported to have antipsychotic effects. The purpose of this study was to further investigate if these effects would be seen using a MK-801-induced rat model of aspects of schizophrenia. MK-801 is an NMDA receptor-antagonist known to produce hyperactivity, deficits in prepulse inhibition (PPI) and social withdrawal, behaviours which correlate well with some of the positive, cognitive and negative symptoms of schizophrenia. We also tested the effect of the atypical antipsychotic clozapine as a comparator.
Methods: Following 4 days of acclimatisation to the holding room, rats were familiarised to startle chambers on day 5 and their prepulse inhibition (PPI) was determined on day 6 after intraperitoneal injection with cannabidiol (3–30 mg/kg), clozapine (1–10 mg/kg) or vehicle and MK-801 (0.3–0.6 mg/kg) or vehicle. On day 9, rats were familiarised to the social interaction testing arena and on day 10, following the same treatments as administered on day 6, the rats' levels of social interaction and locomotor activity were determined.
Results: MK-801 induced disruption of PPI, hyperactivity and social withdrawal. Cannabidiol by itself at 10 mg/kg disrupted PPI although this was accompanied by a significant reduction in startle response. Cannabidiol also caused hyperactivity but had no effect on social behaviour. Cannabidiol was unable to inhibit the MK-801-induced disruption of PPI or hyperactivity however it appeared to partially normalise MK-801-induced social withdrawal. Clozapine only partially inhibited MK-801-induced disruption of PPI but was able to normalise MK-801-induced hyperactivity and social withdrawal.
Conclusion: In conclusion while cannabidiol by itself had propsychotic activity, like clozapine it showed partial antipsychotic activity in an MK-801-induced model of aspects of schizophrenia. Additional behavioural studies using a range of species, strains, animal models and testing paradigms would be required to conclusively establish the antipsychotic potential of cannabidiol.
Policy of full disclosure: None.

P-07-005
Attention deficit induced by deletion of CB1 cannabinoid receptor is not reversed by haloperidol and risperidone treatment in the prepulse inhibition test

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Objective: Deficient prepulse inhibition (PPI) of the acoustic startle response has been reported repeatedly in patients with schizophrenia. In addition, atypical antipsychotics "normalized" PPI in these patients. The present study investigated whether deletion of the cannabinoid CB1 receptors in mice induced a deficit in PPI and the possible "normalization" by typical or atypical antipsychotic treatment.
Methods: Male mice lacking CB1 receptor (CB1KO) and wildtype (WT) were used. Evaluation of sensorimotor gating was carried out determining the amplitude (ASR) and the PPI of the acoustic startle response. Five types of trials were used: pulse alone (120 dB), three with prepulse (68, 71 and 77 dB) and no stimulus trial. After a baseline determination of PPI response, the effects of chronic haloperidol and risperidone oral administration were tested in PPI at 4, 8 and 12 days of treatment. Three doses of haloperidol (0.01, 0.03 and 0.09 mg/kg) and risperidone (0.015, 0.03 and 0.06 mg/kg) were administered twice a day. The 4, 8 and 12 days sessions were performed between 3 and 5 h after the last dose administered.
Results: CB1KO mice showed significantly higher baseline ASR and decreased baseline PPI compared to WT mice. Chronic oral treatment with haloperidol significantly reduced ASR in both genotypes whereas significantly reduced PPI in WT mice only. Chronic oral treatment with risperidone significantly reduced ASR and PPI in both

genotypes. However, the reduction of PPI levels was restricted to the lower intensity of prepulse used (68 dB).
Conclusion: These results suggest that mice lacking CB1 receptor display a PPI deficit resistant to antipsychotic treatment. Therefore, the CB1KO mice may be considered a new model for evaluation of new potential therapeutic agents for treating antipsychotic-resistant schizophrenia.
Policy of full disclosure: None.

P-07-006
T-817MA, a novel neurotrophic agent, prevents loss of GABAergic parvalbumin-positive neurons and sensorimotor gating deficits in rats transiently exposed to MK-801 in the neonatal period

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Objective: T-817MA [1-{3-[2-(1-benzothiophen-5-yl)ethoxy]propyl} azetidin-3-ol maleate] is a newly synthesized neuroprotective agent for the treatment of psychiatric disorders characterized by cognitive disturbances, such as Alzheimer's disease. Cognitive impairment has also been suggested to be a cardinal feature of schizophrenia. We herein sought to determine whether T-817MA would ameliorate sensorimotor gating deficits and loss of parvalbumin (PV)-positive γ-aminobutyric acid (GABA) neurons in the brain of rats transiently exposed to MK-801, an N-methyl-D-aspartate receptor blocker, in the neonatal stage.
Methods: Prepulse inhibition (PPI) was examined in rats treated neonatally with MK-801 (postnatal day; PD 7-10, 0.2 mg/kg/day, s.c.) or vehicle at PD 35 and PD 63. The number of PV-positive GABAergic neurons in the medial prefrontal cortex (mPFC) and the hippocampus was measured after the behavioral assessments. T-817MA (10 or 20 mg/kg), haloperidol (1 mg/kg), risperidone (1 mg/kg), or vehicle was administered for 14 days (on PD 49–62). The number of PV-positive GABAergic neurons in the mPFC and the hippocampus was counted.
Results: Fourteen-day administration of T-817MA dose-dependently ameliorated PPI disruption induced by neonatal MK-801 treatment. Furthermore, the higher dose T-817MA prevented the MK-801-induced decrease in PV-positive neurons in the mPFC and hippocampus.
Conclusion: Rats transiently exposed to MK-801 in the neonatal stage produced impaired sensorimotor gating and histological changes related to the pathophysiology of schizophrenia. Treatment with T-817MA around puberty ameliorated these derangements, suggesting that T-817MA may provide a novel therapeutic approach for schizophrenia.
Policy of full disclosure: Mr. H Hattori and Dr. N Iwakami are employees of Toyama Chemical Co. Ltd that developed T-817MA.

P-07-007
Effects of risperidone on development and expression of nicotine-induced locomotor sensitization in rats*

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Objective: It has been shown that atypical antipsychotics significantly reduce smoking and alcohol consumption in schizophrenia patients. However, our knowledge about the effect of risperidone, especially on nicotine abuse is limited. We aimed to test the effects of risperidone in an animal model of nicotine-induced locomotor sensitization, which represents initial neuroadaptations and continued behavioral changes in nicotine-type dependence.
Methods: All procedures in the present study were performed in accordance with the rules in the Guide for the Care and Use of Laboratory Animals adopted by National Institutes of Health (USA) and the Declaration of Helsinki. Adult male Wistar rats, weighing 207-313 g, were subjects. To investigate the effect of risperidone on the development of nicotine induced locomotor sensitization, rats were pretreated with risperidone (0.025 and 0.050 mg/kg) 30 min before the nicotine (0.5 mg/kg, base) treatment, and locomotor activity was recorded for 30 min. This procedure was repeated every day for eight sessions. After a six-day drug-free period, rats were challenged with nicotine (0.5 mg/kg). In order to reveal the effect of risperidone on the expression of nicotine-induced locomotor sensitization, a new batch of rats were injected with nicotine for 8 sessions. After a 6-day drug-free period, rats were pretreated with risperidone (0.025 and 0.050 mg/kg) or vehicle 30 min before the nicotine (0.5 mg/kg) challenge injection.
Results: Repeated administration of nicotine produced robust locomotor sensitization in rats. Risperidone pretreatment (0.050 mg/kg) blocked the expression but not the development of nicotine-induced locomotor sensitization in rats.
Conclusion: Our results suggest that risperidone can block the continuation of nicotine-type addictive behavior, but it is ineffective on early adaptations in the initiation phase of nicotine addiction. Thus, this drug may have a limited beneficial effect in treatment of nicotine dependence.
Policy of full disclosure: *This study has been accepted for publication in SYNAPSE. This study was supported by the Scientific and Technological Research Council of Turkey (TUBITAK) (Grant No: 105S387, SBAG 3194).

P-07-008
Effects of cannabidiol on schizophrenia-like behavioral deficits presented by spontaneously hypertensive rats (shr)

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Objective: Recently, we have described that Spontaneously Hypertensive Rats (SHR) present schizophrenia-like behavioral alterations—namely deficits in an emotional context processing task, in prepulse inhibition of startle and in social interaction as well as hyperlocomotion—that are specifically attenuated by antipsychotics and worsened by proschizophrenia manipulations (Calzavara et al. Schizophrenia Bull. 2009; Calzavara et al. submitted; Levin et al. submitted). Cannabidiol (CBD), a Cannabis sativa constituent, have been suggested as a potential antipsychotic and anxiolytic agent (Zuardi et al. Rev. Bras. Psiquiatr. 2008). The aim of the present work was to investigate the effects of CBD on the behavioral deficits presented by SHR.
Methods: Different doses of CBD (1–60 mg/kg) were administered to adult Wistar rats and SHR prior to the following behavioral tasks: contextual fear conditioning, prepulse inhibition of startle (PPI) and social interaction/locomotion. Data were analyzed by two-way ANOVA (strain $\times$ drug) followed by Duncan's test when appropriate.
Results: The lowest dose of CBD was able to revert the fear conditioning deficit presented by SHR. Neither the social interaction and the PPI deficits nor the hyperlocomotion presented by this strain were modified by CBD at any dose tested.

Conclusion: Although CBD does not seem to present antipsychotic property for some of the behaviors tested, our results suggest that it could be a useful agent to treat the emotional processing abnormalities in schizophrenia.
Policy of full disclosure: None.

P-07-009
New hydroxysulfonamide with analgesic, anticonvulsant and tranquilizer activity

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Objective: Activation of nociceptive system often leads to nervous regulation disorders resulting in convulsive attacks. Meanwhile, it has been established that certain medications with analgesic effect can intensify convulsive attacks. In this connection, there arises a problem of searching for new compounds with antinociceptive and anticonvulsive effects. In current investigation we studied new endo-2-aminomethylbicyclo[2.2.1]hept-5-en derivative with sulfonamide and sulfolan fragment.
Methods: Experiments were carried out upon white mice (22–28 g). Acute toxicity (LD50) of synthesized compound, determined by Prozorovsky modification of Litchfield & Wilcoxon method, is 730 mg/kg. Analgesic effect of the compound has been investigated by the "hot plate" method at 55°C, the data obtained were compared to initial background. Anticonvulsive activity has been established under corazole spasms test. Tranquilizing activity of the compound has been studied on the test of barbituric sleep duration increase caused by hexenale. Medication (in a dose of 1/10 LD50) was injected to animals 30 min before the experiment. Medication effect was compared to the control group of animals injected with isotonic solution of sodium chloride.
Results: Investigated new sulfolan-containing compound demonstrates analgesic (145%), anticonvulsant (50%) and tranquilizer (127%) activity. Its activity was estimated in percentage to the control group of animals. Thereby, observed effects enable to consider the examined compound as perspective substance for therapy of pain syndrome in the conditions of enhanceable convulsive readiness.
Conclusion: It is necessary to mark that new sulfolan-containing compound under investigation along with low tranquilizing action demonstrates analgesic and anticonvulsive activity. Further research can ground its introduction in clinical practice.
Policy of full disclosure: None.

P-08 Outcome

P-08-001
Clinical and social correlates of "Duration of Untreated Psychosis" (DUP): results from the Catalan Early Psychosis Specific Intervention Programme (EPSIP)

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Objective: To examine the demographic, social and clinical correlates of DUP in patients with first-episode psychosis and compare the differences in these characteristics between patients with long and short DUP.

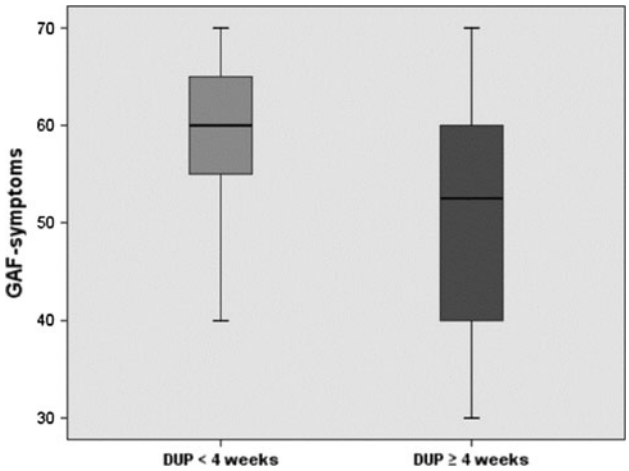

Fig. 1 Differences in GAF-symptoms regarding duration of untreated psychosis (DUP)

Methods: Retrospective study of consecutive admissions to EPSIP. Inclusion criteria: age between 18 and 35 years-old; first-episode of psychosis; and less than a year of symptoms' evolution. Data were collected through a socio-demographic and clinic questionnaire and the GAF scale. Non-parametric test for independent groups and correlation test were used to study demographic, social and clinical variables regarding DUP. The sample was dichotomized into short or long DUP, using a median split (SPSS 18.0).
Results: In our sample ($n = 41$), the median DUP was 4 weeks. The DUP was heavily skewed, with 75.6% ($n = 31$) of the patients having an appropriate treatment within 20 weeks from the onset of psychotic symptoms. There was no significant association of DUP with demographic and social variables. Regarding clinical variables, we found a statistically significant association between DUP and GAF-symptoms ($P = 0.035$; $r = -0.33$) and psychiatric admission history ($P = 0.034$; $r = -0.33$). Likewise,when the sample was divided into two groups significant differences were observed with the longer DUP group showing lower score in GAF-symptoms ($P = 0.041$; 51.4 vs. 59.0) and a higher number of patients without psychiatric admissions previous at the onset of psychotic episode ($P = 0.026$;18 vs. 5) (Fig. 1).
Conclusion: The median DUP found in this study was shorter than expected, but consistent with other studies. On the other hand, our findings suggest that a longer DUP might be influenced by clinical variables (i.e.GAF-symptoms score, prior contact with psychiatric services) more than by socio-demographic variables.Early recognition of predictors of prolonged DUP might have an impact on reducing DUP and potentially improving the prognosis.
Policy of full disclosure: The authors have no conflicts of interest to report.

P-08-002
Severity of outcome in early psychosis: risk and protective factors in a 7-year retrospective study

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Objective: Nowadays 20–40% of people who have a high-risk mental state, according to the criteria for progression to first-episode psychosis proposed by McGorry, developed schizophrenia within a year. The aim of our study was to assess whether it is possible to identify

predictor factors affective and non-affective psychosis in order to hypothesize a model of early intervention and prevention of disabling outcomes in psychosis.
Methods: Multiple linear regression was applied to investigate associations between various independent variables with disease severity parameters, such as the indices of hospitalization (number of admissions per year and hospital stays per year) and assessment scores with the BPRS and GAF scales in subjects with diagnosis of schizophrenia (70.3%) and with mood disorders with psychotic features (29.7%).
Results: The total sample was composed of 167 subjects (111 males and 56 females) between 14 and 35 years, admitted from 2002 to 2009 in the Acute Psychiatric Unit of San Filippo Neri Hospital in Rome. Multivariate analysis shows that early age of onset of psychiatric symptoms, in particular onset between 14 and 19 years, and drug abuse were the only tested variables that significantly influenced the severity, in both samples. The family context and social relationships played an important role on reducing severity indexes in psychotic patients.
Conclusion: With our study, we tested the predictive weight of some risk and protective factors that identified the outcome of the psychotic disorders in terms of severity. In particular, the controversial results on the predictive role of the DUP on the outcome of psychosis, in according with several international studies, has to pay attention to the use of healthcare resources in order not to disperse them.
Policy of full disclosure: None.

P-08-003
Predictors of short- and long-term clinical outcome in schizophrenic psychosis: the Northern Finland 1966 Birth Cohort study

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Objective: Since the outcome in schizophrenia is clearly heterogeneous and often poor, identification of specific predictors of outcome would be useful in clinical practice. Methodological issues and the use of selected samples limit the generalization of the previous studies. Our aim was to find clinically relevant predictors of the short- and long-term clinical outcome of schizophrenia using variables that in preceding studies have shown prognostic importance.
Methods: We utilized the Northern Finland 1966 Birth Cohort, which is an unselected, general population birth cohort based on 12,058 live-born children. Subjects ($n = 103$) with schizophrenia, schizophreniform psychosis, and schizoaffective disorder were followed up for an average of 16.4 years. We used information on psychiatric hospital treatments, premorbid factors and symptoms during the first hospitalization, and interviews (PANSS) to collect predictor and outcome data. We predicted the short- (2-year) and long-term (10 years or more) outcome with these variables. We also used the measures of the early outcome to predict the long-term outcome.
Results: Poor premorbid social adjustment, being single at the onset of the illness, early onset age and insidious onset were all associated with a poorer short-term clinical outcome. The most important predictors of the long-term outcome were early onset, insidious onset, being single at the time of onset and having suicidal ideations around onset since they predicted the use of hospital treatment and lack of remission after 10 years of follow-up.
Conclusion: This population-based study indicates that clinical and sociodemographic factors around the onset of illness are significant when predicting the outcome in schizophrenia. These prognostic factors should be taken into account in clinical practice.
Policy of full disclosure: None.

P-08-004
Clinical versus cognitive symptoms as predictors of outcome in psychosis: a longitudinal study

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Objective: Cognitive impairment and clinical symptoms have been associated with functioning in patients with schizophrenia. But discrepant results on the influence of cognition and clinical symptoms on functional outcome were obtained since now. The objective of the present study was to examine the predictive value of clinical and cognitive variables on outcome in psychosis.
Methods: A study was held with 45 patients with FEP from 3 main hospitals in the Basque Country (Spain).All patients underwent cognitive, clinical, and functional evaluations at base line and at 1 year longitudinally. The cognitive measures included were: the Stroop test, Vocabulary sub-test from WAIS-III, the WCST, and Trail Making Test. The clinical and functional measures included were: the PANNS, The Young Scale, The Montgomery-Asberg scale, and the GAF (Global Assessment of Functioning).
Results: Follow-up data were available for 16 patients for 1 year. A regression analysis was done with the functioning as a dependent variable during 1 year. The measure obtained with the Number of Correct Categories was the only one which had an effect on functioning after 1 year ($B = 0.67$, $P \leq .05$, $R^2 = 0.45$) remained significant when functioning at base line was controlled in the regression analysis. The rest variables were excluded from the model.
Conclusion: None of the clinical variables were significant in the model, and only one cognitive variable, Number of Correct Categories, was significant in the model. These findings emphasize that cognitive dysfunctions have a role on functional outcome in first episode psychosis.
Policy of full disclosure: This study was partially funded by the Health Department of the Basque Government (2008111010) and EITB-Maratoia (BIO 09/EM/015).

P-08-005
Early psychosis intervention: a recovery-oriented project in South Tyrol

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Objective: The first psychotic episode is a dramatic and upsettingly event for patients and relatives. Early recognition of symptoms and providing specific psychosocial and medical interventions are fundamental in order to avoid the high risk of biopsychosocial toxicity and chronicity. Nevertheless a huge amount of subjects suffering from the onset of psychosis loses their contact with the psychiatric community. The aim of this project, as a part of a national intervention study, was the application of an innovative approach guaranteeing systematically and efficiently psychotic patients at onset and their relatives the process of recovery.
Methods: From January 2010 to March 2011 a multi-professional teamwork operates on outpatients setting coordinating with the caregivers of the patient's district specific interventions including pharmaco- and psychotherapy as well as psychoeducation.
Results: 15 months the beginning of the project, 24 cases have been identified, with an average age of 28 years. Among these, 16 had the first contact during the first hospitalization, 8 at Community Center. 2

subjects have rejected the treatments in advance, the remaining 22 are still followed by the psychiatric Service (14 from more than 9 months). 18/22 patients (81%) underwent individual CBT and family-psychoeducation as well as the standard treatment (psychopharmacological support, nursing, social). None of the patients was re-admitted in the hospital.
Conclusion: In the treatment of the psychosis at the onset, ad-hoc psychiatric interventions, performed by an expert teamwork, in partnership with other Services' operators, support in joining the recovery process, increasing the accessibility, the timeliness and continuity in the medical care path.
Policy of full disclosure: None.

P-08-006
Key issues in recovering from first episode psychosis: a factor analysis of the Psychosis Recovery Inventory (PRI)

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Objective: Recovering from first-episode psychosis can be a multifaceted experience. Conventional studies focused on objective outcome measures. The Psychosis Recovery Inventory (PRI, 2005) was designed to capture subjective aspects of the recovery experience. We explored key dimensions in how patients experience their illnesses and treatment through factor analysis of the PRI.
Methods: The PRI is a self-report instrument originally derived from qualitative interview of recovering first-episode patients. A comprehensive range of items include common issues such as adherence, side effects, and insight. Less common but nevertheless important issues include effort to understand illness, perceived impact of illness, perceived extent of recovery and relapse risks. Factor analysis was conducted to identify key dimensions of recovery experience.
Results: 48 male and 72 female adult outpatients (age 25–55, mean 37.80) completed the PRI six-months following treatment of the first-episode psychosis. They are participating in a larger RCT study of Early Intervention for adult FEP patients (JCEP Project). PANSS subscale scores were: positive (1.31 ± 0.53); negative (1.44 ± 0.61); general (1.29 ± 0.36). Factor analysis of the PRI (Principal Component Analysis with Varimax rotation) identified 5 significant factors with eigenvalues above 1, accounting for 50% of the total variance. The five independent factors are (1) perceived impacts of illness; (2) experience of cognitive impairments; (3) perceived needs for medication; (4) items related to "sealing over" attitude and (5) insight.
Conclusion: This analysis identified key domains from patients' perspective on their recovery experience. Independent domains identified include some less familiar domains such as appreciation for impact of illness, subjective cognitive difficulties, and sealing over attitude. Awareness of these domains provides directions for developing focused intervention approaches.
Policy of full disclosure: The JCEP project is funded by The Hong Kong Jockey Club Charities Trust.

P-08-007
Factors contributing to stigma resistance in patients with schizophrenia

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Objective: Persons with mental illnesses, especially those suffering from schizophrenia face stigma attached to their condition. The fight against stigma might profit from people resisting stigma. Stigma resistance, an individual's capacity to counteract the stigma of mental illness, emerged as a separate construct in our study (Sibitz et al. 2011). However, the very nature of stigma resistance has still not been fully revealed. The aim of our study is to shed more light on stigma resistance and to explore its genesis.
Methods: Qualitative interviews were carried out with 32 patients with schizophrenia following a semi-structured guideline. Transcripts of recorded interviews are coded and analysed thematically using a modified, grounded theory approach.
Results: Stigma resistance relates to being immune to stigma and being able to counteract stigma. Stigma resistance unfolds in communicative matters, like speaking about psychological symptoms or developing a selective openness. Other helpful strategies to counteract stigma are humour or degradation facing stigmatising persons. Regarding the development of stigma resistance it was considered helpful to expose oneself to possible stigmatising situations when the individual's precondition was stable, but to save oneself situations that were prone to be harmful. Protective factors were a happy childhood and a supportive family and social network, risk factors were lack of money, lack of possibilities and a constantly stigmatising environment.
Conclusion: Stigma resistance is a new and promising concept, which can be embedded into the bigger current scientific research of resilience, i.e. an individual's ability to withstand and bounce back from stress and adversity (Rutter et al. 2006). Further research should focus on the development of a robust scale for the assessment of stigma resistance to prove its value as an independent variable, as well as an outcome variable of individual therapeutic interventions and public health action.
Policy of full disclosure: None.

P-08-008
The influence of self-stigma on success in work or study among people with schizophrenia

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Objective: Accumulating research has revealed that self-stigma has a negative impact on the well-being of people with schizophrenia and is associated with a loss of self-esteem, hope and experienced quality of life. Persons who stigmatize themselves experience more symptoms and depression. The percentage of persons with schizophrenia who have a high level of self-stigma is large (41.7%). We expect that people with high levels of self-stigma will behave in accordance with their self-stigmatizing cognitions. Therefore, they invest less in finding work, social contacts or other relevant domains. Research has shown that the majority of people with schizophrenia considers they are not capable of concurring for a job. Only a minority (25%) thinks they can hold a job which is appropriate with their level of education, knowledge and experience. There is high unemployment under persons with schizophrenia (90%). We expect that self-stigma plays a role in this high unemployment.
Methods: Persons with schizophrenia ($n = 110$) are assessed with measures of self-stigma, insight, symptoms, social cognition, work status and demographic variables. After controlling for the effects of demographic and illness-related factors, the authors used hierarchical multiple regression analysis to investigate the effects of self-stigma on success in work or study.
Results: Results of this study will be presented.
Conclusion: Based on the results we will develop a new treatment for diminishing self-stigma related to work or study in persons with schizophrenia. The treatment will be evaluated in a pilot study in the Netherlands.
Policy of full disclosure: None.

P-08-009
Clinical and social dimensions of disability at schizophrenic spectrum disorders patients with anhedonia: impact on quality of life

N. Orlova (URISFPDA, Kiev, Ukraine), M. Shkliar

Objective: Disability is necessary component of QoL at schizophrenic patients.This is significant in respect of patients with anhedonia which have disability as a result of mental illness. As a rule that patients have lower level of social functioning and QoL, have a lot of problems with they cannot solve themselves. As a consequence increase a number of hospitalizations on "social causes".
Methods: clinical and anamnesis analyzes.
Results: 60 (50%) patients with negative paranoid schizophrenia (NS) (295.30), 60 (50%) patients with postpsychotic depression (PPD) (295.60) with anhedonia. Mean age were 33.94(±0,96) years, more than under 40. Men dominated than women (65 and 35% respectively). At 52.5% patients illness duration was under 5 years, with début in young age (to 29 years—42.5%). Number of disability patients were 50.83%. Almost 1/3 of patients had more than 5 years disability duration, 1/3 of them received it more than 10 years ago. Patients have relatively high educational level but numbers of working and learning patients were 35.83%. Patients had social problems like inability to home owners and as consequence necessity in outside care, problems with plan and balance of a budget, social contacts poverty. 84% of patients had no persistent family relations (single—61%, divorced—21%, widowed—2%). Almost 2/3 of patients were passive, inert in everyday life, most of the day does not busy. A lot of them completely lost their social position, being indifferent (20.9%), dependent (24.2%) or being in subordinating relations (22.3%). All patients had severe QoL but in NS group it consisted 38.83 ± 1.02 ($rs \approx 0.282$; $P \leq 0.05$).
*Conclusion: A*nalysis pointed at low level of social functioning and quality of life at disability schizophrenia spectrum disorders patients with anhedonia. So in addition to biological correcting of negative symptoms high level instability of marital relations demands the family therapy and Communication Skills Training.
Policy of full disclosure: None.

P-08-010
The ITHACA-Toolkit (German version): validation of an interview manual and toolkit to assess human rights and physical health of residents in psychiatric and social care institutions

H. Zäske (LVR Klinikum, Heinrich-Heine-University, Duesseldorf, Germany), W. Gaebel

Objective: In 2006, the UN adopted the Convention on the Rights of Persons with Disabilities (CRPD). The convention defines disabled people as actors with guaranteed rights, e.g., for social participation on equal terms, not only as passive recipients of social welfare. States that ratified the convention are committed to take action to provide the rights of people with disabilities. Apart from case histories and visitation reports, a methodology to assess the human rights situation of persons in psychiatric or psycho-social institutions does not yet exist. The ITHACA project was conducted in 15 European countries to develop and validate a consistent methodology to assess the human rights situation of people living in psychiatric and social care institutions.
Methods: Focus groups with service users were conducted to identify relevant topics and then to discuss a draft version of the interview manual. 6 different psychiatric institutions (psychiatric hospitals and departments, residential care homes, community mental health services) were visited by a visitation team of former mental health service users and professionals. Visitation sites were selected as best-practice examples, most of them on recommendation of service users.
Results: 44 Interviews were conducted with patients, residents and staff members. Based on the feedback of all participating sites in Europe, both manual and toolkit have been revised and are online freely available in 13 languages. The final version comprises 30 topics. The interviewer can choose on which parts and topics he focuses depending on the visitation's purpose and setting.
Conclusion: The ITHACA interview manual and toolkit is a comprehensive and flexible tool to assess various aspects of health care quality and the human rights situation of patients and residents in psychiatric and psycho-social services. It has been proved suitable for different frameworks as visitation commissions, quality management and further education.
Policy of full disclosure: None.

P-09 Neuropsychology I: Basic

P-09-001
Age at onset and executive function in schizophrenia

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Objective: There seems to be agreement on the fact that early onset schizophrenia (EOS) patients have poorer neurocognitive functioning and outcome than adult onset schizophrenia (AOS). We wanted to use measures of executive functioning to examine whether the differences between the EOS and the AOS group are solely based on the age effect.
Methods: Executive functioning were assessed using Wisconsin Card Sorting Test and The Stroop test on 31 adolescents with EOS, 174 adults with AOS, 66 healthy adolescent controls, and 174 healthy adult volunteers. Both patient groups were assessed early in the course of their illness and were matched to their respective control groups on age and gender.
Results: The adolescents patients performed significantly worse than adult patients on most measures of executive functioning. However, when controlling for developmental differences in the control group, the results were no longer significant. Both the adolescent and adult patient group had executive deficits of approximately 0.8–1.8 SD below their respective control groups.
Conclusion: The results contrast earlier literature which consistently have reported EOS to have poorer cognitive functioning than AOS. This indicates that EOS and AOS are not qualitatively different illnesses, rather that they are two manifestations of the same disorder.
Policy of full disclosure: None.

P-09-002

Cognition and functioning of patients with first psychotic episode and relation with the brain derived neurotrophic factor

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Objective: Brain-derived neurotrophic factor (BDNF) promotes growth and maintenance of connections, serves as a neurotransmitter modulator, and participates in plasticity mechanisms. The cognition of the patients who suffer a first episode of psychotic (FEP) is altered and there is a reduction in their functioning. In this study, we analyze the relation between the BDNF and the cognitive performance and prognosis in patients with recent psychosis.
Methods: 45 patients with a FEP were selected from the Basque Country. The diagnoses for psychotic disorder were made using the SCID-I and DSM-IV. Plasma BDNF levels were measured using the BDNF Sandwich ELISA Kit. All patients were assessed clinically three times over a year using PANSS, GAF and Strauss Carpenter scales. Battery of cognitive tests (Wechsler Memory Scale and WAIS-III) was applied 6 months after the acute episode.
Results: We observed a positive correlation between BDNF levels after 6 months of treatment and five cognitive domains: abstract verbal reasoning ($r = 0.468$), motor and processing speed ($r = 0.397$), learning capacity ($r = 0.559$), immediate memory ($r = 0.409$) and delayed memory ($r = 0.382$). Also,the patients with lower BDNF plasma levels at baseline at 6 months follow-up had worse social activity (0.61 vs. 0.89; $t = -2.137$; $P = 0.041$) and functioning (0.69 vs. 0.93; $t = 2.109$; $P = 0.044$).The BDNF levels increased along the follow up, after the pharmacological treatment (basal-1 month: $Z = -2.88$; $P \leq 0.004$ and 1–6 months: $Z = -2.23$; $P \leq 0.05$).
Conclusion: Our results suggest that BDNF is associated with cognitive impairment seen after a FPE and with their prognosis. After the pharmacological treatment, the BDNF levels increase significatively but it's necessary, at list, 6 moths of treatment to obtain normal levels. Further investigations of the role of this neurotrophin in the symptoms associated with onset of psychosis are warranted.
Policy of full disclosure: None.

P-09-003

Sustained attention and working memory, but not executive function, deficits follow a familial pattern in schizophrenia

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Objective: Cognitive deficits are core features of schizophrenia and as there is increasing evidence for a familial pattern, they are considered putative endophenotypes. This study assessed the familial pattern of cognitive deficits in remitted-schizophrenia patients and their unaffected siblings, using an extensive battery of tasks that have so far yielded mixed findings in performance differences.
Methods: Sixteen patients, 16 unaffected siblings and 17 healthy control subjects underwent neuropsychological tasks assessing sustained attention (Degraded Continuous Performance test, DCPT; Span of Apprehension test, SOA), working memory (N-back sequential letter task) and executive function (Wisconsin Card Sorting test, WCST; Stroop Interference test, SIT; Verbal fluency). The distribution of all variables using the Kolmogorov–Smirnov test was examined and parametric or non-parametric tests were applied, as appropriate.
Results: The groups did not differ in age, years of education, gender and smokers ratios (all P values > 0.09). Both the patient and the siblings group had prolonged reaction times compared to controls in sustained attention tasks [DCPT: patients $P < 0.001$, siblings $P = 0.005$; SOA: patients $P < 0.001$, siblings $P = 0.01$]. In the SOA task, the control group also had more correct responses compared to both patients ($P = 0.003$) and siblings ($P = 0.011$). Both groups committed more false alarms in the N-back task (patients $P = 0.031$, siblings $P = 0.007$), but only the patients performance was poorer in the executive function tasks (patients all P values < 0.009; siblings all P values > 0.08).
Conclusion: These findings further support sustained attention and working memory deficits as potential endophenotypes of schizophrenia. The lack of difference in executive function between the siblings and the controls is in agreement with the law heritability rates of executive function. Reaction time and false alarm rates are suggested as additional useful endophenotypic measures that could potentially account for differences in performance in tasks that are not purported to examine the specific measures per se.
Policy of full disclosure: None.

P-09-004

Impaired top-down processing in schizophrenia in the perception of a hollow mask revealed with fMRT and event-related-potentials

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Objective: Visual illusions can reveal mechanisms of perception that try to make our world around us meaningful. In order to perceive our environment around us as meaningful the interaction between bottom–up and top–down processing has to be intact. In this study we use the principles of the 'hollow-mask illusion' to investigate this interaction. The hollow-mask illusion occurs when a hollow mask is perceived (incorrectly) as a normal face. It is understood to be a process that involves the generation of hypotheses about the three-dimensional shape of faces by interpreting the bottom-up signals received from the eyes using conceptual and perceptual knowledge (top–down processing). Healthy volunteers perceive a hollow mask as a normal face, presumably due to the strength of constraining top-down influences, while patients with schizophrenia do not. However the neural mechanisms underpinning this effect remain poorly understood.
Methods: We used functional magnetic resonance imaging and event related potentials to investigate the hollow-mask illusion in schizophrenic patients and healthy controls. The primary aim of this study was to use measures effective connectivity arising from dynamic causal modelling (DCM).
Results: We identified differences between the two groups in effective connectivity. In particular, there was a strengthening of bottom–up processes, and weakening of top–down ones, during the presentation of 'hollow' faces for the patients. In contrast, the controls exhibited a strengthening of top–down processes when perceiving the same stimuli.
Conclusion: These findings suggest that schizophrenic patients rely on stimulus-driven processing and are less able to employ conceptually-driven top-down strategies during perception, where incoming sensory data are constrained with reference to a generative model that entails stored information from past experience.
Policy of full disclosure: None.

P-09-005
Neural correlates of impaired volition in schizophrenia

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Objective: Saccadic eye movement tasks are particularly useful to distinguish between stimulus-driven and volitional behavior. Recent studies showed that schizophrenia patients are slowed in the initiation of volitional but not visually guided (i.e. stimulus-driven) saccades, suggesting a deficit in the volitional initiation of action. The present study aimed at identifying the neural substrates of this putative deficit.
Methods: Fifteen schizophrenia patients and 15 healthy controls underwent functional magnetic resonance imaging while performing volitional and visually guided saccades.
Results: Preliminary analyses suggest that the slowing in volitional saccade initiation is associated with reduced activation in the supplementary motor area (SEF) in schizophrenia patients.
Conclusion: This result may indicate a neural substrate of disrupted volition in schizophrenia.
Policy of full disclosure: None.

P-09-006
Mechanisms of prediction in patients with psychosis

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Objective: Prediction is an estimate about what will happen in future extrapolated from the present. In daily life, we use prediction together with sensory input and feedback to generate and control action. The oculomotor pursuit system represents a valuable model for studying sensory processing and its use for action planning within a well-characterized neural circuitry. Recent laboratory and imaging studies suggest that patients with psychosis utilize predictive mechanisms to overcome feed forward sensory transformation deficits. Predictive mechanisms may therefore be crucial for action planning in patients with psychosis.
Methods: The present study assessed patients with schizophrenia ($N = 18$) and bipolar disorder ($N = 18$) and matched healthy controls ($N = 20$) on blocks of predictable pursuit ramps at 8 and 16°/s. Three different aspects of prediction were evaluated by blanking off the visible target either at the beginning, the middle or the end of ramps. By this procedure, an anticipatory component could be differentiated from a short-term velocity storage component and a more general action plan. Parameters of interest included eye velocity gain (eye velocity/target velocity) in periods with and without visible targets, eye acceleration and deceleration and its latencies related to target blanking.
Results: First results show that while patients with psychosis are impaired in using and timing anticipation of upcoming events they rely on prediction based on short-term velocity storage to continue ongoing movements to a higher extent than healthy controls even when the visible target is blanked off. Eye velocity gain in patients was reduced in all conditions with visible targets replicating previous findings. In all, there were only slight differences between patients with schizophrenia and bipolar disorder.
Conclusion: Our findings support the hypothesis that distinct mechanisms of prediction such as utilization of working memory information help patients with psychosis to optimize their performance.
Policy of full disclosure: None.

P-09-007
Impaired pantomime in schizophrenia: association with frontal lobe function

S. Walther (University of Bern Psychiatry, Switzerland), T. Vanbellingen, S. Bohlhalter

Objective: Schizophrenia patients suffer from disturbances of thought, motor coordination and affect mainly related to dysfunction of frontotemporal networks. Recent brain imaging data suggest that gesture performance, particularly in the pantomime domain, may critically depend on frontal lobe function. Hence, the goal of the present study was to investigate gesture production and its relationship to behavioral assessments in schizophrenia. We hypothesized an association of gesture performance and measures of frontal lobe function.
Methods: In total, 23 right handed patients with schizophrenia (14 male) were assessed with the standardized Test of Upper Limb Apraxia (TULIA) as well as clinical rating scales including PANSS, Modified Rogers Scale (MRS), UPDRS (motor part III), Abnormal Involuntary Movement Scale (AIMS), MMSE and Frontal Assessment Battery (FAB). In the TULIA test, assessed for both sides separately, patients were requested to perform 48 gestures in two main domains: imitation (on seen gesture) and pantomime (on verbal command). Performance was monitored by video and ratings were done blinded. Exploratory tests were performed using independent T-tests and Spearman correlations.
Results: Gestural deficits were seen in 35% of the patients (imitation deficits in 17%, pantomime deficits in 35%). Patients with gestural deficits had higher scores in the MRS, PANSS positive and PANSS total. Furthermore, they were more impaired in the FAB. Extrapyramidal symptoms, involuntary movements, quantitative motor activity, medication, duration of illness and negative symptoms were not associated with gestural performance. FAB scores strongly correlated with pantomime performance ($r = 0.67$, $P = 0.001$).
Conclusion: Mild gestural deficits, related mainly to impaired pantomime, are prevalent in schizophrenia and strongly associated with frontal lobe function. In contrast, these deficits are independent of motor functioning. The finding is in line with the well-established frontal dysconnectivity in schizophrenia. Furthermore, they support the notion that the neural basis of gestures may be domain-specific.
Policy of full disclosure: None.

P-09-008
Negative capability: a poetic-based cognitive resource in early psychosis

M. Lanzaro (RDASH Psychiatry, Scunthorpe, UK)

Objective: The "jumping to conclusions" response style has been interpreted as reflecting a data gathering reasoning bias and participants to studies with at-risk mental state may present a difficulty in tolerating uncertainty along with impaired working memory. The aim of this paper is to suggest that there will be room for poets arguments, like Johns Keats', to inform cognitive techniques whose target is the faulty appraisal or interpretation of anomalous experiences and events.
Methods: This is a review of the literature regarding reasoning biases in prodromic stages of psychoses, alongside with an analysis of Keats' theory of "negative capability".
Results: The inability to tolerate ambiguity was encompassed in Keats' theory of "negative capability", expressed in his letter to his

brother dated Sunday, 21 December 1817: "I mean Negative Capability, that is when man is capable of being in uncertainties, mysteries, doubts without any irritable reaching after fact and reason (…)". Nearly a century ago (whilst Kraepelin was postulating that there is a specific brain pathology underlying each of the major psychiatric disorders), Keats had the strong intuition that great (and "sane") people have the ability to accept that not everything can be resolved, that the truths found in the imagination access holy authority. In the 1930s, the American philosopher John Dewey cited Keatsian negative capability as having influenced his own philosophical pragmatism, and said of Keats' letter that it "contains more of the psychology of productive thought than many treatises".
Conclusion: Negative capability is a state of intentional open-mindedness, which seemed somehow deficient in studies of individuals with a "jumping to conclusions" response style. Encouragingly, contemporary research is beginning to address applications of exciting new cognitive theoretical models for early psychosis in clinical practice. Keats' theory may be very useful to inform a peculiar innovative technique and approach.
Policy of full disclosure: None.

P-09-009
Data gathering reasoning bias in patients with at-risk mental states: cognitive and poietic techniques

M. Lanzaro (RDASH Psychiatry, Scunthorpe, UK), Max Lanzaro

Objective: The "jumping to conclusions" response style has been interpreted as reflecting a data gathering reasoning bias and several studies show that patients with at-risk mental state may present a difficulty in tolerating uncertainty along with impaired working memory. This interestingly was encompassed in Keats' theory of "negative capability", expressed in his letter to his brother of 21 December 1817: "I mean Negative Capability, that is when man is capable of being in uncertainties, mysteries, doubts without any irritable reaching after fact and reason (…)". Nearly a century ago (whilst Kraepelin was postulating that there is a specific brain pathology underlying the major psychiatric disorders), Keats had the intuition that "sane" people have the ability to accept that not everything can be immediately resolved: This "being in uncertainty is a place between the mundane, ready reality and the multiple potentials of a more fully understood existence". Negative capability is a state of intentional open-mindedness paralleled in the literary and philosophic stances of other writers.
Methods: Qualitative review of the relevant literature.
Results: The aim of this review is to suggest there should be room for poets' arguments to inform new cognitive techniques whose target is the faulty appraisal or interpretation of anomalous experiences and events.
Conclusion: In the 1930s, the American philosopher John Dewey cited Keatsian negative capability as having influenced his philosophical pragmatism, and said of Keats' letter that "contains more psychology of productive thought than many treatises". Encouragingly, modern and contemporary research is beginning to address applications of exciting new cognitive theoretical models for psychosis in clinical practice.
Policy of full disclosure: None.

P-09-010
Electrophysiological markers in bipolarity

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Objective: Making differential diagnosis between a bipolar disorder and a schizophrenic pathology with mood disorder is often difficult. The aim the study was to test whether the ERP'S component could differentiate between these two disorders.
Methods: Twenty-seven patients meeting de the bipolar disorder in DSM IV in a remission phase of 6 months minima were tested with auditory ERP's and CNV. The results were comparated with results obtained with twenty night patients meeting the DSM IV diagnosis of schizophrenia with mood disorders. These schizophrenic patients were also in a remission phase since a minimal of sixth months. There were tested in the same condition with similar ERP'S component. We studied amplitude and latency of N100, MMN, P200, N200, P300 and CNV.
Results: We observed same delays of latency and reduction of the amplitude for P300 in both pathologies. That suggests that temporo-parietal lobes disturbances underlying by difficulties in the attention processes are similar in the two pathologies. Differences were noticed at the level of N100, MMN, P200 and CNV amplitude. It could be the sign of a better reactivity in stimuli in bipolarity as well as a better conservation for executive functions (Table 1).
Conclusion: ERP, s could be contributing in differential diagnosis for bipolarity and schizophrenia. He could constitute a help to the patrician for a better prescription and for evaluation of illness evolution. These observations have to be confirmed by a larger study with more patients and in a longer duration.
References:
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Policy of full disclosure: None.

Table 1 Results

	Latency N100	Amplitude N100	Latency MMN	Amplitude MMN	Latency P200	Amolitude P200	Latency N200
BP	98.0	5.0	148.0	4.8	173.6	7.3	214.9
SCH	105.7	4.4	151.8	3.6	181.0	4.8	214.7
	Latency N200	Amplitude N200	Latency P300	Amplitude P300	P50 inhibition	Latency CNV	Amplitude CNV
BP	214.9	5.4	330.8	9.7	25 OUI	1,163.3	21.6
SCH	214.7	3.5	325.4	7.0	2 OUI	1,223.8	9.8

P-09-011
Measuring mismatch negativity (MMN) in the rat: methodological considerations for translational studies of schizophrenia

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Objective: MMN is a frontal negative deflection in ERPs generated to infrequent "oddball" deviant sounds that violate regularities in background standard sounds. Reduced MMN is a robust finding in schizophrenia and meets many of the criteria for an endophenotype. As MMN is sensitive to the functional integrity of the glutamate NMDA receptor (NMDAR) system, it is potentially a valuable tool in assessing rodent models of schizophrenia focussed on glutamate dysfunction. However, before proceeding down this path, it essential to determine that MMN-like activity in the rodent (i) is not due to greater refractoriness of ERP generators to standard sounds, (ii) meets the hallmark criterion for MMN of a memory-based comparison process and (iii) exhibits sensitivity to local probability effects.
Methods: Epidural ERPs in awake Wistar rats were recorded using 4 oddball conditions in which regular background sounds were occasionally (20%) interrupted by a deviant sound, either a high/low frequency deviant, or a short/long deviant, and control conditions in which varying background sounds intervened between deviants occurring at the same probability (20%) as the deviant oddball, thus eliminating any regularity in background sounds.
Results: ERP responses to both high frequency and long duration oddball deviants showed evidence of MMN: both were negatively displaced relative to a common regular standard and a deviant with many standards. The response to high frequency deviants (but not long duration deviants) was also sensitive to local temporal context of preceding stimulus regularity in that it increased with the number of standards prior to the deviant sound.
Conclusion: Only MMN-like responses to high frequency deviants met two crucial MMN criteria, namely, a memory-based comparison process and sensitivity to local probabilities in terms of the number of standards preceding a deviant and shows promise as an endophenotype in animal models of schizophrenia.
Policy of full disclosure: Funded by the Schizophrenia Research Institute, Hunter Medical Research Institute and the University of Newcastle

P-10 Neuropsychology II: clinical

P-10-001
Differences in the internalizing attributional style of patients with a first episode psychosis depending on their cognitive and insight impairment

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Objective: The model reported by Startup (1996) proposed a model of lack of insight in psychosis which explains that patients with neurocognitive deficits will have only average insight with the deficit due to the cognitive decline. However, patients without neurocognitive impairment will either have good insight, or have poor insight which is secondary to psychological factors (such as neglection). The objective of this study was to test the Startup′s model with the attributional style as psychological factor to explain lack of insight in patients with psychosis who perform cognitively normal.
Methods: A study was held with 32 patients with FEP from 3 main hospitals in the Basque Country (Spain), and 44 controls.All patients underwent clinical and functional evaluations. The measures included were: the Scale to Assess Unawareness of Mental Disorder (SUMD), the Attributional Style Questionnaire (ASQ), Stroop test, Vocabulary sub-test from WAIS-III and Trail Making Test. In order to test Startup's hypothesis, we selected only those patients with lack of insight. Then, we compared attributional style of patients regarding their cognition (normal or impaired).
Results: There was no significant difference between controls and patients in age ($P > 0.005$) and educational level ($P > 0.005$). Patients were divided into two groups according to their cognitive performance (within normal limits and impaired cognitive performance) and insight scores (preserved insight and lack of insight). Then we compared attributional scores of patients with lack of insight. The ANOVA test ($t = 1.32$; $df = 17$) shows internalizing attributional style for negative events is high when the patient has poor insight and good cognition ($x = 4.42$; SD $= 0.76$) and low when both cognition and insight are preserved ($x = 3.94$; SD $= 0.75$).
Conclusion: Our result suggests that internalizing attributional style plays a significant role on insight when cognition is preserved. These results are consistent with Startup's model, taking the EA as the psychological factor.
Policy of full disclosure: This study was partially funded by the Health Department of the Basque Government (2008111010) and EITB-Maratoia (BIO 09/EM/015).

P-10-002
Neurocognition and social cognition in early prodromal state of psychosis: preliminary results

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Objective: Impaired social cognition and neurocognition has been repeatedly demonstrated in patients with schizophrenia, but the specific cognitive deficits in subjects clinically at high risk for psychosis require further clarification. The aim of this study was to investigate neurocognitive functioning in subjects with "at risk mental state for psychosis" (ARMS) compared with healthy controls (HC) and schizophrenic patients.
Methods: We examined the performance of 40 healthy controls, 47 ARMS individuals and 28 schizophrenia patients using the Cambridge Automated Neuropsychological Test Battery and the Emotions Battery of the University of Pennsylvania computerized Neuropsychological Battery. ARMS subjects putatively met early prodromal state of schizophrenia, mainly characterized by the presence of basic symptoms. All ARMS individuals met the risk criterion cognitive-perceptive basic symptoms (COPER) using the SPI-A (Schizophrenia Proneness Instrument, Adult version). A one-way ANOVA was performed to determine group differences.
Results: There were several differences in Emotional processing between ARMS and HC with more poorly performance in emotion recognition and discrimination, facial memory tasks in ARMS subjects. ARMS individuals were significantly more likely to attribute emotions to neutral faces. At the same time differences between HC and schizophrenia patients were more prominent and significant in most parameters of emotion recognition and discrimination. ARMS individuals had significantly greater reaction times when compelling emotion recognition tasks. ARMS subjects

performed significantly worse in terms of executive functioning, visual memory and sustained attention then HC and better then schizophrenia patients.
Conclusion: Deficit in neurocognitive functioning is related to the presence of basic symptoms and early prodromal state of schizophrenia. The performance of the ARMS group is between that of the schizophrenia patients and control groups.
Policy of full disclosure: None.

P-10-003
Facial emotion recognition in subjects a ultra high risk for psychosis: a review

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Objective: This review aims to explore the difficulties in recognizing facial emotions in individuals at high risk for psychosis (UHR) and argues that such difficulties may be potential markers of vulnerability for developing psychosis.
Methods: We used national and international electronic databases; Medline, Lilacs and Scielo virtual library, from 2000 to 2011, and the following descriptors were used: "Emotion Recognition", "Early Psychosis" and "Ultra High Risk".
Results: The search resulted in 28 articles, 12 for meeting the inclusion criteria, three others were selected for being cited in the articles mentioned and addressed the theme. The other 14 articles were excluded for evaluated emotion recognition in patients with first episode and/or chronic schizophrenia. Individuals at UHR for psychosis show impairment in several aspects of emotion recognition, especially in the ability to identify negative facial emotions. They also identify neutral expressions as negative.
Conclusion: These impairments in emotion recognition could be a predictor of conversion to psychosis, although it still has not been possible to exclude the influence of initial positive symptoms in the emotion recognition changes observed in this population. The studies presented some limitations concerning the criteria for UHR. Some of them follow the SIPS/SOPS criteria while others used genetic risk, schizophrenia relatives and schizotypy personality traits, according to the SPQ criteria. Other limitations presented concerning the use of various psychometric measures for the assessment of emotion recognition.
Policy of full disclosure: None.

P-10-004
Mental States at risk of psychosis in youth adult: relationship between cognitive symptoms and basic symptoms

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Objective: Despite the longitudinal research define the cognitive deficits in youth as a predictive aspect of psychosis (Reichenberg et al. 2010; Levine & Rabinowitz 2010), the relationship between neuropsychological tests and clinical scales in this area shows mixed results (Rund et al. 2004). The choices related to establishing criteria for sample selection and use of measuring instruments appear methodologically critical elements that can explain these differences (McGorry, Yung & Killackey et al. 2008).
Methods: This study aims at investigating assessment and identification of mental states at risk of psychosis and the hypothesis of a correlation between the neurocognitive function with basic symptoms of young adults. Participants were members of a representative cohort of 10 males and 6 females younger than or equal to 30 years. The diagnosis of mental state at risk was carried out through the use of two semi-structured interviews (for positive and negative symptoms, Structural Interview for Prodromal Syndromes—SIPS; for the basic symptoms, The Schizophrenia Prediction Instrument for Adults—SPI-A) and a self-report scale completed by the subject (Frankfurter Beschwerde-Fragebogen—FBF) following the guidelines currently in use (Ministry of Health 2009). It was administered a neurocognitive test battery that assessed working memory/fluency, attention, shifting, planning, problem solving, executive function, verbal learning, impulsivity and motor speed.
Results: Performance deficits in young adults with basic symptoms relative to the performance of the controls were found for some but not all cognitive tasks, indicating a selective deficit. In particular, when compared with normative data, subjects showed lower scores in tests of sustained attention in tasks of long-term memory and visual-spatial categorization.
Conclusion: Preliminary analysis showed impairment in subjects on some tests related to executive functions. The finding suggests the usefulness of these tests as clinical, diagnostic and therapeutic tools in evaluations of young adults with basic symptoms.
Policy of full disclosure: None.

P-10-006
The efficacy of Integrated Psychological Therapy (IPT) for middle-aged schizophrenia patients

D. R. Mueller (Univ. Hospital of Psychiatry, University of Bern, Switzerland), S. J. Schmidt, V. Roder

Objective: Cognitive deficits are present in schizophrenia patients independent of age. Only few empirical data exist whether psychotherapeutic interventions can reduce cognitive deficits in middle-aged or elderly schizophrenia patients. Older, more chronified patients are thought to have little potential for change and have become the often forgotten population in research. An exception may represent the Integrated Psychological Therapy (IPT), a group-based cognitive-behavioral therapy approach combining interventions on cognition and social skills, which has been evaluated in studies including middle-aged inpatients.
Methods: Out of a total sample of 36 independent IPT studies we selected those studies evaluating the cognitive part of IPT in comparison to treatment as usual control condition (TAU). Finally, a total sample of 15 studies ($n = 632$ patients) could be selected. Afterwards we categorized the studies into those including middle-aged patients (age > 40 years) and younger patients. A standard meta-analytic procedure was used in calculating within effect sizes (ES) for IPT and TAU separately related to the two age categories.
Results: Middle-aged participants on IPT showed higher effects in neurocognition and social cognition (ES $> .89$) compared to younger patients under IPT (ES $< .60$). In social functioning no marked difference was evident between the age-categories. However, middle-aged and younger patient samples under IPT both reached the level of significance during therapy in all these parameters. But in negative symptom reduction, only the middle-aged patients did (ES $= .36$). With regard to TAU, the results were opposite to those of the IPT groups: only younger patients showed some significant change on a lower level in cognition and social functioning (ES $> .20$), but middle-aged patients did not (ES $< .12$).
Conclusion: Results clearly show no change in middle-aged patients without cognitive intervention, and a strong efficacy for IPT intervention independent of patients' age. Evidence-based therapy should

be implemented in psychiatric rehabilitation with middle-aged and elderly schizophrenia patients.
Policy of full disclosure: None.

P-10-007
Clinical and cognitive outcomes in schizophrenia/psychosis after cognitive remediation with REHACOP

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Objective: The efficacy of cognitive remediation in patients with psychosis has been widely recognized for cognitive impairment. However, clinical symptoms, particularly negative symptoms do not show the same pattern of improvement. Therefore, the goal of this study was to test if clinical symptoms improve after cognitive remediation with REHACOP program.
Methods: Seventy-two patients with first-episode psychosis (FEP) and schizophrenia were randomly allocated into experimental or control groups. The patients allocated on the experimental group ($N = 44$) received a cognitive rehabilitation treatment using REHACOP. They attended 36 sessions of 90 min during 3 months. Patients under control condition ($N = 28$) received Occupational Therapy during the same period of time. Both groups received treatment as usual. Patients underwent clinical and neuropsychological pre- and post treatment assessments.
Results: Repeated measures of MANOVA showed that experimental group improved significantly in most cognitive domains, when compared to controls. Group (REHACOP vs.1 Control) × Time (pre vs. post-treatment) interactions were significant for attention ($F = 12.36$, $P < 0.001$), verbal memory ($F = 5.30$, $P < 0.05$), processing speed ($F = 5.30$, $P < 0.05$), and executive functioning ($F = 4.13$, $P < 0.05$). On the contrary, verbal fluency ($F = 3.75$, $P = 0.56$) did not show significant improvement in any of the groups. Regarding clinical symptoms (PANSS), Group × Time interaction was significant for negative symptoms ($F = 4.24$, $P < 0.05$), showing that experimental group obtained significant improvement when compared to controls. Nevertheless, positive ($F = 1.23$, $P = 0.29$), disorganization ($F = 0.28$, $P = 0.60$), excitement ($F = 1.87$, $P = 0.18$) and emotional distress ($F = 0.07$, $P = 0.79$) symptoms did not significantly improved.
Conclusion: Our findings with a large sample of patients suggest that REHACOP is an effective cognitive remediation program for minimizing existing cognitive but also negative clinical symptoms. The relevance of this finding is strength by the strong relation that both, cognitive and negative symptoms present with functional outcome in psychosis.
Policy of full disclosure: This study was partially funded by the Department of Health and Instituto de Salud Carlos III (Beca FIS Grant number PIO70245); Educational and Science Department of the Basque Goverment (beca del Programa de Formación de Investigadores del Departamento de Educación. Universidades e Investigación); and EITB-Maratoia (BIO09/EM/023).

P-10-008
Effect of cardiovascular exercise on mental and physical health in patients with schizophrenia

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Objective: Even when treated with antipsychotic medication patients with schizophrenia often suffer from positive and negative symptoms and manifest psychiatric co-morbidities such as depression. In addition, patients with schizophrenia have increased morbidity and mortality rates with low cardiovascular fitness levels and overweight as major contributors. This single blind RCT investigated whether a 6-month cardiovascular exercise training (2 h a week) decreased psychotic and depressive symptoms and increased cardiovascular fitness levels in patient with schizophrenia.
Methods: 64 patients with schizophrenia (age: 29.6 ± 7.6 years) were included. Symptoms were measured by the Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987) and Montgomery and Åsberg Depression Rating Scale (MADRS; Montgomery and Åsberg 1979). Cardiovascular fitness (VO2max and WATTmax) was determined by a Maximal Exercise Tolerance Test (Godfrey 1974). Body mass index (BMI) was calculated. Subjects were randomly assigned to cardiovascular exercise or occupational therapy. Drop-out was higher in the occupational therapy than the exercise group (Chi-square 8.327, $P = .016$). Compliance level was set at 60 percent leaving 33 patients (16 exercise vs. 17 occupational therapy) for analyses. SPSS 18.0 was used for analyzing data. Repeated measures general linear models investigated the effects of intervention on PANSS, MADRS, VO2max and WATTmax and BMI.
Results: PANSS total and MADRS score decreased after exercise versus occupational therapy ($F = 16.926$, $P = .000$; $F = 6.012$, $P = .020$). A trend increase in VO2max ($F = 3.202$, $P = .084$), an increase in WATTmax in the exercise versus occupational therapy group were found ($F = 15.105$, $P = .001$) but no change in BMI ($F = 1.992$, $P = .168$).
Conclusion: Exercise effectively decreases schizophrenic and depressive symptoms and increases to a lesser degree fitness in patients with schizophrenia. Results suggest cardiovascular exercise should be offered in patients with schizophrenia. Additional treatments strategies should be developed to improve physical health.
Policy of full disclosure: This study is financially supported by a research grant from the Diabetes Foundation (2007.00.040) and Eli Lilly Pharmaceuticals.

P-10-009
Enhancing synaptic plasticity and cognition by aerobic exercise and cognitive training in chronic schizophrenia: design for a randomised controlled trial

B. Malchow (Dept. of Psychiatry, University Medical Center, Goettingen, Germany), T. Wobrock, P. Falkai

Objective: In a first pilot study we observed that following aerobic exercise training, relative hippocampal volume increased significantly in patients (12%) and healthy subjects (16%), with no change in the non-exercise group of patients (−1%) (Pajonk et al. 2010). The aim of this randomized controlled trial is to replicate the results of our first pilot study and to explore if aerobic exercise combined with cognitive training leads to improvement of cognition in chronic schizophrenia compared to a placebo condition. Furthermore, the investigation is designed to show whether these effects are lasting and whether they could be used to improve cognitive dysfunction in chronic schizophrenia.
Methods: The study will be a randomised, controlled trial comparing the combination of physical aerobic exercise and cognitive training with the participation in the sports program (cycling) alone or with an alternative activity, spending the same amount of time but without an impact on physical activity (table football) in combination with computerized cognitive training (CogPack). All conditions will be provided over a 3 months period. Primary outcome measures will be a significant improvement of the sum score in the VLMT as determined when entering the study and after 3 months (primary endpoint) and

after 6 months (secondary endpoint). Secondary outcome measures will be an improvement of the PANSS negative subscore, improvement in quality of life domains (WHO-QoL), an increase of hippocampal volume and an elevation of NAA-concentration (MRS). All parameters measured when entering the study, after 3 and after 6 months.
Results: Preliminary results will be shown if already suitable.
Conclusion: First conclusions for future studies regarding the impact of aerobic exercise may be drawn.
Policy of full disclosure: None.

P-10-010
No effect of aerobic exercise on the amygdala and vermis cerebelli in patients with chronic schizophrenia

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Objective: Reduced volumes and structural alterations of certain brain regions have been repeatedly reported in patients with chronic schizophrenia. For the amygdalae and the cerebellum results are inconclusive. Exercise training was found to increase substantially the hippocampal volume in patients with chronic schizophrenia (Pajonk et al. 2010). In this investigation the effects of exercise training on the volume of the amygdalae and vermis cerebelli were to be studied.
Methods: In a randomised controlled study eight patients with schizophrenia and eight healthy subjects performed ergometric cycling three times a week in 30 min sessions for a duration of 3 months. Another eight patients with schizophrenia played table football to the same extent and in a similar environment. At baseline and endpoint MRT scanning for volumetric assessment were performed.
Results: There were no changes in the volumes, both for the amygdalae and the vermis cerebelli before and after exercise training and no difference between patients performing exercise or playing table football. Accordingly, there were no significant correlations between changes in the aerobic fitness and the volume changes. The volumes of amygdalae and vermis cerebelli at baseline did not differ between healthy subjects and schizophrenic patients.
Conclusion: Although the exercise intervention proved to have a substantial impact on the growth of the hippocampus, the volumes of amygdala and vermis cerebelli did not change. This indicates that exercise training is not a stimulus for global brain development. We postulate specific neuronal changes in particular brain regions subsequent to physical exercise training that occur in the hippocampus but not in the amygdala or the vermis cerebelli.
Policy of full disclosure: None.

P-10-011
In schizophrenia requirements of stereopsis prevent foveal fixation of the target of attention

H. Korn (Eichstaett, Germany)

Objective: In several recent investigations the authors have reported a disorder of fixation in schizophrenic patients. The present paper describes the case of an unmedicated hyperopic and hyperphoric patient with chronic schizophrenia in whom an inability had been found to deliberately converge with the left eye from a distant to a near target in a test developed by the author—despite evidence of stereopsis. The deficiency was suddenly overcome when working with a laser display, which was accompanied by the transformation of that eye's hyperopia into an emmetropia and finally into a myopia. By correcting the resulting anisometropia with a contact lens instead of spectacles—which had caused an optical aniseikonia—and of the hyperphoria with prismatic glasses, binocular fixation of the near target of selective attention was reestablished and the patient's psychotic problems disappeared.
Methods: Two hypotheses are discussed concerning the causes of the abnormal compensation of the aniseikonia by reducing convergence and accommodation of the eye with the smaller image. It is attributed to an inversion of the left foveal disparity stimulus transforming the foveally stimulated convergence and accommodation into divergence and disaccommodation, thus magnifying the smaller image. The vulnerability for the inversion is imputed to an ambivalence concerning the attribution of foveal disparities to the nasal or the temporal half, due to a reversed crossing of foveal projections in the Chiasma Opticum.
Results: The inversion of the foveal convergence stimulus leads to a dissociation of the binocular and the head-and-body axis—i.e. between localisation of surroundings and the acting self. It feeds the patient's memory and emotions with perceptions she is not interested in mentally.
Conclusion: The resulting psychiatric disorder can be prevented today by detecting the difference of magnitude with the Aniseikonia Inspector, available via Internet, and correcting the optical anisometropia by contact lenses or corneal surgery. See homepage: http://www.schizo-binoc.de.
Policy of full disclosure: None.

P-11 Psychosocial Treatment

P-11-001
Processes of therapy in cognitive behavioral therapy for psychosis: a study in progress

M. Wiesjahn (Clinical Psychology, Philipps-Universität Marburg, Germany), E. Jung, W. Rief, T. Lincoln

Objective: Cognitive Behavioral Therapy has been demonstrated to be an effective treatment for psychotic disorders. However, it is unknown why and in which phase of therapy symptom reduction occurs. The questions addressed in this study are (1) What factors are relevant to symptom change in CBT-p? More specifically: Does positive change in specific domains, such as therapeutic alliance, control beliefs, dysfunctional cognitions about self and symptoms and social support predict treatment success?; (2) Are there systematic patterns of symptom change and which factors predict these patterns?; (3) Do the factors that are relevant to treatment success and the patterns of change differ between patients with psychotic disorders and patients with other mental-health problems?; (4) Do the factors that are relevant to treatment success and the patterns of change differ between patients who take antipsychotic medication and those who do not?
Methods: $N = 75$ patients will be included. The sample will consist of 50 patients diagnosed with psychotic disorders including patients who do not take antipsychotic medication. The comparison group will consist of 25 patients with diagnoses representative of outpatient psychotherapy patients. Patients with psychotic disorders will be treated with CBT-p based on Lincoln (2006). The comparison group will be treated with disorder-specific CBT interventions. Symptoms will be assessed before and after therapy (i.a. PANSS, CAPE, CDSS). Potential factors of efficiency will be measured before therapy and at several sessions during the therapy (i.a. HAQ, IPQ-S, DAS, BCIS, F-sozU). Individual symptoms will be assessed with individualized

session sheets after each therapy session. Data will be analyzed with hierarchical linear models.
Results: First results are expected in 2012.
Conclusion: The longitudinal assessment of symptoms and factors of efficiency aims to obtain a differentiated picture of the therapy processes in CBT-p.
Policy of full disclosure: None.

P-11-002
Predictors for the early therapeutic alliance in cognitive behavioral therapy for psychosis

E. Jung (Clinical Psychology, Philipps-Universität Marburg, Germany), M. Wiesjahn, T. Lincoln

Objective: Therapeutic alliance has been shown to be an important factor of efficiency in psychotherapy. Different client and therapist characteristics influence the therapeutic alliance. Among patients with schizophrenia less negative symptoms and a higher level of global and social functioning have been associated with better therapeutic alliance. The aim of this study was to replicate these findings and to investigate additional factors that predict the early therapeutic alliance.
Methods: Subjects were participants of a randomized clinical trial of Cognitive Behavioral Therapy for outpatients with psychotic disorders ($N = 80$). Baseline assessment of potential predictors included symptom scales (PANSS, SCL, CDSS, BDI) and ratings of general and social functioning (GAF, RFS). Therapeutic alliance was rated by patients and therapists after each session (STEP; Krampen 2002). Fifty-nine patients' ratings and sixty therapists' ratings were included in the analysis.
Results: Correlations between patient and therapist alliance ratings varied strongly between the sessions. Therefore correlations between baseline characteristics and early therapeutic alliance (mean of the first five sessions) were calculated separately for patient and therapist ratings. Significant negative correlations appeared between negative symptoms (PANSS-N) and patients' and therapists' ratings of the therapeutic alliance. Additionally, patient ratings showed significant negative correlations with general symptoms (PANSS-G) and depression (CDSS) and a positive correlation with global functioning (GAF). Regression analysis revealed only negative symptoms to be a significant predictor for patients' and therapists' ratings of the therapeutic alliance.
Conclusion: Higher levels of negative symptoms before therapy are related to lower quality of early therapeutic alliance. This result is consistent with previous findings. Other baseline characteristics did not contribute to explaining differences in the therapeutic alliance. Thus, therapists working with patients with higher levels of negative symptoms should focus particularly on building a good therapeutic alliance.
Policy of full disclosure: None.

P-11-003
Eagerness to understand illness in adult first-episode psychosis patients

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Objective: Understanding of one's illness facilitates a better self-management in recovery. First-episode patients face a challenge in understanding the complex illness underlying their psychosis. Psycho-education is a key component in early intervention. Patients show a range of eagerness to understand illness, which may contribute to psycho-education outcome. 'Eagerness to understand illness' (EUI) is an understudied variable. We use the Psychosis Recovery Inventory (PRI, 2005) to explore factors relating to EUI.
Methods: The PRI is a self-report instrument derived from qualitative accounts of first-episode patients. It includes various domains in the recovery experience (adherence; side effects; insight; perceived impact of illness; perceived extent of recovery; perceived relapse risks and EUI). We explore the relationship between EUI and other clinical and PRI domains in a sample of adult first-episode patients.
Results: 48 male and 72 female adult outpatients (age 25–55, mean 37.80) completed the PRI 6-months following treatment of first-episode psychosis. They participated in a larger RCT study of Early Intervention for adult FEP patients (JCEP Project). PANSS subscale scores were: positive (1.31 ± 0.53); negative (1.44 ± 0.61); general (1.29 ± 0.36). Calgary Depression Scale score was 3.15 ± 3.78. EUI score was summated from 4 PRI 'Eagerness' items. EUI is significantly correlated with (1) perceived impact of illness ($r = 0.54$, $P < 0.001$); (2) side effect ($r = 0.28$, $P = 0.002$); (3) perceived relapse risk ($r = 0.27$, $P = 0.003$) and (4) depressive symptoms ($r = 0.27$, $P = 0.003$). Stepwise multiple regression identified items (1) and (3) as significant predictors for EUI.
Conclusion: This study identified perceived impact of illness and perceived relapse risk as key factors contributing to patients' EUI. The results suggest the first step to enhance psycho-education outcome may be to facilitate appreciation of the impact of illness.
Policy of full disclosure: The JCEP project is funded by The Hong Kong Jockey Club Charities Trust.

P-11-004
Psychoeducation in schizophrenia: results of a survey of all psychiatric providers in the Czech Republic in 2009

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Objective: Psychoeducation in schizophrenia is a low-cost intervention that can prevent relapse. The goal of this survey was to evaluate where, when and how psychoeducation for schizophrenia is provided in the Czech Republic.
Methods: A questionnaire adapted from German version of Questionnaire about psychoeducation (Rummel-Kluge et al. 2006) was sent to all relevant psychiatric providers.
Results: Psychoeducation questionnaire was sent to 113 providers, both from health and social sector. 45 provide psychoeducation, 33 out of them are inpatient units. 9 providers offer more forms of psychoeducation. 16 does not provide any psychoeducation and 52 did not reply even after two prompts. Group psychoeducation (GP) for patients is the most frequent form (44). GP for relatives only and GP for patients and relatives together is provided only by 15 providers. Typically, GP for patients is offered to inpatients (57%), the group is diagnostically heterogenous (61%), and lead by psychiatrist (53%) or psychologist (39%). The programme consists usually of 6–10 lessons (47%), less than 5 lessons are offered by 27% providers. Both GP for relatives only (13 providers) and for relatives and patients in one group (10 providers) are diagnostically heterogenous (61.5%), lead by psychiatrist (69%). The programme consists of less than 5 lessons (70%).
Conclusion: The most effective form of psychoeducation—family psychoeducation is offered only by 15 providers. Despite the evidence, that participants wish to receive disease- specific

psychoeducation after discharge from the hospital, most providers offer only inpatient and diagnostically heterogenous programmes.
References:
Rummel-Kluge Ch., Pitschel-Walz G., Bauml J., and Kissling W. Psychoeducation in Schizophrenia—Results of a Survey of All Psychiatric Institutions in Germany, Austria, and Switzerland. Schizophrenia Bulletin, 2006; 32 (4):765–775
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P-11-005
The influence of psychoeducative family intervention in schizophrenic patients on perceived quality of life

W. Gassmann (Vitos Philippshospital Psychotherapy, Riedstadt, Germany), O. Christ, H. Berger

Objective: Psychoeducative interventions (PEI) can help to improve the quality of life (QOL) of schizophrenic patients (Sibitz et al. 2006). For now, there is no PEI that also includes social environment (SE). We developed and evaluated the effect of a new psychoeducative family intervention (PEFI) for patients with schizophrenic disorders and their SE on QOL.
Methods: In a randomized longitudinal study the effect of PEFI on QOL, assessed four times with the Quality of Life Questionnaire (WHOQOL-Bref), was compared to a control group (CG; $N = 21$). The PEFI Group (PG; $N = 25$) received ten training sessions while the CG was treated as usual. In the first five PEFI sessions information about the disease, possibilities of treatment and strategies of crisis prevention was given to the patients. The last five sessions include skill acquisition (e.g. active listening, coping with stress, etc.). The times between the assessments were 3, 9 and 12 months. SPSS 15 was used for statistical analysis and the last observation carried forward method (LOCF) was used for missing data.
Results: No significant differences were observable due to high standard deviation in all groups, but higher values in PG than in the CG were observable in the last three assessments. Differences between the comparison of the assessments one and two, one and three and one and four, showed partly negative values in the CG (-3.7, 0.9, -1.6) but positive values in the PEFI Group (3.4, 6.2, 6.0). In general differences between CG and PEFI showed small effect sizes (Cohen's *d*: .09–.26).
Conclusion: Although there are no significant results, according to (Sibitz 2006) a positive trend in the PG shows an enhancement in the QOL, while the CG shows a random walk tendency with negative effects on QOL. Further studies are discussed regarding sample size and LOCF method.
Policy of full disclosure: None.

P-11-006
The effect of family psychoeducational intervention on family burden and patients' quality of life in Iranian outpatients with schizophrenia

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Objective: This study explored the effectiveness of family psychoeducation for schizophrenia on relatives' burden and patients' quality of life and investigated the relationship between patients' quality of life and family burden.
Methods: Seventy Iranian outpatients with a diagnosis of schizophrenia disorder and their caregivers were randomly allocated to either experimental ($n = 35$) or control groups ($n = 35$). The patients in the experimental group received antipsychotic drug treatment and a psychoeducational program was arranged for their caregivers, while the patients in the control group received a routine care. At baseline, immediately post intervention and 1 month later, validated tools were used to assess patients' quality of life and family burden.
Results: Psychoeducational Intervention significantly reduced family burden and a significant improvement was found in patients' quality of life. The results indicated a significant linear relationship between patients' quality of life and family burden.
Conclusion: These results suggest that even short-term Psychoeducational Intervention for family members of schizophrenic patients can improve the outcomes of patients and their families.
Policy of full disclosure: None.

P-11-009
Identification of psychosocial necessities associated with aging in schizophrenia

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Objective: Recovery is one emergent objective in the treatment of schizophrenia. This construct is based in one positive perspective of the mental health. The schizophrenia life course is associated with one improving in the quality of live as well as one decline in the severity of the symptoms. The purpose of the study is to detect the psychosocial necessities related to aging in schizophrenia.
Methods: The study has two stages. Firstly we used qualitative methodology by mean of nominal groups. One hundred and six people composed by schizophrenia patients (mean age 44 years), relatives and professionals detected forty psychosocial needs related with aging. They were grouped in one 10-item scale (Psychosocial Risk Scale—PRS). In the second step, this scale was administered to a different sample of 39 schizophrenia subjects and 8 subjects with affective disorders. HONOS, BPRS, Clinical Global Impression and Global Functioning were measured. Inter-rater and test–retest reliability were studied. Principal components analysis with varimax rotation was used to determine the dimensional structure of the psychosocial needs.
Results: Three dimensions explained the 65.2% of the variance in the PRS. They were "personal development" (36.2%, composed by economical resources, health habits, occupation and environment factors); "personal autonomy" (14.7%, composed by housing, family and primary care team) and "psychiatric treatment" (14.3%, composed by pharmacological treatment and mental health team). The global inter-rater reliability was Spearman's Rho = 0.85 ($P < 0.001$, bilateral) and test–retest Spearman's Rho = 0.81 ($P < 0.001$, bilateral). The psychosocial risk correlates Spearman's Rho = 0.46 ($P < 0.001$, bilateral) with the clinical global impression, but did not importantly correlated with the rest of tests.
Conclusion: Personal development is the most important dimension to take in account for the recovery of schizophrenia people during the process of aging.
Policy of full disclosure: This work has received funding from the Junta de Castilla y León (Spain) (SAN/1056/2010) and from AstraZeneca Foundation.

P-11-010
A group treatment protocol for comorbid personality disorder

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Objective: Co-morbidity of personality disorders in schizophrenia is at least as common as in a normal population. Personility disorders or traits can influence treatment of schizophrenia patients. In borderline personality disorder, schema therapy has been proven to be effective in reducing borderline personality disorder–specific and general psychopathologic dysfunction and improving quality of life. Schema therapy helps patients to change life patterns—or schemas—using cognitive, behavioral, and emotion-focused techniques. To examine the effectiveness of schema therapy for schizophrenia patients with personality disorders or traits, this study was initiated.
Methods: A literature in PubMed and Medline was done to examine the results of schema therapy and group therapy for patients with psychotic disorders and comorbid personality disorders or traits. On the basis of the findings it was investigated whether a protocol cognitive schema therapy in a group had to be adjusted. To evaluate the effectiveness of this treatment group a pilot study was started. A pre- and post-test was done to investigate changes in psychopathology, personality traits, therapeutic relationship, quality of life and schemas.
Results: Preliminary results show that some adaptions should be made in the protocol for this patient population, particularly in time and use of experiential techniques. The protocol will be presented as well as the first results of the pilot study.
Conclusion: Clinicians should be aware of the patterns and extent of personality disorder comorbidities that exist in schizophrenia. A new group therapy protocol for comorbid personality disorder or traits based on schema therapy is presented and discussed.
Policy of full disclosure: None.

P-11-011
Psychological group therapy for panic disorder with or without agoraphobia

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Objective: We present a group psychological therapy programme for panic disorder with or without agoraphobia. It is aimed at adult patients whose main diagnosis is panic disorder with or without agoraphobia.
Methods: The programme consists of ten fortnightly 90-min sessions. Groups have a minimum of 8 and maximum of 14 members Assessment is carried out, before and after therapy, by PSWQ (Meyer, Miller, Metzger and Borkovec, 1990), the Inventory of Agoraphobia (E. Echeburúa 1992), the Adaptatioin Scale (Echeburúa 1987), the Panic Belief Questionnaire (Greenberg, 1989), the Avoidance Scale Fear and Beck's Depression Inventory. The programme consists of three phases:

1. Psychoeducational phase, in which explanations are given of what a panic attack is, what its symptoms are, its causes, the importance of thoughts in the attack, and what agoraphobia is.
2. Learning phase, in which patients learn techniques of anxiety control and cognitive restructuring and are taught such strategies as diaphragmatic breathing, relaxing, distraction, self-discipline and positive imagination.
3. Exposure phase. Firstly, exercises of interoceptive exposure. Afterwards, patients are systematically exposed to avoided situations and security behaviours are eliminated, in order to solve the problems of agoraphobia. All sessions follow the same structure, which is typical of cognitive-behavioural orientation therapies:

Results: Of the 12 patients, only two had to drop. The analysis of the results shows that, 100% of the participants were highly satisfied with the programme. They had all had one or more attacks of anxiety in the last month, but in all cases, with limited symptoms and they undergone them with acceptance and coping. It should be stressed that patients began the exposure phase spontaneously from Session 3 and with no exception, they had all noticed moderate-to-high improvement in agoraphobic avoidance.
Conclusion: Psychological group therapy is an effective and efficient option for panic disorder, and should be taken into account by public health services.
Policy of full disclosure: See affiliation.

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