

Unassigned abstracts

HPA axis dysfunction in psychiatry: Genetic background

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HPA axis dysfunction is a key neurobiological finding in major depression (MDD) and in a number of other stress related psychiatric disorders. Hyperdrive of corticotropin releasing hormone (CRH) is at the core of HPA axis dysregulation in MDD. The liability to develop CRH hyperdrive is a complex trait, partially determined by genetic factors. A main functional candidate gene for the regulation of the HPA axis is the gene encoding for the glucocorticoid receptor (GR). Transgenic mice with functional GR gene impairment show profound behavioral changes and elevated plasma corticotropin responses to stress. In humans, several GR polymorphisms were shown to influence HPA axis function. Recently, our group published a positive association finding between polymorphisms in the 5' region of the GR gene and recurrent MDD in two separate populations (1).

The action of the glucocorticoid receptor is tightly regulated by a number of co-chaperones. Binder et al. (2) found significant associations of response to antidepressants and polymorphisms in the FKBP5 gene, a glucocorticoid receptor–regulating co-chaperone of hsp-90.

Several other candidate genes are of interest, such as the CRH receptor 1 and CRH receptor 2 genes, the CRH binding protein gene (3), the AVP receptor gene and the mineralocorticoid receptor gene. These and other genetic determinants of HPA axis function, from our own studies and from the literature, will be discussed.

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Transmission disequilibrium of chromosome 22q11-13 marks in Chinese Han mixed pedigrees of schizophrenia and mood disorder

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Background: Several genome-wide linkage scans have reported that chromosome 22q11-13 might contain susceptibility loci for both schizophrenia and mood disorder.

Methods: We genotyped 44 Chinese Han family trios with mixed family history of schizophrenia and mood disorder with 11 DNA microsatellite markers on chromosome 22q11-13. These markers spanned 56.55 cM on 22q11-13 with mean intervals of 5.66 cM and average heterozygosity 0.71. The transmission disequilibrium test (TDT) was used to search for susceptibility loci to schizophrenia and mood disorder.

Results: Including all family trios regardless of proband diagnosis, we found six markers associated with susceptibility to psychotic disorders, including D22S420 ($\chi^2=4.76$, $df=1$, $P=0.029$) %3001D22S277 ($\chi^2=5.44$, $df=1$, $P=0.020$) %3001D22S315 (allele 5, $\chi^2=7.00$, $df=1$, $P=0.008$; allele 7, $\chi^2=-4.83$, $df=1$, $P=0.028$; allele 11, $\chi^2=4.00$, $df=1$, $P=0.046$) %3001D22S274 (allele 7, $\chi^2=-5.40$, $df=1$, $P=0.020$; allele 10, $\chi^2=6.23$, $df=1$, $P=0.013$) %3001D22S1160 ($\chi^2=-4$, $df=1$, $P=0.046$) and D22S1161 ($\chi^2=5.14$, $df=1$, $P=0.023$). When grouped separately into schizophrenia and mood disorder according to proband diagnosis, four markers D22S420 ($\chi^2=7.36$, $df=1$, $P=0.007$) %3001D22S315 (allele 5, $\chi^2=4$, $df=1$, $P=0.046$; allele 7, $\chi^2=-8.89$, $df=1$, $P=0.003$) %3001D22S1161 ($\chi^2=6.23$, $df=1$, $P=0.013$) and D22S280 ($\chi^2=4$, $df=1$, $P=0.046$) were significantly associated with schizophrenia, but were not significantly associated with mood disorder, D22S274 (allele 7, $\chi^2=5$, $df=1$, $P=0.025$; allele 10, $\chi^2=6$, $df=1$, $P=0.014$) were significantly associated with mood disorder only, and D22S277 ($\chi^2=4$, $df=1$, $P=0.046$) was associated with both schizophrenia and mood disorder.

Conclusions: These results indicate that chromosome 22q11-13 contains the susceptibility loci to schizophrenia and mood disorder, and that overlapping regions may be shared by these disorders.

Attitudes of nurses towards schizophrenia

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Objectives: According to the recent literature, stigma connected to schizophrenia has a negative impact on the commencement, process and the outcome of the treatment. The aim of this study was to investigate the attitude of nurses from our local community towards schizophrenia.

Methods: This study engaged 166 nurses (8 male, 158 female) employed at the Clinical Hospital in Osijek and the Primary Medical Care in Osječko-baranjska County. The subjects have filled out the

Canadian Community Antistigma Questionnaire during 3 mental health lectures for nurses.

Results: Out of total of 166 nurses, 74.7% (124) of them has heard something about schizophrenia in the last couple of months. 45.8% (76) of nurses was employed at the institution that treated patients with mental illness. 34.3% (57) of nurses personally knew someone who was diagnosed with schizophrenia or were treated for schizophrenia themselves. The results have shown an extensive knowledge of the facts related to schizophrenia among the nurses in our local community. It has also emerged that the attitude to the person with schizophrenia is more negative, and the level of stigma is higher as the higher emotional involvement is required.

Conclusion: Medical staff has a good level of knowledge about schizophrenia. Emotional acceptance of the person with schizophrenia is lower as the closer contact is required. Because the results show a certain degree of stigma to schizophrenia in the population of nurses in our local community, it would be necessary to develop specific anti-stigma programs for medical staff.

The Danish OPUS-trial: RCT of standard treatment versus integrated treatment in first episode psychosis. 5 years follow-up

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Aim: To evaluate the effects of integrated treatment for first-episode psychotic patients.

Method: In a randomised clinical trial of 547 first-episode patients with schizophrenia spectrum disorders, effects of integrated treatment and standard treatment was compared. The integrated treatment lasted for two years and consisted of assertive community treatment with programmes for family-involvement and social skills training. Standard treatment offered contact with a community mental health centre. Patients were assessed at entry and after one, two and five years by investigators that were not involved in treatment.

Results: At the one-year and two-year follow-up psychotic and negative symptoms changed in favour of integrated treatment. Patients in integrated treatment had significantly less co-morbid substance abuse, better adherence to treatment, and more satisfaction with treatment. Use of bed days was 22 percent less in integrated treatment than in standard treatment. Results of five-year follow-up will be presented.

Conclusion: Integrated treatment improved clinical outcome and adherence to treatment. The improvement in clinical outcome was consistent in the one-year and two-year follow-ups.

Outcome and its predictors in schizophrenia - The northern Finland 1966 birth cohort

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Background and aims: Follow-up studies of schizophrenia have reported divergent rates of outcomes. In addition to definition and

measurement challenges, one reason for divergence may be due to sampling biases. Our aim was to report clinical and social outcomes of schizophrenia in the longitudinal, unselected, population-based Northern Finland 1966 Birth Cohort, and describe associated factors.

Methods: Subjects with DSM-III-R schizophrenia (N=109) were followed prospectively from mid-pregnancy up to age 35 years. Used outcome measures were positive and negative symptoms, global clinical impression, use of antipsychotics, psychiatric hospitalisations, social and occupational functioning. Several definitions of good and poor outcomes were explored, and predictors of outcomes were analysed.

Results: In a subsample of 59 cases with complete information of outcomes, good clinical outcome varied from 10% to 59%, and good social outcome 15-46%, depending on definition of outcomes. Poor clinical outcome varied 41-77% and poor social 37-54%. Two subjects recovered fully using the most stringent definition of outcome. Lack of friends in childhood, father's high social class, lower school performance and earlier age of illness onset predicted poor outcomes. When the whole sample was considered, early infant development around the age of 1 year was associated with worse course of illness.

Conclusions: Outcomes were heterogeneous and relatively poor in this sample of relatively young schizophrenia subjects. The results were influenced by the definitions and measurements of outcomes. Persons having a sub-optimal developmental trajectory with poor social contacts, poor school performance, and early age of illness onset seem to have the worst outcome.

Familial risk and prodromal features of psychosis in adolescents aged 15-16 years in the northern Finland 1986 birth cohort

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Background and aims: Subjects with family history of psychosis and with prodromal symptoms are at risk for schizophrenia. The aim was to study whether adolescents with familial risk have more commonly prodromal features.

Methods: Members (N= 9,215) of the Northern Finland 1986 Birth Cohort, an unselected general population cohort, were invited to participate in a field survey conducted during 2001-2002. At the ages of 15-16 years, the study included a 21-item PROD-screen questionnaire developed for screening prodromal psychotic symptoms with 12 specific questions for psychosis (Heinimaa et al. 2003). The scale measured symptoms for last six months. The Finnish Hospital Discharge Register was used to find out parental psychoses during 1972-2000.

Results: Of the males 24% and 37% of the females were screen positives for prodromal features at the age of 15-16 years. Of the offspring, 1.8% had parents with psychosis. The prevalence of screen positives was 26% in males and 36% in females with familial risk for psychosis.

Conclusion: Prodromal features of psychosis are prevalent in adolescence. It may be difficult to screen adolescent subjects at risk for developing schizophrenia with a questionnaire in a general population, especially as these symptoms do not appear to be more common among subjects with familial risk.

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The efficacy of weight management training in patients with schizophrenia

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Introduction: In this study, we want to evaluate the efficacy of a preventive weight management training. We hypothesize that this training will reduce weight gain, pathological metabolic parameters and will increase drug compliance and subjective well-being.

Method: 69 schizophrenic patients were included in this study, in all patients olanzapine was newly initiated. They were randomly assigned to verum and control group. Patients in the verum group attended the training every second week for 24 weeks. Physical and chemical parameters were measured regularly, and also eating behaviour, physical activity, quality of life, mental state and psychosocial adaptation.

Results/Discussion: 28 patients dropped out during the first 4 weeks of intervention. The data of the remaining 41 patients (verum group N=21, control group N=20) was analysed. During the intervention there was no significant difference between the groups regarding weight-gain. Both groups gained weight slightly (verum group 3.02±4.06kg, control group 2.80±4.84kg). Concerning triglycerides we found an interaction effect of time and group ($F(1)=6.697$, $p=.025$), the same was found on the second scale of the questionnaire for eating behaviour (FEV), which measures to what degree eating behaviour is disturbed ($F(1)=8.381$, $p=.013$) and on the social functioning scale of the SF-36 ($F(2,38)=3.34$, $p=.032$). Regarding glucose tolerance challenge, there was a significant group effect at the first time of measure after intake of the glucose-dilution ($F(1)=9.15$, $p=.016$). Our results do not support the hypothesis that the intervention has the desired effects on body weight, but it influenced positively other metabolic parameters, eating behaviour and social functioning.

Near-infrared spectroscopy for the guidance of inhibitory rTMS treatment of auditory verbal hallucinations in schizophrenic patients

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Background and aims: Auditory verbal hallucinations (AVHs) are among the most frequent and disabling symptoms of schizophrenic diseases. In approximately one quarter of patients, AVHs have to be considered as therapy-refractory with regard to pharmacological

treatment options. This group of patients may benefit from a treatment protocol with repetitive Transcranial magnetic stimulation (rTMS) aiming on an inhibition of AVH-associated increased activity of auditory brain areas in the temporal cortex. However, optimal protocols for the guidance and control of such innovative treatment regimens are still lacking.

Methods: We propose the application of a non-invasive optical imaging technique (functional Near-Infrared Spectroscopy; fNIRS) for the measurement of the AVH-related activity of the auditory cortex, for the guidance of the rTMS-treatment and for the control of a treatment success on the brain metabolic level.

Results: In the reported patient, NIRS measurement indicated AVH-related activity in the left auditory cortex which strongly decreased after a period of three weeks with daily inhibitory rTMS treatment, in parallel with drastically diminished AVHs.

Conclusions: This is the first report of a NIRS-guided and –controlled inhibitory rTMS treatment of therapy-refractory AVHs in a schizophrenic patient. Given the excellent clinical applicability of the applied methods, the combination of fNIRS and rTMS might have the potential to establish new treatment options in psychiatry aiming on the modulation of pathological regional brain activity patterns.

The effect of long term treatment with olanzapine on neuropsychological prefrontal test in schizophrenia

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Background: Neuropsychological studies show the positive effect of treatment with atypical neuroleptics on cognitive functions in schizophrenia. The aim of this study was to assess the effect of olanzapine on prefrontal functions during 12-months of treatment in schizophrenia.

Methods: The study was performed in 48 schizophrenic patients, aged 20-48, who were treated with the generic olanzapine (Zolafren - Adamed, Poland). Psychometric evaluation was done using PANSS. Neuropsychological assessments included Wisconsin Card Sorting Test (WCST) and Trail Making Test and Stroop Color-Word Interference Test. The measurements were performed before, after 3, 6 and 12 months of treatment. The daily dose of olanzapine was 5-25mg/day (mean 14.9 mg/day) after 3 month of treatment, and 5-20 mg (mean 13.6 mg/day), after 6 and 12 months of treatment.

Results: The intensity of psychopathology on PANSS was at baseline 99 points, and after 3, 6 and 12 months of treatment 63, 54 and 51p, respectively, with significant systematic improvement during olanzapine treatment ($p<0.001$, ANOVA Friedman Test). After 3 month of treatment, there was a significant amelioration on TMT, Stroop, and WCST-conceptual responses. After 3, 6 and 12 months of treatment significant improvements on TMT, Stroop and WCST were observed. The level of cognitive improvement was assessed with the decrease on negative symptoms. After 3 month – this correlated with improvement on TMT and WCST-perseverative errors, and after 6 and 12 months with TMT A and WCST perseverative errors.

Conclusions: The results obtained show a significant improvement of psychopathology and neuropsychological frontal lobe tests after long-term treatment with olanzapine.

Schizophrenia research: Ethical questions

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Although the ethical issues concerning schizophrenia research have evolved considerably over the last decade, there are many questions that remain only incompletely resolved.

Ethical concerns involved in schizophrenia research have been raised from the doubts about the competency of the potential research participants to valid informed consent. Another issues addressed in this presentation are drug discontinuation, medication-free intervals and placebo control groups in research on schizophrenia, problem of financial payments to participants in clinical research, consequences of exclusion of potentially suicidal patients from biological and therapeutical research, question of research approaches to prodromal and early phase of schizophrenia and discrimination against the individuals with the potential genetic risk for schizophrenia.

Recent studies suggest that the strongest predictors of decisional incompetency of patients with schizophrenia are cognitive impairment and severity of negative symptoms. On the other hand, age, education, severity of positive and depressive symptoms and level of insight have only minimal predictive value. We can also say that the presence of diagnosis of schizophrenia is not enough to indicate that a patient is unable to give valid consent to research participation.

Although we must confirm that many questions of etiology, prevention or treatment of schizophrenia are not satisfactory resolved just because we are not able to realize ethically acceptable studies, we must hope that development in this new area of schizophrenia research will improve the risk/benefit ratio of research approaches and bring clearly defined values, guidelines and standards.

An objective diagnostic decision support for schizophrenia

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Background and aims: This method rests on a 50 year long tradition of Psychophysiological experiments at the Dept of Psychiatry in Lund, Sweden. Our branch has focused on Psychoacoustics since 1983, and found significant aberrant functioning of auditory perceptual mechanisms in schizophrenia. Some of these are possible to assess by ABR (auditory brain-stem responses). The assessments may be used to support the diagnostic decision process by demonstrating a biological dysfunction typical for the disease.

Method: ABR measurements of twenty-three paranoid schizophrenics and matched controls for age and sex were compared. Eleven patented complex auditory stimuli, which schizophrenics earlier have been shown to perceive incorrectly, were presented. The ABR-measuring technique has been specifically adapted for the purpose.

Results: When subjects were presented with a standard complex stimulus and a high-pass filtered one, schizophrenics showed statistically significant aberrances for wave V of the latter in the ABR, corresponding to the activity of colliculus inferior of the brain-stem. Furthermore, there was a significant change of activity regarding the two sides of the brain-stem, indicating a change of perceptual (grouping) activity in them.

Conclusions: This finding is just one example within the Schizo-Detect method, aimed at helping medical personnel to ascertain the diagnosis of schizophrenia. It shows that different complex sound stimuli are treated in specific ways by schizophrenic patients.

Together with the results from the ten remaining stimuli and further details of the ABR-curves, a diagnostic validity well over 90% has been achieved up till now.

Encoding deficit during face processing within the fusiform face area in schizophrenia

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Background and aims: Face processing is crucial for social interaction, but impaired in schizophrenia in terms of delays and misperceptions of identity and affective content. One important functional region for early stages of human face processing is the right fusiform face area. Thus, this region might be affected in schizophrenia. Aim of the study was to investigate whether face processing deficits are related to dysfunctions of the right fusiform face area in schizophrenics compared to controls.

Methods: In a rapid event-related fMRI design encoding of new faces as well as the recognition of newly learned, famous, and unknown faces was investigated in 13 schizophrenics and 21 healthy controls. Region of interest analysis was applied to each individual's right fusiform face area and tested for group differences.

Results: Controls displayed more BOLD activation during the memorization of faces that were later successfully recognized. In schizophrenics this effect was not present. During the recognition task schizophrenics had lower BOLD responses, less accuracy, as well as longer reaction times to famous and unknown faces.

Conclusions: Our results support the hypothesis that impaired face processing in schizophrenia is related to early stage deficits during the encoding and immediate recognition of faces.

Cognitive remediation in schizophrenia: An evidence-based treatment approach?

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The vast majority of schizophrenic patients demonstrates poor performance in different aspects of cognitive processing. Some of these cognitive deficits clearly have been identified as rate-limiting factors in social functioning. Over the past years, a series of meta-analyses has summarized the evidence for the benefits of cognitive remediation approaches. However, there are marked discrepancies between their findings.

The present contribution aims to provide a conclusive survey of the available evidence for the efficacy of cognitive remediation as derived from these meta-analyses and the findings of an own recent meta-analysis of all randomized controlled trials published in peer-reviewed journals.

Relevant meta-analyses and randomized controlled trials were identified by searching several electronic data bases and by hand-searching of reference lists. In order to compare the findings of the existing meta-analyses the reported effect sizes were transformed into a standardized effect size measure. For the own meta-analysis weighted mean effect size differences between comparison groups regarding various types of outcome were estimated. Their significance was tested by confidence intervals and heterogeneity tests were applied to examine the consistency of the effects.

The findings of systematic reviews covering cognitive remediation approaches differ considerably depending on the methodological rigor of included studies and the cognitive function targeted. The present meta-analysis provides support for small to medium improvements in attention, executive functioning and social cognition tasks, indicates small reductions in negative symptoms and a moderate transfer effect on social functioning. However, the durability of the effects remains unclear since follow-up data are missing.

ECT practice in Australia

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Objective: To determine the characteristics of electroconvulsive therapy (ECT) practice in Australia.

Method: From October 1, 2002 to February 29, 2004, a 29-item questionnaire was sent to 136 hospitals in Australia.

Results: 113 hospitals (83%) completed the questionnaire. ECT was available in 90 hospitals. A total of 7,469 patients received 58,499 ECTs from 356 psychiatrists, which gives an average course length of 8.5 treatments. ECT utilization as assessed by the crude treated-person and crude administration rates were 37.85 persons and 296.47 administrations per 100,000 population per annum, respectively. 63.4% of patients were female. Brief-pulse devices were used in all hospitals. EEG monitoring was used routinely in 80 hospitals. Unilateral ECT was used twice as often as bilateral ECT. 82.3% of ECT treatments were given to patients with major depression, 9.6% with schizophrenia, 4.9% with mania, and 1.7% with catatonia. Patients who received ECT were in age group over 65 years (38.4%), followed by 45–64 years (28.3%), 25–44 years (26.3%), 18–24 years (6.9%), and less than 18 years (0.2%). Unmodified ECT was not used in any hospital. 1,196 patients received continuation ECT in 83 hospitals and 1,044 received maintenance ECT in 77. There was no case of ECT-related death during a survey period.

Conclusion: ECT use in Australia is high. ECT training programs for psychiatry residents were acceptable. The pattern of use is similar to that of the United States.

ECT practice in Asia

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Objective: To obtain information on ECT practice in Asia.

Method: From September 1, 2001 to August 31, 2003, a 29-item questionnaire was sent to 977 institutions in 45 countries in Asia.

Results: 334 institutions (34%) in 29 countries replied, of which 257 institutions in 23 countries had ECT. 39,875 patients (men: women = 1.56: 1) received 240,314 ECTs from 1,919 psychiatrists during the survey period. Brief-pulse device was used in 103 institutions, 60 did not know the type of their ECT devices. Thymatron or MECTA devices were used in 58 institutions, 115 respondents did not

know the brand of their ECT devices. EEG monitoring was used routinely in 59 institutions. Bilateral ECT was always used in 202 institutions. Patients commonly received ECT were schizophrenia (41.8%), major depressive disorder (32.4%), mania (14%), catatonia (6.9%), drug abuse (1.8%), and dysthymia (1.6%). 26,167 ECTs (73%) were given to patients age group 18–44 years, 2,138 ECTs (5.4%) to children and adolescent, and 1,581 ECTs (4%) to age group 65 and above. 22,194 patients (55.7%) received unmodified ECT totally of 129,906 treatments (54%) at 141 institutions in 14 countries. Continuation ECT was done in 115 institutions in 17 countries and maintenance ECT was done in 63 institutions in 14 countries.

Conclusions: ECT is commonly practiced in Asia. Unmodified ECT accounted for 54% of treatments. There was no formal training in any institution.

A prospective study of metabolic disease and monitoring practices in antipsychotic-treated community psychiatric patients

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Background and aims: Recent guidelines and consensus statements recommend stringent monitoring of metabolic function in individuals receiving antipsychotic drugs. We aimed prospectively to study the evolution of metabolic dysfunction in a cohort of antipsychotic-treated subjects with severe mental illness from across the diagnostic spectrum. We also investigated monitoring practices for metabolic disease and cardiovascular risk.

Methods: A prospective cohort study of 106 community-treated psychiatric patients from across the diagnostic spectrum from the Northeast of England. Detailed anthropometric and metabolic assessment was undertaken.

Results: A high prevalence of undiagnosed and untreated metabolic disease was present at baseline assessment. Mean follow-up time was 599.3 (SD ± 235.4) days. Body mass index ($p < 0.005$) and waist circumference ($p < 0.05$) had significantly increased at follow-up, as had the number of individuals who were either overweight or obese. Fifty-three per cent of individuals had hypertriglyceridemia, and 31% had hypercholesterolemia, but only 7% were receiving lipid-lowering therapy. A number of individuals on 'high risk' drugs with regard to glucose homeostasis disorders reverted from impaired fasting glucose to normoglycemia during the follow-up period. Monitoring practices were poor. Recording of measures of adiposity occurred in 0% of individuals, and >50% of subjects had neither blood glucose nor lipids monitored during the follow-up period.

Conclusions: This cohort has a high prevalence of metabolic disease and heightened cardiovascular risk. Despite the publication of a number of recommendations regarding physical health screening in this population, monitoring rates are poor, and physical health worsened during the 19 month follow-up period.

Assessing the needs of pregnant women and mothers with severe mental illness

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Background and aims: There is an absence of instruments to assess the complex needs of pregnant women and mothers with severe

mental illness. We aimed to develop a standardised assessment of need for pregnant women and mothers with severe mental illness.

Methods: Staff and service users identified relevant domains of need. Professional experts and service users were then surveyed and asked to rate the importance of the domains of the CAN-M (Camberwell Assessment of Need – Mothers). Reliability was established using 36 service user-staff pairs. Concurrent validity was assessed with the Global Assessment of Functioning.

Results: Inter-rater and test-retest reliability coefficients for unmet needs indicated excellent reliability. Relevant CAN-M domains correlated with the Global Assessment of Functioning symptom ($p=0.05$) and disability ($p < 0.01$) subscales.

Conclusions: The CAN-M is a reliable, valid instrument for assessing the needs of pregnant women and mothers with severe mental illness.

Nicotinic cholinergic mechanisms in the regulation of brain DNA-methyltransferase 1 (DNMT1) expression

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Perturbation of epigenetic mechanisms, which is likely associated with an overexpression of DNA-methyltransferase 1 (DNMT1) in telencephalic GABAergic neurons of schizophrenia (SZ) patients, participates in the pathophysiology of cognitive disorders.

We hypothesize that tobacco abuse, which is very frequent in SZ patients, may be an attempt to self-medicate cognitive dysfunction by reducing DNMT1 overexpression.

In mice treated with nicotine (4.5mg/kg/sc twice a day for 5 days) and decapitated 2,4,8,12 or 24 hrs after the last dose of nicotine, we counted the number of DNMT1 mRNA- and protein-positive neurons in various brain areas using a two-dimensional counting method.

Mice receiving nicotine exhibited a 30-40% decrease in the number of DNMT1 mRNA- and protein-positive neurons in layers I and II of cingulate, piriform, somatosensory cortices and caudate-putamen. A single dose of nicotine causes only marginal changes in DNMT1 mRNA expression.

The high affinity nicotinic receptor antagonist mecamylamine (2mg/kg/sc twice a day for 5 days) given along with nicotine attenuates the nicotine-induced decrease of DNMT1 mRNA-positive neurons in various brain areas.

We also found that cortical layer I and hippocampal GABAergic neurons include high levels of $\alpha 4$ and $\alpha 7$ nicotinic acetylcholine receptor (nAChR) subunits which can then mediate the action of nicotine on GABAergic interneurons. The observation that repeated injections of nicotine decrease the DNMT1 mRNA and protein expression in telencephalic layer I and II cortical GABAergic neurons suggests that in these neurons, nAChR may have an impact on the epigenetic modulation of chromatin remodeling.

Correlation between serum androgen levels and neuropsychological functions in schizophrenia

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Background: Older literature had repeatedly documented that physically frail male schizophrenics tended to be withdrawn with apathy, blunted affect and poor prognosis. However, in female

schizophrenics, signs of virilism portend poor prognosis and severe deterioration. Three published studies of 92 male schizophrenics, from India, Iran and Japan, showed negative correlations between testosterone (T) levels and negative symptoms.

Methods: Twenty-eight (18 male and 10 female) patients, aged 25-67 (mean=34.8) years, who fulfilled DSM-IV TR criteria for schizophrenia were selected, with the approval of local ethical committee. Serum levels of T, dihydrotestosterone and DHEA were estimated by radioimmunoassay. Neuropsychological tests were administered for each patient. Pearson correlation test, linear regression analysis and independent 't' test were used for statistical analysis.

Results: Mean PANSS score for all 28 patients was 82.3; 18 patients had predominantly positive symptoms and 10 had predominantly negative symptoms. Independent 't' test did not show any significant difference for any of the serum hormone levels between the groups of patients based on PANSS scores. However, when women were excluded, T levels were significantly lower in negative symptom dominant group ($p=0.05$). A correlation between serum T levels, but not of other hormones, and the total scores on all neuropsychological test results was also noted ($p=0.017$); verbal fluency showed the greatest correlation, followed by working memory. But when women were excluded, this significance disappeared.

Conclusions: Negative symptoms correlate negatively with T levels, but only in men. Neuropsychological findings correlate with T levels as well.

Functional dissection of SLITRK1 signaling

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Background and aims: Tourette syndrome (TS) is a neuropsychiatric disorder characterized by motor and vocal tics and associated complex behavioral abnormalities. There is strong support for a genetic basis to the disorder, however, the precise pattern of transmission and the identification of underlying genes has remained elusive. Recently, mutations in a gene termed SLIT- and NTRK-like family, member 1 (SLITRK1) have been shown to lead to rare forms of TS and associated disorders. The SLITRK family (SLITRK 1-6) includes neuronal transmembrane proteins that can control neurite outgrowth. Structurally, SLITRK family members are characterized by two leucine-rich repeat (LRR) domains located on the extracellular/intralumenal domain, a single transmembrane domain, and an intracellular/cytoplasmic domain that is of varying lengths. SLITRK1 has a cytoplasmic domain that is most different from the others, being both the shortest (53 amino acids), and lacking conserved potential sites of tyrosine phosphorylation. We are using molecular methods to dissect SLITRK1 signaling and metabolism.

Methods: We developed a bait from the human SLITRK1 protein and used it to screen libraries for SLITRK1-interacting proteins. In addition, we studied the metabolism of SLITRK1 in situ.

Results: We completed screens of both an adult and a fetal brain library and are characterizing the validated SLITRK1-interacting proteins. We have also characterized SLITRK1 metabolism and the effects of SLITRK1 mutations on its metabolism.

Conclusions: SLITRK1-interacting proteins may represent susceptibility loci for TS and related disorders, and are likely involved in the development of the central nervous system.