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The spectrum of risk and concomitant factors in stuttering is generally thought to be wide and heterogeneous. However, only a few studies have examined these factors using information from large databases. We examined the data on 11,905 Swiss conscripts from 2003. All cases with high psychiatric screening scores indicating “caseness” for a psychiatric disorder were excluded, among them potential malingerers, so that 9,814 records remained. The analyses rely on self-reported information about stuttering in childhood, problems at birth, problems in school, mental disorders of parents and relatives, childhood adversity and socio-demographic information. Statistical modelling was done using logistic regression and path analysis models. Risk factors determined in the logistic regression include premature birth, probable attention deficit hyperactive disorder, alcohol abuse of the parents, obsessive-compulsive disorder in parents and relatives, having a disabled mother and having a parent from a foreign country. There is no overwhelmingly strong risk factor; all odds ratios are about 2 or below. In conclusion, large databases are helpful in revealing less obvious and less frequent risk factors for heterogeneous disorders such as stuttering. Obviously, not only secondary analyses, but also systematical large scale studies would be required to complete the complex epidemiological puzzle in stuttering. An extensive examination of young adults who were initially assessed in childhood might provide the most promising design.


The aim of this naturalistic study was to evaluate the potential influence of the duration of untreated illness (DUI)—defined as the time elapsed between the occurrence of the first mood episode and the first adequate pharmacological treatment with mood stabilizers—on the clinical course of bipolar disorder (BD). Three hundred and twenty outpatients (n = 320) with a DSM-IV diagnosis of BD—either Type I or Type II—were interviewed; their clinical features were collected and they were naturalistically followed-up for 5 years. At the end of the follow-up observation, the sample was subdivided into two groups: one group with a DUI < or =2 years (n = 65) and another group with a DUI >2 years (n = 255). The main demographic and clinical variables were analyzed and compared
between the two subgroups of patients using chi-square tests for dichotomous variables or Mann-Whitney U tests for continuous variables. Patients with a longer DUI showed a higher frequency of suicide attempts ($Z = -2.11, P = 0.035$), a higher number of suicide attempters ($\chi^2(2) = 4.13, df = 1, P = 0.04$), and a longer duration of illness ($Z = -6.79, P < 0.0001$) when compared to patients with a shorter DUI. Moreover, patients with a longer DUI had a depressive first episode more frequently than patients with a shorter DUI ($\chi^2(2) = 11.28, df = 2, P = 0.004$). A further analysis performed dividing the total sample into two subgroups on the basis of a DUI of 6 years (corresponding to the median value of the DUI in the study sample) confirmed prior findings. Results indicate a potential association between a longer DUI and a worse outcome in BD, particularly in terms of suicidality, and confirm the clinical relevance of early diagnosis and pharmacological intervention with mood stabilizers in BD.


To evaluate the potential impact of early childhood problems on the chronicity of mood disorders. A representative cohort from the population was prospectively studied from ages 19/20 to 39/40. Unipolar (UP) and bipolar disorders (BP) were operationally defined applying broad Zurich criteria for bipolarity. Chronicity required the presence of symptoms for more days than not over 2 years prior to an interview, or almost daily occurrence for 1 year. A family history and a history of childhood problems were taken at ages 27/28 and 29/30. Data include the first of multiple self-assessments with the Symptom-Checklist-90 R at age 19/20, and mastery and self-esteem assessed 1 year later. A factor analysis of childhood problems yielded two factors: family problems and conduct problems. Sexual trauma, which did not load on either factor, and conduct problems were unrelated to chronicity of UP or BP or both together. In contrast, childhood family problems increased the risk of chronicity by a factor of 1.7. An anxious personality in childhood and low self-esteem and mastery in early adulthood were also associated with chronicity. Childhood family problems are strong risk factors for the chronicity of mood disorders (UP and BP). The risk may be mediated partly by anxious personality traits, poor coping and low self-esteem.


Olanzapine is described as a multi-acting receptor-targeted antipsychotic agent. Although regional differences of dopamine D(2) receptor occupancy, i.e., limbic selectivity, were reported for olanzapine, contradictory results were also reported. We measured dopamine D(2) receptor occupancy of olanzapine in extrastriatal regions in patients with schizophrenia using positron-emission tomography with [(11)C]FLB457 and the plasma concentrations of olanzapine. Ten patients with schizophrenia taking 5-20 mg/day of olanzapine participated. Dopamine D(2) receptor occupancy in the temporal cortex ranged from 61.1 to 85.8%, and plasma concentration was from 12.7 to 115.4 ng/ml. The ED(50) value was 3.4 mg/day for dose and 10.5 ng/ml for plasma concentration. The ED(50) values obtained in this study were quite similar to those previously reported in the striatum. In conclusion, although the subjects and methods were different from previous striatal occupancy studies, these results suggest that limbic occupancy by olanzapine may not be so different from that in the striatum.

Bipolar disorder (BD) has been associated with a proinflammatory state in which TNF-alpha seems to play a relevant role. The aim of the present study was to evaluate the plasma levels of TNF-alpha and its soluble receptors (sTNFR1 and sTNFR2) in BD patients in mania and euthymia in comparison with control subjects. We evaluated 53 BD patients (34 in mania and 19 in euthymia) and 38 healthy subjects. All subjects were assessed by the Mini-International Neuropsychiatry Interview (MINI-Plus). Patients were also evaluated by the Young Mania Rating Scale (YMRS) and by Hamilton Depression Rating Scale (HDRS). Plasma TNF-alpha and its soluble receptors were measured by ELISA. The plasma TNF-alpha and sTNFR2 levels did not differ between groups, but higher sTNFR1 levels were found in BD patients. Of note, BD patients in mania had higher sTNFR1 levels than BD patients in euthymia and controls. The sTNFR1 and sTNFR2 levels correlated with BD duration, and sTNFR2 levels correlated with age of patients. Our data indicate a proinflammatory status in BD patients during mania and further suggest that inflammatory mechanisms may be involved with the pathophysiology of BD.


Major Depressive Disorder (MDD) and antidepressant therapy response are largely based on behavioral criteria, which are known to correlate at best modestly with biological measures. Therefore, it is not surprising that the search for peripheral biological markers (biomarkers) being assessed in distant biological systems such as body fluids has not yet resulted in clinically convincing measures for MDD diagnostics or treatment evaluation. Imaging genetics studies, however, have been successful in the search for intermediate imaging phenotypes of MDD and treatment response that are directly related to the neurobiological underpinnings of MDD, but are not suitable for a broad clinical use today. Hence, we argue that intermediate phenotypes derived from imaging genetics studies should be utilized as substitutes of behaviorally assessed psychiatric diagnoses or therapy response in the search for easily accessible peripheral biomarkers. This article will further cover the current state of peripheral and neural biomarker research.


Instruments for self-rating in depression are available, but their psychometric properties have not been fully explored; discrepancies with clinician ratings have been identified. This study was longitudinal with 85 patients fulfilling the DSM-III-R diagnosis of Seasonal Affective Disorder. Self-reporting versions (definitely and semidefinitely anchored) corresponding to the Hamilton Depression Scale (HAMD), the Hamilton Subscale (HAM), and the Bech-Rafaelsen Melancholia Scale (MES) were compared to each other and the clinician-rated version. The unidimensional property of the sum score in each scale was tested by the item-response theory model ad modum Rasch. The scales were also tested for their sensitivity to discriminate between placebo and citalopram therapy. The sum scores and the sum score variances of the definite self-rating versions did not differ significantly from the sum scores of the corresponding observer scales at any of the five time points. The semidefinite scales significantly over-scored at all time points. The convergent validity between corresponding definite self-ratings and observer ratings was very high with correlations exceeding 0.90. Only item responses from the MES, the HAM, and their corresponding definite versions of the self-rating questionnaires DMQ and DHAM were accepted by the Rasch analysis, and only these four valid scales discriminated significantly between the effect of citalopram and placebo treatment. Our results are limited to patients with moderate depression. Two new self-report scales with unparalleled construct validity, reliability, sensitivity, and convergent validity have been identified.
(DMQ and DHAM). We have also identified a crucial importance of format for the means and variances of self-rating scales. These findings are of high practical and scientific value.


The goal of the study was twofold: (1) to investigate the effect of different diagnostic criteria on prevalence estimates of adult attention deficit hyperactivity disorder (ADHD), and (2) to provide prevalence estimates of adult ADHD for the first time in a Hungarian sample. Subjects between 18 and 60 years were included in the screening phase of the study (N = 3,529), conducted in 17 GP practices in Budapest. Adult self-report scale 6-item version was used for screening. Out of 279 positively screened subjects 161 subjects participated in a clinical interview and filled out a self-report questionnaire to confirm the diagnosis. Beside DSM-IV diagnostic criteria, we applied four alternative diagnostic criteria: 'No-onset' (DSM-IV criteria without the specific requirement for onset); full/Sx (DSM-IV "symptoms only" criteria); and reduced/Sx (DSM-IV "symptoms only" criteria with a reduced threshold for symptom count). Crude prevalence estimates adjusted for the specificity and sensitivity data of the screener were 1.35% in the 'DSM-IV' group, 1.64% in the 'No-onset' group, 3.65% in the 'Sx/full' group and 4.16% in the 'Sx/reduced' group. Logistic regression analysis showed that ADHD was significantly more prevalent with younger age and male gender \(\text{chi}(2) = 14.46; P = 0.0007\). Prevalence estimates corrected for the 'not-interviewed' subsample and adjusted for specificity and sensitivity data of the screener was 2.3% in males, 0.91% in females; 2.02% in the < or =40 years age group and 0.70% in the >40 years age group, based on DSM-IV diagnostic criteria. Prevalence rates found in this study are somewhat lower, but still are in line with those reported in the literature.


Behavioural and neuropsychological vulnerability have been associated with an increased risk of psychosis. We investigated whether certain clusters of premorbid behavioural and personality-related signs and symptoms were predictors of nonaffective and/or affective psychosis and schizophrenia, respectively, in a 50-year follow-up of an unselected general community population. Total population cohorts from the same catchment area in 1947 (n = 2,503) and 1957 (n = 3,215) that had been rated for behavioural items and enduring symptoms were followed up to 1997 regarding first-incidence of DSM-IV nonaffective and/or affective psychosis. Attrition was 1-6%. The influence of the background factors, aggregated in dichotomous variables (predictors), on time to occurrence of nonaffective and/or affective psychosis was assessed by means of Cox regression models. In multivariate models the predictors nervous-tense, blunt-deteriorated, paranoid-schizotypal and tired-distracted were significantly associated with subsequent nonaffective and/or affective psychosis. In simple models, down-semidepressed, sensitive-frail and easily hurt were significantly associated with development of psychosis. When schizophrenia was analysed separately nervous-tense remained significant in the multivariate model, although blunt-deteriorated, paranoid-schizotypal and tired-distracted did not; and abnormal-antisocial reached significance. To conclude, we found some evidence for anxiety-proneness, affective/cognitive blunting, poor concentration, personality cluster-A like traits and interpersonal sensitivity to be associated with general psychosis vulnerability.

Poor sleep is linked to poorer daily functioning and increased risk of psychiatric symptoms. With respect to pain, the relation is bi-directional; poor sleep exacerbates pain, while greater pain adversely affects sleep. Moreover, perception of pain is subject to cognitive-emotional processes. Surprisingly, no data are available from non-clinical samples of young adults. The aim of the present study was therefore to investigate the relation between sleep and pain as a function of quality of life and depressive symptoms in young adults. The direction of influence between sleep and pain was statistically tested with two different structural equation models (SEMs). A total of 862 participants (639 women, 223 men; mean age: 24.67; SD = 5.91) completed a series of validated self-report questionnaires assessing sleep, quality of life, depressive symptoms and cognitive-emotional elaboration of pain. Sleep, pain, quality of life, and depressive symptoms were interrelated. The first SEM suggested both a direct and an indirect influence of pain on sleep, whereas the second SEM suggested that sleep had only an indirect influence on pain. Irrespective of the SEM, the relation between sleep and cognitive-emotional elaboration of pain was mediated by quality of life and depressive symptoms. For a non-clinical sample of young adults, findings did support the bidirectional relation between poor sleep and increased cognitive-emotional elaboration of pain, though other cognitive-emotional processes such as depressive symptoms and quality of life should be taken into account.


The septal nuclei are assumed to play a significant role in the pathophysiology of schizophrenia and affective disorders. The aim of this study was to morphometrically characterize the septal nuclei in patients with schizophrenia, bipolar disorder, and major depressive disorder, when compared with healthy control subjects. We analyzed the septal nuclei by determining the density and size of the neurons in postmortem brains in 17 patients with schizophrenia, 8 patients with bipolar disorder, 7 patients with major depressive disorder, and 14 control subjects matched for age and gender. There was a significant reduction in the neuronal density, but not in the mean cross-sectional area, in the lateral septal nucleus (P = 0.013) in patients with bipolar disorder when compared with control subjects. There were no significant changes in the neuronal density of the septal nuclei of the medial and lateral cell groups in patients with schizophrenia and major depressive disorder when compared with control subjects. There was a significant negative correlation between neuronal density in the lateral septal nucleus and disease duration in patients with major depressive disorder (P = 0.037, r = -0.9). The histopathological abnormality of the decreased neuronal density in the lateral septal nucleus, which is an important limbic region involved in emotions, might be a neuropathological correlate of bipolar disorder.


Recent transcranial sonography (TCS) studies showed that disruption of echogenic midbrain line, corresponding to basal limbic system and raphe nuclei (RN) within, might represent functional marker for the development of depression. Major depressive disorder (MDD) is one of the most common psychiatric disorders associated with suicidal ideation. We initiated this study to assess the usefulness of TCS recording in a group of MDD patients and in MDD patients who also reported
suicidal ideation, on the assumption that TCS might serve as a screening method for differentiating patients at risk of suicide. Altogether 71 subjects: 17 patients with MDD, 14 patients with MDD who also reported suicidal ideation and 40 healthy controls, were studied using TCS by two independent physicians. Reduced raphe echogenicity was found in 8 of 17 (47%) of the patients with MDD but only in 6 of 40 (15%) controls. In patients with suicidal ideations that finding was even more pronounced (12 of 14, 86%) with the highest frequency of completely not visible TCS RN finding (10 of 14, 72%). Data showed that altered echogenicity of the RN is frequent in patients with suicidal ideation. Normal RN echogenicity in MDD patients was associated with less severe depressive symptoms and rarely with the presence of suicidal ideations. As far as we know, these are the first ever obtained results which show that TCS might help differentiating MDD patients with suicidal risk or eventually predict good disease recovery based on the findings of RN hypo- or normoechogenicity.


The cavum septum pellucidum (CSP), a putative marker of neurodevelopmental anomaly, has been associated with an increased risk of several psychiatric disorders. The purpose of this study was to evaluate the CSP in patients with obsessive-compulsive disorder (OCD) compared with healthy control subjects. Seventy-one patients with OCD and 71 healthy volunteers matched for age and sex were evaluated with magnetic resonance imaging. We evaluated the CSP using criteria employed in previous studies: presence of the CSP, length of the CSP, and overall size of the CSP, measured in five grades, ranging from grades 0 (no CSP) to 4 (severe CSP). We evaluated OCD symptom severity using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). The CSP presence was significantly greater in the OCD group (60.6%) than in control subjects (29.6%), and CSP size grade was significantly larger in the OCD group (chi(2) = 15.609, P = 0.004). CSP length showed no significant group difference. Among patients with OCD, those with a CSP had higher scores on the obsession subscale of the Y-BOCS than those without a CSP (Z = -2.358, P = 0.018), while they did not show significant difference from those without a CSP in the compulsion subscale of the Y-BOCS, age, duration of illness, or age at onset. These results indicate that neurodevelopmental alterations in midline structures might contribute to the pathogenesis of OCD.


Adrenergic alpha2A receptor gene (ADRA2A) is one of the most promising candidate genes for ADHD pharmacogenetics. Thus far, three studies have investigated the association between the ADRA2A -1291 C>G polymorphism and the therapeutic response to methylphenidate (MPH) in children with ADHD, all of them with positive results. The aim of this study is to investigate, for the first time, the association between three ADRA2A polymorphisms (-1291 C>G, -262 G>A, and 1780 C>T) and the response to MPH in adults with ADHD. The sample comprises 165 Brazilians of European descent evaluated in the adult ADHD outpatient clinic of the Hospital de Clínicas de Porto Alegre. The diagnostic procedures followed the DSM-IV criteria. Drug response was assessed by both categorical and dimensional approaches, through the scales Swanson, Nolan, and Pelham Rating scale version IV and the Clinical Global Impression-Severity Scale, applied at the beginning and after the 30th day of treatment. We found no evidence of association between the three ADRA2A polymorphisms and the therapeutic response to MPH treatment. Our findings do not support a significant role for the ADRA2A gene in ADHD pharmacogenetics, at least among adult patients.

Weight gain leading to obesity is a frequent adverse effect of treatment with atypical antipsychotics. However, the degree of its independent contribution to the risk of coronary heart disease events in patients treated with these drugs has not been elucidated. The aim of this study is to determine whether obesity is an independent risk factor for the 10-year risk of coronary heart disease events in psychiatric patients treated with atypical antipsychotics. We used the Framingham method, which is based on age, gender, blood pressure, smoking, and plasma levels of total and high-density lipoprotein cholesterol, to estimate the 10-year risk of coronary heart disease events in patients treated with second-generation antipsychotics who were obese (N = 44; mean age 38.1 years, 54.5% men) or normal weight (N = 83; mean age 39.9 years, 47.0% men). Excluded were patients with metabolic syndrome and those taking antihypertensive, hypoglycemic, and lipid-lowering drugs. The 10-year risk of coronary artery disease events was very low and virtually identical in the obese and normal weight patients (2.3 +/- 3.5 vs. 2.6 +/- 4.6, P = 0.68), despite excess of 12 BMI units (P < 0.0001) and 15.7 cm waist circumference (P < 0.0001) in the obese. The risk was similar in obese and normal weight men (3.8 +/- 5.9 vs. 2.8 +/- 3.4, P = 0.45) and women (1.7 +/- 3.7 vs. 1.5 +/- 2.5, P = 0.83). The validity of the 10-year prediction for risk of coronary heart disease events in the mentally ill based on the Framingham score system requires prospective confirmation. Obesity does not appear to be an independent predictor for the 10-year risk of coronary heart disease events in patients without metabolic syndrome treated with second-generation antipsychotics.


Olfactory identification deficit appears to be an enduring feature of schizophrenia, but it is unclear whether it is specific to schizophrenia or present in psychotic disorders in general. The aim of the present study was to compare olfactory identification and olfactory preference in schizophrenia and bipolar disorder. Individuals with schizophrenia or bipolar disorder and demographically matched healthy participants were given the University of Pennsylvania Smell Identification Test (UPSIT) to assess olfactory identification ability. To examine olfactory hedonic judgment, participants were also asked to indicate their preference for each UPSIT item on a 5-point rating scale, immediately after odor identification. Clinical symptoms and social competence were also assessed. Both schizophrenic and bipolar groups showed olfactory identification deficits compared with the healthy controls, but schizophrenic patients were more impaired than bipolar patients on the UPSIT accuracy. Interestingly, both bipolar and schizophrenic patients rated odors to be more pleasant than did healthy controls, but all groups preferred odors that they could correctly identify to unidentified smells. Restricted range of preference ratings was associated with the severity of negative symptoms in schizophrenia, and with mania in bipolar disorder. Social competence was associated with better olfactory identification performance. These findings suggest that olfactory identification and preference are compromised in bipolar disorder as well as in schizophrenia, but the precise nature of these abnormalities needs to be further elucidated.


The presence of the metabolic syndrome is an important risk factor for cardiovascular disease and diabetes. The short- and long-term metabolic safety of sertindole was compared to that of risperidone in a subset of patients enrolled in the sertindole cohort prospective (SCoP) study, an open randomized study. In 261 randomized patients, there were moderate increases in mean weight,
BMI, and waist circumference during treatment with either sertindole or risperidone; after 12 weeks, the increase in weight was 1.3 and 1.1 kg, respectively, and after 36 weeks, it was 2.2 and 2.0 kg, respectively. From baseline to last assessment (up to 60 weeks), weight gains of 1.8 and 1.7 kg for sertindole and risperidone, respectively, were observed. Similar proportions of patients (sertindole: 17% versus risperidone: 16%) had weight increases >/= 7% from baseline to last assessment. The mean changes from baseline in triglycerides, total cholesterol, HDL-cholesterol, LDL-cholesterol, plasma glucose and blood pressure were small and not clinically relevant in both treatment groups. No patient in either of the groups developed type 2 diabetes during the study. At last assessment, the prevalence of metabolic syndrome (International Diabetes Federation) was 17% in the sertindole group and 26% in the risperidone group and the incidence of metabolic syndrome was 7% in the sertindole group and 10% in the risperidone group. Treatment with either sertindole or risperidone did not appear to be associated with an increased comparative risk of developing metabolic syndrome. In general, the metabolic effects of sertindole and risperidone were similar.


Panic disorder (PD) is characterized by recurrent panic attacks that are defined as distinct episodes of intense fear, accompanied by symptoms related to physical arousal. Because most patients interpret these symptoms as signs of serious somatic disease (e.g., a heart attack), utilization of healthcare services is high in PD sufferers. PD can become debilitating, interfering significantly with patients' lives. Fortunately, effective treatments are available, but a considerable proportion of patients do not respond sufficiently. The aim of this paper is to outline some promising research strategies aimed at improving established treatments.


Serotonin (5-HT) pathways play an important role in the pathophysiology of anorexia nervosa (AN). In this study, we investigated functional characteristics of the platelet 5-HT transporter and platelet 5-HT content in AN patients at various stages of their illness in comparison to healthy control woman (HCW) controlling for the 5-HTTLPR deletion/insertion polymorphism and other confounding variables. Fasting blood samples of 58 acutely underweight AN patients (acAN, BMI = 15.2 +/- 1.4), 26 AN patients of the initial acAN sample after short-term/partial weight restoration (BMI = 17.3 +/- 0.9), 36 weight-recovered AN patients (recAN, BMI = 20.7 +/- 2.2) and 58 HCW (BMI = 21.6 +/- 2.0) were assessed for kinetic characteristics of platelet 5-HT uptake (V (max), K (m)) and platelet 5-HT content. Plasma leptin served as an indicator of malnutrition. Mean V (max) and K (m) values were significantly higher in recAN subjects in comparison to HCW (2.05 +/- 0.62 vs. 1.66 +/- 0.40 nmol 5-HT/10(9) platelets min and 432 +/- 215 vs. 315 +/- 136 nmol, respectively) but there were no differences in platelet 5-HT content (464.8 +/- 210.6 vs. 472.0 +/- 162.2 ng 5-HT/10(9) platelets). 5-HT parameters in acAN patients and HCW were similar. 5-HTTLPR variants were not related to 5-HT platelet variables. In the longitudinal part of the study we found significantly increased 5-HT content but unchanged 5-HT uptake in AN patients after short-term/partial weight restoration. Our results highlight the importance of malnutrition for the interpretation of abnormalities in neurotransmitter systems in AN. Changes in platelet 5-HT transporter activity were related to the stage of the illness but not to 5-HTTLPR genotype. Increased V (max) and K (m) in recovered AN patients might mirror adaptive modulations of the 5-HT system.

The hippocampus seems to be affected in MDD, and brain-derived neurotrophic factor (BDNF) has positive effects on neurogenesis within the hippocampus. Although there are inconsistencies among study results, a smaller hippocampal volume in depressed patients is thought to be related to the pathophysiology of the disease. We looked at the correlation between serum BDNF (sBDNF) levels and hippocampal volumes (HCV) of first-episode MDD patients (18 female, 7 male; mean age = 32.1 +/- 9.3) and healthy controls (17 female, 5 male; mean age = 29.7 +/- 6.4). Region of interest analysis was conducted on the images acquired via MRI. sBDNF levels and HCV correlated only in the MDD group (right: r = 0.46, P = 0.02; left: r = 0.47, P = 0.02); however, HCV did not differ between MDD patients and healthy controls (right: F = 2.45, df = 1.46, P > 0.05; left: F = 0.05, df = 1.46, P > 0.05). BDNF may be a factor underlying HCV differences between MDD and healthy control subjects, which become apparent as severe and multiple episodes are experienced.


Why are savagery and violence so omnipresent among humans? We suggest that hunting behaviour is fascinating and attractive, a desire that makes temporary deprivation from physical needs, pain, sweat, blood and, ultimately, the willingness to kill tolerable and even appetitive. Evolutionary development into the "perversion" of the urge to hunt humans, that is to say the transfer of this hunt to members of one's own species, has been nurtured by the resultant advantage of personal and social power and dominance. While a breakdown of the inhibition towards intra-specific killing would endanger any animal species, controlled inhibition was enabled in humans in that higher regulatory systems, such as frontal lobe-based executive functions, prevent the involuntary derailment of hunting behaviour. If this control--such as in child soldiers for example--is not learnt, then brutality towards humans remains fascinating and appealing. Blood must flow in order to kill. It is hence an appetitive cue as is the struggling of the victim. Hunting for men, more rarely for women, is fascinating and emotionally arousing with the parallel release of testosterone, serotonin and endorphins, which can produce feelings of euphoria and alleviative pain. Bonding and social rites (e.g. initiation) set up the constraints for both hunting and violent disputes. Children learn which conditions legitimate aggressive behaviour and which not. Big game hunting as well as attack of other communities is more successful in groups--men also perceive it as more pleasurable. This may explain the fascination with gladiatorial combat, violent computer games but as well ritualized forms like football.


Despite the fact that alcoholism is a severe public health problem of worldwide proportions, only a limited number of medications is used as coadjuvant treatment. The objectives of this study were to analyse the use of disulfiram for alcohol-dependent patients and the immediate interruption of treatment following medication prescription. This is a transversal study of 810 patients who attended the Alcohol and Drug Research Unit (UNIAD) during the 2000-2006 period. The study showed that both male and female patients who had remained under treatment during the first year used proportionally more disulfiram than those who remained for lesser time under treatment, and immediate treatment interruption was statistically more significant in this latter group of patients.
after prescription of this medication. Although disulfiram is an old medication, it seems that this drug can be useful for keeping alcohol-dependent patients under outpatient treatment.


Although perinatal complications are hypothesized to be risk factors for the development of anorexia nervosa (AN), no study to date explored this issue using a discordant sibling design. This type of design allows to explore whether the risk for obstetric complications is itself a consequence of the genetic vulnerability for AN (covariation model) or whether obstetric complications increase the risk of AN independently of (additive model), or in interaction with (interaction model), the disorder’s genetic liability. The presence of perinatal complications was assessed through review of the obstetric records of 60 AN subjects, 60 unaffected sisters, and 70 healthy subjects. Unaffected sisters and healthy controls were compared in relation to perinatal characteristics and complications. There was no evidence for an elevated rate of complications in unaffected siblings of AN patients. Mothers with a positive psychiatric history tended to have more perinatal complications. Perinatal complications seem to be independent risk factors that may interact with, but are not caused by, familial risk factors for AN. In terms of prevention, a particular attention should be paid to mothers with a lifetime history of psychiatric disorders.


The insanity defense in the United States is available to provide a legal excuse for those whose criminal acts were due to serious mental illness. To an underappreciated extent, the evolution of the insanity defense is integrally related to the evolution of conceptions of psychopathic disorders and their relevance, or determined lack thereof, to the insanity defense. As legal and mental health professionals discuss the ideal insanity defense and whether psychopathic disorders should be qualifying or disqualifying conditions, any practical outcome of such discussions must take into account the politics of the insanity defense. When this is done, it becomes apparent that the insanity
defense itself, even for serious, psychotic mental disorders, is withering under relentless attack and must be advanced and defended without diluting its salient importance by including psychopathic disorders.


The role of the amygdala during facial emotion recognition (FER) tasks as well as its clinical implications in schizophrenia patients remains unclear. While most of authors have reported hypoactivation, recently it has been suggested that patients may also exhibit hyperactivation. We studied amygdalar response during a previously validated FER task using (18)[F] fluorodeoxyglucose positron emission tomography ((18)FDG-PET) technique in ten right-handed healthy volunteers and 11 right-handed non acute patients with schizophrenia. Both groups underwent two scans on different days in a random order; each consisted of 17 1/2 min of continuous emotional and control tasks. Statistical Parametric Mapping (SPM) 2 analysis with a region of interest approach was carried out. Left amygdalar hyperactivation among the schizophrenia group was shown in both emotional and control tasks when compared to healthy subjects. The right amygdala showed no differential activation in any of the tasks. Patients diagnosed with schizophrenia exhibit a non-task specific amygdalar hyperactivation during a continuous emotional and non-emotional task when compared to matched healthy controls.


There is evidence that high alcohol use is associated with an increase in mortality. Little is known about long-term effects of problematic alcohol consumption in non-clinical (community) populations. The aim of our study was to obtain data on this and related issues in a representative rural community sample assessed longitudinally over a period of 20 years. Assessments focused on a baseline survey from 1980 to 1984 and 20-year follow-up from 2001 to 2004. Based on expert interviews and standardized self-rating scales (e.g. MALT; Munich Alcoholism Test), the following three groups were defined (a) severe alcohol problems, (b) moderate alcohol problems, and (c) no alcohol problems. Mortality and hazard rates were analyzed with logistic and Cox regression adjusted for several health risk factors. From an original community sample of 1,465 individuals, 448 were deceased at 20-year follow-up. Participation rates were high. Baseline prevalence according to the MALT was 1.6% for severe alcohol problems and 4.0% for moderate alcohol problems. Over the 20-year time span, individuals with severe alcohol problems had a significantly elevated risk for dying earlier than the group with no alcohol problems (2.4 times higher). Mortality for those with moderate alcohol problems at baseline had a non-significantly elevated 20-year mortality risk (1.5 times higher) compared to those with no alcohol problems. Cox survival analyses corroborate these findings from multiple sequential logistic regression analyses. In discussing the mortality risk of persons with alcohol problems, the severity of the alcohol problems must be taken into account.

The N1 component of the auditory evoked potential (AEP) is a robust and easily recorded metric of auditory sensory-perceptual processing. In patients with schizophrenia, a diminution in the amplitude of this component is a near-ubiquitous finding. A pair of recent studies has also shown this N1 deficit in first-degree relatives of schizophrenia probands, suggesting that the deficit may be linked to the underlying genetic risk of the disease rather than to the disease state itself. However, in both these studies, a significant proportion of the relatives had other psychiatric conditions. As such, although the N1 deficit represents an intriguing candidate endophenotype for schizophrenia, it remains to be shown whether it is present in a group of clinically unaffected first-degree relatives. In addition to testing first-degree relatives, we also sought to replicate the N1 deficit in a group of first-episode patients and in a group of chronic schizophrenia probands. Subject groups consisted of 35 patients with schizophrenia, 30 unaffected first-degree relatives, 13 first-episode patients, and 22 healthy controls. Subjects sat in a dimly lit room and listened to a series of simple 1,000-Hz tones, indicating with a button press whenever they heard a deviant tone (1,500 Hz; 17% probability), while the AEP was recorded from 72 scalp electrodes. Both chronic and first-episode patients showed clear N1 amplitude decrements relative to healthy control subjects. Crucially, unaffected first-degree relatives also showed a clear N1 deficit. This study provides further support for the proposal that the auditory N1 deficit in schizophrenia is linked to the underlying genetic risk of developing this disorder. In light of recent studies, these results point to the N1 deficit as an endophenotypic marker for schizophrenia. The potential future utility of this metric as one element of a multivariate endophenotype is discussed.


An increasing number of controlled studies strongly support an antidepressant effect of high-frequency repetitive transcranial magnetic stimulation (rTMS) over the left dorsolateral prefrontal cortex. However, these data come from highly selected study populations. Whether rTMS is a feasible therapeutic tool for the treatment of depression under naturalistic condition has not yet been addressed. Here, we report results from 232 depressive patients [aged 20-76 years, baseline Hamilton Depression Rating Score (HDRS-21) 24.0 +/- 7.3] treated with rTMS add-on to continued psychopharmacological treatment in a naturalistic clinical setting. Two thousand stimuli of 20-Hz rTMS were applied daily over the left dorsolateral prefrontal cortex with an intensity of 110% of motor threshold. Treatment duration was individually planned and varied between 10 and 20 sessions. In average, patients received 13 +/- 6.1 rTMS sessions. In 90% of the cases, treatment was terminated regularly. No severe side effects were observed. Only four patients stopped rTMS treatment because of side effects. Ratings with the HDRS-21 before and after treatment were available in 130 patients. The average improvement of the HDRS-21 in this subsample was 9.0 +/- 9.2 points. Fifty-three patients had an improvement of 50% or more. These results document that rTMS is feasible, safe and well tolerated under naturalistic conditions.


Cognitive impairment and deficits in social skills have been largely documented in patients with schizophrenia and are increasingly recognized as rate-limiting factors for recovery. Evidence has been provided that cognitive training and social skills training (SST) are effective to treat cognitive and social skills impairment in schizophrenia; however, the translation of improved performance on cognitive or social skills tasks into improved functional outcome is controversial. According to recent
reviews, interventions providing cognitive training in conjunction with psychosocial rehabilitation have a greater impact on functional outcome than either intervention alone suggesting that the two treatment approaches may work together in a synergistic fashion. The present pilot study was designed to test the hypothesis that an integrated rehabilitation program, including individualized cognitive and SST, is more effective than the structured leisure activities (SLA) carried out in many Italian Mental Health Departments. The primary outcome measure was subjects’ personal and social functioning as assessed by the Interview for the assessment of disability. The study is based on a controlled design including randomization to treatment groups, blind assessments and stable pharmacological treatment. Subjects were recruited among patients attending three psychiatric facilities located in the Italian region Campania. Thirty patients were randomized to the experimental program “social skills and neurocognitive individualized training” (SSANIT), and 30 to SLA. The two programs were matched for the overall duration as well as frequency and duration of the sessions. The two groups of patients did not differ at baseline on psychopathology, neurocognitive and personal/social functioning. After 6 months of treatment, personal and social functioning was significantly better in patients assigned to SSANIT than in those assigned to usual rehabilitation activities practiced in Mental Health Departments. No advantage was observed for either program on psychopathological and cognitive outcome indices. As for other integrated programs, also for SSANIT further studies are needed to verify generalization and persistence of the observed gains, and to clarify most adequate length and doses of the therapeutic intervention as well as the relative contribution of each program component to its impact on subjects’ disability.


Verbal and visuospatial working memory (WM) impairment is a well-documented finding in psychiatric patients suffering from major psychoses such as schizophrenia or bipolar affective disorder. However, in major depression (MDD) the literature on the presence and the extent of WM deficits is inconsistent. The use of a multitude of different WM tasks most of which lack process-specificity may have contributed to these inconsistencies. Eighteen MDD patients and 18 healthy controls matched with regard to age, gender and education were tested using process- and circuit-specific WM tasks for which clear brain-behaviour relationships had been established in prior functional neuroimaging studies. Patients suffering from acute MDD showed a selective impairment in articulatory rehearsal of verbal information in working memory. By contrast, visuospatial WM was unimpaired in this sample. There were no significant correlations between symptom severity and WM performance. These data indicate a dysfunction of a specific verbal WM system in acutely ill patients with MDD. As the observed functional deficit did not correlate with different symptom scores, further, longitudinal studies are required to clarify whether and how this deficit is related to illness acuity and clinical state of MDD patients.


Decreased volumes of subgenual cingulate (SGC) have been reported primarily among familial bipolar patients, which is one of the hallmarks of an endophenotype. In order to investigate specificity of SGC volume abnormalities to familial mood disorders and to test whether SGC volumes represent an endophenotype for BD, we measured SGC volumes in young affected and unaffected relatives of bipolar patients (high-risk design) and in sporadic bipolar patients. We included 20 unaffected, 15 affected offspring of bipolar I or bipolar II parents, 18 controls, and 19 sporadic bipolar patients between 15 and 30 years of age. SGC volumes were measured on 1.5 T 3D
anatomical MRI images using standard methods. We also combined the effect sizes from all published studies of sporadic patients with mood disorders (N = 61) and controls (N = 84) using random-effect models. We found comparable SGC volumes among unaffected, affected offspring of BD parents and controls (F = 0.7, df = 2; 50, P = 0.47). Likewise no SGC abnormalities were found between sporadic bipolar and control subjects (F = 2.31, df = 1; 34, P = 0.14). When combining all available data from sporadic patients, there were no differences in left (SDM 0.19, 95% CI -0.13 to 0.51) or right (SDM -0.11, 95% CI -0.47 to 0.26) SGC volumes between sporadic bipolar patients and controls. The limitations of the study are cross-sectional design and inclusion of both bipolar I and bipolar II probands. In conclusion, SGC volume abnormalities were absent in unaffected, affected relatives of bipolar patients as well as sporadic bipolar patients and thus did not meet criteria for endophenotype.


Neuregulin-1 (NRG-1) is a putative susceptibility gene for schizophrenia but the neurocognitive processes that may involve NRG-1 in schizophrenia are unknown. Deficits in antisaccade (AS) and smooth pursuit eye movements (SPEM) are promising endophenotypes, which may be associated with brain dysfunctions underlying the pathophysiology of schizophrenia. The aim of this study was to investigate the associations of NRG-1 genotypes with AS and SPEM in schizophrenia patients and healthy controls. Patients (N = 113) and controls (N = 106) were genotyped for two NRG-1 single nucleotide polymorphisms (SNPs); SNP8NRG222662, a surrogate marker for the originally described Icelandic NRG-1 risk haplotype, and SNP8NRG243177, which has recently been associated with individual differences in brain function. Subjects underwent infrared oculographic assessment of AS and SPEM. The study replicates previous findings of impaired AS and SPEM performance in schizophrenia patients (all P < 0.005; all s = 0.5-1.5). SNP8NRG243177 risk allele carriers had marginally increased variability of AS spatial error (P = 0.050, = 0.3), but there were no significant genotype effects on other eye movement variables and no significant diagnosis-by-genotype interactions. Generally, risk allele carriers (G allele for SNP8NRG222662 and T allele for SNP8NRG243177) had numerically worse performance than non-carriers on most AS and SPEM variables. The results do not suggest that NRG-1 genotype significantly affects AS and SPEM task performance. However, the power of the sample to identify small effects is limited and the possibility of a type II error must be kept in mind. Larger samples may be needed to reliably investigate such gene effects on oculomotor endophenotypes.


During an intense four-level community-based intervention program conducted in Nuremberg (490,000 inhabitants) in 2001 and 2002 [Nuremberg Alliance Against Depression (NAD)], the number of suicidal acts (main outcome completed + attempted suicides) had dropped significantly (-21.7%), a significant effect compared with the baseline year and the control region (Wuerzburg, about 290,000 inhabitants). To assess the sustainability of the intervention effects the number of suicidal acts was assessed in the follow-up year (2003), after the termination of the 2-year intervention. Also, in the follow-up year (2003), the reduction in suicidal acts compared with the baseline year in Nuremberg (2000 vs. 2003: -32.4%) was significantly larger than that in the control region (P = 0.0065). The reduction was even numerically larger than that of the intervention years (2001, 2002). Thus, 1 year after the end of the main intervention, preventive effects on suicidality of the NAD remain at least
stable. The four-level intervention concept appears to be cost-effective and is presently implemented in many European regions.


Capacity to consent is a basic prerequisite for participation of patients as probands in research. However, mental illness often impairs this competence. Therefore, in psychiatric research, the first obligation is to assess a mentally ill patient's competence to consent. This is not a simple task. Informed consent should be viewed not only as a legal must, but also as a chance to build up a trusting patient-psychiatrist relationship. This is called for by respect for the autonomy and dignity of the patient. Specifically, competence to consent is related to the specific intervention; the validity of a consent requires that the patient understands the intervention-related medical information, comprehends its significance and consequences, and can appreciate its meaning for himself. Research with patients who lack this competence to consent validly meets a major problem: an uncovered need for research in frequent major psychiatric disorders exists, but a substantial number of patients with these illnesses cannot consent validly. Several guidelines for dealing with this problem will be discussed. Mentally ill patients who are willing to participate in needed research are a rare resource. This must be protected by the virtue of the clinical researcher who has to take great pains over the strict adherence to ethical guidelines.


Depression rating scales play a decisive role in the assessment of the severity of depression and the evaluation of the efficacy of antidepressant treatments. The Hamilton Depression Rating Scale (HAMD) is regarded as the 'gold standard'; nevertheless, studies suggest that the Inventory of Depressive Symptomatology (IDS) is more sensitive to detect symptom changes. The aim of the present study was to investigate whether the IDS is more sensitive in detecting changes in depression symptoms in patients with mild major, minor or subsyndromal depression (MIND). Biweekly IDS-C(28) and HAMD(17) data from 340 patients of a 10-week randomized, placebo-controlled trial comparing the effectiveness of sertraline and cognitive-behavioural therapy in patients with MIND were analysed. We investigated sensitivity to change for both scales (1) from assessment-to-assessment, (2) in relation to depression severity level, and (3) in relation to DSM-IV depression criterion symptoms. The IDS-C(28) was more sensitive in detecting changes in depression symptomatology over the treatment course as well as for different severity levels, especially in patients with a low depression severity. It assesses the DSM-IV criteria more thoroughly, is better able to track the change of cognitive symptoms and to identify residual symptoms. Both scales are well able to assess depressive symptomatology. However, the IDS-C(28) surpasses the HAMD(17) in detecting small changes especially in the core symptoms of depression. This is important for an optimal treatment by capturing early improvements, enabling prompt reactions and detecting residual symptoms.

Psychomotor symptoms related to an impairment of the nigrostriatal dopaminergic system are frequent in major depression (MD). Repetitive transcranial magnetic stimulation (rTMS) has been discussed as a new treatment option for MD. In neurobiological terms, an influence of high-frequency rTMS on dopaminergic neurotransmission has previously been shown by several studies in animals and humans. Therefore, an improvement of psychomotor symptoms by rTMS could be assumed. The aim of this pilot study was to investigate the effect of high-frequency rTMS on psychomotor retardation and agitation in depressive patients. We investigated the effect of left prefrontal 10 Hz rTMS on psychomotor retardation and agitation in 30 patients with MD. Patients were randomly assigned to real or sham rTMS in addition to a newly initiated standardized antidepressant medication. We found a trend in the reduction of agitation (t(28) = 1.76, p = 0.09, two-tailed), but not in the reduction of retardation. Furthermore, no general additional antidepressant effect of rTMS was observed. Although there was no statistical significant influence of high-frequency rTMS on psychomotor symptoms in depressive patients, the results showed a trend in the reduction of psychomotor agitation in MD. This effect should be systematically investigated as the primary end point in further studies with larger sample sizes.


According to the so-called telescoping effect, there is a gender-specific course of alcohol dependence with women starting alcohol use later than men and having a faster development of harmful consequences. There are inconsistent data regarding a telescoping effect in opiate dependence. In each of six European centres, 100 opiate addicts were investigated by a structured interview (mainly the EuropASI and CIDI) at admission to various kinds of treatment (TREAT project). In a secondary analysis of the TREAT data, women and men were compared regarding age at onset of heroin use and the current severity of addiction. In addition, a comparison of female (n = 140) and male (n = 140) addicts matched for age and study centre were carried out. Eventually, multiple logistic and linear regressions were done with the interaction term of gender and time of regular consumption as predictor for the severity of dependence, besides, other sociodemographic variables. There was no difference between genders regarding the age at onset of regular heroin consumption. Up to 4 years of regular consumption, there are gender-specific differences in the course of opiate dependence, e.g. a faster progression of legal problems in men and social problems in women. There were no differences in the severity of dependence other than more economic problems for women. A telescoping effect could only partially be observed in this large sample of opiate addicts. A gender-specific course was limited to the first years of consumption, and included domains with a faster progression for men. It has to be assumed that opiate dependence is a rapidly developing disorder with early chronification. Afterwards, only individual courses with influences of the national treatment system were observed.


The role of a functional polymorphism in the transcriptional control region of serotonin transporter gene (5-HTTLPR, SERTPR) has been studied intensively in major depression and in the response to selective serotonin inhibitors (SSRIs) in major depression. The findings have been contradictory, although majority of the studies indicate that the short allele is associated with poor response to SSRIs in major depression. In the present study, we evaluated the association of 5-HTTLPR with treatment response to SSRI medication in Finnish Caucasian MDD patients. A secondary purpose was to study the possible association of this particular polymorphism with major depressive disorder. The
aim of the study was to replicate the previous findings in this area. Primary outcomes of the treatment were remission, defined by an exit score of seven or less, and response, defined by a reduction of at least 50% on the MADRS. We had also a control population of 375 healthy blood donors, as a secondary objective was to evaluate the possible association of this particular polymorphism with major depressive disorder. Twenty-nine of the 85 (34.1%) patients reached the remission and 58.8% achieved the predefined response criteria. The I/I genotype of 5-HTTLPR was presented in 51.7% of those patients who achieved remission vs. 25.0% in the non-remitters (P = 0.03). The result remained statistically significant after adjusting for age, gender, medication and MADRS points at the study entry. However, the small sample size limits the reliability of this result.


While an interactive effect of genes with adverse life events is increasingly appreciated in current concepts of depression etiology, no data are presently available on interactions between genetic and environmental (G x E) factors with respect to personality and related disorders. The present study therefore aimed to detect main effects as well as interactions of serotonergic candidate genes (coding for the serotonin transporter, 5-HTT; the serotonin autoreceptor, HTR1A; and the enzyme which synthesizes serotonin in the brain, TPH2) with the burden of life events (#LE) in two independent samples consisting of 183 patients suffering from personality disorders and 123 patients suffering from adult attention deficit/hyperactivity disorder (aADHD). Simple analyses ignoring possible G x E interactions revealed no evidence for associations of either #LE or of the considered polymorphisms in 5-HTT and TPH2. Only the G allele of HTR1A rs6295 seemed to increase the risk of emotional-dramatic cluster B personality disorders (p = 0.019, in the personality disorder sample) and to decrease the risk of anxious-fearful cluster C personality disorders (p = 0.016, in the aADHD sample). We extended the initial simple model by taking a G x E interaction term into account, since this approach may better fit the data indicating that the effect of a gene is modified by stressful life events or, vice versa, that stressful life events only have an effect in the presence of a susceptibility genotype. By doing so, we observed nominal evidence for G x E effects as well as main effects of 5-HTT-LPR and the TPH2 SNP rs4570625 on the occurrence of personality disorders. Further replication studies, however, are necessary to validate the apparent complexity of G x E interactions in disorders of human personality.


Schizophrenia clinical practice guidelines are developed to provide expert- and evidence-based advice to practicing psychiatrists in order to improve the management of this disorder. However, the application of these guidelines in everyday health care can still be described as nonsatisfying. Within the project “Guideline-supported quality management in outpatient treatment”, we investigated whether guideline adherence and quality of outcome can be improved by implementing a computer-based, guideline-oriented decision-support system. Therefore, a disease-specific decision-support system was developed interactively presenting guidelines to support the physicians decision-making process during the treatment of schizophrenia patients. We evaluated the system in a control group design: An experimental group consisting of 15 psychiatrists in private practice used the decision-support system, thus documenting the treatment of schizophrenic patients. Guideline-based
algorithms were interactively and case specifically displayed on the PC-screen as soon as predefined triggers were met. A first control group in Munich provided treatment-as-usual, documenting the treatment via paper-pencil. Two further physician groups served as additional comparison groups: one also documented electronically using the decision-support system, however without receiving electronic guideline support, the second group carried out traditional quality circles while also using the paper-pencil approach. As a result of the intervention, we observed a strong initial but time-limited improvement with respect to the core aspects of outpatient treatment in schizophrenia in the experimental group. The findings suggest that decision-support systems, despite their limitations, can be used to enhance treatment outcome in schizophrenia outpatient care.


An increasing number of longitudinal cohort studies have identified a risk increase for dementia by the chronic use of drugs with anticholinergic properties. The respective data from the German Study on Aging, Cognition and Dementia in Primary Care Patients (AgeCoDe) also showing risk increase (hazard ratio = 2.081) are reported here. The mechanisms by which the risk increase is transported are still unknown. Irritation of compensated alterations of cholinergic transmission at the predementia stage of Alzheimer’s disease (AD) or acceleration of neuroinflammation by disturbance of the anti-inflammatory effect of cholinergic innervation are discussed. In terms of dementia prevention, centrally acting anticholinergic drugs should be strictly avoided, because of long-term dementia risk increase in addition to acute negative effects on cognition.


Deficits in executive functions, e.g. voluntary selection, are considered central to the attention-deficit/hyperactivity disorder (ADHD). The aim of this simultaneous EEG/fMRI study was to examine associated neural correlates in ADHD patients. Patients with ADHD and healthy subjects performed an adapted go/no-go task including a voluntary selection condition allowing participants to freely decide, whether to press the response button. Electrophysiologically, response inhibition and voluntary selection led to fronto-central responses. The fMRI data revealed increased medial/lateral frontal and parietal activity during the voluntary selection task. Frontal brain responses were reduced in ADHD patients compared to controls during free responses, whereas parietal brain functions seemed to be unaffected. These results may indicate that selection processes are related to dysfunctions, predominantly in frontal brain regions in ADHD patients.


The objective of the European Post-marketing Observational Serdolect((R)) (EPOS) Study was to compare the safety of treatment with Serdolect (sertindole) with that of usual treatment in patients with schizophrenia, in normal European clinical practice. The EPOS was a multicentre, multinational,
referred, cohort study. Patients were enrolled at 226 centres in ten European countries. The study was prematurely terminated in 1998 as a result of the temporary market suspension of sertindole. Termination of the study reduced the number of patients recruited from the planned 12,000 to 2,321. While the power of the study was weakened, it did provide useful mortality information, which may be useful for future long-term studies. Crude mortality in the sertindole and non-sertindole groups was 1.45 (95% confidence interval, CI 0.53-3.16) and 1.50 (CI 0.72-2.76) deaths/100 patient-years exposed, respectively. There were no more cardiac deaths in the sertindole group than in the non-sertindole group. QT interval prolongation did not translate into an increased risk of death. Sertindole was well tolerated and caused few extrapyramidal symptoms. Although CIs remained large, this post-marketing study does not provide any evidence against the use of sertindole under normal conditions. Sertindole was well tolerated and posed no significant safety problems.


The aim of this study was to determine whether there was any relationship between hippocampal volume, and glucocorticoid regulation, and cognitive dysfunctions in drug-naïve major depressive disorder (MDD) patients during their first episode. Twenty drug-free female MDD patients in their first episode and 15 healthy females as control subjects were included in the study. All subjects underwent 3.0 Tesla (T) magnetic resonance imaging (MRI), comprehensive neuropsychological testing and dexamethasone suppression tests (DST). The volumes of the right and left hippocampus of the patients were found to be significantly smaller than those of the controls. Patients were found to have significantly lower scores on measures of attention, working memory, psychomotor speed, executive functions, and visual and verbal memory fields. The performance of the patients only in the recollection memory and memory of reward-associated rules were positively correlated with hippocampal volumes. The volumes of the left and right hippocampus did not correlate with basal or post-dexamethasone cortisol levels. Our findings indicate that depressed patients have smaller hippocampi even in the earlier phase of their illness. Further research efforts are needed to explain the mechanisms that are responsible for the small hippocampus in depressed patients.


Altered neuroplasticity contributes to the pathophysiology of schizophrenia. However, the idea that antipsychotics may act, at least in part, by normalizing neurogenesis has not been consistently supported. Our study seeks to determine whether hippocampal cell proliferation is altered in adult rats pretreated with ketamine, a validated model of schizophrenia, and whether chronic administration with neuroleptic drugs (haloperidol and risperidone) affect changes of cell genesis/survival. Ketamine per se has no effect on cell proliferation. Its withdrawal, however, significantly induced cell proliferation/survival in the hippocampus. Risperidone and haloperidol supported cell genesis/survival as well. During ketamine withdrawal, however, their application did not affect cell proliferation/survival additionally. TUNEL staining indicated a cell-protective potency of both neuroleptics with respect to a ketamine-induced cell death. As RT-PCR and Western blot revealed that the treatment effects of risperidone and haloperidol seemed to be mediated through activation of VEGF and MMP2. The mRNA expression of NGF, BDNF, and NT3 was unaffected. From the respective receptors, only TrkA was enhanced when ketamine withdrawal was combined with risperidone or haloperidol. Risperidone also induced BCL-2. Ketamine withdrawal has no effect on the expression of VEGF, MMP2, or BCL-2. It activated the expression of BDNF. This effect was
normalized by risperidone or haloperidol. The findings indicate a promoting effect of risperidone and haloperidol on survival of young neurons in the hippocampus by enhancing the expression of the anti-apoptotic protein BCL-2 and by activation of VEGF/MMP2, whereby an interference with ketamine and thus a priority role of the NMDA system was not evident.


Patients' attitudes toward side effects of antidepressants are likely to differ according to gender, which has not yet been fully addressed in the literature. From the 228,310 registrants, 1,305 participants who had received antidepressant drugs within the past year were identified with the Yahoo Japan research monitor through four-step screening procedures. Participants were asked as to which side effect(s) they had experienced, whether they had reported those side effects to their physicians, and whether they had taken any action to counteract them. The questionnaire was completed by 1,187 participants. Side effects were reported in 73.4% of the participants; the prevalence of self-reported side effects was significantly higher in men than women (80.4% vs. 68.3%, P <0.05). The percentage of participants who reported side effects to their physicians widely differed depending on the nature of their experience, ranging from 45.7% to 89.9%; the lowest was for sexual dysfunction. The percentage of participants who had taken any action to relieve side effects varied among side effects from 26.3% for sexual dysfunction to 89.5% for dry mouth. Moreover, a lower percentage of women had reported sexual dysfunction to physicians (36.6% vs. 60.7%, P <0.05) and had taken any action to counteract the problem (19.8% vs. 36.9%, P <0.05). Given that patients experienced with antidepressants are likely to be reluctant to report sexual side effects, physicians should be cognizant of the potential presence of sexual dysfunction in patients who are taking antidepressants, especially for women.


To date, pain perception is thought to be a creative process of modulation carried out by an interplay of pro- and anti-nociceptive mechanisms. Recent research demonstrates that pain experience constitutes the result of top-down processes represented in cortical descending pain modulation. Cortical, mainly medial and frontal areas, as well as subcortical structures such as the brain stem, medulla and thalamus seem to be key players in pain modulation. An imbalance of pro- and anti-nociceptive mechanisms are assumed to cause chronic pain disorders, which are associated with spontaneous pain perception without physiologic scaffolding or exaggerated cortical activation in response to pain exposure. In contrast to recent investigations, the aim of the present study was to elucidate cortical activation of somatoform pain disorder patients during baseline condition. Scalp EEG, quantitative Fourier-spectral analyses and LORETA were employed to compare patient group (N = 15) to age- and sex-matched controls (N = 15) at rest. S1, SII, ACC, SMA, PFC, PPC, insular, amygdale and hippocampus displayed significant spectral power reductions within the beta band range (12-30 Hz). These results suggest decreased cortical baseline arousal in somatoform pain disorder patients. We finally conclude that obtained results may point to an altered baseline activity, maybe characteristic for chronic somatoform pain disorder.

Evidence for white matter abnormalities in patients with schizophrenia is increasing. Decreased fractional anisotropy (FA) in interhemispheric commissural fibers as well as long-ranging fronto-parietal association fibers belongs to the most frequent findings. The present study used tract-based spatial statistics to investigate white matter integrity in 35 patients with schizophrenia and 35 healthy volunteers. We found that patients exhibited significantly decreased FA relative to healthy subjects in the corpus callosum, the cerebral peduncle, the left inferior fronto-occipital fasciculus, the anterior thalamic radiation, the right posterior corona radiata, the middle cerebellar peduncle, and the right superior longitudinal fasciculus. Increased FA was detectable in the inferior sections of the corticopontine-cerebellar circuit. Present data indicate extended cortical-subcortical alterations of white matter integrity in schizophrenia using advanced data analysis strategies. They corroborate preceding findings of white matter structural deficits in mainly long-ranging association fibers and provide first evidence for neuroplastic changes in terms of an increased directionality in more inferior fiber tracts.


The underlying pathophysiological mechanisms in Tourette’s syndrome (TS) are still unclear. Increasing evidence supports the involvement of infections, possibly on the basis of an altered immune status. Not only streptococci but also other infectious agents may be involved. This study investigates the association between the neurotrophic agents Chlamydia, Toxoplasma and TS. 32 patients with TS and 30 healthy matched controls were included. For each individual, IgA/IgG antibody titers against Chlamydia trachomatis/pneumoniae and Toxoplasma gondii were evaluated and analyzed with Fisher’s exact test. We found a significantly higher rate of TS patients with elevated antibody titers against Chlamydia trachomatis (P = 0.017) as compared to controls. A trend toward a higher prevalence in the Tourette’s group was shown for Toxoplasma (P = 0.069). In conclusion, within the TS patients a higher rate of antibody titers could be demonstrated, pointing to a possible role of Chlamydia and Toxoplasma in the pathogenesis of tic disorders. Because none of these agents has been linked with TS to date, a hypothesis is that infections could contribute to TS by triggering an immune response. It still remains unclear whether tic symptoms are partly due to the infection or to changes in the immune balance caused by an infection.


To examine disease and treatment characteristics of patients with schizophrenia treated with electroconvulsive therapy (ECT). We examined charts from 79 patients diagnosed with schizophrenia (n = 55), persistent delusional disorders (n = 7), and schizoaffective disorders (n = 17) between 2003 and 2008. We recorded age, sex, indication for ECT, number of ECT sessions, ECT series, outcome, maintenance ECT, use of antipsychotics, duration of illness, and duration of the current exacerbation. All patients were taking antipsychotics at the time of enrolment in the study. Acute ECT included 2-26 sessions; maintenance ECT (M-ECT) was given to 18 patients for up to 12 years. Initial indications for ECT included psychosis (n = 28), pronounced affective symptoms (n = 28), delirious states (n = 20), and M-ECT (n = 3). Most patients experienced excellent/good outcomes (n = 66), but others experienced moderate (n = 8) or poor (n = 5) outcomes. No factors were identified that predicted treatment responses in individual patients. ECT proved to be effective in a population of patients that were severely ill with treatment-refractory schizophrenia. This does not imply that the patients were cured from schizophrenia. Rather, it reflects the degree of relief from psychosis and disruptive
behaviour, as described in the patient charts. The treatment was often offered to patients after considerable disease durations.


We introduce a diagnostic map that was calculated by robust non-metric multidimensional scaling based on AMDP symptom profiles of patients with schizophrenic and affective disorders to demonstrate a possibility to combine the categorical and the dimensional perspective at the same time. In the diagnostic map, a manic, a depressive, and a non-affective cluster clearly emerged. At the same time, the mania dimension \( r = 0.82 \), the depression dimension \( r = 0.68 \), and the apathy dimension \( r = 0.74 \) showed high multiple regression values in the map. We found substantial overlaps of the diagnostic groups with regard to the affective spectrum but irrespective of the ICD-10 classification. Within this sample, we found the association and quality of mood symptoms to be a structuring principle in a diagnostic map. We demonstrate that this approach represents a promising way of combining the categorical and the dimensional perspective. As a practical implementation of these findings, a multidimensional diagnostic map could serve as an automated diagnostic tool based on psychopathological symptom profiles.


Early-onset bipolar disorder is an impairing condition that is strongly associated with genetic inheritance. Neurocognitive deficits are core traits of this disorder which seem to be present in both young and adult forms. Deficits in verbal memory and attention are persistent within euthymic phases in bipolar adults, adolescents, and children. In younger samples, including type I or II and not otherwise specified patients, executive functions are not widely impaired and the existence of visual-spatial deficits remains unclear. The main aim of this study was to compare the neurocognitive performance in young stabilized type I or II bipolar patients and healthy controls. Fifteen medicated adolescents with bipolar disorder and 15 healthy adolescents, matched in age and gender, were compared on visual-spatial skills (reasoning, memory, visual-motor accuracy) and executive functioning (attention and working memory, set-shifting, inhibition) using t-tests and MANCOVA. Correcting for verbal competence, MANCOVA showed that patients performed significantly worse than controls in letters and numbers sequencing \( P = 0.003 \), copy \( P < 0.001 \) and immediate recall \( P = 0.007 \) of the Rey Complex Figure Test, interference of the Stroop Color-Word Test \( P = 0.007 \) and non-perseverative errors on the Wisconsin Card Sorting Test \( P = 0.038 \). Impaired cognitive performance was found in young bipolar patients in working memory, visual-motor skills, and inhibitory control.


Evidence-based medicine (EBM) is becoming the guiding principle for clinical treatment decisions. But evidence remains a loosely defined term. Multiple criteria for evidence criteria have been proposed. Most influential evidence criteria give priority to meta-analyses because they promise an objective procedure to combine the outcomes of all informative, putatively conflicting studies on the same issue in an overall score. However, we claim that meta-analyses are of limited informative value for the following six reasons: (1) meta-analyses are often "overpowered" with clinically
irrelevant results that might emerge as highly significant; (2) there is serious concern of publication biases with "negative" studies not being published; (3) meta-analyses consider the variation in the results of the empirical studies included to be random noise, however, the variability of results across studies can be informative; (4) the result of a meta-analysis depends on the strategy used to identify the included empirical studies; (5) the quality of conclusions from meta-analyses depends on the statistical tests used to combine the results of the separate studies; (6) the qualitative conclusions drawn from the meta-analytical combination of individual studies may depend on specific design aspects of the individual studies. Thus, meta-analyses are primarily a method to generate hypotheses through an a posteriori analysis of treatment effects.


A conflict of interests occurs when a doctor is unduly influenced by a secondary interest (i.e., a personal incentive) in his acts concerning one of the primary interests to which he is professionally committed (the welfare of patients, the progress of science, or the education of students or residents). One specific variety of conflicts of interests has monopolized the attention of the scientific and lay press: the financial conflicts of interests arising from the relationships between doctors and drug companies. A large literature has described the many, sometimes subtle, ways by which a psychiatrist can be influenced in his prescribing habits or research activities by his relationships with the industry. Some empirical evidence is now available in this area. On the other hand, it has been pointed out that the current debate on this issue is sometimes "affectively charged" or fails to take into account that the interests of patients, families and mental health professionals and those of the industry may be often convergent. Other types of conflicts of interests are beginning now to be discussed. There is evidence that the allegiance of a researcher to a given school of thought may influence the results of studies comparing different psychotherapeutic techniques, thus colliding with the primary interest represented by the progress of science. Political commitment is also emerging as a source of conflicts of interests. Financial and non-financial conflicts of interests are widespread in psychiatric practice and research. They cannot be eradicated, but must be managed more effectively than is currently the case.


Long-term relapse prevention is the biggest challenge in treating alcohol-dependent patients. It is equally based on psychotherapy and pharmacotherapy. Psychotherapy includes motivational interviewing, community reinforcement, cognitive behavioural therapy, motivational enhancement, twelve-step facilitation, social network behaviour therapy, cue exposure, etc. For pharmacological treatment, we dispose of disulfiram, acamprosate and naltrexone. Reviews and meta-analyses reveal only modest effect sizes of these approaches probably because they are usually tested in large and heterogeneous samples where "one size does not fit all". However, attempts to form more homogeneous subgroups for which specific psychotherapies should be more effective ("matching") also failed. We suppose that this failure may have to do with the fact that these studies used only psychopathology and behavioural analyses as a basis for subtyping. Things look more promising once biologically defined endophenotypes are used as well in order to form more homogeneous subgroups. For example, naltrexone treatment seems more effective in carriers of a specific variant of the mu-opioid receptor gene. The same could be true for acamprosate if a newly found polymorphism was used to preselect potential responders. Very recently biological differences between patient groups are also being detected using functional imaging. Naltrexone is suggested to work better in a subgroup of patients with higher cue reactivity when shown appetitive alcohol pictures. MR spectroscopy of brain glutamate levels may detect potential acamprosate responders.
On such a basis, an individualised approach in the treatment of alcoholism ("personalised medicine") seems to hold promise.


Depression is a severe neuropsychiatric disorder affecting approximately 10% of the world population. Despite this, the molecular mechanisms underlying the disorder are still not understood. Novel technologies such as proteomic-based platforms are beginning to offer new insights into this devastating illness, beyond those provided by the standard targeted methodologies. Here, we will show the potential of proteome analyses as a tool to elucidate the pathophysiological mechanisms of depression as well as the discovery of potential diagnostic, therapeutic and disease course biomarkers.


On the basis of impaired glutamatergic transmission and the potential role of astrocytes in schizophrenia, we treated cultured astrocytes with MK-801, an NMDA-receptor antagonist, to investigate whether the resulting proteome changes are similar to those we found in our earlier proteome analysis of schizophrenia human brain tissue as well as to better comprehend the role of astrocytes in the disorder. Indeed, there are similarities. Furthermore, to verify the efficacy of clozapine and its effect over the proteome, we treated MK-801-treated astrocytes with clozapine. Interestingly, clozapine reversed protein changes induced by MK-801. The treatment of cell cultures with neural transmission agonists and antagonists might provide useful insights about psychiatric disorders.


Social learning is essential for adaptive behavior in humans. Neurofeedback based on functional magnetic resonance imaging (fMRI) trains control over localized brain activity. It can disentangle learning processes at the neural level and thus investigate the mechanisms of operant conditioning with explicit social reinforcers. In a pilot study, a computer-generated face provided a positive feedback (smiling) when activity in the anterior cingulate cortex (ACC) increased and gradually returned to a neutral expression when the activity dropped. One female volunteer without previous experience in fMRI underwent training based on a social reinforcer. Directly before and after the neurofeedback runs, neural responses to a cognitive interference task (Simon task) were recorded. We observed a significant increase in activity within ACC during the neurofeedback blocks, correspondent with the a-priori defined anatomical region of interest. In the course of the neurofeedback training, the subject learned to regulate ACC activity and could maintain the control even without direct feedback. Moreover, ACC was activated significantly stronger during Simon task after the neurofeedback training when compared to before. Localized brain activity can be controlled by social reward. The increased ACC activity transferred to a cognitive task with the potential to
reduce cognitive interference. Systematic studies are required to explore long-term effects on social behavior and clinical applications.


Several studies have demonstrated that structural brain change is detectable in the hippocampus in both patients, with schizophrenia and major depression. Only few studies, however, compared both clinical disease entities directly and no larger study has tried to take different disease stages into account. The objectives of this study are to investigate whether hippocampal volumes are reduced in patients with schizophrenia and those with major depression with the same duration of illness compared to healthy controls and to assess further changes at different disease stages. A total of 319 inpatients and healthy controls were enrolled and investigated with magnetic resonance imaging (MRI). Hippocampal volumes were measured using the segmentation software BRAINS. Bilateral hippocampal volume reductions were detected in both schizophrenic and depressed patients compared to healthy control (HC) subjects. Although younger, schizophrenic (SZ) patients showed in their MRI scans significant bilaterally reduced hippocampal volumes compared to patients with major depression. Although the hippocampal reductions were similar at the onset of symptomatic manifestation of both diseases, there was a further significant reduction of the left hippocampus in the recurrently ill SZ subgroup. The data suggest rather dynamic structural brain alterations in schizophrenia compared to major depression. Here, the presented application of the comparative neuroscience approach, by the use of large neuroimaging MRI databases, seems highly valuable. In the field of psychiatry, with its still controversial operationalized descriptive diagnostic entities, the cross-nosological approach provides a helpful tool to better elucidate the still unknown brain pathologies and their underlying molecular mechanisms beyond a single nosological entity.


Some studies suggest seasonality of suicide attempts in females, but not in males. The reasons for this gender difference remain unclear. Only few studies addressed the question whether gender differences in seasonality of suicide attempts reflect gender differences in the choice of method for suicide attempts, with inconsistent results. So, this study aimed to analyze the association of gender with seasonality in suicide attempts by persons living in two Northern Bavarian regions [city of Nuremberg (480,000 inhabitants) and region of Wuerzburg (270,000 inhabitants)] between 2000 and 2004. We addressed this question by focussing on the frequency of suicide attempts in relation to the seasons. The sample consisted of 2,269 suicide attempters (882 males and 1,387 females). The overall seasonality was assessed using the chi(2) test for multinomials. Moreover, the ratio of observed to expected number of suicide attempts (OER) with 95% confidence intervals within each season was calculated. As a result, overall distribution of suicide attempts differed significantly between seasons for women (chi(2) = 9.19, df = 3, P = 0.03), but not for men. Female suicide attempts showed a trough in the spring (decline compared to the expected value by 10%; OER = 0.9, 95% CI = 0.8-1.0). This trough was restricted to female low-risk suicide attempts (decline by 13%; OER = 0.87, 95% CI = 0.77-0.98). No seasonality was found for men. Seasonality of high-risk methods was more pronounced than that of low-risk methods; however, no significant gender differences were found concerning this aspect. The overall distribution of the sub-types of suicidal acts (parasuicidal gestures, suicidal pauses, suicide attempts in the strict sense) showed seasonality neither for males
nor for females. Whereas seasonality was absent in male suicide attempters, the frequency of low-risk suicide attempts in females was 13.1% lower than expected in the spring.


Several studies suggest that attention to emotional content is related to specific changes in central information processing. In particular, event-related potential (ERP) studies focusing on emotion recognition in pictures and faces or word processing have pointed toward a distinct component of the visual-evoked potential, the EPN (‘early posterior negativity’), which has been shown to be related to attention to emotional content. In the present study, we were interested in the existence of a corresponding ERP component in the auditory modality and a possible relationship with the personality dimension extraversion-introversion, as assessed by the NEO Five-Factors Inventory. We investigated 29 healthy subjects using three types of auditory choice tasks: (1) the distinction of syllables with emotional intonation, (2) the identification of the emotional content of adjectives and (3) a purely cognitive control task. Compared with the cognitive control task, emotional paradigms using auditory stimuli evoked an EPN component with a distinct peak after 170 ms (EPN 170). Interestingly, subjects with high scores in the personality trait extraversion showed significantly higher EPN amplitudes for emotional paradigms (syllables and words) than introverted subjects.


Sensorimotor gating deficits are relevant in schizophrenia and can be measured using prepulse inhibition (PPI) of the startle reflex. It is conceivable that such deficits may hinder the cognitive functions in schizophrenia patients. In this study, using PPI and a neuropsychological battery, we studied this possibility in a group of 23 acute, neuroleptic-free schizophrenia patients and 16 controls. A non-significant decrease in PPI was found in the patients as compared to the controls, as well as significant differences in the performance of Trail A and B in Wisconsin Card Sorting and Digit/Symbol Tests. No statistically significant correlations between PPI and neuropsychological performance were found after the correction for multiple comparisons in any group. Our results suggest that PPI deficits in schizophrenia patients may not contribute to the cognitive deficits typical of that illness, at least in patients with a non-significant PPI decrease.


Gray matter (GM) volume deficits have been described in patients with schizophrenia (Sz) and bipolar disorder (BD), but to date, few studies have directly compared GM volumes between these syndromes with methods allowing for whole-brain comparisons. We have used structural magnetic resonance imaging (MRI) and voxel-based morphometry (VBM) to compare GM volumes between 38 Sz and 19 BD chronic patients. We also included 24 healthy controls. The results revealed a widespread cortical (dorsolateral and medial prefrontal and precentral) and cerebellar deficit as well as GM deficits in putamen and thalamus in Sz when compared to BD patients. Besides, a subcortical GM deficit was shown by Sz and BD groups when compared to the healthy controls, although a putaminal reduction was only evident in the Sz patients. In this comparison, the BD patients showed
a limited cortical and subcortical GM deficit. These results support a partly different pattern of GM deficits associated to chronic S2 and chronic BD, with some degree of overlapping.


To date, few studies have addressed the relationship between brain structure alterations and responses to atypical antipsychotics in schizophrenia. To this end, in this study, magnetic resonance imaging (MRI) and voxel-based morphometry (VBM) were used to assess the relationship between the brain volumes of gray (GM) and white (WM) matters and the clinical response to risperidone or olanzapine in 30 schizophrenia patients. In comparison with healthy controls, the patients in this study showed a bilateral decrease in the anterior medial cerebellar hemispheres, the rectal gyrus and the insula, together with bilateral increases in GM in the basal ganglia. Both patient groups had a significantly smaller volume of WM in a region encompassing the internal and external capsules as compared to the controls. We found an inverse association between striatal size and the degree of clinical improvement, and a direct association between the degree of insular volume deficit and its improvement. The non-responder patient group showed a significant decrease in their left rectal gyrus as compared with the responder group. This study reveals a pattern of structural alterations in schizophrenia associated with the response to risperidone or olanzapine.


While the impact of mentally ill patients’ perceptions of their key relatives’ expressed emotion is well examined with regard to relapse, there is a paucity of evidence concerning the impact on their key relatives’ burden. The present study aims to evaluate the relative prognostic value of expressed and perceived emotion on caregivers’ stress outcome within a 3-year follow-up period. Yearly follow-up data of the key relatives of 16 first-hospitalized schizophrenic and 34 depressed patients were available including expressed and perceived emotion and different dimensions of caregivers’ stress outcome: objective and subjective burden, well-being, psychological symptoms and subjective quality of life. Multiple linear regression analyses were computed to assess the relative impact of expressed and perceived emotion. All dimensions of burden were significantly and consistently correlated with caregivers’ expressed emotion and patients’ perceived criticism on the bivariate level. On the multivariate level, however, expressed criticism appeared to be the most relevant predictor, followed by perceived resignation. Data indicate that the impact of the patients’ perceived criticism on caregivers’ stress outcome is limited. More attention should be paid to patients’ perceived resignation which may be an unidentified stress contributor for caregivers so far.


While neuroticism has been intensely investigated in caregivers of patients with serious somatic disorders, studies in caregivers of patients with mental illness are lacking. Additionally, most studies are cross-sectional not allowing conclusions about long-term effects of personality factors. The present study examines the impact of personality factors on the course of subjective burden and psychological well-being by a mediational model in a sample of caregivers of first hospitalized patients with schizophrenia or depression within a 2-year follow-up period. At baseline, 83 caregivers
could be enrolled in the study, the drop-out rate was about 23% at 2-year follow-up. Personality factors were assessed by the German version of the NEO-FFI (Borstenau and Costa 1993) only at baseline. At each follow-up, subjective burden was assessed by the FBQ (Moller-Leimkuhler acc. to Pai and Kapur (Brit J Psychiat 138:332-335, 1981)), and psychological well-being by the SCL-90 R (Derogatis in SCL-90-R, administration, scoring and procedures. Manual for the r(revised) version. John Hopkins University School of Medicine, Baltimore, 1977). Among the personality factors, neuroticism turned out to be the most relevant predictor of subjective burden and self-rated symptoms, showing direct as well as indirect effects. The direct effects on caregivers’ mental health were mediated to a considerable amount by subjective burden. The mediational model was stable across time and even revealed increasing indirect effects of neuroticism. Caregivers’ neuroticism as a dispositional trait plays a crucial role in the course of the stress process. As neuroticism is associated with perceptual distortion, the latter should be targeted by long-term family interventions in order to reduce subjective burden and enhance mental health of the caregivers.


Proof of efficacy of a psychotropic medicinal product is the key point of clinical psychopharmacology. This especially concerns the licensing of a new compound, but apart from this special case, lots of efficacy questions need to be answered in clinical psychopharmacology, such as, e.g. the question of the efficacy of a combination therapy. The methodology of the scientific proof of efficacy has already had a long tradition and has been developed further in the recent past under different aspects. Especially the double-blind randomised parallel group comparison has been developed as a design of highest methodological standard. However, often designs have their place and justification under certain conditions and in relation to certain questions. Although in the recent past, with the over-emphasis of so-called effectiveness studies, the inherent methodological limitations of these studies have not been addressed properly (Moller in Eur Arch Psychiatry Clin Neurosci 258:257-270, 2008), which in consequence devaluated the scientific merits of the classical double-blind randomised control group study designs in the view of those colleagues, who are not that experienced in study design issues. Therefore, it seems to be timely and necessary to review the principle standards and problems concerning the proof of efficacy in clinical psychopharmacology.


Given the limited explanatory power of the available neurobiological findings, results of long-term follow-up studies should still be considered as one criterion among others in the development of psychiatric classification systems regarding schizophrenia and affective disorders. A total of 323 first hospitalized inpatients of the Psychiatric Department of the University Munich were recruited at index time and followed up after 15 years. The full follow-up evaluation including several standardized assessment procedures (AMDP, PANSS, SANS, DAS, GAS) could be performed in 197 patients. The patients originally diagnosed according to ICD-9 were re-diagnosed according to ICD-10 and DSM-IV, using SCID among others. Schizophrenic patients had a much poorer outcome than affective or schizoaffective patients in terms of negative syndrome, deficit syndrome, psychosocial impairments and GAS results, and a higher prevalence of a chronic course. The logistic regression analyses performed to find optimized predictor combinations for the prognosis of a chronic course found, for example, the total Strauss-Carpenter Scale score, male gender and several other psychopathological syndromes to be relevant predictors. The findings reflect some long-term related validity for the differentiation between schizophrenia and affective disorders. The Strauss-Carpenter
Scale, male gender as well as several psychopathological syndromes are the most relevant predictors for chronicity.


Psychopharmacotherapy should now be regulated in the sense of evidence-based medicine, as is the case in other areas of clinical treatment in medicine. In general this is a meaningful development, which principally will have a positive impact on routine health care in psychiatry. But several related problems should not be ignored. So far consensus on an internationally accepted evidence graduation could not be reached due to several difficulties related to this. For example, focussing on the results of meta-analyses instead of considering relevant single studies results in a decision-making logic which is in conflict with the rationale applied by drug authorities in the licensing process. Another example is the relevance of placebo-controlled trials: if randomized placebo-controlled phase-III studies are prioritized in the evidence grading, the evidence possibly deviates too far from the conditions of routine clinical care due to the special selection of patients in those studies. However, a grading primarily based on active comparator trials could lead to wrong conclusions about efficacy. This concerns especially the so-called "effectiveness" studies and other forms of phase-IV studies with their less restrictive methodological rigidity. Attempts to regulate psychopharmacotherapy in the sense of evidence-based medicine come closer to their limits the more complex the clinical situation and the respective decision-making logic are. Even in times of evidence-based medicine a large part of complex clinical decision-making in psychopharmacotherapy still relies more on clinical experience and a consensus on clinical experience, traditions and belief systems than on results of efficacy oriented phase-III and effectiveness-oriented phase-IV clinical studies.


The mini-mental state examination (MMSE) has been widely used as a screening instrument for cognitive disorders. Age, schooling and many other sociodemographic and health variables may be associated with a worse performance on the MMSE. The objectives of this study were to investigate the distribution of MMSE percentiles in a large Brazilian community-based elderly sample, divided according to age and schooling, and to evaluate the impact of sociodemographic and health variables on groups of elderly people with lower cognitive performance. The MMSE was applied to a sample of 2,708 adults, aged 60 years and older. Of this population, 1,563 individuals were living in the city of Sao Paulo, while 1,145 were living in the city of Ribeirao Preto. The subjects were divided into six groups according to the amount of schooling that they had received (no formal education, 1-4 and >/=5 years) and age (<75 and >/=75 years old). To each one of the subgroups a stepwise logistic regression was applied, considering the following dependent variable: subjects who scored under or above the 15th percentile on MMSE. High scores on a depression scale, high scores on a memory complaints scale and low socio-economic levels were associated with poorer performance on the MMSE. Being currently employed and being married were related to higher scores on the test. Many sociodemographic and health variables can influence MMSE performance, with impacts depending on age and schooling. Clinicians and primary care physicians should pay attention to variables that may be associated with worse cognitive performance.


The genetic factors determining the progression of prodromal syndromes to first episode schizophrenia have remained enigmatic to date. In a unique prospective multicentre trial, we assessed whether variants at the D-amino acid oxidase activator (DAOA)/G72 locus influence progression to psychosis. Young subjects with a prodromal syndrome were observed prospectively for up to 2 years to assess the incidence of progression to schizophrenia or first episode psychosis. Of the 82 probands with a prodromal syndrome, 21 probands experienced progression to psychosis within the observation period. Assessment of nine common variants in the DAOA/G72 locus yielded two variants with the predictive value for symptom progression: all four probands with the rs1341402 CC genotype developed psychosis compared with 17 out of 78 probands with the TT or CT genotypes (chi2 = 12.348; df = 2; p = 0.002). The relative risk for progression to psychosis was significantly increased in the CC genotype: RR = 4.588 (95% CI = 2.175-4.588). Similarly, for rs778294, 50% of probands with the AA genotype, but only 22% of probands with a GG or GA genotype progressed to psychosis (chi2 = 7.027; df = 2; p = 0.030). Moreover, haplotype analysis revealed a susceptibility haplotype for progression to psychosis. This is one of the first studies to identify a specific genetic factor for the progression of prodromal syndromes to schizophrenia, and further underscores the importance of the DAOA/G72 gene for schizophrenia.


Studies using diffusion tensor imaging (DTI) have shown multifocal reduction in anisotropy of white matter fibre tracts in schizophrenia, and a few of these also suggest changes in apparent diffusion coefficient (ADC). In this study, we assessed ADC in 18 patients with schizophrenia and 18 healthy controls using a voxel-based approach. We did not find evidence of statistically significant changes in ADC in either direction at P < 0.05 (FDR corrected) using different smoothing filter sizes; only at an uncorrected threshold of P < 0.001 did we find an increase in a small right prefrontal area close to our previous FA finding. Our findings therefore do not support ADC changes to be a marker of white matter or grey matter abnormalities in schizophrenia. Changes in other parameters like fractional anisotropy (FA) might be a more sensitive indicator of white matter pathology in this disorder.


The purpose of the present study was to explore 5HT1A-mediated cortisol release in major depressive disorder (MDD) patients in order to determine whether the degree of 5HT1A-receptor sensitivity can predict response to treatment with selective serotonin reuptake inhibitors (SSRIs). We examined whether the sensitivity of the 5HT1A receptor, as measured by the difference in salivary cortisol levels immediately before and 90 min following the administration of a single dose of the 5HT1A-selective agonist buspirone, predicted treatment outcome following an 8-week, fixed-dose, open trial of the SSRI escitalopram in 17 outpatients with MDD. Change in cortisol levels before and 90 min after the administration of buspirone were not found to predict treatment outcome, whether defined as clinical response (50% or greater reduction in symptom severity), or remission of symptoms. In conclusion, in the present study, we did not find that the change in salivary cortisol levels following the administration of a 5HT1A-selective agonist predicted treatment outcome following an 8-week, fixed-dose, open-label trial of the SSRI escitalopram among outpatients with
MDD. Although the 5HT1A-desensitization hypothesis is still a valid one, the results of the present study could not provide any evidence in support.


The purpose of this analysis was to explore the potential role of anxious MDD as a treatment predictor and moderator in major depressive disorder (MDD) using a large escitalopram clinical trial dataset. Individual patient-level data from 13 double-blinded, randomized, controlled trials in patients with MDD were pooled. Both univariate, last observation carried forward (LOCF) analyses and repeated measurements analyses without imputation (MMRM) were carried out for change in symptom scores, response and remission rates. Of 3,919 patients, 48.0% were classified as having anxious MDD depression (HAMD) somatization/anxiety subscale score >/=7 at baseline. Patients with anxious MDD were less likely to report symptom improvement on some outcome measures than patients without anxious MDD (predictor analysis). Specifically, the difference in response rates for patients with vs. patients without anxious MDD according to the MADRS (55.6% vs. 57.7%, respectively) was not statistically different. However, the difference in remission rates for patients with versus without anxious MDD according to the MADRS (37.6% vs. 44.1%, respectively) was statistically significant. Escitalopram was more effective than placebo, and as effective as the SSRIs and SNRIs, in the treatment of anxious MDD. The present analysis provides some evidence that the presence of an anxious MDD subtype is a predictor of poor response. There was no difference in the response to treatment of patients with or without anxious MDD to escitalopram, SSRIs, or SNRIs. The present analysis did not support the notion that SNRIs are more effective than escitalopram in the treatment of anxious MDD, nor was there evidence to support treatment moderating effects for anxious MDD.


In the present study, we examined several metabolic parameters in a group of 19 acutely depressed inpatients with major depression (DSM-IV) at baseline and investigated their development after 4 weeks of antidepressant treatment with reboxetine (8-12 mg per day). We performed oral glucose tolerance tests and additionally assessed free saliva cortisol and post-dexamethasone cortisol levels, as well as whole cholesterol, HDL- and LDL-cholesterol, triglycerides, free fatty acids, waist and hip circumference, heart rate, systolic and diastolic blood pressure. Furthermore, we evaluated the incidence of a metabolic syndrome and investigated the metabolic changes in depressed patients with and without a metabolic syndrome. We found 42.1% of patients to fulfill the criteria for a metabolic syndrome. Overall, reboxetine was well tolerated with essentially no side effects during the observation period. A 4-week treatment with reboxetine showed a beneficial effect on several metabolic parameters that was independent from treatment outcome and could therefore theoretically be attributed to the pharmacological profile of the drug. Due to the preliminary character of the present investigation, no conclusions about the clinical efficacy of reboxetine can be drawn.

The aim of the study was to report on the clinical utility of naturalistic adjunctive treatment with valproate (VPA) in a group of panic disorder (PD) patients with comorbid bipolar disorder (BD) or otherwise resistant to antidepressants. The hypothesis was that these patients might not respond because of coexisting low-grade mood instability and adjunctive VPA treatment might ameliorate PD symptoms. A group of 47 patients with lifetime comorbid BD (n = 35, 74.5%) or otherwise resistant to antidepressants (n = 12, 25.6%), from a population of 326 consecutive outpatients with PD-Agoraphobia evaluated and treated at the Psychiatric Institute of the University of Pisa from 1991 to 1995, and followed for a period of 3 years. All patients were evaluated at baseline and at least every 2 months by means of an intensive interview including semi-structured and structured instruments (SCID, Life-Up, and Panic Disorder/Agoraphobia Interview). Mean dosage was 687 (SD = 234) mg/day (min 400, max 1,500 mg/day). Adjunctive treatment with VPA was well tolerated by all subjects, and there was no treatment interruption because of side effects or adverse events. All antidepressant-resistant subjects and 31 of 35 (88.6%) patients with bipolar comorbidity achieved symptomatological remission. During the observation period, 7 (58.3%) among resistant subjects and 17 (48.6%) of bipolar patients had a relapse of panic disorder after remission. Survival analysis of remission durations and onset relapses for PD and Agoraphobia did not show significant differences between the two groups. Relapses of Agoraphobia were less frequent and more delayed than those for panic. According to the results, VPA seems to be an effective and a well-tolerated adjunctive treatment in PD patients who were resistant to antidepressant therapy or had BD in comorbidity. The results of the study support the hypothesis of resistance to antidepressant treatment being related to mood instability.


Suicidal behavior and mood disorders are one of the world's largest public health problems. The biological vulnerability for these problems includes genetic factors involved in the regulation of the serotonergic system and stress system. The hypothalamic-pituitary-adrenal (HPA) axis is a neuroendocrine system that regulates the body's response to stress and has complex interactions with brain serotonergic, noradrenergic and dopaminergic systems. Corticotropin-releasing hormone and vasopressin act synergistically to stimulate the secretion of ACTH that stimulates the biosynthesis of corticosteroids such as cortisol from cholesterol. Cortisol is a major stress hormone and has effects on many tissues, including on mineralocorticoid receptors and glucocorticoid receptors in the brain. Glucocorticoids produce behavioral changes, and one important target of glucocorticoids is the hypothalamus, which is a major controlling center of the HPA axis. Stress plays a major role in the various pathophysiological processes associated with mood disorders and suicidal behavior. Serotonergic dysfunction is a well-established substrate for mood disorders and suicidal behavior. Corticosteroids may play an important role in the relationship between stress, mood changes and perhaps suicidal behavior by interacting with 5-HT1A receptors. Abnormalities in the HPA axis in response to increased levels of stress are found to be associated with a dysregulation in the serotonergic system, both in subjects with mood disorders and those who engage in suicidal behavior. HPA over-activity may be a good predictor of mood disorders and perhaps suicidal behavior via abnormalities in the serotonergic system.

The present study examined data on symptom patterns in the week prior to admission for suicide attempt, in a nationwide representative sample of patients. Socio-demographic, clinical, and treatment data was gathered for 1,547 patients admitted over a 12-day index period during the year 2004 to 130 public and 36 private psychiatric facilities in Italy. Patients were evaluated in terms of whether they had been admitted for having attempted suicide or not. A detailed checklist was used to assess symptom pattern at admission; diagnoses were based on ICD-10 categories. Two-hundred thirty patients (14.8%) in the sample had been admitted for suicide attempt. Patients with depression or with personality disorders were more frequently observed among suicide attempters. First-contact patients were significantly more likely to have been admitted after a suicide attempt, the only exception being individuals with bipolar disorder, manic phase. No diagnosis was statistically related to admission after suicide attempt, once symptoms pattern at admission had been accounted for. Disordered eating behavior, depressive symptoms, substance abuse, and non-prescribed medication abuse were positively related to attempted suicide, as were any traumatic events in the week prior to admission; symptoms of psychosis (hallucinations/delusions) and lack of self-care were negatively associated with suicide attempt admission. Greater attention to symptoms immediately preceding or concomitant with admission after a suicide attempt can be a key factor in establishing the best treatment plan and discharge strategy, the most effective community-service referral, and targeted intervention programmes for patients hospitalized for a suicide attempt.


The Study aimed to assess clinical and social outcomes following involuntary admissions over 1 year and identify socio-demographic and clinical patient characteristics associated with more or less favourable outcomes. Seven hundred and seventy-eight involuntary patients admitted to one of 22 hospitals in England were assessed within the first week after admission and at 1 month, 3 month and 12 month follow-ups. Outcome criteria were symptom levels, global functioning, objective social outcomes, and subjective quality of life (SQOL). Baseline characteristics and patients' initial experience were tested as predictors. Symptom levels and global functioning improved moderately. Objective social outcomes showed a small, but statistically significant deterioration, and SQOL a small, but significant improvement at 1 year. In multivariable analyses, admission due to risk to oneself and receiving benefits predicted poorer symptom outcomes. Female gender and higher perceived coercion were associated with better objective social outcomes, whilst higher initial satisfaction with treatment predicted more positive SQOL at follow-ups. Over a 1-year period following involuntary hospital admission, patients on average showed only limited health and social gains. Different types of outcomes are associated with different predictor variables. Patients' initial experience of treatment, in the form of perceived coercion or satisfaction with treatment, has predictive value for up to a year following the admission.


The objective of this study is to examine the association of psychological distress to high-sensitivity C-reactive protein (hsCRP) levels and to examine the potential mediating role of health behaviours and pathophysiological factors. A total of 883 (393 men and 490 women) subjects, aged 36-56 years, participated in a population-based, cross-sectional study from 1997 to 1998 in Piekamaki, Finland. Various clinical, biochemical and behavioural factors were measured, including hsCRP concentration. Psychological distress was measured using the 12-item General Health Questionnaire (GHQ-12). Subjects with low psychological distress (0 points in GHQ-12) were younger and more physically
active, and their mean hsCRP level was lower when compared to subjects with medium (1-3 points) or high (4-12 points) psychological distress (1.26 +/- 1.36, 1.53 +/- 1.75 and 1.70 +/- 1.68 mg/l, respectively, P for linearity = 0.003). Psychological distress was also associated with high relative cardiovascular risk (hsCRP >3.00 mg/l). After adjusting for gender, age, BMI, smoking, use of alcohol and leisure time physical activity, odds ratios for hsCRP >3.00 mg/l in the groups that had medium and high psychological distress were 1.32 (95% CI: 0.81-2.16) and 1.79 (95% CI: 1.05-3.04), respectively, compared with the low distress group (P for linearity 0.032). Psychological distress was associated with elevated hsCRP levels representing high relative cardiovascular risk. This association remained after adjusting for health behaviours and pathophysiological factors, supporting a direct, physiological link between psychological distress and inflammation. CRP could be an important pathophysiological mechanism through which psychological factors are associated with cardiovascular disease.


Although classical and atypical antipsychotics may have different neurotoxic effects, their underlying mechanisms remain to be elucidated, especially regarding neuroglial function. In the present study, we compared the atypical antipsychotic risperidone (0.01-10 muM) with the typical antipsychotic haloperidol (0.01-10 muM) regarding different aspects such as glutamate uptake, glutamine synthetase (GS) activity, glutathione (GSH) content, and intracellular reactive oxygen species (ROS) production in C6 astroglial cells. Risperidone significantly increased glutamate uptake (up to 27%), GS activity (14%), and GSH content (up to 17%). In contrast, haloperidol was not able to change any of these glial functions. However, at concentration of 10 muM, haloperidol increased (12%) ROS production. Our data contribute to the clarification of different hypothesis concerning the putative neural responses after stimulus with different antipsychotics, and may establish important insights about how brain rewiring could be enhanced.


There are several hypotheses on functional neuronal networks that modulate mood states and which might form the neuroanatomical basis of bipolar disorder. The thalamus has been reported to be a key structure within the circuits that modulate mood states and might thus play an important role within the aetiology of the bipolar affective disorder. Nevertheless, structural brain imaging studies on the thalamus volume of bipolar patients have shown heterogeneous results. Using structural MRI scanning, we compared the thalamus volume of 41 euthymic bipolar patients to the thalamus volume of 41 well-matched healthy controls. Taking the concomitant medication as a co-variable within the patient group, the analysis of variance revealed a significantly smaller relative volume of the right thalamus in patients not treated with lithium when compared with healthy controls. In contrast, there are no significant differences concerning the thalamus volume between all euthymic bipolar patients and healthy controls. The study only shows findings of a transverse section. No longitudinal analysis was performed. More detailed information on patients' pharmacological histories could not be obtained. In conclusion, this result may be interpreted as an indication of the impact of the thalamus in the pathogenesis of the bipolar I disorder and emphasises the need for further longitudinal studies in bipolar patients with special attention paid to the concomitant medication, in particular to the role of lithium.
Melatonin secretion is synchronized to the sleep/wake cycle and has been suggested to have somnogenic properties. Sleep/wake cycle disruption and alterations in the secretory pattern of melatonin is present in various psychiatric disorders. The objective of this study was to investigate the sleep architecture and the presence of depression in individuals with low endogenous melatonin levels. The study included 16 participants (mean age 30.3 +/- 14.9 years). The first night of testing included psychiatric evaluation followed by melatonin secretion profile evaluation by Dim Light Melatonin Onset test and then standard montage polysomnographic testing. On the second night, only polysomnographic testing was carried out with an imposed sleep period of 8 h. Low endogenous melatonin secretors (LEMS) showed no discernible peaks in melatonin secretion compared to normal secretors (controls). LEMS demonstrated significant alterations in rapid eye movement sleep but not in non-rapid eye movement sleep along with poor sleep initiation and quality compared to controls. 55.6% of the low melatonin secretors group presented with subsyndromal depression. Melatonin has significant bearing on sleep architecture and a lack of melatonin may desynchronize endogenous rhythms allowing subsyndromal depression to manifest.

The purpose of the present study was to establish a short paradigm for the examination of classical aversive conditioning processes for application in patients with anxiety disorders. We measured behavioral, autonomic and neural correlates of the paradigm in healthy subjects, applying functional magnetic resonance imaging (fMRI) and measurement of skin conductance. Therefore, neutral visual stimuli were paired with an unpleasant white noise as unconditioned stimulus. Twenty healthy subjects performed three experimental phases of learning: familiarization, acquisition and extinction. Subjective ratings of valence and arousal after each phase of conditioning as well as skin conductance measurement indicated successful conditioning. During acquisition, fMRI results showed increased activation for the conditioned stimulus (CS+) (unpaired) when compared with the non-conditioned stimulus (CS-) in the right amygdala, the insulae, the anterior cingulate cortex and the parahippocampal gyrus, all regions known to be involved in emotional processing. In addition, a linearly decreasing activation in the right amygdala/hippocampus for the CS- across the acquisition phase was found. There were no significant differences between CS+ and CS- during extinction. In conclusion, the applicability of this paradigm for the evaluation of neural correlates in conditioning and extinction processes has been proven. Thus, we present a promising paradigm for the examination of the fear-circuit in patients with anxiety disorders and additionally effects of cognitive-behavioral interventions.

Previous studies pointed out the high prevalence of the metabolic syndrome among patients with bipolar disorder and major depression. A link between depression and a metabolic syndrome remains in dispute despite these studies. This study was conducted to evaluate the occurrence of the metabolic syndrome in depressive inpatients, to analyze the association between the severity of depression and the metabolic syndrome and to screen specific laboratory values in the course of depressive illness. 60 acute depressive patients were recruited for the study and underwent psychometric testing [21-item Hamilton Depression Rating Scale (HAMDS), Beck Depression Inventory.
(BDI), Clinical Global Impression Scale (CGI) and Global Assessment of Functioning Scale (GAF)] and a metabolic syndrome screening using the modified criteria of the American National Cholesterol Education Program (NCEP) Treatment Panel III (ATPIII). Moreover, CRP, cholesterol, HDL-cholesterol, fasting glucose, triglyceride and leptin levels were measured. 42 patients were reexamined in state of (partial) remission. Depression was reassessed using the 21-item HAMD, and laboratory values were analyzed a second time. 25% of the depressive patients fulfilled the criteria of metabolic syndrome (MS+). Only in the MS+ group, a positive correlation between triglyceride blood levels and severity of depression became evident as well in the state of acute depression as in the state of remission. In the group of patients without metabolic syndrome, laboratory values were not associated with severity of depression. An association between metabolic parameters and the course of depression could only be detected in the group of patients with metabolic syndrome. These findings suggest that, in these patients, a beneficial outcome of depressive illness may improve the metabolic situation.


Mismatch negativity (MMN) is an auditory event-related potential indicating auditory sensory memory and information processing. The present study tested the hypothesis that chronic cannabis use is associated with deficient MMN generation. MMN was investigated in age- and gender-matched chronic cannabis users (n = 30) and nonuser controls (n = 30). The cannabis users were divided into two groups according to duration and quantity of cannabis consumption. The MMNs resulting from a pseudorandomized sequence of 2 x 900 auditory stimuli were recorded by 32-channel EEG. The standard stimuli were 1,000 Hz, 80 dB SPL and 90 ms duration. The deviant stimuli differed in duration (50 ms) or frequency (1,200 Hz). There were no significant differences in MMN values between cannabis users and nonuser controls in both deviance conditions. With regard to subgroups, reduced amplitudes of frequency MMN at frontal electrodes were found in long-term (>/=8 years of use) and heavy (>/=15 joints/week) users compared to short-term and light users. The results indicate that chronic cannabis use may cause a specific impairment of auditory information processing. In particular, duration and quantity of cannabis use could be identified as important factors of deficient MMN generation.


Clinical trials with several measurement occasions are frequently analyzed using only the last available observation as the dependent variable [last observation carried forward (LOCF)]. This ignores intermediate observations. We reanalyze, with complete data methods, a clinical trial previously reported using LOCF, comparing placebo and five dosage levels of moclobemide in the treatment of outpatients with panic disorder to illustrate the superiority of methods using repeated observations. We initially analyzed unprovoked and situational, major and minor attacks as the four dependent variables, by repeated measures maximum likelihood methods. The model included parameters for linear and curvilinear time trends and regression of measures during treatment on baseline measures. Significance tests using this method take into account the structure of the error covariance matrix. This makes the sphericity assumption irrelevant. Missingness is assumed to be unrelated to eventual outcome and the residuals are assumed to have a multivariate normal distribution. No differential treatment effects for limited attacks were found. Since similar results were obtained for both types of major attack, data for the two types of major attack were combined. Overall downward linear and negatively accelerated downward curvilinear time trends were found. There were highly significant treatment differences in the regression slopes of scores during treatment on baseline observations. For major attacks, all treatment groups improved over time. The flatter regression slopes, obtained with higher doses, indicated that higher doses result in uniformly
lower attack rates regardless of initial severity. Lower doses do not lower the attack rate of severely ill patients to those achieved in the less severely ill. The clinical implication is that more severe patients require higher doses to attain best benefit. Further, the significance levels obtained by LOCF analyses were only in the 0.05-0.01 range, while significance levels of <0.00001 were obtained by these repeated measures analyses indicating increased power. The greater sensitivity to treatment effect of this complete data method is illustrated. To increase power, it is often recommended to increase sample size. However, this is often impractical since a major proportion of the cost per subject is due to the initial evaluation. Increasing the number of repeated observations increases power economically and also allows detailed longitudinal trajectory analyses.


This paper proposes a new cognitive model to explain the aetiology of delusions irrespective of diagnosis and/or phenomenology. The model hypothesises the influence of two processes in the formation and maintenance of delusions; (i) impaired perceptual abilities, particularly affect perception, which fosters the encoding of (ii) idiosyncratic semantic memories, especially those with an affective/self-referential valence. Previous research has established that schizophrenia patients with delusions have impaired semantic memory function. In the current paper we sought to provide evidence for (ii) abnormal semantic processing in persons with delusions with an alternative aetiology. Performance of four cases with a significant delusion post a traumatic brain injury was examined on a broad range of semantic memory tests. Overall semantic processing was impaired in the four cases relative to a normative healthy control sample. Cases performed better on tasks which required categorical identification, relative to the novel production of semantic information, which was poor in all four of the cases. These data offer preliminary evidence for our hypothesis of impaired semantic processing in persons with delusions. Findings will need to be empirically verified in larger sample groups and in those with alternative aetiologies.


The interplay of psychotic and affective symptoms is a crucial challenge in understanding the pathogenesis of psychosis. In this study, we analyzed the interplay between two subclinical psychosis symptoms dimensions, and one depression symptoms dimension, using longitudinal data from Zurich. The Zurich study started in 1979 with a representative sample of 591 participants who were aged 20/21. Follow-up interviews were conducted at age 23, 28, 30, 35, and 41. The psychiatric symptoms were assessed with a semi-structured interview and the SCL 90-R. In this study, we analyzed three SCL-90-R subscales: the depression symptoms dimension and two distinct symptoms dimensions of subclinical psychosis, one representing a schizophrenia nuclear symptom dimension, the other representing a schizotypal symptoms dimension. Modeling was done with hybrid latent growth models, thereby including simultaneous and cross-lagged effects. The interplay between the two subclinical psychosis symptoms dimensions and the depression symptoms dimension includes several intertwined pathways. The schizotypal symptoms dimension has strong direct effects on the schizophrenia nuclear symptoms dimension, but also on the depression symptoms dimension. The latter has for its part an effect on the schizophrenia nuclear symptoms dimension. The main driving force within the dynamic interplay between depression and psychosis symptoms is a schizotypal symptoms dimension, which represents social and interpersonal deficiencies, ideas of reference,
suspiciousness, paranoid ideation, and odd behavior. It does not only directly influence subclinical nuclear schizophrenia symptoms but also the symptoms of depression.


Indicated prevention is currently one of the most promising approaches to fight the individual and societal burden associated with psychosis and particularly schizophrenia. The number of studies is still limited, yet encouraging results have been reported from pharmacological and psychotherapeutic trials. Furthermore, it has become clear that persons characterized by the at-risk criteria are already ill and do not only need preventive intervention but also treatment. As is indicated by a recent study successfully using omega-3 fatty acids for both purposes, it may be promising to develop and investigate interventions especially for the at-risk state, independent of their effectiveness in manifest disease states. An overview on the current findings and ongoing research in this area is provided.


Disgust may be a key emotion and target for psychotherapeutic interventions in borderline personality disorder (BPD) and posttraumatic stress disorder (PTSD) at explicit and implicit-automatic levels. However, automatically activated disgust reactions in individuals with these disorders have not been studied. Disgust and its correlation with childhood abuse were assessed in women with BPD, but without PTSD; women with PTSD, but without BPD; women with BPD and PTSD; and healthy women. Disgust sensitivity, anxiety and depression were measured by self-report. Implicit disgust-prone (relative to anxiety-prone) self-concept was assessed using the Implicit Association Test. Women with BPD and/or PTSD reported more disgust sensitivity than controls. The implicit self-concept among patients was more disgust-prone (relative to anxiety-prone) than in controls. Women with BPD, with PTSD, or BPD and PTSD did not differ significantly in self-reported disgust levels or implicit disgust-related self-concept. Among women with BPD and/or PTSD, current psychiatric comorbidity (major depression, anxiety disorder, eating disorder, or substance-related disorder) did not affect disgust-related variables. More severe physical abuse in childhood was associated with a more anxiety-prone (less disgust-prone) implicit self-concept. Independent of psychiatric comorbidity, disgust appears to be elevated at implicit and explicit levels in trauma-related disorders. Psychotherapeutic approaches to address disgust should take implicit processes into account.


Meritocratic worldviews that stress personal responsibility, such as the Protestant ethic or general beliefs in a just world, are typically associated with stigmatizing attitudes and could explain the persistence of mental illness stigma. Beliefs in a just world for oneself ("I get what I deserve"), however, are often related to personal well-being and can be a coping resource for stigmatized individuals. Despite these findings in other stigmatized groups, the link between worldviews and the stigma of psychiatric disorders is unknown. We measured just world beliefs for self and others as well as endorsement of the Protestant ethic in 85 people with schizophrenia, schizoaffective or affective disorders and 50 members of the general public. Stigmatizing attitudes toward people with mental illness (perceived responsibility, perceived dangerousness, general agreement with negative
stereotypes) were assessed by self-report. Using a response-latency task, the Brief Implicit Association Test, we also examined guilt-related implicit negative stereotypes about mental illness. We found a consistent positive link between endorsing the Protestant ethic and stigmatizing self-reported attitudes in both groups. Implicit guilt-related stereotypes were positively associated with the Protestant ethic only among members of the public. Among people with mental illness, stronger just world beliefs for self were related to reduced self-stigma, but also to more implicit blame of persons with mental illness. The Protestant ethic may increase (self-)stigmatizing attitudes; just world beliefs for oneself, on the other hand, may lead to unexpected implicit self-blame in stigmatized individuals. Public anti-stigma campaigns and initiatives to reduce self-stigma among people with mental illness should take worldviews into account.


We performed the factor analysis of the Polish version of the Hypomania Check List (HCL-32) scale and assessed the utility of HCL-32 in discriminating patients with treatment-resistant and treatment non-resistant depression. The study included 1,051 patients with single or recurrent depressive episode among which 569 met the criteria for treatment-resistant depression. The Polish version of HCL-32 was employed to all patients. The Cronbach's alpha for entire scale was 0.93 which indicates high degree of consistency. The factor analysis of the scale yielded three factors with item loadings of 0.4 or more. Factor 1, comprising ten items connected with elevated mood and increased activity explained more than half of total variance, Factor 2 (two items) was connected with sexual activity, and factor 3 (three items) with irritability. The mean score of HCL-32 was significantly higher in treatment-resistant versus non-resistant depression (11.9 +/- 8.3 vs. 8.5 +/- 7.7, respectively, P < 0.001). Also, the percentage of patients having positive response to 14 or more items of the scale was significantly higher in treatment-resistant than in non-resistant depression (43.9 vs. 30.0%, respectively, P < 0.001). Therefore, using Polish version of HCL-32 we have confirmed the association between bipolarity and worse response to antidepressants in patients with mood disorders.


The pathogenesis, pathophysiology, and pharmacotherapy of sleep bruxism (SB) are still not fully understood. We investigated symptomatology, objective and subjective sleep and awakening quality of middle-aged bruxers compared with controls and acute effects of clonazepam 1 mg compared with placebo by polysomnography and psychometry. Twenty-one drug-free bruxers spent 3 nights in the sleep lab, 21 age- and sex-matched controls 2 nights. Clinically, bruxers exhibited deteriorated PSQI, SAS, SDS and IRLSSG measures, polysomnographically impaired sleep maintenance, increased movement time, stage shift index, periodic leg movements (PLM) and arousals and psychometrically deteriorated subjective sleep and awakening quality, evening/morning well-being, drive, mood, drowsiness, attention variability, memory, and fine motor activity. As compared with placebo, clonazepam significantly decreased the SB index in all patients (mean: -42 +/- 15%). Sleep efficiency, maintenance, latency, awakenings and nocturnal wake time, the stage shift index, S1, PLM, the arousal index, subjective sleep and awakening quality, and fine motor activity improved.

The interaction of psychopathological states and psychosocial functioning determine the long-term course of schizophrenia and its treatment. To be able to achieve this interplay better, exact assessment of psychosocial functioning is needed besides measurement of psychopathology. Using the Personal and Social Performance (PSP) Scale, examination of the association between psychosocial functioning and psychopathology was conducted in a sample of 103 patients with chronic schizophrenia. Rating instruments were in addition Global Assessment of Functioning Scale and Social and Occupational Functioning Assessment Scale, as well as Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression Scale, and Mini-ICF-APP-Rating for Mental Disorders (Mini-ICF-APP). Besides good psychometric properties for the PSP scale in this chronic sample, we found, as expected, significant associations between the two relevant outcome domains: results showed significant negative correlations between PSP and PANSS. Findings prove the close interplay between social functioning and psychopathology in the chronic course of schizophrenia.


Generalized anxiety disorder (GAD) is characterized by excessive and persistent worrying. Neural substrates of this disorder are insufficiently understood, which relates to functional as well as to structural brain abnormalities. Especially, findings on the neuroanatomy of GAD have been inconsistent and were predominantly derived from pediatric samples. Therefore, we studied adult patients. Thirty-one women (16 patients with GAD and 15 healthy control participants) underwent structural MRI scanning. Gray matter volumes for specific brain regions involved in worrying, anticipatory anxiety, and emotion regulation were analyzed by means of voxel-based morphometry. Relative to controls, patients with GAD had larger volumes of the amygdala and the dorsomedial prefrontal cortex (DMPFC). Moreover, patients' self-reports on symptom severity were positively correlated with volumes of the DMPFC and the anterior cingulate cortex. Patients with GAD show localized gray matter volume differences in brain regions associated with anticipatory anxiety and emotion regulation. This abnormality may represent either a predisposition for GAD or a consequence of disorder-specific behavior, such as chronic worrying. This issue should be addressed in future MRI studies.


To determine if NMDA receptor alterations are present in the cerebellum in schizophrenia, we measured NMDA receptor binding and gene expression of the NMDA receptor subunits in a post-mortem study of elderly patients with schizophrenia and non-affected subjects. Furthermore, we assessed influence of genetic variation in the candidate gene neuregulin-1 (NRG1) on the expression of the NMDA receptor in an exploratory study. Post-mortem samples from the cerebellar cortex of ten schizophrenic patients were compared with nine normal subjects. We investigated NMDA receptor binding by receptor autoradiography and gene expression of the NMDA receptor subunits NR1, NR2A, NR2B, NR2C and NR2D by in situ hybridization. For the genetic study, we genotyped the NRG1 polymorphism rs35753505 (SNP8NRG221533). Additionally, we treated rats with the antipsychotics haloperidol or clozapine and assessed cerebellar NMDA receptor binding and gene expression of subunits to examine the effects of antipsychotic treatment. Gene expression of the
NR2D subunit was increased in the right cerebellum of schizophrenic patients compared to controls. Individuals carrying at least one C allele of rs35753505 (SNP8NRG221533) showed decreased expression of the NR2C subunit in the right cerebellum, compared to individuals homozygous for the T allele. Correlation with medication parameters and the animal model revealed no treatment effects. In conclusion, increased NR2D expression results in a hyperexcitable NMDA receptor suggesting an adaptive effect due to receptor hypofunction. The decreased NR2C expression in NRG1 risk variant may cause a deficit in NMDA receptor function. This supports the hypothesis of an abnormal glutamatergic neurotransmission in the right cerebellum in the pathophysiology of schizophrenia.


Psychiatry in Germany is characterized by high relevance both individually and socioeconomically, and by the burden caused by mental disorders as lifelong diseases. This is comparable to most industrialized countries in the world. For Germany, the role of psychiatry in Nazi-Germany has to be critically discussed and still remains incompletely researched. Another more current focus has to be directed to attracting the most promising young students to the discipline. Psychiatry promises to profit especially from new approaches that combine scientific and clinical expertise in education and professional career.


Nightmares are defined as disturbing mental experiences that generally occur during REM sleep and often result in awakening. Whereas the number of publications addressing nightmare frequency and psychopathology, nightmare etiology and treatment is increasing rapidly in the last few years, nightmare content has been studied very rarely in a systematic way, especially in adults. The present study investigated nightmare frequency and the frequency of various nightmare topics in a representative German sample. The five most common themes were falling, being chased, paralyzed, being late, and the deaths of close persons. Even though several effects can be explained by the continuity hypothesis of dreaming, further research is needed to investigate the possible metaphoric relationship between nightmare topics like falling or being chased and waking-life stressors.


Animal experiments have shown that early developmental lesions of the entorhinal cortex lead, after a prolonged interval, to an enhanced mesolimbic dopamine release and an increased locomotor activity in rats. Hence, disturbed shape of the entorhinal cortex might indicate maturational abnormalities relevant for psychotic symptoms in schizophrenia. We used an automated surface-based MRI method to perform a region of interest analysis of entorhinal cortical surface area, folding and thickness in 59 patients with schizophrenia and 59 healthy controls. We postulated the entorhinal cortical surface area, folding index, and thickness to be significantly smaller in patients with schizophrenia. Additionally, we expected the complexity of the entorhinal cortical shape to be
associated with psychotic symptoms in schizophrenia. Our ROI analysis showed a significant thinner left entorhinal cortex. In addition, our data demonstrate a positive correlation between left entorhinal cortical surface area and folding index and severity of psychotic symptoms. In conclusion, we present new evidence for the involvement of the entorhinal cortex in the pathogenesis of schizophrenia. As cortical folding is a stable neuroanatomical parameter terminated in early neonatal stages, our data give reason to assume that the vulnerability to develop psychotic symptoms might be manifest at an early level of brain maturation.


The self-medication hypothesis attempts to explain the extraordinary high levels of cigarette smoking in schizophrenia; patients may smoke in an attempt to reduce their cognitive deficits, symptoms, or the side effects of antipsychotics. In a previous report, we detected beneficial performance in attention and working memory in patients with first-episode psychosis who smoked compared to non-smoking patients soon after stabilization. In the present study, we examine differences in the course of those deficits 12 months after the initiation of antipsychotic treatment. We also explore the association between smoking and symptoms and side effects of medication. Neuropsychological assessments were performed at baseline, month 6 and month 12 using a computerized battery that included measures of sustained attention (Continuous Performance Test CPT-O), selective attention (Stroop interference task) and working memory (CPT-XO). Patients met the criterion of fitting in the same smoking category throughout the study: non-smoker (n = 15; 0 cigarettes/day) and smoker (n = 26; >15 cigarettes/day). The non-smoking patients showed significant cognitive improvements, whereas smoking patients lost their superior baseline performance, which was probably obtained through nicotinic stimulation, at the 6- and 12-month assessments due to a static course of deficits. Smokers did not obtain any cognitive benefit after instauration of treatment and worsen their symptoms over the first year. These results suggest that smoking may constitute a marker of a more severe illness. Smoking was not associated with fewer extrapyramidal side effects. Smoking might improve attention and working memory to a similarly modest extent as atypical antipsychotics and could reflect an effort to ameliorate these cognitive dysfunctions previous to treatment instauration.


Few case series studies have addressed the issue of treatment response in patients with obsessive-compulsive disorder (OCD) and comorbid post-traumatic stress disorder (PTSD), and there are no prospective studies addressing response to conventional treatment in OCD patients with a history of trauma (HT). The present study aimed to investigate, prospectively, the impact of HT or PTSD on two systematic, first-line treatments for OCD. Two hundred and nineteen non-treatment-resistant OCD outpatients were treated with either group cognitive-behavioral therapy (GCBT n = 147) or monotherapy with a selective serotonin reuptake inhibitor (SSRI n = 72). Presence of HT and PTSD were assessed at intake, as part of a broader clinical and demographical baseline characterization of the sample. Severity and types of OCD symptoms were assessed with the Yale-Brown Obsessive-Compulsive Scale (YBOCS) and the Dimensional YBOCS (DYBOCS), respectively. Depression and anxiety symptoms were measured with the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI). Both treatments had 12-week duration. Treatment response was considered as a categorical [35% or greater reduction in baseline YBOCS scores plus a Clinical Global Impression-Improvement rating of better (2) or much better (1)] and continuous variable (absolute number
reduction in baseline YBOCS scores). Treatment response was compared between the OCD + HT group versus the OCD without HT group and between the OCD + PTSD group versus the OCD without PTSD group. Parametric and non-parametric tests were used when indicated. Data on HT and PTSD were available for 215 subjects. Thirty-eight subjects (17.67% of the whole sample) had a positive HT (OCD + HT group) and 22 subjects (57.89% of the OCD + HT group and 10.23% of the whole sample) met full DSM-IV criteria for PTSD. The OCD + HT and OCD without HT groups presented similar response to GCBT (60% of responders in the first group and 63% of responders in the second group, p = 1.00). Regarding SSRI treatment, the difference between the response of the OCD + HT (47.4%) and OCD without HT (22.2%) groups was marginally significant (p = 0.07). In addition, the OCD + PTSD group presented a greater treatment response than the OCD without PTSD group when treatment response was considered as a continuous variable (p = 0.01). The age when the first trauma occurred had no impact on treatment response. In terms of specific OCD symptom dimensions, as measured by the DYBOCS, OCD treatment fostered greater reductions for the OCD + PTSD group than for the OCD without PTSD group in the scores of contamination obsessions and cleaning compulsions, collecting and hoarding and miscellaneous obsessions and related compulsions (including illness concerns and mental rituals, among others). The OCD + PTSD group also presented a greater reduction in anxiety scores than the OCD without PTSD group (p = 0.003). The presence of HT or PTSD was not related to a poorer treatment response in this sample of non-treatment-resistant OCD patients. Unexpectedly, OCD patients with PTSD presented a greater magnitude of response when compared with OCD without PTSD patients in specific OCD symptom dimensions. Future studies are needed to clarify if trauma and PTSD have a more significant impact on the onset and clinical expression of OCD than on the conventional treatment for this condition, and whether OCD stemming from trauma would constitute a subtype of OCD with a distinct response to conventional treatment.


This study investigated gender differences in facial expression as a reaction to various emotional stimuli in two groups of schizophrenia patients. The first group consisted of hospitalized patients (22 men and 13 women) who were tested at three points in time. The second group consisted of outpatients (21 men, 8 women) who were tested at two points in time. In addition, the facial behaviour of two control groups was investigated (17 men and 12 women; 18 men and 14 women, respectively). Facial activity was videotaped, whilst participants watched emotion-eliciting video clips and participated in an emotion-inducing interview, and measured using the Facial Action Coding System. In agreement with our expectations, schizophrenia patients showed significantly less facial activity overall than healthy control participants. Contrary to expectations, however, female patients did not display more facial activity compared to male schizophrenia patients. This finding contrasts with those of healthy participants in previous studies where women tended to show more facial activity than men. It was further expected that in non-psychotic patients (i.e. outpatients), gender differences would be more clearly apparent and female schizophrenia patients would show considerably more facial activity than male patients, with findings more or less comparable to the gender differences found in healthy controls. However, no significant interaction was found between patient group (in- vs. outpatients) and gender. The different explanations for these findings are considered in this study.

Obstetric complications play a role in the pathophysiology of schizophrenia. However, the biological consequences during neurodevelopment until adulthood are unknown. Microarrays have been used for expression profiling in four brain regions of a rat model of neonatal hypoxia as a common factor of obstetric complications. Animals were repeatedly exposed to chronic hypoxia from postnatal (PD) day 4 through day 8 and killed at the age of 150 days. Additional groups of rats were treated with clozapine from PD 120-150. Self-spotted chips containing 340 cDNAs related to the glutamate system ("glutamate chips") were used. The data show differential (up and down) regulations of numerous genes in frontal (FR), temporal (TE) and parietal cortex (PAR), and in caudate putamen (CPU), but evidently many more genes are upregulated in frontal and temporal cortex, whereas in parietal cortex the majority of genes are downregulated. Because of their primary presynaptic occurrence, five differentially expressed genes (CPX1, NPY, NRXN1, SNAP-25, and STX1A) have been selected for comparisons with clozapine-treated animals by qRT-PCR. Complexin 1 is upregulated in FR and TE cortex but unchanged in PAR by hypoxic treatment. Clozapine downregulates it in FR but upregulates it in PAR cortex. Similarly, syntaxin 1A was upregulated in FR, but downregulated in TE and unchanged in PAR cortex, whereas clozapine downregulated it in FR but upregulated it in PAR cortex. Hence, hypoxia alters gene expression regionally specific, which is in agreement with reports on differentially expressed presynaptic genes in schizophrenia. Chronic clozapine treatment may contribute to normalize synaptic connectivity.


Previous studies of lymphocyte distribution in schizophrenia have yielded inconsistent results, as summarized in the present study. Based on our own original data, potential confounds that might explain these variations are analyzed and discussed. Blood samples from 26 patients with acute paranoid schizophrenia were investigated in comparison with 32 matched healthy controls by flow cytometry (CD3, CD4, CD8, CD19, and CD56 phenotyping). A subgroup of drug-free patients was followed up after 6 weeks of treatment. Cotinine levels and the free cortisol index (FCI) were provided in order to control for medication, smoking, and stress. Cotinine levels correlated with natural killer (NK) cell counts (CD3/CD56(+): r = -0.383, P = 0.003) while the FCI was related to B cell numbers (CD19(+): r = 0.390, P = 0.003). Considering these covariates, a lower level of T helper cells (P = 0.010), a reduced CD4/CD8 ratio (P = 0.029), and elevated B cells (P = 0.008) were found during acute psychosis. After 6 weeks of medication, an inverse pattern was observed in initially drug-free patients: total T cell (P = 0.005), T helper (P = 0.003), and T suppressor/cytotoxic cells (P = 0.005) increased, while B cell counts declined (P = 0.049). In conclusion, acute paranoid schizophrenia may be accompanied by a reduced T cell defense and a shift towards B cell immunity, which normalizes in response to treatment. In addition to disease stage or subtype and medication, cigarette smoking and stress are important co-factors.


Attention-deficit hyperactivity disorder (ADHD) is a common disorder with estimated prevalence of 5% in children and 3.4% in adults. Psychiatric disorders are a frequent concomitant feature. Restless legs syndrome (RLS) may mimic the symptoms of ADHD. The aim of the study is to evaluate whether the presence of RLS predicts occurrence of psychiatric disorders in parents of children with ADHD. Thirty-seven parents of 26 children with ADHD were examined for RLS and for lifetime prevalence rates of psychiatric disorders and personality disorders based on the Structured Clinical Interview for DSM-IV Diagnoses (SCID). Prevalence rates in parents were 29.7% for RLS, 67.6% for Axis I and 40.5%
for Axis II disorders. Mothers revealed higher rates for depression, anxiety disorders and ADHD than fathers, whereas personality disorders occurred at higher rates in fathers. The presence of RLS predicted a diagnosis of ADHD (odds ratio (OR) 21.9), agoraphobia (OR = 20.4) and any anxiety disorder (OR = 8.5). Although limited by the small sample size, we found evidence for increased rates of cluster B personality disorders (OR = 59.3) in parents with RLS. All parents of the latter group (100%) reported a positive family history of psychiatric disorders which was not the case in parents without RLS (69.2%) excluding the index children with ADHD. RLS seems to indicate increased vulnerability for psychiatric disorders, i.e., ADHD and anxiety disorders, in a subgroup of parents from ADHD children. Synaptic dysfunction affecting dopaminergic transmission among other transmitter systems may be a common final pathway related to the phenotypic spectrum of ADHD.


Previous literature has suggested an important role of inferior frontal gyrus, which mainly consists of Brodmann's Area (BA) 44 and 45, in the pathophysiology of schizophrenia. While recent neuroimaging techniques have revealed differential functional correlates of BA 44 and 45 in healthy individuals, previous studies have not yet separately evaluated the gray matter volume reduction of BA 44 and 45 and their relationships to psychotic symptoms in patients with schizophrenia. In the present study, magnetic resonance images were obtained from 29 right-handed male patients with schizophrenia and from 29 age- and handedness-matched healthy male controls. The reliable manual tracing methodology was employed to measure the gray matter volume of BA 44 and BA 45. The severities of psychotic symptoms were evaluated using the five-factor model of positive and negative syndrome scale in the patient group. A significant gray matter volume reduction of both the BA 44 and BA 45 was found bilaterally in the patients with schizophrenia compared with the healthy controls. Among these inferior frontal sub-regions, reduced volume of right BA 45 revealed the largest effect size. In addition, the reduced volume of BA 45 in left hemisphere showed a significant association with the increased severity of delusional behavior, while the severity of disorganized and positive symptoms were correlated with the bilateral BA 45 volumes in the patient group. The findings support an important role of inferior frontal gyrus in the pathophysiology of schizophrenia. The present study further demonstrated that BA 45 might especially contribute to the production of psychotic symptoms in the patients with schizophrenia.


The description of the heterogeneous phenomenological, pathophysiological, and etiological nature of schizophrenia is under way; however, the relationships between heterogeneity levels are still unclear. We performed a robust cross-sectional study, including a systematic neuropsychological battery, assessment of clinical symptoms, neurological soft signs, morphogenetic anomalies and smell identification, and measurement of event-related potentials on 50 outpatients with schizophrenia in their compensated states. An explorative fuzzy cluster analysis revealed two subgroups in this sample that could be distinguished from each other on symptomatological, cognitive and neurological levels. The patterns of cognitive dysfunctions and neurological developmental anomalies equally indicate that there may be hemispherical differences between the patients belonging to the different clusters.
The pathophysiology of autistic spectrum disorder (ASD) is not fully understood and there are no diagnostic or predictive biomarkers. Proteomic profiling has been used in the past for biomarker research in several non-psychiatric and psychiatric disorders and could provide new insights, potentially presenting a useful tool for generating such biomarkers in autism. Serum protein pre-fractionation with C8-magnetic beads and protein profiling by matrix-assisted laser desorption/ionisation-time of flight-mass spectrometry (MALDI-ToF-MS) were used to identify possible differences in protein profiles in patients and controls. Serum was obtained from 16 patients (aged 8-18) and age-matched controls. Three peaks in the MALDI-ToF-MS significantly differentiated the ASD sample from the control group. Sub-grouping the ASD patients into children with and without comorbid Attention Deficit and Hyperactivity Disorder, ADHD (ASD/ADHD+ patients, n = 9; ASD/ADHD- patients, n = 7), one peak distinguished the ASD/ADHD+ patients from controls and ASD/ADHD- patients. Our results suggest that altered protein levels in peripheral blood of patients with ASD might represent useful biomarkers for this devastating psychiatric disorder.


Under the Euthanasia Program of Nazi Germany, more than 200,000 psychiatric patients were killed by doctors in psychiatric institutions. After summarising the historical facts and the slow and still going-on process of illuminating and understanding what happened, some ethical consequences are drawn. What can we learn from history? The following aspects are addressed: the special situation of psychiatry in times of war, bioethics and biopolitics, the responsibility of the psychiatrist for the individual patient, the effects of hierarchy on personal conscience and responsibility, the unethical "curable-uncurable" distinction and the atrocious concept that persons differ in their value.


The cholinergic system is essential in mediating cognitive processes. Although there has been extensive research regarding cholinergic receptor subsystems, the specific contribution of the muscarinic and nicotinic receptor system to cognitive processes still has not been sufficiently explored. In the present study, we examined the selective contribution of muscarinic and nicotinic antagonism to cognitive performance in healthy human subjects. A single-blind, double-dummy, time-elapsed, repeated measures cross-over design was used on 15 healthy males. Subjects completed a neuropsychological test battery assessing a wide range of cognitive domains after 0.4 mg scopolamine (intravenous), 0.2 mg/kg mecamylamine (max. 15 mg; oral) or placebo. Subjects were tested under three conditions: placebo/placebo (PP), scopolamine/placebo (SP) and mecamylamine/placebo (MP). Results show that scopolamine significantly impaired the free recall and recognition performance in the verbal learning test. No other cognitive domain was affected, neither by scopolamine nor by mecamylamine. In line with the existing literature, antagonism of muscarinic receptors resulted in specific cognitive impairments, predominantly memory performance.
Elevations of serum homocysteine levels are a consistent finding in alcohol addiction. Serum S100B levels are altered in different neuropsychiatric disorders but not well investigated in alcohol withdrawal syndromes. Because of the close connection of S100B to ACTH and glutamate secretion that both are involved in neurodegeneration and symptoms of alcoholism the relationship of S100B and homocysteine to acute withdrawal variables has been examined. A total of 22 male and 9 female inpatients (mean age 46.9 +/- 9.7 years) with an ICD-10 diagnosis of alcohol addiction without relevant affective comorbidity were examined on admission and after 24, 48, and 120 h during withdrawal. S100B and homocysteine levels in serum were collected, and severity of withdrawal symptoms (AWS-scale), applied withdrawal medication, initial serum ethanol levels and duration of addiction were recorded. Serum S100B and homocysteine levels declined significantly (P < .05) over time. Both levels declined with withdrawal syndrome severity. Females showed a trend to a more intense decline in serum S100B levels compared to males at day 5 (P = .06). Homocysteine levels displayed a negative relationship to applied amount of clomethiazole (P < .05) and correlated with age of onset of addiction. No withdrawal seizures were recorded during the trial. As it is known for homocysteine, S100B revealed to decline rapidly over withdrawal treatment in alcoholism. This effect is more pronounced in female patients. S100B could be of relevance in the neurobiology of alcohol withdrawal syndromes. It may be indirectly related to the level of stress level or glutamatergic activity during alcohol withdrawal.


Tourette's syndrome (TS) is a developmental neuropsychiatric disorder characterized by motor and vocal tics as well as psychiatric comorbidities. Recently, differences in maturation of cortical networks using functional connectivity metrics have been described for this disorder. However, adult data on subcortical networks are scarce. In particular, the connectivity of the amygdala, for which a role in the pathophysiology of TS has been established, has not been examined so far. We studied 15 adult TS patients (11 male, aged 30.4 +/- 9.7y) and 15 age- and sex-matched controls (11 male, aged 32.0 +/- 9.3y) in a functional magnetic resonance imaging study at 1.5T using a simple motor task. We corrected for possible confounds introduced by tics, motion and brain-structural differences as well as age, sex, and medication. Task performance was monitored by simultaneous MR-compatible video-recording. Data were analyzed using an independent component approach sensitive to functional connectivity patterns. A stable component comprising both amygdalae could be identified across all subjects. Additionally, we observed a highly significant increase in coupling between/within amygdalae in the TS group when compared to controls, although behavioral data obtained during scanning did not show significant differences. These findings are expected to add to our understanding of the functional architecture of Tourette's syndrome.


Agoraphobia (with and without panic disorder) is a highly prevalent and disabling anxiety disorder. Its neural complexity can be characterized by specific cues in fMRI studies. Therefore, we developed a fMRI paradigm with agoraphobia-specific stimuli. Pictures of potential agoraphobic situations were
generated. Twenty-six patients, suffering from panic disorder and agoraphobia, and 22 healthy controls rated the pictures with respect to arousal, valence, and agoraphobia-related anxiety. The 96 pictures, which discriminated best between groups were chosen, split into two parallel sets and supplemented with matched neutral pictures from the International Affective Picture System. Reliability, criterion, and construct validity of the picture set were determined in a second sample (44 patients, 28 controls). The resulting event-related "Westphal-Paradigm" with cued and uncued pictures was tested in a fMRI pilot study with 16 patients. Internal consistency of the sets was very high; parallelism was given. Positive correlations of picture ratings with Mobility Inventory and Hamilton anxiety scores support construct validity. FMRI data revealed activations in areas associated with the fear circuit including amygdala, insula, and hippocampal areas. Psychometric properties of the Westphal-Paradigm meet necessary quality requirements for further scientific use. The paradigm reliably produces behavioral and fMRI patterns in response to agoraphobia-specific stimuli. To our knowledge, it is the first fMRI paradigm with these properties. This paradigm can be used to further characterize the functional neuroanatomy of panic disorder and agoraphobia and might be useful to contribute data to the differentiation of panic disorder and agoraphobia as related, but conceptually different clinical disorders.


Structural magnetic resonance imaging (MRI) studies reveal evidence for brain abnormalities in obsessive-compulsive disorder (OCD), for instance, reduction of gray matter volume in the prefrontal cortex. Disturbances of gyrification in the prefrontal cortex have been described several times in schizophrenia pointing to a neurodevelopmental etiology, while gyrification has not been studied so far in OCD patients. In 26 OCD patients and 38 healthy control subjects MR-imaging was performed. Prefrontal cortical folding (gyrification) was measured bilaterally by an automated version of the automated-gyrification index (A-GI), a ratio reflecting the extent of folding, from the slice containing the inner genu of the corpus callosum up to the frontal pole. Analysis of covariance (ANCOVA, independent factor diagnosis, covariates age, duration of education) demonstrated that compared with control subjects, patients with OCD displayed a significantly reduced A-GI in the left hemisphere (p = 0.021) and a trend for a decreased A-GI in the right hemisphere (p = 0.076). Significant correlations between prefrontal lobe volume and A-GI were only observed in controls, but not in OCD patients. In conclusion, prefrontal hypogyrification in OCD patients may be a structural correlate of the impairment in executive function of this patient group and may point to a neurodevelopmental origin of this disease.


Self/other (i.e., internal/external) source monitoring is one of the leading paradigms for the study of hallucinations in schizophrenia. The cognitive processes that underlie hallucinations are theorized to transform self-generated (internal) cognitive events into other-generated (external) cognitive events. These proposed cognitive operations also appear to play a role in producing analogous types of errors in self/other source monitoring, namely a memory bias whereby recalled material that was self-generated is misremembered as other-generated, referred to as an externalization bias. Internalization biases are more frequent in groups of hallucinating schizophrenia patients than in other groups. One source of measurement error that is inherent in the study of the externalization bias is that, even for never-previously viewed items, there is a tendency to guess an external source under conditions of uncertainty. If such guessing takes place in response to self-generated but
Relapse of major depressive disorder (MDD) is a common clinical problem. Identifying relapse predictors could lead to strategies that reduce relapse risk. This study is designed to determine whether residual symptoms predict relapse risk during the continuation/maintenance treatment of MDD. 570 MDD patients received open-label fluoxetine for 12 weeks. Under double blind conditions, 262 patients who responded by week 12 were randomly assigned to continue fluoxetine or switch to placebo for 52 weeks or until relapse. Residual symptoms were measured using the Symptom Checklist-90 and the Symptom Questionnaire. The relationship between residual symptom severity and relapse risk was assessed. Without adjusting for overall residual symptom severity, a greater severity of residual obsessive-compulsive and phobic anxiety symptoms predicted greater relapse risk. After adjusting for overall residual symptom severity, only severity of phobic anxiety symptoms predicted relapse risk. The predictive value of phobic anxiety symptoms with respect to relapse risk was independent of treatment assignment. The results indicated that there may be a specific pattern of residual symptoms associated with depressive relapse during antidepressant continuation/maintenance, which is unrelated to treatment assignment. Future studies are needed to further explore the relationship between residual symptoms and relapse risk in MDD. Clinical implications: (1) It is important to treat residual symptoms among antidepressant responders/remitters in order to decrease relapse risk. (2) Clinicians should target residual phobic anxiety symptoms in order to decrease relapse risk. (3) Clinicians should target residual obsessive-
compulsive symptoms in order to decrease relapse risk. Limitations: (1) limited generalizability due to inclusion/exclusion criteria; (2) lack of active comparator treatment group; (3) post hoc analysis.


Most studies point to an increased prevalence of metabolic syndrome (MS) and an increased risk of coronary heart disease (CHD) in schizophrenia patients with MS. The aims of this study were to compare the prevalence of MS in schizophrenia patients with the general population, to explore the clinical correlates and predictors of MS and to evaluate the risk for CHD within 10 years. Consecutive 319 patients, aged 18-75 years, with a diagnosis of schizophrenia according to the DSM-IV were enrolled. The ATP-III, the ATP-IIIA and the IDF criteria were used to define MS. 10-year risk of CHD events was calculated with the Framingham score. One hundred nine (34.2%) patients met the ATP-III criteria, 118 (37%) the ATP-IIIA and 133 (41.7%) the IDF criteria for MS. Patients with MS were older, had a later onset of illness and an older age at first hospitalization. The prevalence of MS in schizophrenia patients was higher from the general population only within the 20-29 age group. Patients with MS had a higher age and sex-corrected 10-year risk of CHD events. The only predictor of MS was the age of illness onset. In conclusion, countries where the general population prevalence of MS is already too high, schizophrenia patients younger than 30 years of age might be under higher risk of morbidity and mortality related with MS. This study points to the necessity for aggressive interventions to correct MS in schizophrenia as early as possible, within the first 10 years of post detection.


The aims of this study were to examine the nature and extent of cognitive impairment in first-episode early-onset psychosis (FE-EOP) soon after their stabilisation and to search for potential differences according to specific diagnostic sub-groups of patients. As part of a Spanish multicentre longitudinal study, 107 FE-EOP patients and 98 healthy controls were assessed on the following cognitive domains: attention, working memory, executive functioning, and verbal learning and memory. Three diagnostic categories were established in the patient sample: schizophrenia (n = 36), bipolar disorder (n = 19), and other psychosis (n = 52). Patients performed significantly worse than controls in all cognitive domains. The three diagnostic sub-groups did not differ in terms of impaired/preserved cognitive functions or degree of impairment. FE-EOP patients show significant cognitive impairment that, during this early phase, seems to be non-specific to differential diagnosis.


The negative symptoms of schizophrenia have been considered to be a psychiatric form of the frontal lobe syndrome. However, no studies have compared these two disorders at the clinical level. In this study, 12 negative symptom schizophrenic patients and 11 patients with behavioural variant frontotemporal dementia (bv-FTD) were rated for negative symptoms and for occurrence of frontal lobe behaviours in everyday life. They were also rated for speech disorder and were given a series of executive tests. Both patient groups showed positive ratings on negative symptoms and frontal lobe behaviours in daily life; however, the schizophrenic patients had higher negative symptom scores
and the bv-FTD patients had higher carer ratings on frontal behaviours in daily life. Both groups were impaired on the executive tests, but the bv-FTD patients showed significantly greater impairment on verbal fluency and a test requiring inhibition of prepotent responses. A minority of the bv-FTD patients unexpectedly showed speech abnormalities typically associated with schizophrenia. The findings indicate that the negative syndrome in schizophrenia and the frontal lobe syndrome resemble each other clinically in important respects. Some of the differences may be attributable to the additional presence of disinhibition in the frontal lobe syndrome.


Besides the ventral tegmental area and the nucleus accumbens as the most investigated brain reward structures, several reports about the relation between volume and activity of the amygdala and drug-seeking behavior have emphasized the central role of the amygdala in the etiology of addiction. Considering its proposed important role and the limited number of human protein expression studies with amygdala in drug addiction, we performed a human postmortem proteomic analysis of amygdala tissue obtained from 8 opiate addicts and 7 control individuals. Results were validated by Western blot in an independent postmortem replication sample from 12 opiate addicts compared to 12 controls and 12 suicide victims, as a second “control sample”. Applying 2D-electrophoresis and MALDI-TOF-MS analysis, we detected alterations of beta-tubulin expression and decreased levels of the heat-shock protein HSP60 in drug addicts. Western blot analysis in the additional sample demonstrated significantly increased alpha- and beta-tubulin concentrations in the amygdala of drug abusers versus controls (P = 0.021, 0.029) and to suicide victims (P = 0.006, 0.002). Our results suggest that cytoskeletal alterations in the amygdala determined by tubulin seem to be involved in the pathophysiology of drug addiction, probably via a relation to neurotransmission and cellular signaling. Moreover, the loss of neuroprotection against stressors by chaperons as HSP60 might also contribute to structural alteration in the brain of drug addicts. Although further studies have to confirm our results, this might be a possible pathway that may increase our understanding of drug addiction.


Working memory (WM) deficits are a neuropsychological core finding in patients with schizophrenia and also supposed to be a potential endophenotype of schizophrenia. Yet, there is a large heterogeneity between different WM tasks which is partly due to the lack of process specificity of the tasks applied. Therefore, we investigated WM functioning in patients with schizophrenia using process- and circuit-specific tasks. Thirty-one patients with schizophrenia and 47 controls were tested with respect to different aspects of verbal and visuospatial working memory using modified Sternberg paradigms in a computer-based behavioural experiment. Total group analysis revealed significant impairment of patients with schizophrenia in each of the tested WM components. Furthermore, we were able to identify subgroups of patients showing different patterns of selective deficits. Patients with schizophrenia exhibit specific and, in part, selective WM deficits with indirect but conclusive evidence of dysfunctions of the underlying neural networks. These deficits are present in tasks requiring only maintenance of verbal or visuospatial information. In contrast to a seemingly global working memory deficit, individual analysis revealed differential patterns of working memory impairments in patients with schizophrenia.

The search of the genetic predictors of response to antidepressants is a rapidly expanding field. A large number of clinical studies are reporting partly inconsistent results. Emerging new results focus on new candidate single nucleotide polymorphisms--particularly in the 5HT2a-receptor gene and the gene coding for the co-chaperone FKBPS. The impact of the 5HTTLPR polymorphism on therapeutic outcome and side effects under treatment with SSRIs has to be viewed in a more complex manner than previously proposed. All replicable genetic associations display only a very modest effect. Despite of enormous research efforts, currently pharmacogenetics of therapeutic effects and of side effects of antidepressants are unable to guide decisions on the selection of the most beneficial drug for an individual patient.

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Alzheimer's disease (AD) and mild cognitive impairment (MCI), the transitional clinical stage between cognition in normal aging and dementia, have been linked to abnormalities in brain perfusion. Pulsed arterial spin labeling (PASL) is a magnetic resonance imaging (MRI) technique for evaluating brain perfusion. The present study aimed to determine regional perfusion abnormalities in 19 patients with mild dementia in AD and 24 patients with MCI as compared to 24 cognitively healthy elderly controls using PASL. In line with nuclear imaging methods, lower perfusion in patients with MCI and AD was found mainly in the parietal lobe, but also in angular and middle temporal areas as well as in the left middle occipital lobe and precuneus. Our data imply that PASL may be a valuable instrument for investigating perfusion changes in the transition from normal aging to dementia and indicate that it might become an alternative to nuclear imaging techniques in AD diagnostics.


The presence of comorbidity in major psychoses (e.g., schizophrenia and psychotic subtypes of bipolar disorder and major depressive disorder) seems to be the rule rather than the exception in both DSM-IV and ICD-10. Examining comorbidity in major psychoses, however, requires an investigation into the different levels of comorbidity (either full-blown and subsyndromal) which should be analyzed in both psychopathological and medical fields. On one hand, the high prevalence of psychiatric comorbidity in major psychoses may be the result of the current nosographic systems. On the other hand, it may stem from a common neurobiological substrate. In fact, comorbid psychopathological conditions may share a biological vulnerability, given that dysfunction in specific brain areas may be responsible for different symptoms and syndromes. The high rates of comorbidity in major psychoses require targeted pharmacological treatments in order to effectively act on both the primary diagnosis and comorbid conditions. Nevertheless, few controlled trials in comorbid
major psychoses had been carried out and treatment recommendations in this field have mostly an empirical basis. The aim of the present article is to provide a comprehensive and updated overview in relation to epidemiological and clinical issues of comorbidity in major psychoses.


To assess the clinical validity of individual DSM-IV criteria for hypomania. In an international sample of 5,635 patients with major depressive episodes (Bridge Study), DSM-IV criteria for hypomania (stem questions, number and quality of symptoms, duration and exclusion criteria) were systematically assessed and their validity analysed on the basis of clinical data including family history, course, and other clinical characteristics. Three stem questions for hypomania, irritability, elevated mood and the added question of increased activity, showed comparable validity. The results support the current DSM-IV requirement for a higher symptom threshold (4 of 7 hypomanic symptoms) in cases of irritable mood. Longer durations of hypomanic episodes were associated with higher scores on all validators. The results did not support the DSM-IV durational requirements for hypomanic episodes (4 days) and manic episodes (7 days). Brief hypomanic episodes of 1, 2 or 3 days were valid and would meet validity criteria for inclusion. The three exclusion criteria in DSM-IV (hypomania due to the use of antidepressants or of other substances, or to other medical conditions) were found to exclude patients with bipolar depression and should therefore not be retained. These results support several revisions of the DSM-IV concept of hypomanic episodes: specifically, the inclusion of increased activity as a gate question, the inclusion of 1 or 2 to 3-day episodes and the elimination of all exclusion criteria.


To evaluate the potential impact of early childhood problems on the chronicity of mood disorders. A representative cohort from the population was prospectively studied from ages 19/20 to 39/40. Unipolar (UP) and bipolar disorders (BP) were operationally defined applying broad Zurich criteria for bipolarity. Chronicity required the presence of symptoms for more days than not over 2 years prior to an interview, or almost daily occurrence for 1 year. A family history and a history of childhood problems were taken at ages 27/28 and 29/30. Data include the first of multiple self-assessments with the Symptom-Checklist-90 R at age 19/20, and mastery and self-esteem assessed 1 year later. A factor analysis of childhood problems yielded two factors: family problems and conduct problems. Sexual trauma, which did not load on either factor, and conduct problems were unrelated to chronicity of UP or BP or both together. In contrast, childhood family problems increased the risk of chronicity by a factor of 1.7. An anxious personality in childhood and low self-esteem and mastery in early adulthood were also associated with chronicity. Childhood family problems are strong risk factors for the chronicity of mood disorders (UP and BP). The risk may be mediated partly by anxious personality traits, poor coping and low self-esteem.


Association of some neurotropic viruses like Borna Disease virus and Herpes virus with schizophrenia is better explained. However, the role of West Nile virus (WNV) infection in schizophrenia is not well
documented. Therefore, this study was performed to investigate possible association between schizophrenia and presence of antibodies and WNV RNA in schizophrenic patients. For this, 200 blood samples from patients with schizophrenia and 200 from control groups were collected in Istanbul, Turkey. WNV RNA was not detected in any of the 200 patients and 200 controls analyzed by real-time RT-PCR. One hundred and twelve sera of schizophrenic patients and 162 of controls were analyzed for the presence of IgG antibodies to WNV by a commercial IgG-ELISA (Euroimmun, Germany). Antibodies to WNV were detected in 6 schizophrenic patients and 5 controls. ELISA positive patients had antipsychotic therapy. The difference between groups in terms of seropositivity to WNV was not statistically significant (p = 0.887, p = 0.148). Known symptoms of schizophrenia were observed in these patients, and interestingly majority had close contact to cats in the past and come from agricultural area of Turkey where potential area of mosquitoes and bird habitat. In conclusion, the results of this study show that antibodies to WNV in people do not seem to be associated with schizophrenia. However, detecting antibodies to WNV in schizophrenic patients suggests that WNV infection should be considered in endemic areas as it may play role in psychiatric diseases.


Attentional deficits are prominent in schizophrenia, affecting nearly all cognitive functions. Human attention comprises three essential components: alerting, orienting and executive control. For the assessment of these functions, the attention network test (ANT) has been proposed and used in healthy controls and patients. In schizophrenia, the ANT has revealed behavioral deficits; however, the corresponding neural correlates have not been examined. In the present study, neural correlates of attention were investigated in 17 schizophrenia patients and 17 healthy controls using the ANT with fMRI. Behavioral deficits emerged in the alertness system with a reduced efficiency for temporal cues. In fMRI, changes were observed for all three domains-alerting, orienting and conflict-and revealed hyper- as well as hypoactivation in patients. Affected regions during alerting comprised a broad fronto-temporo-parieto-occipito-cerebellar network, while differences during orienting mainly tapped fronto-parietal regions and during conflict processing a thalamo-frontal-temporal occipital network including the postcentral regions. In general, hyperactivations were positively correlated with more severe psychopathological symptoms.


Current gold standard approaches to the treatment of depression include pharmacotherapeutic and psychotherapeutic interventions with social support. Due to current controversies concerning the efficacy of antidepressants in randomized controlled trials, the generalizability of study findings to wider clinical practice and the increasing importance of socioeconomic considerations, it seems timely to address the uncertainty of concerned patients and relatives, and their treating psychiatrists and general practitioners. We therefore discuss both the efficacy and clinical effectiveness of antidepressants in the treatment of depressive disorders. We explain and clarify useful measures for assessing clinically meaningful antidepressant treatment effects and the types of studies that are useful for addressing uncertainties. This includes considerations of methodological issues in randomized controlled studies, meta-analyses, and effectiveness studies. Furthermore, we summarize the differential efficacy and effectiveness of antidepressants with distinct pharmacodynamic properties, and differences between studies using antidepressants and/or
psychotherapy. We also address the differential effectiveness of antidepressant drugs with differing modes of action and in varying subtypes of depressive disorder. After highlighting the clinical usefulness of treatment algorithms and the divergent biological, psychological, and clinical efforts to predict the effectiveness of antidepressant treatments, we conclude that the spectrum of different antidepressant treatments has broadened over the last few decades. The efficacy and clinical effectiveness of antidepressants is statistically significant, clinically relevant, and proven repeatedly. Further optimization of treatment can be helped by clearly structured treatment algorithms and the implementation of psychotherapeutic interventions. Modern individualized antidepressant treatment is in most cases a well-tolerated and efficacious approach to minimize the negative impact of otherwise potentially devastating and life-threatening outcomes in depressive disorders.


Current gold standard in the treatment of depression includes pharmacotherapeutic and psychotherapeutic strategies together with social support. Due to the actually discussed controversies concerning the differential efficacy of antidepressants, a contribution to a comprehensive clarification seems to be necessary to avert further deterioration and uncertainty from patients, relatives, and their treating psychiatrists and general practitioners. Both efficacy and clinical effectiveness of antidepressants in the treatment of depressive disorders can be confirmed. Clinically meaningful antidepressant treatment effects were confirmed in different types of studies. Methodological issues of randomized controlled studies, meta-analyses, and effectiveness studies will be discussed. Furthermore, actual data about the differential efficacy and effectiveness of antidepressants with distinct pharmacodynamic properties and about outcome differences in studies using antidepressants and/or psychotherapy are discussed. This is followed by a clinically oriented depiction-the differential clinical effectiveness of different pharmacodynamic modes of action of antidepressants in different subtypes of depressive disorders. It can be summarized that the spectrum of different antidepressant treatments has broadened during the last decades. The efficacy and clinical effectiveness of antidepressants is statistically significant and clinically relevant and proven repeatedly. For further optimizing antidepressant treatment plans, clearly structured treatment algorithms and the implementation of psychotherapy seem to be useful. A modern individualized antidepressant treatment in most cases is a well-tolerated and efficacious tool to minimize the negative impact of the otherwise devastating and life-threatening outcome of depressive disorders.


Bipolar disorder (BD) has been associated with a proinflammatory state in which TNF-alpha seems to play a relevant role. The aim of the present study was to evaluate the plasma levels of TNF-alpha and its soluble receptors (sTNFR1 and sTNFR2) in BD patients in mania and euthymia in comparison with control subjects. We evaluated 53 BD patients (34 in mania and 19 in euthymia) and 38 healthy subjects. All subjects were assessed by the Mini-International Neuropsychiatry Interview (MINI-Plus). Patients were also evaluated by the Young Mania Rating Scale (YMRS) and by Hamilton Depression Rating Scale (HDRS). Plasma TNF-alpha and its soluble receptors were measured by ELISA. The plasma TNF-alpha and sTNFR2 levels did not differ between groups, but higher sTNFR1 levels were found in BD patients. Of note, BD patients in mania had higher sTNFR1 levels than BD patients in euthymia.
and controls. The sTNFR1 and sTNFR2 levels correlated with BD duration, and sTNFR2 levels correlated with age of patients. Our data indicate a proinflammatory status in BD patients during mania and further suggest that inflammatory mechanisms may be involved with the physiopathology of BD.


Brief hypomania lasting less than 4 days may impair functioning and help to detect bipolarity. This study analyzed brief hypomania that occurred in patients with bipolar disorder who were diagnosed according to the DSM-IV criteria. Daily self-reported mood ratings were obtained from 393 patients (247 bipolar I and 146 bipolar II) for 6 months (75,284 days of data, mean 191.6 days). Episodes of hypomania were calculated using a 4, 3, 2, and single day length criterion. Brief hypomania occurred frequently. With a decrease in the minimum criterion from 4 days to 2 days, there were almost twice as many patients with an episode of hypomania (102 vs. 190), and more than twice as many episodes (305 vs. 863). Single days of hypomania were experienced by 271 (69%) of the sample. With a 2-day episode length, 33% of all hypomania remained outside of an episode. There was no significant difference in the percent of hypomanic days outside of an episode between patients with bipolar I and II disorders. There were no significant differences in the demographic characteristics of patients who met the 4-day minimum as compared with those who only experienced episodes of hypomania using a shortened length criterion. Decreasing the minimum length criterion for an episode of hypomania will cause a large increase in the number of patients who experience an episode and in the aggregate number of episodes, but will not distinguish subgroups within a sample who meet the DSM-IV criteria for bipolar disorder. Frequency may be an important dimensional aspect of brief hypomania. Clinicians should regularly probe for brief hypomania.


Instruments for self-rating in depression are available, but their psychometric properties have not been fully explored; discrepancies with clinician ratings have been identified. This study was longitudinal with 85 patients fulfilling the DSM-III-R diagnosis of Seasonal Affective Disorder. Self-reporting versions (definitely and semidefinitely anchored) corresponding to the Hamilton Depression Scale (HAM-D), the Hamilton Subscale (HAM), and the Bech-Rafaelsen Melancholia Scale (MES) were compared to each other and the clinician-rated version. The unidimensional property of the sum score in each scale was tested by the item-response theory model ad modum Rasch. The scales were also tested for their sensitivity to discriminate between placebo and citalopram therapy. The sum scores and the sum score variances of the definite self-rating versions did not differ significantly from the sum scores of the corresponding observer scales at any of the five time points. The semidefinite scales significantly over-scored at all time points. The convergent validity between corresponding definite self-ratings and observer ratings was very high with correlations exceeding 0.90. Only item responses from the MES, the HAM, and their corresponding definite versions of the self-rating questionnaires DMQ and DHAM were accepted by the Rasch analysis, and only these four valid scales discriminated significantly between the effect of citalopram and placebo treatment. Our results are limited to patients with moderate depression. Two new self-report scales with unparalleled construct validity, reliability, sensitivity, and convergent validity have been identified (DMQ and DHAM). We have also identified a crucial importance of format for the means and variances of self-rating scales. These findings are of high practical and scientific value.
The septal nuclei are assumed to play a significant role in the pathophysiology of schizophrenia and affective disorders. The aim of this study was to morphometrically characterize the septal nuclei in patients with schizophrenia, bipolar disorder, and major depressive disorder, when compared with healthy control subjects. We analyzed the septal nuclei by determining the density and size of the neurons in postmortem brains in 17 patients with schizophrenia, 8 patients with bipolar disorder, 7 patients with major depressive disorder, and 14 control subjects matched for age and gender. There was a significant reduction in the neuronal density, but not in the mean cross-sectional area, in the lateral septal nucleus (P = 0.013) in patients with bipolar disorder when compared with control subjects. There were no significant changes in the neuronal density of the septal nuclei of the medial and lateral cell groups in patients with schizophrenia and major depressive disorder when compared with control subjects. There was a significant negative correlation between neuronal density in the lateral septal nucleus and disease duration in patients with major depressive disorder (P = 0.037, r = -0.9). The histopathological abnormality of the decreased neuronal density in the lateral septal nucleus, which is an important limbic region involved in emotions, might be a neuropathological correlate of bipolar disorder.

Subjective quality of life (QoL) and psychosocial functioning constitute important treatment outcomes in schizophrenia. We aimed to investigate the relationship between them in schizophrenia patients living in the community. Symptom severity and insight were assessed with the Positive and Negative Syndrome Scale (PANSS) in 76 community schizophrenia patients. Social functioning was measured with the Portuguese version of Personal and Social Performance (PSP) scale, and subjective QoL was measured with the Portuguese version of the WHO Quality of Life Measure-Abbreviated Version (WHOQoL-Bref). The majority of patients were single (78%) and unemployed/inactive (74%). Mean PSP total score was 55.5, and mean scores on WHOQoL-Bref domains ranged from 54.1 to 63.0. Greater symptom severity and worse insight were significantly associated with worse functioning in all PSP domains. Symptoms were more moderately correlated with QoL, with no significant correlations between QoL and positive symptoms and insight levels. Partial correlations controlling for symptom severity revealed no significant associations between social functioning and subjective QoL. Symptom severity may exert a greater influence on social functioning than on subjective QoL; however, social functioning was not associated with subjective QoL. The results suggest these constructs might be independent and should be assessed separately. A broader research approach, with increased attention to social and psychological factors, may help identify treatment targets to improve schizophrenia patients' social functioning and QoL.

Visually scored and power spectral analyses (PSA) of polysomnography (PSG) recordings reveal abnormalities in alcohol dependence (AD) and major depressive disorder (MDD), including deficiencies in slow wave activity (SWA) during non-rapid eye movement (NREM) sleep. SWA
parameters reflect the integrity of the homeostatic sleep drive, which have not been compared in those with AD or MDD. Ten men with AD were compared with 10 men with MDD and 10 healthy controls (HCs), all aged 20-40 years. They maintained an 11 pm to 6 am sleep schedule for 5-7 days, followed by 3 consecutive nights of PSG in the laboratory: night 1 for adaptation/screening; night 2 for baseline recordings; and night 3 as the challenge night, delaying sleep until 2 am. SWA was quantified with PSA across 4 NREM periods. Men with AD generated the least SWA at baseline. In response to sleep delay, HC men showed the expected SWA enhancement and a sharper exponential decline across NREM periods. Both the MDD and the AD groups showed a significantly blunted SWA response to sleep delay. Men with MDD had the least SWA in the first NREM period (impaired accumulation of sleep drive), whereas men with AD had the slowest SWA decay rate (impaired dissipation of sleep drive). These results suggest that both SWA generation and its homeostatic regulation are impaired in men with either AD or MDD. Finding interventions that selectively improve these different components of sleep homeostasis should be a goal of treatment for AD and MDD.

16. Busse S, Bernstein HG, Busse M, Bielau H, Brisch R, Mawrin C, Muller S, Sarnyai Z, Gos T, Bogerts B, Steiner J (2011) Reduced density of hypothalamic VGF-immunoreactive neurons in schizophrenia: a potential link to impaired growth factor signaling and energy homeostasis. Eur Arch Psychiatry Clin Neurosci. Protein expression of VGF (nonacronymic) is induced by nerve/brain-derived growth factor, neurotrophin 3, and insulin. VGF is synthesized by neurons in the paraventricular (PVN) and supraoptic (SON) nuclei of the hypothalamus. After enzymatic processing, smaller VGF-derived peptides are secreted into the cerebrospinal fluid (CSF) or blood. These peptides play important roles by improving synaptic plasticity, neurogenesis, and energy homeostasis, which are impaired in schizophrenia. Based on previous observations of neuroendocrine and hypothalamic deficits in schizophrenia and to determine whether increased levels of the VGF fragment 23-62 in CSF, which have been described in a recent study, were related to changes in hypothalamic VGF expression, an immunohistochemical study was performed in 20 patients with schizophrenia and 19 matched control subjects. N- (D-20) and C-terminal (R-15) VGF antibodies yielded similar results and immunolabeled a vast majority of PVN and SON neurons. Additionally, D20-VGF immunohistochemistry revealed immunostained fibers in the pituitary stalk and neurohypophysis that ended at vessel walls, suggesting axonal transport and VGF secretion. The cell density of D20-VGF-immunoreactive neurons was reduced in the left PVN (P = 0.002) and SON (P = 0.008) of patients with schizophrenia. This study provides the first evidence for diminished hypothalamic VGF levels in schizophrenia, which might suggest increased protein secretion. Our finding was particularly significant in subjects without metabolic syndrome (patients with a body mass index <28.7 kg/m(2)). In conclusion, apart from beneficial effects on synaptic plasticity and neurogenesis, VGF may be linked to schizophrenia-related alterations in energy homeostasis.

17. Chiesa A, Crisafulli C, Porcelli S, Han C, Patkar AA, Lee SJ, Park MH, Jun TY, Serretti A, Pae CU (2011) Influence of GRIA1, GRIA2 and GRIA4 polymorphisms on diagnosis and response to treatment in patients with major depressive disorder. Eur Arch Psychiatry Clin Neurosci. The present study is aimed to exploring whether some single nucleotide polymorphisms (SNPs) within GRIA1, GRIA2 and GRIA4 could be associated with major depressive disorder (MDD) and whether they could predict clinical outcomes in Korean in-patients, respectively, treated with antidepressants. One hundred forty-five (145) patients with MDD and 170 healthy controls were genotyped for 17 SNPs within GRIA1, GRIA2 and GRIA4. Baseline and final clinical measures, including the Montgomery-Asberg Depression Rating Scale (MADRS) for patients with MDD, were recorded. No association was observed between alleles, genotypes and haplotypes under investigation and clinical and demographical variables. As a secondary finding, a marginal association was observed between
rs4302506 and rs4403097 alleles within GRIA2 and age of onset in patients with MDD. Our findings provide evidence for a possible association between rs4302506 and rs4403097 SNPs and age of onset in patients with MDD. However, taking into account that the several limitations of our study including the moderately small sample size of our study, our findings should be considered with caution and further research is needed to draw more definitive conclusions.


Current research focuses on delineating the neurobiological boundaries between familial risk for schizophrenia (SZ) and bipolar disorder (BD). Available evidence suggests that inhibitory control may be affected in both disorders. Inhibitory control relies on the dual processes of contextual information maintenance and response inhibition. This study investigated the effect of familial risk of SZ or BD on these two aspects of inhibitory control. Seventeen healthy first-degree relatives of patients with BD (BD-R), 15 healthy relatives of patients with SZ (SZ-R) and 23 demographically matched controls were compared in terms of their performance during Controlled Oral Word Association (COWA), which measures contextually driven response selection, and during the Hayling Sentence Completion Test (HSCT), which assesses contextual response selection and inhibition. Compared to controls and BD-R, SZ-R showed deficits in contextual information processing that resulted in spontaneous errors in the COWA as well as deficits in response inhibition during the HSCT that resulted in higher error rates. BD-R also showed deficits in response inhibition during the HSCT relative to controls, which were, however, less pronounced than in SZ-R. Both relatives groups had longer response times. Our results suggest that failure in contextual maintenance is primarily associated with familial risk for SZ, while response inhibition may be a shared marker of familial risk for both disorders.


Adrenergic alpha2A receptor gene (ADRA2A) is one of the most promising candidate genes for ADHD pharmacogenetics. Thus far, three studies have investigated the association between the ADRA2A -1291 C>G polymorphism and the therapeutic response to methylphenidate (MPH) in children with ADHD, all of them with positive results. The aim of this study is to investigate, for the first time, the association between three ADRA2A polymorphisms (-1291 C>G, -262 G>A, and 1780 C>T) and the response to MPH in adults with ADHD. The sample comprises 165 Brazilians of European descent evaluated in the adult ADHD outpatient clinic of the Hospital de Clinicas de Porto Alegre. The diagnostic procedures followed the DSM-IV criteria. Drug response was assessed by both categorical and dimensional approaches, through the scales Swanson, Nolan, and Pelham Rating scale version IV and the Clinical Global Impression-Severity Scale, applied at the beginning and after the 30th day of treatment. We found no evidence of association between the three ADRA2A polymorphisms and the therapeutic response to MPH treatment. Our findings do not support a significant role for the ADRA2A gene in ADHD pharmacogenetics, at least among adult patients.

Central nervous system (CNS) monoamine deficits have been linked to a number of pathological conditions such as major depressive disorder. Individual biological variations in 5-hydroxyindoleacetic acid (5-HIAA), homovanillic acid (HVA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) might account for the variation in responses of neurotransmitter systems observed after the administration of clomipramine. The prolactin response to clomipramine has been widely used to assess CNS functioning. This open label study investigates the prolactin response induced by clomipramine in the plasma of healthy volunteers and whether it is related to changes in monoamine metabolites. The effects of clomipramine challenge on prolactin, 5-HIAA, HVA and MHPG were measured in 12 healthy volunteers. Samples were drawn directly before and 50 min after clomipramine infusion. A statistically significant increase in serum prolactin concentrations was measured in women 50 min after CMI infusion, but not in men. We found no significant increases in the serum monoamine metabolite concentrations 50 min after CMI infusion. Changes in HVA and 5-HIAA correlated statistically significantly and positively with the amount of prolactin release in the whole sample. Furthermore, positive correlations were found between (50-0 min) 5-HIAA and (50-0 min) HVA, although we did not find a correlation between (50-0 min) prolactin and (50-0 min) MHPG after clomipramine challenge. The pronounced prolactin release in healthy adult women might indicate a higher physiological sensitivity. Correlations between intra-individual changes in HVA, 5-HIAA and serum prolactin might indicate a central nervous effect of clomipramine on monoamine turnover. We conclude that monoamine changes in relation to prolactin response after clomipramine challenge may be suitable for characterizing the relationship between central serotonergic and dopaminergic function.


Weight gain leading to obesity is a frequent adverse effect of treatment with atypical antipsychotics. However, the degree of its independent contribution to the risk of coronary heart disease events in patients treated with these drugs has not been elucidated. The aim of this study is to determine whether obesity is an independent risk factor for the 10-year risk of coronary heart disease events in psychiatric patients treated with atypical antipsychotics. We used the Framingham method, which is based on age, gender, blood pressure, smoking, and plasma levels of total and high-density lipoprotein cholesterol, to estimate the 10-year risk of coronary heart disease events in patients treated with second-generation antipsychotics who were obese (N = 44; mean age 38.1 years, 54.5% men) or normal weight (N = 83; mean age 39.9 years, 47.0% men). Excluded were patients with metabolic syndrome and those taking antihypertensive, hypoglycemic, and lipid-lowering drugs. The 10-year risk of coronary artery disease events was very low and virtually identical in the obese and normal weight patients (2.3 +/- 3.5 vs. 2.6 +/- 4.6, P = 0.68), despite excess of 12 BMI units (P < 0.0001) and 15.7 cm waist circumference (P < 0.0001) in the obese. The risk was similar in obese and normal weight men (3.8 +/- 5.9 vs. 2.8 +/- 3.4, P = 0.45) and women (1.7 +/- 3.7 vs. 1.5 +/- 2.5, P = 0.83). The validity of the 10-year prediction for risk of coronary heart disease events in the mentally ill based on the Framingham score system requires prospective confirmation. Obesity does not appear to be an independent predictor for the 10-year risk of coronary heart disease events in patients without metabolic syndrome treated with second-generation antipsychotics.


The aim of this study is to investigate possible associations between a set of single-nucleotide polymorphisms (SNPs) within 10 genes with Schizophrenia (SCZ) and response to antipsychotics in
Korean in-patients treated with antipsychotics. Two hundred and twenty-one SCZ in-patients and 170 psychiatrically healthy controls were genotyped for 42 SNPs within ABCB1, ABCB4, TAP2, CLOCK, CPLX1, CPLX2, SYN2, NRG1, SHTR1A and GPRIN2. Baseline and final clinical measures, including the Positive and Negative Symptoms Scale (PANSS), were recorded. Rs10042486 within SHTR1A was associated with both SCZ and clinical improvement on PANSS total scores as well as on PANSS positive and PANSS negative scores. The haplotype analyses focusing on the four, three and two blocks' haplotypes within SHTR1A confirmed such findings as well. We did not observe any significant association between the remaining genetic variants under investigation in this study and clinical outcomes. Our preliminary findings suggest that rs10042486 within SHTR1A promoter region could be associated with SCZ and with clinical improvement on PANSS total, positive and negative scores in Korean patients with SCZ. However, taking into account the several limitations of our study, further research is needed to draw more definitive conclusions.


Olfactory identification deficit appears to be an enduring feature of schizophrenia, but it is unclear whether it is specific to schizophrenia or present in psychotic disorders in general. The aim of the present study was to compare olfactory identification and olfactory preference in schizophrenia and bipolar disorder. Individuals with schizophrenia or bipolar disorder and demographically matched healthy participants were given the University of Pennsylvania Smell Identification Test (UPSIT) to assess olfactory identification ability. To examine olfactory hedonic judgment, participants were also asked to indicate their preference for each UPSIT item on a 5-point rating scale, immediately after odor identification. Clinical symptoms and social competence were also assessed. Both schizophrenic and bipolar groups showed olfactory identification deficits compared with the healthy controls, but schizophrenic patients were more impaired than bipolar patients on the UPSIT accuracy. Interestingly, both bipolar and schizophrenic patients rated odors to be more pleasant than did healthy controls, but all groups preferred odors that they could correctly identify to unidentified smells. Restricted range of preference ratings was associated with the severity of negative symptoms in schizophrenia, and with mania in bipolar disorder. Social competence was associated with better olfactory identification performance. These findings suggest that olfactory identification and preference are compromised in bipolar disorder as well as in schizophrenia, but the precise nature of these abnormalities needs to be further elucidated.


A recent randomized, open-label, relapse prevention trial (ConstaTRE) compared outcomes with risperidone long-acting injectable (RLAI) versus the oral atypical antipsychotic quetiapine. This study also included a small descriptive arm in which patients could also be randomized to aripiprazole. Results of this exploratory analysis are described here. Clinically stable adults with schizophrenia or schizoaffective disorder previously treated with oral risperidone, olanzapine, or an oral conventional antipsychotic were randomized to RLAI or aripiprazole. Efficacy and tolerability were monitored for up to 24 months. A total of 45 patients were treated with aripiprazole (10-30 mg/day) and 329 patients with RLAI (25-50 mg i.m. every 2 weeks). Relapse occurred in 27.3% (95% CI: 15.0-42.8%) of aripiprazole-treated and 16.5% (95% CI: 12.7-21.0%) of RLAI-treated patients. Kaplan-Meier estimates of mean (standard error) relapse-free period were 313.7 (20.4) days for aripiprazole and 607.1 (11.4) days for RLAI patients. Remission was achieved by 34.1% (95% CI: 20.5-49.9%) of aripiprazole and 51.1% (95% CI: 45.5-56.6%) of RLAI patients. Clinical global impression-change was improved ("minimally improved" to "very much improved") in 26.4% with RLAI and 15.9% with
Aripiprazole patients. Tolerability was generally good for both treatment groups. Weight gain (7.0% with RLAI vs. 4.4% with aripiprazole), extrapyramidal adverse events (AEs) (10.3% vs. 4.4%), and potentially prolactin-related AEs (4.6% vs. 0%) were more common with RLAI treatment, and gastrointestinal disorders were more common in aripiprazole-treated patients (22.2% vs. 6.1%). Time-to-relapse in stable patients with schizophrenia or schizoaffective disorder was numerically longer in RLAI-treated patients than in aripiprazole-treated patients although not statistically significant. Both treatments were generally well tolerated.


The presence of the metabolic syndrome is an important risk factor for cardiovascular disease and diabetes. The short- and long-term metabolic safety of sertindole was compared to that of risperidone in a subset of patients enrolled in the sertindole cohort prospective (SCoP) study, an open randomized study. In 261 randomized patients, there were moderate increases in mean weight, BMI, and waist circumference during treatment with either sertindole or risperidone; after 12 weeks, the increase in weight was 1.3 and 1.1 kg, respectively, and after 36 weeks, it was 2.2 and 2.0 kg, respectively. From baseline to last assessment (up to 60 weeks), weight gains of 1.8 and 1.7 kg for sertindole and risperidone, respectively, were observed. Similar proportions of patients (sertindole: 17% versus risperidone: 16%) had weight increases >/=7% from baseline to last assessment. The mean changes from baseline in triglycerides, total cholesterol, HDL-cholesterol, LDL-cholesterol, plasma glucose and blood pressure were small and not clinically relevant in both treatment groups. No patient in either of the groups developed type 2 diabetes during the study. At last assessment, the prevalence of metabolic syndrome (International Diabetes Federation) was 17% in the sertindole group and 26% in the risperidone group and the incidence of metabolic syndrome was 7% in the sertindole group and 10% in the risperidone group. Treatment with either sertindole or risperidone did not appear to be associated with an increased comparative risk of developing metabolic syndrome. In general, the metabolic effects of sertindole and risperidone were similar.


The psychological well-being dimension and depressive symptoms are both important variables in an individual's health. In this study, we evaluated the World Health Organization 5-item well-being index (WHO-Five) internal and external validities, and accuracy in detecting depression. A total of 1,128 individuals between 18 and 65 years old from a rural Brazilian population were included. Cronbach's alpha and factor analysis were performed for internal validation. Demographic variables means were compared, receiver operating characteristic (ROC) curve was constructed, and sensitivity, specificity and positive and negative predictive values for different cutoff points were calculated for external validation and accuracy in detecting depression. Cronbach's alpha was 0.83, and only one factor was responsible for 59% of common variances, with an eigenvalue of 2.96. Higher WHO-Five scores were associated with being man, from oldest age category and retired. It was also related to better general health self-perception and negative screening in the Beck Depression Inventory (BDI). Based on BDI, the area under the curve was 67.37. A sensitivity of 66.75% and a negative predictive value of 91/92% for cutoffs <19/20 were detected. WHO-Five showed internal and external validities when used to measure the well-being dimension and to be a useful tool for depression screening.

Little research on the prevalence and correlates of adult ADHD has been conducted outside the United States. The aim of the present study was to estimate the prevalence and correlates of adult ADHD in a large representative sample of the German population aged 18-64 years (n = 1,655). Two self-rating screening instruments to assess childhood and adult ADHD symptomatology were used to estimate the prevalence of ADHD. A 4-item screening tool was used to assess probable cases of current depression and anxiety (Patient Health Questionnaire). The estimated crude prevalence rate of current ADHD was 4.7%. Adult ADHD was significantly associated with lower age, low educational level, unemployment, marital status (never married and divorced), and rural residency. No association was found with gender. Adult ADHD was strongly associated with positive screening results for depression and anxiety. ADHD is a common disorder of adulthood, is associated with significant social impairment and psychiatric co-morbidity, and should receive further research attention.


The aim of this naturalistic observational study was to investigate EEG alterations in patients under olanzapine treatment with a special regard to olanzapine dose and plasma concentration. Twenty-two in-patients of a psychiatric university ward with the monodiagnosis of paranoid schizophrenia (ICD-10: F20.0), who received a monotherapy of olanzapine were included in this study. All patients had a normal alpha-EEG before drug therapy, and did not suffer from brain-organic dysfunctions, as verified by clinical examination and cMRT scans. EEG and olanzapine plasma levels were determined under steady-state conditions (between 18 and 22 days after begin of treatment). In 9 patients (40.9%), pathological EEG changes (one with spike-waves) consecutive to olanzapine treatment were observed. The dose of olanzapine was significantly higher in patients with changes of the EEG than in patients without changes (24.4 mg/day (SD: 8.1) vs. 12.7 mg/day (SD: 4.8); T = -4.3, df = 21, P < 0.001). In patients with EEG changes, the blood plasma concentration of olanzapine (45.6 mg/l (SD: 30.9) vs. 26.3 mg/l (SD: 21.6) tended to be also higher. The sensitivity of olanzapine dosage to predict EEG changes was 66.7%, the specificity 100% (Youden-index: 0.67). EEG abnormalities during olanzapine treatment are common. These are significantly dose dependent. Thus, EEG control recordings should be mandatory during olanzapine treatment with special emphasis on dosages exceeding 20 mg per day, although keeping in mind that EEGs have only a limited predictive power regarding future epileptic seizures.


Research on social cognition focuses on several human abilities with a huge diversity in the approaches to tap the different functions. Empathy, for instance, is a rather elaborated human ability, and several recent studies point to significant impairments in patients suffering from psychiatric disorders, such as schizophrenia or autism. Neuroimaging data from these patients commonly indicate neural dysfunctions accompanying the behavioral deficits. Studying the neural correlates of social cognition is of particular importance, because deficits in these domains may explain the major dysfunctions in psychiatric disorders that prevent effective (re)integration into work and social life. It has also become clearer that social cognition deficits, similar to emotion dysfunctions, may represent trait markers and endophenotypes of the diseases. However, there are several challenges for future studies on social cognitive dysfunctions: on the one hand, the
complexity of the constructs and thus the variety of definitions which make it hard to develop adequate tasks. On the other hand, results are needed that particularly address the disorder specificity of these impairments, as well as their potential as endophenotypes via analyzing people at high-risk and their relatives.


Attention deficit hyperactivity disorder (ADHD) is now recognized as a common disorder both in child and adult psychiatry. Adult patients with a diagnosis of ADHD (n = 572) and community controls (n = 675) responded to auto-questionnaires rating past and present symptoms of ADHD, co-morbid conditions, including migraine, treatment history and work status. The prevalence of migraine was significantly higher in the patient group compared to the controls (28.3% vs. 19.2%, P < 0.001, OR = 1.67, CI 1.28-2.17). The difference from controls was particularly marked for men (22.5% vs. 10.7%, P < 0.001, OR = 2.43, CI 1.51-3.90) but was also significant for women (34.4% vs. 24.9%, P = 0.008, OR = 1.58, CI 1.13-2.21). In both patients and controls, migraine was associated with symptoms of mood and anxiety disorders. These findings point to a co-morbidity of migraine with ADHD, and it is possible that these patients represent a clinical and biological subgroup of adult patients with ADHD.


Although perinatal complications are hypothesized to be risk factors for the development of anorexia nervosa (AN), no study to date explored this issue using a discordant sibling design. This type of design allows to explore whether the risk for obstetric complications is itself a consequence of the genetic vulnerability for AN (covariation model) or whether obstetric complications increase the risk of AN independently of (additive model), or in interaction with (interaction model), the disorder's genetic liability. The presence of perinatal complications was assessed through review of the obstetric records of 60 AN subjects, 60 unaffected sisters, and 70 healthy subjects. Unaffected sisters and healthy controls were compared in relation to perinatal characteristics and complications. There was no evidence for an elevated rate of complications in unaffected siblings of AN patients. Mothers with a positive psychiatric history tended to have more perinatal complications. Perinatal complications seem to be independent risk factors that may interact with, but are not caused by,
familial risk factors for AN. In terms of prevention, a particular attention should be paid to mothers with a lifetime history of psychiatric disorders.


There is evidence that high alcohol use is associated with an increase in mortality. Little is known about long-term effects of problematic alcohol consumption in non-clinical (community) populations. The aim of our study was to obtain data on this and related issues in a representative rural community sample assessed longitudinally over a period of 20 years. Assessments focused on a baseline survey from 1980 to 1984 and 20-year follow-up from 2001 to 2004. Based on expert interviews and standardized self-rating scales (e.g. MALT; Munich Alcoholism Test), the following three groups were defined (a) severe alcohol problems, (b) moderate alcohol problems, and (c) no alcohol problems. Mortality and hazard rates were analyzed with logistic and Cox regression adjusted for several health risk factors. From an original community sample of 1,465 individuals, 448 were deceased at 20-year follow-up. Participation rates were high. Baseline prevalence according to the MALT was 1.6% for severe alcohol problems and 4.0% for moderate alcohol problems. Over the 20-year time span, individuals with severe alcohol problems had a significantly elevated risk for dying earlier than the group with no alcohol problems (2.4 times higher). Mortality for those with moderate alcohol problems at baseline had a non-significantly elevated 20-year mortality risk (1.5 times higher) compared to those with no alcohol problems. Cox survival analyses corroborate these findings from multiple sequential logistic regression analyses. In discussing the mortality risk of persons with alcohol problems, the severity of the alcohol problems must be taken into account.


The N1 component of the auditory evoked potential (AEP) is a robust and easily recorded metric of auditory sensory-perceptual processing. In patients with schizophrenia, a diminution in the amplitude of this component is a near-ubiquitous finding. A pair of recent studies has also shown this N1 deficit in first-degree relatives of schizophrenia probands, suggesting that the deficit may be linked to the underlying genetic risk of the disease rather than to the disease state itself. However, in both these studies, a significant proportion of the relatives had other psychiatric conditions. As such, although the N1 deficit represents an intriguing candidate endophenotype for schizophrenia, it remains to be shown whether it is present in a group of clinically unaffected first-degree relatives. In addition to testing first-degree relatives, we also sought to replicate the N1 deficit in a group of first-episode patients and in a group of chronic schizophrenia probands. Subject groups consisted of 35 patients with schizophrenia, 30 unaffected first-degree relatives, 13 first-episode patients, and 22 healthy controls. Subjects sat in a dimly lit room and listened to a series of simple 1,000-Hz tones, indicating with a button press whenever they heard a deviant tone (1,500 Hz; 17% probability), while the AEP was recorded from 72 scalp electrodes. Both chronic and first-episode patients showed clear N1 amplitude decrements relative to healthy control subjects. Crucially, unaffected first-degree relatives also showed a clear N1 deficit. This study provides further support for the proposal that the auditory N1 deficit in schizophrenia is linked to the underlying genetic risk of developing this disorder. In light of recent studies, these results point to the N1 deficit as an endophenotypic marker for schizophrenia. The potential future utility of this metric as one element of a multivariate endophenotype is discussed.

An increasing number of controlled studies strongly support an antidepressant effect of high-frequency repetitive transcranial magnetic stimulation (rTMS) over the left dorsolateral prefrontal cortex. However, these data come from highly selected study populations. Whether rTMS is a feasible therapeutic tool for the treatment of depression under naturalistic condition has not yet been addressed. Here, we report results from 232 depressive patients [aged 20-76 years, baseline Hamilton Depression Rating Score (HDRS-21) 24.0 +/- 7.3] treated with rTMS add-on to continued psychopharmacological treatment in a naturalistic clinical setting. Two thousand stimuli of 20-Hz rTMS were applied daily over the left dorsolateral prefrontal cortex with an intensity of 110% of motor threshold. Treatment duration was individually planned and varied between 10 and 20 sessions. In average, patients received 13 +/- 6.1 rTMS sessions. In 90% of the cases, treatment was terminated regularly. No severe side effects were observed. Only four patients stopped rTMS treatment because of side effects. Ratings with the HDRS-21 before and after treatment were available in 130 patients. The average improvement of the HDRS-21 in this subsample was 9.0 +/- 9.2 points. Fifty-three patients had an improvement of 50% or more. These results document that rTMS is feasible, safe and well tolerated under naturalistic conditions.


The stigma of mental illness is a severe burden for people suffering from mental illness both in private and public life, also affecting their relatives, their close social network, and the mental health care system in terms of disciplines, providers, and institutions. Interventions against the stigma of mental illness employ complementary strategies (e.g., protest, education, and contact) and address different target groups (e.g., school children and teachers, journalists, stakeholders). Within this framework, the World Psychiatric Association has adopted an Action Plan with the goal to improve the image of psychiatry and to reduce potential stigmatizing attitudes toward psychiatry and psychiatrists. To evaluate such interventions, a questionnaire has been developed that assesses opinions and attitudes toward psychiatrists and psychiatry in different samples of medical specialists (psychiatrists and general practitioners). The questionnaire comprises scales about perceived stigma in terms of the perception of societal stereotypes, self-stigma in terms of stereotype agreement, perceived stigma in terms of structural discriminations, discrimination experiences, stigma outcomes, and attitudes toward a second medical discipline. It is available in several languages (Arab, English, German, Japanese, Polish, and Spanish) and can easily be adapted for utilization in other medical specialties.


Major depressive disorder (MDD) is associated with increased volumes of visceral fat and a high prevalence of the metabolic syndrome. In turn, affective disorders are frequently found in patients with borderline personality disorder (BPD). It is therefore unclear whether BPD per se may influence body composition. In order to clarify a potential relationship between BPD and body composition, we measured visceral fat content (VFC) in young depressed women with and without comorbid BPD and
related this parameter to various features of the metabolic syndrome. Visceral fat content was measured by magnetic resonance imaging in 22 premenopausal women with MDD only, in 44 women with comorbid MDD and BPD, in 12 female BPD patients without MDD, and in 34 healthy women (CG). Data showed that depressed women without comorbid BPD had a 335% higher VFC and women with comorbid BPD had a 250% higher VFC than the CG women. When controlling for age, data showed significant effects of MDD on VFC (F = 8.4; P = 0.005). However, BPD, with or without MDD, was not related to VFC. Young depressed women with and without comorbid BPD display increased visceral fat content when compared to control subjects and may therefore constitute a risk group for the development of the metabolic syndrome. BPD per se is not an additive risk factor in this context.


The brain-derived neurotrophic factor (BDNF) is a key regulator of synaptic plasticity and has been suggested to be involved in the pathophysiology and pathogenesis of psychotic disorders, with particular emphasis on dysfunctions of the hippocampus. The aim of the present study was to replicate and to extend prior findings of BDNF val66met genotype effects on hippocampal volume and N-acetyl aspartate (NAA) levels. Hundred and fifty-eight caucasians (66 schizophrenic, 45 bipolar, and 47 healthy subjects; 105 subjects underwent MRI and 103 MRS scanning) participated in the study and were genotyped with regard to the val66met polymorphism (rs6265) of the BDNF gene. Hippocampal volumes were determined using structural magnetic resonance imaging (MRI), and measures of biochemical markers were taken using proton magnetic resonance spectroscopy ((1)H-MRS) in the hippocampus and other brain regions. Verbal memory was assessed as a behavioral index of hippocampal function. BDNF genotype did not impact hippocampal volumes. Significant genotype effects were found on metabolic markers specifically in the left hippocampus. In particular, homozygous carriers of the met-allele exhibited significantly lower NAA/Cre and (Glu + Gln)/Cre metabolic ratios compared with val/val homozygotes, independently of psychiatric diagnoses. BDNF genotype had a numerical, but nonsignificant effect on verbal memory performance. These findings provide first in vivo evidence for an effect of the functional BDNF val66met polymorphism on the glutamate system in human hippocampus.


Verbal and visuospatial working memory (WM) impairment is a well-documented finding in psychiatric patients suffering from major psychoses such as schizophrenia or bipolar affective disorder. However, in major depression (MDD) the literature on the presence and the extent of WM deficits is inconsistent. The use of a multitude of different WM tasks most of which lack process-specificity may have contributed to these inconsistencies. Eighteen MDD patients and 18 healthy controls matched with regard to age, gender and education were tested using process- and circuit-specific WM tasks for which clear brain-behaviour relationships had been established in prior functional neuroimaging studies. Patients suffering from acute MDD showed a selective impairment in articulatory rehearsal of verbal information in working memory. By contrast, visuospatial WM was unimpaired in this sample. There were no significant correlations between symptom severity and WM performance. These data indicate a dysfunction of a specific verbal WM system in acutely ill patients with MDD. As the observed functional deficit did not correlate with different symptom
scores, further, longitudinal studies are required to clarify whether and how this deficit is related to illness acuity and clinical state of MDD patients.


Hypocapnia through hyperventilation is a well-known procedure in electroconvulsive therapy (ECT) to enhance seizure activity. However, it has mostly been applied in an uncontrolled manner. Originally intended for a better management of the supraglottic airway, laryngeal masks are more suited to monitor levels of CO(2) during hyperventilation than face masks and thereby provide for the possibility of controlled hyperventilation (CHV). The impact of CHV was retrospectively studied in 114 consecutive patients; 65 of them had received ECT with CHV and 49 had received ECT with uncontrolled hyperventilation (UHV) directly prior to the time period when the laryneal mask was introduced to the ECT treatment procedure. The CO(2) level in the CHV group was aimed at 30 mmHg or below. CHV considerably enhanced the seizure activity leading to changes in clinically determined parameters of the treatment course: the necessity for increasing the electric charge, for re-stimulations (trend) and for bilateral stimulations was lower in the CHV group as compared to the UHV group. The improvement in the Global Assessment of Functioning Scores was not different in both groups. CHV was associated with a higher amount of prolonged seizures, with a reduced number of delirious symptoms after treatments and an attenuating effect on heart rate. Concluding, CHV can help to maintain the applied electric charge low without worsening the clinical outcome. Therefore, it is a helpful technical improvement. However, it should be used carefully with regard to prolonged seizures.


Media reports of suicides have an impact on suicide rates. However, countermeasures to this media effect have not been evaluated. We examined the association between media reports of suicides accomplished with the use of hydrogen sulfide, the voluntary stoppage of sales of suicide-related products, and suicide rates for people in their 20s, 30s, and 40s in Japan. The Box-Jenkins transfer function model was applied to monthly time series data from February 2003 to December 2009 (83 months). In the male suicide time series, media reports of suicide were not related to suicide counts (omega((R)) = 8.988, P = 0.694). Similarly, stopping the sale of bath salts was not related to the number of suicides (omega((S)) = -7.344, P = 0.694). However, in the female suicide time series, media reports of suicide were related to the number of suicides (omega((R)) = 17.225, P = 0.049). Similarly, stopping the sale of bath salts was related to the number of suicides (omega((S)) = -18.545, P = 0.040). The results suggest that stopping the sale of bath salts might be effective in reducing the number of copycat suicides among the women in their 20s, 30s, and 40s. In practice, stopping the sale of suicide-related products might be a potentially effective countermeasure to prevent copycat suicides triggered by media coverage of suicides.


Although several case reports have suggested a relationship between accessing Internet suicide sites and the incidence of suicide, the influence of the Internet on the incidence of suicide is not known. Thus, we examined the association between Internet suicide-related searches and the incidence of
suicide in 20- and 30-year-old individuals in Japan. The Box-Jenkins transfer function model was applied to monthly time series data from January 2004 to May 2010 (77 months). The terms "hydrogen sulfide," "hydrogen sulfide suicide," and "suicide hydrogen sulfide suicide" at (t-11) were related to the incidence of suicide among people aged in their 20 s (P = 0.005, 0.005, and 0.006, respectively) and people aged in their 30 s (P = 0.013, 0.011, and 0.012, respectively). "BBS on suicide" at (t-5) and "suicide by jumping" at (t-6) were related to the incidence of suicide in people aged 30-39 (P = 0.006 and 0.001, respectively). Internet searches for specific suicide-related terms are related to the incidence of suicide among 20- and 30-year-old individuals in Japan. Routine interrogation by a clinician about visiting Internet suicide websites and stricter regulation of these websites may reduce the incidence of suicide among young people.


From the clinical practice and some experimental studies, it is apparent that paranoid schizophrenia patients tend to assign emotional salience to neutral social stimuli. This aberrant cognitive bias has been conceptualized to result from increased emotional arousal, but direct empirical data are scarce. The aim of the present study was to quantify the subjective emotional arousal (SEA) evoked by emotionally non-salient (neutral) compared to emotionally salient (negative) social stimuli in schizophrenia patients and healthy controls. Thirty male inpatients with paranoid schizophrenia psychosis and 30 demographically matched healthy controls rated their level of SEA in response to neutral and negative social scenes from the International Affective Picture System and the Munich Affective Picture System. Schizophrenia patients compared to healthy controls had an increased overall SEA level. This relatively higher SEA was evoked only by the neutral but not by the negative social scenes. To our knowledge, the present study is the first designed to directly demonstrate subjective emotional over-arousal to neutral social scenes in paranoid schizophrenia. This finding might explain previous clinical and experimental data and could be viewed as the missing link between the primary neurobiological and secondary psychological mechanisms of paranoid psychotic-symptom formation. Furthermore, despite being very short and easy to perform, the task we used appeared to be sensitive enough to reveal emotional dysregulation, in terms of emotional disinhibition/hyperactivation in paranoid schizophrenia patients. Thus, it could have further research and clinical applications, including as a neurobehavioral probe for imaging studies.


Cortical development and folding seems to be under environmental as well as genetic control. The aim of our study was to estimate the genetic influence on gyrification and cortical volumes, comparing prefrontal gyrification index (GI) in monozygotic (MZ) and dizygotic (DZ) twin pairs, and unrelated pairs. Twenty-four subjects (6 pairs of MZ and 6 pairs of DZ twins) were included in this study. Prefrontal cortical folding (gyrification) was measured by an automated and manual version of the gyrification index (A-GI, M-GI) according to previously published protocols. MR-imaging was performed and 3 representative slices were selected from coronar MR-imaging scans. The volumes of the total brain, temporal lobes, prefrontal lobes, and cerebellum were analyzed, too. To evaluate similarity in GI, absolute differences in GI, and brain volumes as well as intraclass correlations of twin pairs were compared with regard to twin status. Finally, a control group of unrelated pairs was assembled from the first two study groups and analyzed. Compared to unrelated pairs, twin pairs exhibited more similarity concerning different brain volumes and a trend to more similarity concerning A-GI. MZ twins did not present more similarity concerning GI (automatically and manually
measured) and volume measurements compared to DZ twins. Different factors, like intrauterine factors, postnatal development conditions, and especially environmental factors might account for the differences between related and unrelated pairs. The nonexistence of a pronounced similarity in MZ twins compared to DZ twins concerning prefrontal G1 raises questions about the extent of genetic influence on G1.


Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive neurostimulatory technique widely used in research, diagnostics, and neuro-psychiatric therapy. Despite its growing popularity, basic molecular mechanisms underlying the clinical effects of rTMS have remained largely under-researched. Here, we present a human-derived neuronal cell culture system responsive to rTMS effects. SH-SY5Y neuroblastoma cells were differentiated by retinoic acid treatment for 10 days, resulting in a neuronal phenotype characterized by upregulation of neuronal marker proteins and generation of an action potential in response to depolarizing current step injection. Repetitive magnetic stimulation of these cells resulted in increased intracellular cAMP levels and increased phosphorylation of transcription factor CREB. Pretreatment with ketamine (1 μM) potentiated, while pretreatment with lithium (2 mM) attenuated this cellular response to repetitive magnetic stimulation. In conclusion, we introduce here a novel in vitro system responding to rTMS at the level of second messenger signaling. The use of human-derived cells with neuron-like properties will prove useful for further studies on the cellular effects of rTMS.


Depression rating scales play a decisive role in the assessment of the severity of depression and the evaluation of the efficacy of antidepressant treatments. The Hamilton Depression Rating Scale (HAMD) is regarded as the 'gold standard'; nevertheless, studies suggest that the Inventory of Depressive Symptomatology (IDS) is more sensitive to detect symptom changes. The aim of the present study was to investigate whether the IDS is more sensitive in detecting changes in depression symptoms in patients with mild major, minor or subsyndromal depression (MIND). Biweekly IDS-C(28) and HAMD(17) data from 340 patients of a 10-week randomized, placebo-controlled trial comparing the effectiveness of sertraline and cognitive-behavioural therapy in patients with MIND were analysed. We investigated sensitivity to change for both scales (1) from assessment-to-assessment, (2) in relation to depression severity level, and (3) in relation to DSM-IV depression criterion symptoms. The IDS-C(28) was more sensitive in detecting changes in depression symptomatology over the treatment course as well as for different severity levels, especially in patients with a low depression severity. It assesses the DSM-IV criteria more thoroughly, is better able to track the change of cognitive symptoms and to identify residual symptoms. Both scales are well able to assess depressive symptomatology. However, the IDS-C(28) surpasses the HAMD(17) in detecting small changes especially in the core symptoms of depression. This is important for an optimal treatment by capturing early improvements, enabling prompt reactions and detecting residual symptoms.

In the efficacy evaluation of antidepressant treatments, the total score of the Hamilton Depression Rating Scale (HAMD) is still regarded as the 'gold standard'. We previously had shown that the Inventory of Depressive Symptomatology (IDS) was more sensitive to detect depressive symptom changes than the HAMD17 (Helmreich et al. 2011). Furthermore, studies suggest that the unidimensional subscales of the HAMD, which capture the core depressive symptoms, outperform the full HAMD regarding the detection of antidepressant treatment effects. The aim of the present study was to compare several unidimensional subscales of the HAMD and the IDS regarding their sensitivity to changes in depression symptoms in a sample of patients with mild major, minor or subsyndromal depression (MIND). Biweekly IDS-C28 and HAMD17 data from 287 patients of a 10-week randomised, placebo-controlled trial comparing the effectiveness of sertraline and cognitive-behavioural group therapy in patients with MIND were converted to subscale scores and analysed during the antidepressant treatment course. We investigated sensitivity to depressive change for all scales from assessment-to-assessment, in relation to depression severity level and placebo-verum differences. The subscales performed similarly during the treatment course, with slight advantages for some subscales in detecting treatment effects depending on the treatment modality and on the items included. Most changes in depressive symptomatology were detected by the IDS short scale, but regarding the effect sizes, it performed worse than most subscales. Unidimensional subscales are a time- and cost-saving option in judging drug therapy outcomes, especially in antidepressant treatment efficacy studies. However, subscales do not cover all facets of depression (e.g. atypical symptoms, sleep disturbances), which might be important for comprehensively understanding the nature of the disease depression. Therefore, the cost-to-benefit ratio must be carefully assessed in the decision for using unidimensional subscales.


Eating disorders and, in particular, anorexia nervosa (AN) have morbidity and mortality rates that are among the highest of any mental disorders and are associated with significant functional impairment. More than 25 years ago, several researchers hypothesised that the prerequisite for the development of AN was a family process characterised by an overprotective and conflict-avoiding parent-child interaction. Family studies, however, suggest that AN is a complex genetic disorder that is likely expressed primarily by temperament and specific traits during childhood, including inhibition, perfectionism and harm avoidance. Recent studies have described an impaired flexibility and deficits in social cognition that are independent of body weight and the current state of the eating disorder, providing further evidence for a genetic component of AN. The physiological and psychological alterations and the increasing societal demands that occur during puberty may trigger onset. The starvation process itself is associated with severe alterations of central and peripheral metabolism, especially neuroendocrine and neurotransmitter changes, which are thought to affect the adolescent brain during the vulnerable period of neural restructuring. Long-standing malnutrition during adolescence and young adulthood associated with hormonal and neuropeptide dysfunctions may produce "biological scars" that maintain and accelerate the disorder and likely result in chronic mental disorders in adulthood as well as poor social functioning.

Ventricular enlargement is one of the most consistent abnormal structural brain findings in schizophrenia and has been used to infer brain shrinkage. However, whether ventricular enlargement is related to local overlying cortex and/or adjacent subcortical structures or whether it is related to brain volume change globally has not been assessed. We systematically assessed interrelations of ventricular volumes with gray and white matter volumes of 40 Brodmann areas (BAs), the thalamus and its medial dorsal nucleus and pulvinar, the internal capsule, caudate and putamen. We acquired structural MRI (patients with schizophrenia (n = 64) and healthy controls (n = 56)) and diffusion tensor fractional anisotropy (FA) (untreated schizophrenia n = 19, controls n = 32). Volumes were assessed by manual tracing of central structures and a semi-automated parcellation of BAs. Patients with schizophrenia had increased ventricular size associated with decreased cortical gray matter volumes widely across the brain; a similar but less pronounced pattern was seen in normal controls; local correlations (e.g. temporal horn with temporal lobe volume) were not appreciably higher than non-local correlations (e.g. temporal horn with prefrontal volume). White matter regions adjacent to the ventricles similarly did not reveal strong regional relationships. FA and center of mass of the anterior limb of the internal capsule also appeared differentially influenced by ventricular volume but findings were similarly not regional. Taken together, these findings indicate that ventricular enlargement is globally interrelated with gray matter volume diminution but not directly correlated with volume loss in the immediately adjacent caudate, putamen, or internal capsule.


The role of a functional polymorphism in the transcriptional control region of serotonin transporter gene (5-HTTLPR, SERTPR) has been studied intensively in major depression and in the response to selective serotonin inhibitors (SSRIs) in major depression. The findings have been contradictory, although majority of the studies indicate that the short allele is associated with poor response to SSRIs in major depression. In the present study, we evaluated the association of 5-HTTLPR with treatment response to SSRI medication in Finnish Caucasian MDD patients. A secondary purpose was to study the possible association of this particular polymorphism with major depressive disorder. The aim of the study was to replicate the previous findings in this area. Primary outcomes of the treatment were remission, defined by an exit score of seven or less, and response, defined by a reduction of at least 50% on the MADRS. We had also a control population of 375 healthy blood donors, as a secondary objective was to evaluate the possible association of this particular polymorphism with major depressive disorder. Twenty-nine of the 85 (34.1%) patients reached the remission and 58.8% achieved the predefined response criteria. The l/l genotype of 5-HTTLPR was presented in 51.7% of those patients who achieved remission vs. 25.0% in the non-remitters (P = 0.03). The result remained statistically significant after adjusting for age, gender, medication and MADRS points at the study entry. However, the small sample size limits the reliability of this result.

Although low serum 25-hydroxyvitamin D (25(OH)D) and elevated serum parathyroid hormone (PTH) have been associated with depression in clinical settings, this link in community-dwelling individuals is inconclusive. The present study aimed at examining the association between serum 25(OH)D and PTH levels and the presence of depression in a national population-based household sample of 4,002 Jordanian participants aged >/=25 years. The DASS21 depression scale was used to screen for depression, and serum concentrations of 25(OH)D and PTH were measured by radioimmunoassay. Multiple logistic regression models were used to explore the association between serum 25(OH)D and PTH levels and depression. The unadjusted odds ratio (OR) decreased linearly with increasing quartiles of serum 25(OH)D (P (trend) = 0.00). The OR for having depression was significantly higher among individuals in the first and second quartiles (OR = 1.4, 1.23, respectively) than among those in the fourth quartile (P values = 0.00 and 0.03, respectively). This relationship remained significant after adjusting for age, sex, marital status, education, BMI, serum creatinine, number of chronic diseases (OR = 1.39 and 1.21 and P values = 0.00 and 0.05, respectively) and after further adjustment for exercise, altitude, and smoking (OR = 1.48 and 1.24, respectively, and P values = 0.00 and 0.03, respectively). No significant association was found between serum PTH levels and depression. The decrease in risk of depression among participants started to be significant with serum 25(OH)D levels higher than 42.3 ng/ml (lower limit of the range of the third quartile). This value may help pinpoint the desirable level of serum 25(OH)D to be attained to help aid the prevention and treatment of depression.


Previous studies on the association between affective disorders and the metabolic syndrome yielded inconclusive results. Therefore, we examined the prevalence of the metabolic syndrome in 230 men and women with unipolar major depressive disorder during inpatient treatment and compared it to 1,673 subjects from primary care from a similar region in northern Germany. We used the AHA/NHBLI criteria to determine the rate of metabolic syndrome (MetS) and each single criterion of MetS in both groups. The age-standardized prevalence of MetS was 2.4x as high in patients with major depressive disorder (MDD) compared with data from comparison subjects (41.0% vs. 17.0%). With respect to the single criteria, elevations were found in MDD patients for fasting glucose and triglycerides in both genders, and waist circumference in women. Men in the patient and the comparison groups were found to have higher rates of increased fasting glucose and triglycerides than women in the respective groups. Factors associated with the MetS in MDD patients comprise body mass index and the severity of depression. Our results demonstrate an increased prevalence of the MetS in men and women with MDD. Interventions for the frequently untreated metabolic abnormalities and careful screening for physical health conditions among people with MDD are warranted.


As a relatively large body of research has been published up to now, it may be informative to explore whether the use of endophenotypes has produced consistent findings in attention-deficit hyperactivity disorder (ADHD). We reviewed the results of genetic studies investigating associations between putative susceptibility genes for ADHD and neuropsychological traits relevant for this disorder. A PubMed database search identified 47 studies. Most of them (n = 36) examined a single candidate gene, while seven studies examined two or three genes and only four studies examined 10 genes or more. The most investigated genes were DRD4, DAT1, COMT, MAOA, and DBH. Regarding DRD4, association of high reaction time variability with the 7-R allele absence appears to be the most consistent result. Speed of processing, set shifting, and cognitive impulsiveness were less frequently investigated, but seem to be altered in the 7-R allele carriers. Regarding DAT1, majority of studies reported negative results indicating that this gene may have a modulating effect rather than direct influence on cognitive functioning. The other genes were investigated in fewer studies, and the reported findings need to be replicated. The principal methodological issues that could represent confounding factors and may explain conflicting results are discussed.


Patients' attitudes toward side effects of antidepressants are likely to differ according to gender, which has not yet been fully addressed in the literature. From the 228,310 registrants, 1,305 participants who had received antidepressant drugs within the past year were identified with the Yahoo Japan research monitor through four-step screening procedures. Participants were asked as to which side effect(s) they had experienced, whether they had reported those side effects to their physicians, and whether they had taken any action to counteract them. The questionnaire was completed by 1,187 participants. Side effects were reported in 73.4% of the participants; the prevalence of self-reported side effects was significantly higher in men than women (80.4% vs. 68.3%, P <0.05). The percentage of participants who reported side effects to their physicians widely differed depending on the nature of their experience, ranging from 45.7% to 89.9%; the lowest was for sexual dysfunction. The percentage of participants who had taken any action to relieve side effects varied among side effects from 26.3% for sexual dysfunction to 89.5% for dry mouth. Moreover, a lower percentage of women had reported sexual dysfunction to physicians (36.6% vs. 60.7%, P <0.05) and had taken any action to counteract the problem (19.8% vs. 36.9%, P <0.05). Given that patients experienced with antidepressants are likely to be reluctant to report sexual side effects, physicians should be cognizant of the potential presence of sexual dysfunction in patients who are taking antidepressants, especially for women.


To date, pain perception is thought to be a creative process of modulation carried out by an interplay of pro- and anti-nociceptive mechanisms. Recent research demonstrates that pain experience
constitutes the result of top-down processes represented in cortical descending pain modulation. Cortical, mainly medial and frontal areas, as well as subcortical structures such as the brain stem, medulla and thalamus seem to be key players in pain modulation. An imbalance of pro- and antinociceptive mechanisms are assumed to cause chronic pain disorders, which are associated with spontaneous pain perception without physiologic scaffolding or exaggerated cortical activation in response to pain exposure. In contrast to recent investigations, the aim of the present study was to elucidate cortical activation of somatoform pain disorder patients during baseline condition. Scalp EEG, quantitative Fourier-spectral analyses and LORETA were employed to compare patient group (N = 15) to age- and sex-matched controls (N = 15) at rest. SI, SII, ACC, SMA, PFC, PPC, insular, amygdala and hippocampus displayed significant spectral power reductions within the beta band range (12-30 Hz). These results suggest decreased cortical baseline arousal in somatoform pain disorder patients. We finally conclude that obtained results may point to an altered baseline activity, maybe characteristic for chronic somatoform pain disorder.


Inattention is the most important behavioral feature of adult patients with attention-deficit/hyperactivity disorder (ADHD). Neuroimaging studies in ADHD have demonstrated abnormalities primarily in the frontostriatal circuitry and were mostly conducted in children. We investigated white matter (WM) integrity in adult ADHD patients and the correlation of WM microstructure and neuropsychological parameters in 37 (21 men) never-medicated adult ADHD patients and 34 age- and gender-matched healthy controls. All subjects underwent clinical interviews, rating scales, and neuropsychological tests of attentional performance. Diffusion tensor imaging (DTI) was acquired, and 12 WM regions-of-interest (ROIs) within the attentional network were chosen. Group differences of mean fractional anisotropy (FA) and mean diffusivity (MD) values were calculated for each ROI, and patients' DTI measures were then correlated with measures of attentional performance. FA values in ADHD patients were significantly reduced in the left inferior longitudinal fasciculus (ILF), while MD values were significantly increased in ADHD patients in the frontal portion of the left frontooccipital fasciculus (IFO). In ADHD patients, MD values were negatively correlated with attentional performance in the left ILF. Our findings provide further support for disturbed frontostriatal structural connectivity and also point to an involvement of the left temporal white matter with an impact on attentional performance.


In a retrospective chart review, we examined the effects of ketamine, an N-methyl-d-aspartate (NMDA) receptor antagonist, as electroconvulsive therapy (ECT) anaesthetic in patients suffering from therapy-resistant depression. We included 42 patients who received ECT treatment with either ketamine (n = 16) or the barbiturate thiopental (n = 26). We analysed the number of sessions until completion of ECT treatment (used as a surrogate parameter for outcome), psychopathology as assessed by pre- and post-ECT Mini-Mental State Examination (MMSE) and Hamilton Rating Scale for Depression (HAM-D) scores as well as ECT and seizure parameters (stimulation dose, seizure duration and concordance, urapidil dosage for post-seizure blood pressure management). The ketamine group needed significantly fewer ECT sessions and had significantly lower HAM-D and higher MMSE scores afterwards. As expected, the ketamine group needed more urapidil for blood pressure control. Taking into account the limits inherent in a retrospective study design and the rather small sample
size, our results nonetheless point towards synergistic effects of ECT and ketamine anaesthesia, less cognitive side effects and good tolerability of ketamine.


We evaluated the clinical use and the safety of cerebrospinal fluid diagnostics in 155 patients with the suspected diagnosis of first-episode schizophrenia. Five patients (3.2%) revealed pathological findings that lead to diagnostic re-evaluation and changes in clinical management. No serious adverse events occurred, but we documented 16 (10.3%) cases of mild to moderate headache or local pain at the puncture site. Our results underline the value of lumbar puncture in the clinical workup of first-episode patients with suspected schizophrenia.


To examine disease and treatment characteristics of patients with schizophrenia treated with electroconvulsive therapy (ECT). We examined charts from 79 patients diagnosed with schizophrenia (n = 55), persistent delusional disorders (n = 7), and schizoaffective disorders (n = 17) between 2003 and 2008. We recorded age, sex, indication for ECT, number of ECT sessions, ECT series, outcome, maintenance ECT, use of antipsychotics, duration of illness, and duration of the current exacerbation. All patients were taking antipsychotics at the time of enrolment in the study. Acute ECT included 2-26 sessions; maintenance ECT (M-ECT) was given to 18 patients for up to 12 years. Initial indications for ECT included psychosis (n = 28), pronounced affective symptoms (n = 28), delirious states (n = 20), and M-ECT (n = 3). Most patients experienced excellent/good outcomes (n = 66), but others experienced moderate (n = 8) or poor (n = 5) outcomes. No factors were identified that predicted treatment responses in individual patients. ECT proved to be effective in a population of patients that were severely ill with treatment-refractory schizophrenia. This does not imply that the patients were cured from schizophrenia. Rather, it reflects the degree of relief from psychosis and disruptive behaviour, as described in the patient charts. The treatment was often offered to patients after considerable disease durations.


This paper investigates the structure of psychopathological symptoms. Based on AMDP symptom profiles, a symptom space was calculated by robust nonmetric multidimensional scaling (NMDS) and the symptom structures of a sample dating from 1980 and a sample from 2002/2003 were compared. The method of NMDS presented in this study allows results from other studies to be confirmed and complemented. The symptom factors identified in the past by factor-analytic studies were replicated as clusters in two-dimensional symptom maps. Additionally, some theoretically assumed clusters of symptoms were detected that were not found in previous factor analysis approaches. From the results, which are depicted in a continuous space, new insights can be gained, especially with regard to questions of categorical and dimensional classifications. The comparison of the structural aspects of the symptomatology across more than two decades resulted in only small divergences and allows conclusions to be drawn about the stability of these structures and consequently of the symptom clusters and dimensions.

We introduce a diagnostic map that was calculated by robust non-metric multidimensional scaling based on AMDP symptom profiles of patients with schizophrenic and affective disorders to demonstrate a possibility to combine the categorical and the dimensional perspective at the same time. In the diagnostic map, a manic, a depressive, and a non-affective cluster clearly emerged. At the same time, the mania dimension \((r = 0.82)\), the depression dimension \((r = 0.68)\), and the apathy dimension \((r = 0.74)\) showed high multiple regression values in the map. We found substantial overlaps of the diagnostic groups with regard to the affective spectrum but irrespective of the ICD-10 classification. Within this sample, we found the association and quality of mood symptoms to be a structuring principle in a diagnostic map. We demonstrate that this approach represents a promising way of combining the categorical and the dimensional perspective. As a practical implementation of these findings, a multidimensional diagnostic map could serve as an automated diagnostic tool based on psychopathological symptom profiles.


The aim of the study was to investigate which factors are associated with age at onset in bipolar disorder with a specific focus on excessive alcohol and cannabis use, and the sequence of the onsets of excessive substance use and bipolar disorder. We investigated a naturalistic sample of 151 patients with bipolar I and II disorder receiving psychiatric treatment. Whether the presence of excessive substance use prior to bipolar disorder onset or the type of substance used (alcohol or cannabis) was associated with differences in age at onset was investigated using hierarchical and multiple linear regression analyses, adjusting for potential confounders. Patients with excessive alcohol use had a significantly later onset compared with patients with excessive cannabis use. Excessive general substance use prior to bipolar disorder onset was associated with a later onset. However, excessive cannabis use was associated with an earlier onset whether it preceded or followed bipolar disorder onset, also after adjusting for possible confounders. Excessive use of alcohol or other substances was not independently associated with age at onset in multivariate analyses. Alcohol use was associated with a later onset compared with cannabis use, suggesting different relationships to the onset of bipolar disorder. Lifetime use of cannabis predicted an earlier onset, independent of the sequence of onsets. This indicates that an early onset may increase the risk of cannabis use and that cannabis use may trigger bipolar disorder in vulnerable individuals.


The interrelation between needs for care and quality of life has been described and replicated by several studies. The present work aims to add to the understanding of longitudinal interrelations between needs for care, quality of life, and other outcome measures by analyzing a sample of patients at the onset of schizophrenia. This study relied on data from the EUFEST trial, designed to compare first- and second-generation antipsychotics during 1 year. At baseline, 498 patients have been included. The first (baseline) and the last assessment (12 months after baseline) were used for the analyses. Predictors of quality of life were determined using regression analyses. We tested the complex longitudinal interrelations between baseline and outcome measures with structural
equation models. Unmet needs were not definitively confirmed as a predictor of subsequent quality of life, unless unmet needs changing to no needs were separated from unmet needs changing to met needs. Each unmet need that changed to no need enhanced the quality of life (mean score 1-7) by 0.136 scale points. This study suggests that when studying quality of life and needs for treatment, it is crucial to differentiate whether unmet needs disappeared or whether they were met, as the former has a stronger impact on quality of life.


Mutations of the transcription factor 4 (TCF4) gene cause mental retardation with or without associated facial dysmorphisms and intermittent hyperventilation. Subsequently, a polymorphism of TCF4 was shown in a genome-wide association study to slightly increase the risk of schizophrenia. We have further analysed the impact of this TCF4 variant rs9960767 on early information processing and cognitive functions in schizophrenia patients. We have shown in a sample of 401 schizophrenia patients that TCF4 influences verbal memory in the Rey Auditory Verbal Learning Test. Contrary to expectations, carriers of the schizophrenia-associated allele showed better recognition, thus indicating that while TCF4 influences verbal memory, the TCF4-mediated schizophrenia risk is not determined by the influence of TCF4 on verbal memory. TCF4 does not impact on various other cognitive functions belonging to the domains of attention and executive functions. Moreover, in a pharmacogenetic approach, TCF4 does not modulate the improvement of positive or negative schizophrenia symptoms during treatment with antipsychotics. Finally, we have assessed a key electrophysiological endophenotype of schizophrenia, sensorimotor gating. As measured by prepulse inhibition, the schizophrenia risk allele C of TCF4 rs9960767 reduces sensorimotor gating. This indicates that TCF4 influences key mechanisms of information processing, which may contribute to the pathogenesis of schizophrenia.


Mutations in postsynaptic scaffolding genes contribute to autism, thus suggesting a role in pathological processes in neurodevelopment. Recently, two de novo mutations in SHANK3 were described in schizophrenia patients. In most cases, abnormal SHANK3 genotype was also accompanied by cognitive disruptions. The present study queries whether common SHANK variants may also contribute to neuropsychological dysfunctions in schizophrenia. We genotyped five common coding or promoter variants located in SHANK1, SHANK2 and SHANK3. A comprehensive test battery was used to assess neuropsychological functions in 199 schizophrenia patients and 206 healthy control subjects. In addition, an independent sample of 77 subjects at risk for psychosis was analyzed for replication of significant findings. We found the T allele of the SHANK1 promoter variant rs3810280 to lead to significantly impaired auditory working memory as assessed with digit span (12.5 +/- 3.6 vs. 14.8 +/- 4.1, P < .001) in schizophrenia cases, applying strict Bonferroni correction for multiple testing. This finding was replicated for forward digit span in the at-risk sample (7.1 +/- 2.0 vs. 8.3 +/- 2.0, P = .044). Previously, altered memory functions and reduced dendritic spines and postsynaptic density of excitatory synapses were reported in SHANK1 knock-out mice. Moreover, the atypical neuroleptic clozapine was found to increase SHANK1 density in rats. Our findings suggest a role of SHANK1 in working memory deficits in schizophrenia, which may arise from neurodevelopmental changes to prefrontal cortical areas.
Early-onset bipolar disorder is an impairing condition that is strongly associated with genetic inheritance. Neurocognitive deficits are core traits of this disorder which seem to be present in both young and adult forms. Deficits in verbal memory and attention are persistent within euthymic phases in bipolar adults, adolescents, and children. In younger samples, including type I or II and not otherwise specified patients, executive functions are not widely impaired and the existence of visual-spatial deficits remains unclear. The main aim of this study was to compare the neurocognitive performance in young stabilized type I or II bipolar patients and healthy controls. Fifteen medicated adolescents with bipolar disorder and 15 healthy adolescents, matched in age and gender, were compared on visual-spatial skills (reasoning, memory, visual-motor accuracy) and executive functioning (attention and working memory, set-shifting, inhibition) using t-tests and MANCOVA. Correcting for verbal competence, MANCOVA showed that patients performed significantly worse than controls in letters and numbers sequencing (P = 0.003), copy (P < 0.001) and immediate recall (P = 0.007) of the Rey Complex Figure Test, interference of the Stroop Color-Word Test (P = 0.007) and non-perseverative errors on the Wisconsin Card Sorting Test (P = 0.038). Impaired cognitive performance was found in young bipolar patients in working memory, visual-motor skills, and inhibitory control.

Diffusion tensor imaging (DTI) demonstrates decline of fractional anisotropy (FA) as a marker of fiber tract integrity in Alzheimer’s disease (AD). We aimed to assess the longitudinal course of white matter microstructural changes in AD and healthy elderly control (HC) subjects and to evaluate the effects of treatment with the cholinesterase inhibitor galantamine on white matter microstructure in AD patients. We enrolled 28 AD patients and 11 healthy elderly control subjects (HC). AD patients were randomly assigned to 6-month double-blind galantamine treatment or placebo, with a 6-month open-label extension phase. DTI was performed at baseline, as well as at 6 and 12-month follow-up in AD patients. The HC subjects underwent DTI at baseline and 12-month follow-up without treatment. We measured FA in regions of interest covering the posterior cingulate and corpus callosum. At 6-month follow-up, the AD group showed significant FA decline in the left posterior cingulate. FA decline was significantly preserved in the posterior body of the corpus callosum in AD group with treatment compared to placebo. At 12-month follow-up, the AD patients showed no differences in FA decline between initial treatment and placebo groups after the 6-month open-label extension phase. A significant FA decline occurred in the left posterior cingulate across the AD and HC groups without between-group differences. DTI demonstrated FA decline in intracortically projecting fiber tracts in aging and AD over 1 year. Galantamine had limited impact on regional FA decline, which was not preserved after additional 6-month open-label treatment.

Changes in the clinical presentation of functional disorders and the influence of social and cultural factors can be investigated through the historical case notes from mental hospitals. World War I (WWI) was a potent trigger of functional disorders with neurological or psychiatric symptoms. We analysed 100 randomly selected case files of German servicemen admitted to the Department of Psychiatry of the Charite Medical School of Berlin University during WWI and classified them according to contemporaneous and retrospective modern diagnoses. We compared the clinical presentations with accounts in the German and British medical literature of the time. Most patients obtained the contemporaneous diagnosis of 'psychopathic constitution' or hysteria reflecting the general view of German psychiatrists that not the war but an individual predisposition was the basis for the development of symptoms. The clinical picture was dominated by pseudoneurological motor or sensory symptoms as well as pseudoseizures. Some soldiers relived combat experiences in dream-like dissociative states that partly resemble modern-day post-traumatic stress disorder. Most servicemen were classified as unfit for military service but very few of them were granted compensation. Severe functional disorders of a neurological character could develop even without traumatic exposure in combat, which is of interest for the current debate on triggers of stress disorders. The high incidence of pseudoseizures accords with the psychiatric literature of the time and contrasts with accounts of war-related disorders in Britain. The tendency of German psychiatrists not to send traumatised servicemen back to active duty also distinguished between German and British practice. Our data contribute to the debate on the changing patterns of human responses to traumatic experience and their historical and social context.


The aim of the study was to examine the psychosis continuum in a Latin-American community setting. Data were from the Brazilian Sao Paulo Epidemiologic Catchment Area Study, a cross-sectional survey conducted in two boroughs of the city of Sao Paulo. The Composite International Diagnosis Interview (version 1.1) was applied to a probabilistic sample of 1,464 adults, who were interviewed in their household, in order to identify the presence of psychotic symptoms. A subsample was assessed with Schedules for Clinical Assessment in Neuropsychiatry interview. We described the occurrence of psychotic symptoms, categorized into subgroups according to their clinical impact, disability, and help-seeking behavior. The correlation of socio-demographic variables, depressive symptoms, and alcohol and substance use disorders with those psychotic subgroups was analyzed. Polychotomic logistic regression tested the associations between subgroups of psychosis (clinical and subclinical) and the correlates. Of the total sample, 38.0% presented at least one lifetime psychotic symptom, 1.9% met the criteria for an ICD-10 diagnosis of non-affective psychosis, 5.4% presented clinically relevant psychotic symptoms, and 30.7% endorsed clinically non-relevant symptoms. The most common psychotic symptom was delusion with a plausible explanation (in 18.6%). The presence of any psychiatric diagnosis was associated with the presence of psychotic symptoms (OR range, 1.9-8.9). Subclinical psychosis subgroups were found to be associated with the 18-24 year age bracket, chronic depressive mood, and alcohol use disorder. Our results support the concept of a psychosis continuum in Latin-American populations, suggesting that different risk factors influence their manifestation across the continuum.

Professional athletes are subject to massive somatic, social, and mental stress. Despite great public interest for athletic achievements, the emotional strains thereof are very poorly investigated and discussed. The main reason for this is the widespread assumption that only emotionally very strong athletes are able to compete at the highly professional level and therefore mental disorders do not exist in professional sports. But available research data about the prevalence of mental disorders in this area suggest that this hypothesis must be revised. With respect to depression and the overtraining syndrome, attempts have been made to demonstrate the difficulties with etiology, diagnostics, and treatment for sports psychiatry and psychotherapy. Scientifically, sport psychiatry and psychotherapy can be defined as a discipline, whose focus is the investigation, treatment, and prevention of the extreme and sports-specific emotional strains and disorders. In addition to sport psychology, which focuses mainly on performance enhancement, mental stress, and disorders can hereby be recognized, disorders be treated and the athletic performance sustained. With the foundation of the Task Force for Sports Psychiatry and Psychotherapy at the German Association for Psychiatry and Psychotherapy, scientific research, further education, prevention, and treatment for mental disorders in professional sports will be improved.


On the basis of impaired glutamatergic transmission and the potential role of astrocytes in schizophrenia, we treated cultured astrocytes with MK-801, an NMDA-receptor antagonist, to investigate whether the resulting proteome changes are similar to those we found in our earlier proteome analysis of schizophrenia human brain tissue as well as to better comprehend the role of astrocytes in the disorder. Indeed, there are similarities. Furthermore, to verify the efficacy of clozapine and its effect over the proteome, we treated MK-801-treated astrocytes with clozapine. Interestingly, clozapine reversed protein changes induced by MK-801. The treatment of cell cultures with neural transmission agonists and antagonists might provide useful insights about psychiatric disorders.


Investigating and characterizing the degree and correlates of patient's trust in their treating psychiatrists across a range of psychiatric disorders is of a great clinical relevance to enhance our therapeutic alliance, which has not been addressed in the literature. In this study, outpatients who visited one of the participating psychiatric clinics in Tokyo, Japan between October and November, 2010 were asked to complete the Trust in Physician Scale (TPS), an 11-item self-report questionnaire. A univariate general linear model was used to examine the effects of the following variables on the TPS total score: age, sex, diagnosis, Global Assessment of Functioning score, educational background, physician’s years of practice as a psychiatrist, duration of treatment with their current psychiatrists, sex concordance between patients and their psychiatrists, and whether patients were older than their psychiatrists. Five hundred and four patients were enrolled (mean +/- SD age = 42.8 +/- 13.6 years; 176 men; Psychiatric diagnoses (ICD-10): F0 [N = 8], F2 [N = 72], F3 [N = 252], F4 [N = 147], F6 [N = 22]). A duration of treatment with their current psychiatrist of >= 1 year and a duration of their physician’s clinical expertise as a psychiatrist for >= 10 years were associated with a greater degree of patient's trust in their psychiatrist. Furthermore, patients with a F3 diagnosis showed a significantly higher TPS total score than those with F4. These findings underscore an importance of paying close attention to patients who are relatively new and are not treated by well-experienced
psychiatrists in terms of subjective trust. Furthermore, this likely holds more true for patients with neurotic disorders.


Consisting evidence in animal models has suggested that alterations in brain-derived neurotrophic factor (BDNF) brain expression and release are involved in the pathogenesis of mental illnesses, such as, mood, anxiety, and eating disorders. This hypothesis is supported by data emerging from biochemical studies on serum BDNF levels and genetic studies on the functional polymorphism Val66Met in the BDNF gene in patients and control subjects. Anxiety-related personality traits are associated with several mental disorders. However, they are also measurable in non-affected subjects and, so, may represent a useful "endophenotype" to study the biological correlation of the vulnerability factors in the general population. In this study, we analyzed putative correlations in subjects unaffected by mental disorders between personality traits, serum BDNF levels (N = 107), and the BDNF Val66Met genotype (N = 217). Furthermore, we tested the possible interactions between these variables. A significant correlation has been observed between high scores of harm avoidance (HA) measured by the temperament and character inventory (TCI), and low BDNF serum concentration (r = -0.253, P = 0.009). In addition, an association has been evidenced between low BDNF levels in serum and the BDNF Val/Val genotype (P = 0.021). By analyzing putative concomitant effects of different variables on HA scores in a regression model, we observed a significant correlation only with BDNF serum concentrations (P = 0.022). The study results suggest that a decrease in serum BDNF concentrations may represent a biochemical marker associated with anxiety personality traits also retrievable in the general population.


Several studies suggest that attention to emotional content is related to specific changes in central information processing. In particular, event-related potential (ERP) studies focusing on emotion recognition in pictures and faces or word processing have pointed toward a distinct component of the visual-evoked potential, the EPN ('early posterior negativity'), which has been shown to be related to attention to emotional content. In the present study, we were interested in the existence of a corresponding ERP component in the auditory modality and a possible relationship with the personality dimension extraversion-introversion, as assessed by the NEO Five-Factors Inventory. We investigated 29 healthy subjects using three types of auditory choice tasks: (1) the distinction of syllables with emotional intonation, (2) the identification of the emotional content of adjectives and (3) a purely cognitive control task. Compared with the cognitive control task, emotional paradigms using auditory stimuli evoked an EPN component with a distinct peak after 170 ms (EPN 170). Interestingly, subjects with high scores in the personality trait extraversion showed significantly higher EPN amplitudes for emotional paradigms (syllables and words) than introverted subjects.

Gray matter (GM) volume deficits have been described in patients with schizophrenia (Sz) and bipolar disorder (BD), but to date, few studies have directly compared GM volumes between these syndromes with methods allowing for whole-brain comparisons. We have used structural magnetic resonance imaging (MRI) and voxel-based morphometry (VBM) to compare GM volumes between 38 Sz and 19 BD chronic patients. We also included 24 healthy controls. The results revealed a widespread cortical (dorsolateral and medial prefrontal and precentral) and cerebellar deficit as well as GM deficits in putamen and thalamus in Sz when compared to BD patients. Besides, a subcortical GM deficit was shown by Sz and BD groups when compared to the healthy controls, although a putaminal reduction was only evident in the Sz patients. In this comparison, the BD patients showed a limited cortical and subcortical GM deficit. These results support a partly different pattern of GM deficits associated to chronic Sz and chronic BD, with some degree of overlapping.


To date, few studies have addressed the relationship between brain structure alterations and responses to atypical antipsychotics in schizophrenia. To this end, in this study, magnetic resonance imaging (MRI) and voxel-based morphometry (VBM) were used to assess the relationship between the brain volumes of gray (GM) and white (WM) matters and the clinical response to risperidone or olanzapine in 30 schizophrenia patients. In comparison with healthy controls, the patients in this study showed a bilateral decrease in the anteromedial cerebellar hemispheres, the rectal gyrus and the insula, together with bilateral increases in GM in the basal ganglia. Both patient groups had a significantly smaller volume of WM in a region encompassing the internal and external capsules as compared to the controls. We found an inverse association between striatal size and the degree of clinical improvement, and a direct association between the degree of insular volume deficit and its improvement. The non-responder patient group showed a significant decrease in their left rectal gyrus as compared with the responder group. This study reveals a pattern of structural alterations in schizophrenia associated with the response to risperidone or olanzapine.


While the impact of mentally ill patients’ perceptions of their key relatives’ expressed emotion is well examined with regard to relapse, there is a paucity of evidence concerning the impact on their key relatives' burden. The present study aims to evaluate the relative prognostic value of expressed and perceived emotion on caregivers' stress outcome within a 3-year follow-up period. Yearly follow-up data of the key relatives of 16 first-hospitalized schizophrenic and 34 depressed patients were available including expressed and perceived emotion and different dimensions of caregivers' stress outcome: objective and subjective burden, well-being, psychological symptoms and subjective quality of life. Multiple linear regression analyses were computed to assess the relative impact of expressed and perceived emotion. All dimensions of burden were significantly and consistently correlated with caregivers' expressed emotion and patients' perceived criticism on the bivariate level. On the multivariate level, however, expressed criticism appeared to be the most relevant predictor, followed by perceived resignation. Data indicate that the impact of the patients' perceived criticism on caregivers' stress outcome is limited. More attention should be paid to patients' perceived resignation which may be an unidentified stress contributor for caregivers so far.

While neuroticism has been intensely investigated in caregivers of patients with serious somatic disorders, studies in caregivers of patients with mental illness are lacking. Additionally, most studies are cross-sectional not allowing conclusions about long-term effects of personality factors. The present study examines the impact of personality factors on the course of subjective burden and psychological well-being by a mediational model in a sample of caregivers of first hospitalized patients with schizophrenia or depression within a 2-year follow-up period. At baseline, 83 caregivers could be enrolled in the study, the drop-out rate was about 23% at 2-year follow-up. Personality factors were assessed by the German version of the NEO-FFI (Borstenau and Costa 1993) only at baseline. At each follow-up, subjective burden was assessed by the FBQ (Moller-Leimkuhler acc. to Pai and Kapur (Brit J Psychiat 138:332-335, 1981)), and psychological well-being by the SCL-90 R (Derogatis in SCL-90-R, administration, scoring and procedures. Manual for the r(evised) version. John Hopkins University School of Medicine, Baltimore, 1977). Among the personality factors, neuroticism turned out to be the most relevant predictor of subjective burden and self-rated symptoms, showing direct as well as indirect effects. The direct effects on caregivers' mental health were mediated to a considerable amount by subjective burden. The mediational model was stable across time and even revealed increasing indirect effects of neuroticism. Caregivers' neuroticism as a dispositional trait plays a crucial role in the course of the stress process. As neuroticism is associated with perceptual distortion, the latter should be targeted by long-term family interventions in order to reduce subjective burden and enhance mental health of the caregivers.


The aim of the present study is to identify the relative contribution of patient and caregiver characteristics in a sample of primary carers of patients with chronic mental disorders living in the community. As carers were recruited from caregiver organizations, mainly mothers of an adult child suffering from schizophrenia participated in the study (n = 102). Within a comprehensive transactional stress model, burden was assessed with respect to objective and subjective burden, cognitive-emotional well-being, psychological distress and subjective quality of life. Primary stressors include illness-related characteristics of the patient, and a number of personal dispositions and resources of the caregivers were included as potential moderating variables. Multiple regression analyses were separately calculated for each dimension of burden. Interaction of carers' expressed emotion and external locus of control with the patient's problem with family communication as well as perceived social support was most predictive for objective and subjective burden, whereas carers' neuroticism appeared as the most relevant predictor of their well-being, psychological distress and subjective quality of life. Among the patients' variables, regular employment contributed significantly to reduce carers' distress and enhance their well-being. As the sample was recruited from caregiver organizations, a selection bias has to be taken into account. To reduce caregiver burden, especially mothers' burden, the patients' occupational abilities should be strongly enhanced at an early stage. Family interventions should improve dysfunctional interactions, enhance the carers' social activities and focus more intensely on the carers' own dispositions.


Given the importance of the term 'evidence' in evidence-based medicine (EBM), the meaning of this term is evaluated, going back to the philosophical tradition and current meaning of the terms
‘evidence’ and ‘truth’. Based on this, current problems in the definition of evidence and in the grading of evidence in EBM are described, taking examples from the field of psychiatry and especially pharmacopsychiatry. These problems underline that the use of the term evidence in EBM is inconsistent and inconclusive. This should be fairly stated in all EBM-related publications, especially in EBM-based guidelines, to avoid severe misunderstandings in and outside the field of psychiatry. Although EBM might have increased empirically driven rational decision-making in psychiatry/medicine, the current limitations should be carefully considered.


Alterations of theory of mind (ToM) and empathy were implicated in the formation of psychotic experiences, and deficits in psychosocial functioning of schizophrenia patients. Inspired by concepts of neurocognitive endophenotypes, the existence of a distinct, potentially neurobiologically based social-cognitive vulnerability marker for schizophrenia is a matter of ongoing debate. The fact that previous research on social-cognitive deficits in individuals at risk yielded contradictory results may partly be due to an insufficient differentiation between qualitative aspects of ToM. Thirty-four unaffected first-degree relatives of schizophrenia patients (21 parents, 8 siblings, 5 children; f/m: 30/4; mean age: 48.1 +/- 12.7 years) and 34 controls subjects (f/m: 25/9; mean age: 45.9 +/- 10.9 years) completed the ‘Movie for the Assessment of Social Cognition’-a video-based ToM test-and an empathy questionnaire (Interpersonal Reactivity Index, IRI). Outcome parameters comprised (1) ‘cognitive’ versus ‘emotional’ ToM, (2) error counts representing ‘undermentalizing’ versus ‘overmentalizing’, (3) empathic abilities and (4) non-social neurocognition. MANCOVA showed impairments in cognitive but not emotional ToM in the relatives’ group, when age, gender and neurocognition were controlled for. Relatives showed elevated error counts for ‘undermentalizing’ but not for ‘overmentalizing’. No alterations were detected in self-rated dimensions of empathy. Of all measures of ToM and empathy, only the IRI subscale ‘fantasy’ was associated with measures of psychotic risk, i.e. a history of subclinical delusional ideation. The present study confirmed subtle deficits in cognitive, but not emotional ToM in first-degree relatives of schizophrenia patients, which were not explained by global cognitive deficits. Findings corroborate the assumption of distinct social-cognitive abilities as an intermediate phenotype for schizophrenia.


Genetic factors determining the response to antipsychotic treatment in schizophrenia are poorly understood. A new schizophrenia susceptibility gene, the zinc-finger gene ZNF804A, has recently been identified. To assess the pharmacogenetic importance of this gene, we treated 144 schizophrenia patients and assessed the response of positive and negative symptoms by PANSS. Patients homozygous for the ZNF804A risk allele for schizophrenia (rs1344706 AA) showed poorer improvement of positive symptoms (7.35 +/- 0.46) compared to patients with a protective allele
(9.41 +/- 0.71, P = 0.022). This provides further evidence that ZNF804A is of functional relevance to schizophrenia and indicates that ZNF804A may be a novel target for pharmacological interventions.


The N-methyl-D-aspartate receptor (NMDAR) has been implicated in the pathophysiology of schizophrenia. Administered to healthy individuals, a subanesthetic dose of the noncompetitive NMDAR antagonist ketamine reproduces several psychopathological symptoms commonly observed in patients with schizophrenia. In a counterbalanced, placebo-controlled, double-blind, within-participants study, fifteen healthy subjects were administered a continuous subanesthetic S-ketamine infusion while cortical activation was measured using functional magnetic resonance imaging. While being scanned, subjects performed an overt word generation task. Ketamine-induced psychopathological symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS). Ketamine administration elicited effects on psychopathology, including difficulties in abstract thinking, lack of spontaneity and flow of conversation as well as formal thought disorder. On a behavioral level, verbal fluency performance was unaffected. The PANSS score for formal thought disorder positively correlated with activation measures encompassing the left superior temporal gyrus, the right middle and inferior frontal gyrus and the precuneus. Difficulty in abstract thinking was correlated with pronounced activations in prefrontal as well as in anterior cingulate regions, whereas hyperactivations in the left superior temporal gyrus were found in association with a lack of spontaneity and flow of conversation. In the absence of behavioral impairments during verbal fluency, NMDAR blocking evoked psychopathological symptoms and cortical activations in regions previously reported in schizophrenia patients. The results provide further support for the hypothesis of an NMDAR dysfunction in the pathophysiology of schizophrenia.


Studies using diffusion tensor imaging (DTI) have shown multifocal reduction in anisotropy of white matter fibre tracts in schizophrenia, and a few of these also suggest changes in apparent diffusion coefficient (ADC). In this study, we assessed ADC in 18 patients with schizophrenia and 18 healthy controls using a voxel-based approach. We did not find evidence of statistically significant changes in ADC in either direction at P < 0.05 (FDR corrected) using different smoothing filter sizes; only at an uncorrected threshold of P < 0.001 did we find an increase in a small right prefrontal area close to our previous FA finding. Our findings therefore do not support ADC changes to be a marker of white matter or grey matter abnormalities in schizophrenia. Changes in other parameters like fractional anisotropy (FA) might be a more sensitive indicator of white matter pathology in this disorder.


In recent years, we have witnessed an increase in media attention on the subject of mental illness, which mass media frequently portray as a new phenomenon affecting large sections of the population. Reports about people suffering from mental disorders and on psychiatric or psychotherapeutic clinics, however, are often characterised by their emphasis on stereotypes and one-sided invariably negative attributes both in the choice of wording and the images used. This paper is an attempt to elucidate this apparent contradiction from both a narrative and a socio-
historical perspective. In view of the development of modern moving image formats and storytelling techniques, it seeks to identify possible ways of harnessing the media to present a more considered and differentiated picture of psychiatric disorders and mental illnesses. Professionally moderated discussion forums based on social media techniques are to serve just as well as stories that take account of the narrative universals such as reward, success and human relations.


Schizophrenia is a neuropsychiatric disorder entailing progressive psychotic, cognitive and affective symptoms. Several imaging studies identified brain structure abnormalities in schizophrenia patients, particularly in fronto-temporal regions and evidence for progressive anatomical changes. Here, we synthesised these findings by quantitative coordinate-based meta-analysis, assessing regions of consistently reported brain structure changes, their physiological functions and the correlation of their likelihood with disease duration. The meta-analysis revealed four significant clusters of convergent grey matter reduction, while one cluster indicated higher grey matter values in patients. A voxel-wise analysis revealed a correlation between grey matter reduction and disease duration in the left anterior insula. Functional characterisation revealed significant association with reward, affective processing and language functions. The current analysis allowed the identification of consistent morphometric changes across a large sample of studies in regions that are associated with neurophysiological functions that are altered as hallmarks of schizophrenia psychopathology. The observation that the location of presumably progressive pathology is functionally linked to language and emotion is well in line with increasing deficits in these domains with disease progression in schizophrenia.


The purpose of this analysis was to explore the potential role of anxious MDD as a treatment predictor and moderator in major depressive disorder (MDD) using a large escitalopram clinical trial dataset. Individual patient-level data from 13 double-blinded, randomized, controlled trials in patients with MDD were pooled. Both univariate, last observation carried forward (LOCF) analyses and repeated measurements analyses without imputation (MMRM) were carried out for change in symptom scores, response and remission rates. Of 3,919 patients, 48.0% were classified as having anxious MDD depression (HAMD) somatization/anxiety subscale score >/=7 at baseline. Patients with anxious MDD were less likely to report symptom improvement on some outcome measures than patients without anxious MDD (predictor analysis). Specifically, the difference in response rates for patients with vs. patients without anxious MDD according to the MADRS (55.6% vs. 57.7%, respectively) was not statistically different. However, the difference in remission rates for patients with versus without anxious MDD according to the MADRS (37.6% vs. 44.1%, respectively) was statistically significant. Escitalopram was more effective than placebo, and as effective as the SSRIs and SNRIs, in the treatment of anxious MDD. The present analysis provides some evidence that the presence of an anxious MDD subtype is a predictor of poor response. There was no difference in the response to treatment of patients with or without anxious MDD to escitalopram, SSRIs, or SNRIs. The present analysis did not support the notion that SNRIs are more effective than escitalopram in the treatment of anxious MDD, nor was there evidence to support treatment moderating effects for anxious MDD.

In the present study, we examined several metabolic parameters in a group of 19 acutely depressed inpatients with major depression (DSM-IV) at baseline and investigated their development after 4 weeks of antidepressant treatment with reboxetine (8-12 mg per day). We performed oral glucose tolerance tests and additionally assessed free saliva cortisol and post-dexamethasone cortisol levels, as well as whole cholesterol, HDL- and LDL-cholesterol, triglycerides, free fatty acids, waist and hip circumference, heart rate, systolic and diastolic blood pressure. Furthermore, we evaluated the incidence of a metabolic syndrome and investigated the metabolic changes in depressed patients with and without a metabolic syndrome. We found 42.1% of patients to fulfil the criteria for a metabolic syndrome. Overall, reboxetine was well tolerated with essentially no side effects during the observation period. A 4-week treatment with reboxetine showed a beneficial effect on several metabolic parameters that was independent from treatment outcome and could therefore theoretically be attributed to the pharmacological profile of the drug. Due to the preliminary character of the present investigation, no conclusions about the clinical efficacy of reboxetine can be drawn.


Spontaneous Parkinsonism (SP) in schizophrenia-related disorders is poorly characterized. The objective of this study was to examine the concordance and clinical validity of alternative definitions of SP in patients with nonaffective psychotic disorders. Two-hundred drug-naive patients with nonaffective psychotic disorders were examined for core parkinsonian signs, including bradykinesia, rigidity, and tremor, and diagnosed of SP according to the Simpson-Angus Scale (SAS) cutoff criterion, the UK Parkinson’s disease brain bank (UKPDDBB) criteria, the National Institute of Neurological Disorders and Stroke (NINDS) criteria, and criteria requiring the presence of all three core features (full syndrome criteria). Parkinsonian signs and criteria were examined in relation to a number of relevant clinical variables. The most frequent sign was rigidity (33.5%) followed by bradykinesia (16%) and tremor (12%). The prevalence rate of SP according to the SAS cutoff criterion, the UKPDDBB criteria, the NINDS criteria for possible and probable SP, and the full syndrome criteria were 20.5, 13, 25.5, 18.5, and 4%, respectively. Bradykinesia was specifically related to negative symptoms, rigidity to neurological soft signs, and tremor to dyskinetic movements. The set of criteria showing more associations with clinical variables were the NINDS criteria for probable SP. Patients fulfilling these criteria had higher ratings for poor premorbid adjustment, negative symptoms, dyskinesia, neurological soft signs, and poor global treatment response than those without that diagnosis. The NINDS criteria for probable SP, i.e., presence of any two of the three core parkinsonian signs, seem to be the most suitable for clinical and research purposes.


Suicide and suicidal behaviour are a major health concern worldwide particularly in patients with mood disorders. Family, adoption and twin studies show that genetics influences suicidal behaviour. The serotonin transporter (5HTT) plays an important role in the pathophysiology of mood disorders and may also be involved in suicidal behaviour since 5HTT binding is decreased in the brain of suicide
completers. Because the effect of genomic imprinting in the 5HTT gene on suicidal behaviour has not been investigated, we analysed the parent-of-origin effect (POE) of four 5HTT markers and the differential expression of the 5HTT G2651T (rs1042173) alleles in suicide attempters affected by bipolar disorder. We performed a family based association study and ETDT/QTDT analyses of the rs25531, HTTLPR, VNTR-2 and G2651T polymorphisms in 312 nuclear families with at least one subject affected by bipolar disorder. The main outcomes investigated in this study are bipolar disorder diagnosis, suicide attempts, suicidal behaviour severity and age at onset of bipolar disorder. We also compared the allele-specific mRNA levels in lymphoblastoid cells from 13 bipolar suicide attempters and 8 bipolar non-suicide attempters. Allele 2651T was transmitted significantly more often to bipolar patients (P = 0.042). There was no significant difference between maternal and paternal transmission ratios. Furthermore, there was no significant difference in the ratio of T/G-specific mRNA expression between bipolar attempters and non-attempters. These data do not support a role for differential allelic expression of 5HTT for suicidal behaviour in bipolar disorder. Small sample size and the fact that RNA was obtained from lymphoblastoid cell lines were some of the limitations of this study.


This study presents a visual rating scale for the assessment of cerebral [(18)F]fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) scans to characterize typical findings in dementias associated with frontotemporal lobar degeneration (FTLD) and to differentiate individual patients with FTLD compared to Alzheimer’s disease (AD) and mild cognitive impairment (MCI). A total of 43 cerebral PET scans from patients with FTLD (n = 16, mean age 58.4 years), AD (n = 16, 59.9 years) and MCI (n = 11, 57.9 years) were analysed. Every PET data set was visually rated for seven brain regions on each hemisphere (frontal lobe, temporal lobe, parietal lobe, occipital lobe, basal ganglia, thalamus and cerebellum). The extent of the impairment in metabolism was classified as absent, mild, medium or strong. Using this four-stage visual rating scale, characteristic profiles of metabolic impairment in FTLD, AD, MCI and the FTLD-subgroup FTD (n = 9) could be demonstrated. Patients with FTLD showed a significantly lower metabolism in the left frontal lobe and in the left basal ganglia when compared to AD and to MCI. Complementary analyses using statistical parametric mapping (SPM2) supported the findings of the visual analysis. In detecting FTLD with visual rating, sensitivity/specificity was 81/94% compared to AD and 81/64% compared to MCI. Patients with FTD were correctly attributed to a diagnosis of FTLD with a sensitivity of 89%. This visual rating scale may facilitate the differential diagnosis of FTLD in clinical routine.


The Study aimed to assess clinical and social outcomes following involuntary admissions over 1 year and identify socio-demographic and clinical patient characteristics associated with more or less favourable outcomes. Seven hundred and seventy-eight involuntary patients admitted to one of 22 hospitals in England were assessed within the first week after admission and at 1 month, 3 month and 12 month follow-ups. Outcome criteria were symptom levels, global functioning, objective social outcomes, and subjective quality of life (SQOL). Baseline characteristics and patients’ initial experience were tested as predictors. Symptom levels and global functioning improved moderately. Objective social outcomes showed a small, but statistically significant deterioration, and SQOL a small, but significant improvement at 1 year. In multivariable analyses, admission due to risk to oneself and receiving benefits predicted poorer symptom outcomes. Female gender and higher
perceived coercion were associated with better objective social outcomes, whilst higher initial satisfaction with treatment predicted more positive SQOL at follow-ups. Over a 1-year period following involuntary hospital admission, patients on average showed only limited health and social gains. Different types of outcomes are associated with different predictor variables. Patients' initial experience of treatment, in the form of perceived coercion or satisfaction with treatment, has predictive value for up to a year following the admission.


The objective of this study is to examine the association of psychological distress to high-sensitivity C-reactive protein (hsCRP) levels and to examine the potential mediating role of health behaviours and pathophysiological factors. A total of 883 (393 men and 490 women) subjects, aged 36-56 years, participated in a population-based, cross-sectional study from 1997 to 1998 in Pieksamaki, Finland. Various clinical, biochemical and behavioural factors were measured, including hsCRP concentration. Psychological distress was measured using the 12-item General Health Questionnaire (GHQ-12). Subjects with low psychological distress (0 points in GHQ-12) were younger and more physically active, and their mean hsCRP level was lower when compared to subjects with medium (1-3 points) or high (4-12 points) psychological distress (1.26 +/- 1.36, 1.53 +/- 1.75 and 1.70 +/- 1.68 mg/l, respectively, P for linearity = 0.003). Psychological distress was also associated with high relative cardiovascular risk (hsCRP >3.00 mg/l). After adjusting for gender, age, BMI, smoking, use of alcohol and leisure time physical activity, odds ratios for hsCRP >3.00 mg/l in the groups that had medium and high psychological distress were 1.32 (95% CI: 0.81-2.16) and 1.79 (95% CI: 1.05-3.04), respectively, compared with the low distress group (P for linearity 0.032). Psychological distress was associated with elevated hsCRP levels representing high relative cardiovascular risk. This association remained after adjusting for health behaviours and pathophysiological factors, supporting a direct, physiological link between psychological distress and inflammation. CRP could be an important pathophysiological mechanism through which psychological factors are associated with cardiovascular disease.


The Italian psychiatric reform of 1978 was one of the most radical attempts in history to abolish the practise of custodial psychiatry using legislation. The work of the charismatic reformer Franco Basaglia had four main objectives, which have taken more than 30 years to achieve. Although the creation of outpatient mental health centres and a reduction in involuntary commitments occurred rapidly, the expensive development of small acute psychiatric departments in general hospitals as an alternative to psychiatric hospitals was implemented very slowly. According to a national survey by the Italian Ministry of Health, in 2001, there were a total of 9,300 acute beds for all of Italy, of which as many as 4,000 were in private facilities. With 1.72 acute beds per 10,000 inhabitants, Italy has one of the lowest figures in Europe of psychiatric beds. However, Italy's apparent and often praised low bed requirement places a large burden on families. The implementation of the reform process was most delayed and occurred at its worst in South Tyrol, in North Italy. In an effort to achieve a modern and progressive community-based psychiatric service, in particular one with more specialised services, mental health providers in this region have examined German, Austrian and Swiss models of psychiatric practice.

Electroconvulsive therapy (ECT) is an important treatment for catatonia. We aimed to study the response rate of catatonia treated with ECT and its clinical correlates in a large sample of inpatients. The ECT parameters of all patients (n = 63) admitted with catatonia between the months of January and December 2007 were examined. The number of ECTs administered, seizure threshold, failure to achieve adequate seizures and clinical signs pertaining to catatonia were analyzed. Response was considered as complete resolution of catatonic symptoms with Bush Francis Catatonia Rating Scale (BFCRS) score becoming zero. ECT was mostly started after failed lorazepam treatment except in 6 patients where ECT was the first choice. Patients who responded in 4 ECT sessions were considered fast responders (mean session number for response is 4 sessions) and response with 5 or more ECTs was considered slow response. Fast responders had significantly lower duration of catatonia (19.67 +/- 21.66 days, P = 0.02) and higher BFCRS score at presentation (17.25 +/- 6.21, P = 0.03). Presence of waxy flexibility and gegenhalten (22.60% vs. 0%, P = 0.01) predicted faster response, whereas presence of echophenomena (3.2% vs. 24.0%) predicted slow response. The response rate to catatonia appears to be associated with the severity and duration of catatonia, and the presence of certain catatonic signs.


Earlier studies suggested more severe overall cognitive impairments in deficit versus non-deficit schizophrenia; however, the specific contribution of different cognitive domains to this overall cognitive impairment remains unclear. The purpose of this study was to compare the two subtypes in general cognitive functioning as well as in individual cognitive domains using the composite score approach. One hundred and forty-three patients fulfilling the criteria for the deficit syndrome were compared with 123 patients diagnosed with non-deficit schizophrenia. Neurocognitive functioning was assessed by a neuropsychological test battery measuring the domains of sustained vigilance/attention, working memory, short-term memory, verbal memory, cognitive flexibility, and ideation fluency. Using the raw neuropsychological measures, we calculated a global index of cognitive impairment and domain-specific composite z-scores. Association between these composite scores and the deficit syndrome was examined by logistic regression analysis. After adjusting for relevant covariates including sex, age, education, smoking, and antipsychotic dose, results indicated a significant increase in the likelihood of deficit syndrome as a function of global (OR = 5.40; 95% CI 3.02-9.65) as well as domain-specific impairments (OR > 2 for all individual domains except for short-term memory). Cognitive flexibility was an independent predictor (OR = 2.92; 95% CI 1.47-5.80), whereas other cognitive domains demonstrated no unique contribution to the general cognitive impairment. Patients with deficit schizophrenia suffer from a more severe degree of neurocognitive impairment, which is qualitatively similar to the dysfunction seen in non-deficit schizophrenia. However, our results indicate that cognitive flexibility is specifically impaired in deficit versus non-deficit patients and may therefore represent a core feature of this subtype.


The Trial Criteria in Schizophrenia Working Group was convened in November 2007 to define consensus criteria for clinical trials in patients suffering from acute schizophrenia with special focus on placebo-controlled trials and withdrawal conditions. Clinical trials involving patients give rise to ethical and medico-legal dilemmas. Essential research of new drugs may potentially expose patients
to ineffective treatment regimens or placebo. The complexity of the problem increases when dealing with mentally ill patients. The Working Group’s criteria are thought to cover different aspects important in conducting clinical trials namely to ensure the patient’s safety, to present criteria that would allow the ethics committees to agree to the proposed criteria and to enable the possibility to reasonably conduct and ensure comparable quality of clinical studies in acutely ill patients with schizophrenia. To furthermore counteract current inconsistencies, these criteria should be evaluated using standardized rating scales applying established cut-off criteria. The developed trial criteria cover inclusion and exclusion criteria as well as withdrawal criteria due to non-response or worsening of symptoms.


Since severe stress can induce mental disorder symptoms that interact with vulnerability factors, the Community Assessment of Psychic Experiences (CAPE) was evaluated in a population of 419 young adults who survived an earthquake; results were compared to a database of 1,057 ‘non-exposed’ subjects. Unexpectedly, earthquake survivors showed lower CAPE scores for ‘small’ to ‘medium’ effect size. Post-trauma positive changes or re-appraisal for successful adaptation may explain these findings.


The interplay of psychotic and affective symptoms is a crucial challenge in understanding the pathogenesis of psychosis. In this study, we analyzed the interplay between two subclinical psychosis symptoms dimensions, and one depression symptoms dimension, using longitudinal data from Zurich. The Zurich study started in 1979 with a representative sample of 591 participants who were aged 20/21. Follow-up interviews were conducted at age 23, 28, 30, 35, and 41. The psychiatric symptoms were assessed with a semi-structured interview and the SCL 90-R. In this study, we analyzed three SCL-90-R subscales: the depression symptoms dimension and two distinct symptoms dimensions of subclinical psychosis, one representing a schizophrenia nuclear symptom dimension, the other representing a schizotypal symptoms dimension. Modeling was done with hybrid latent growth models, thereby including simultaneous and cross-lagged effects. The interplay between the two subclinical psychosis symptoms dimensions and the depression symptoms dimension includes several intertwined pathways. The schizotypal symptoms dimension has strong direct effects on the schizophrenia nuclear symptoms dimension, but also on the depression symptoms dimension. The latter has for its part an effect on the schizophrenia nuclear symptoms dimension. The main driving force within the dynamic interplay between depression and psychosis symptoms is a schizotypal symptoms dimension, which represents social and interpersonal deficiencies, ideas of reference, suspiciousness, paranoid ideation, and odd behavior. It does not only directly influence subclinical nuclear schizophrenia symptoms but also the symptoms of depression.


Disgust may be a key emotion and target for psychotherapeutic interventions in borderline personality disorder (BPD) and posttraumatic stress disorder (PTSD) at explicit and implicit-automatic levels. However, automatically activated disgust reactions in individuals with these disorders have not been studied. Disgust and its correlation with childhood abuse were assessed in women with BPD, but without PTSD; women with PTSD, but without BPD; women with BPD and PTSD; and healthy women. Disgust sensitivity, anxiety and depression were measured by self-report. Implicit disgust-prone (relative to anxiety-prone) self-concept was assessed using the Implicit Association Test. Women with BPD and/or PTSD reported more disgust sensitivity than controls. The implicit self-concept among patients was more disgust-prone (relative to anxiety-prone) than in controls. Women with BPD, with PTSD, or BPD and PTSD did not differ significantly in self-reported disgust levels or implicit disgust-related self-concept. Among women with BPD and/or PTSD, current psychiatric comorbidity (major depression, anxiety disorder, eating disorder, or substance-related disorder) did not affect disgust-related variables. More severe physical abuse in childhood was associated with a more anxiety-prone (less disgust-prone) implicit self-concept. Independent of psychiatric comorbidity, disgust appears to be elevated at implicit and explicit levels in trauma-related disorders. Psychotherapeutic approaches to address disgust should take implicit processes into account.


In June 2001, the then president of the Max Planck Society addressed a formal apology to survivors of Nazi medical crimes. Starting from this ritual of repentance, the paper examines the participants' diverse views of how to deal with the medical crimes of National Socialism. In comparison with the DGPPN, it asks about possibilities of going beyond historical retrospection to fulfil the imperative of remembrance.


The interaction of psychopathological states and psychosocial functioning determine the long-term course of schizophrenia and its treatment. To be able to achieve this interplay better, exact assessment of psychosocial functioning is needed besides measurement of psychopathology. Using the Personal and Social Performance (PSP) Scale, examination of the association between psychosocial functioning and psychopathology was conducted in a sample of 103 patients with chronic schizophrenia. Rating instruments were in addition Global Assessment of Functioning Scale and Social and Occupational Functioning Assessment Scale, as well as Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression Scale, and Mini-ICF-APP-Rating for Mental Disorders (Mini-ICF-APP). Besides good psychometric properties for the PSP scale in this chronic sample, we found, as expected, significant associations between the two relevant outcome domains: results showed significant negative correlations between PSP and PANSS. Findings prove the close interplay between social functioning and psychopathology in the chronic course of schizophrenia.

Generalized anxiety disorder (GAD) is characterized by excessive and persistent worrying. Neural substrates of this disorder are insufficiently understood, which relates to functional as well as to structural brain abnormalities. Especially, findings on the neuroanatomy of GAD have been inconsistent and were predominantly derived from pediatric samples. Therefore, we studied adult patients. Thirty-one women (16 patients with GAD and 15 healthy control participants) underwent structural MRI scanning. Gray matter volumes for specific brain regions involved in worrying, anticipatory anxiety, and emotion regulation were analyzed by means of voxel-based morphometry. Relative to controls, patients with GAD had larger volumes of the amygdala and the dorsomedial prefrontal cortex (DMPFC). Moreover, patients’ self-reports on symptom severity were positively correlated with volumes of the DMPFC and the anterior cingulate cortex. Patients with GAD show localized gray matter volume differences in brain regions associated with anticipatory anxiety and emotion regulation. This abnormality may represent either a predisposition for GAD or a consequence of disorder-specific behavior, such as chronic worrying. This issue should be addressed in future MRI studies.


The article evaluates the arguments used by German psychiatrists in the first half of the twentieth century to raise their professional reputation. The arguments, which were used in Wilhelmine Germany and in the 1920s, changed with the establishment of the NS-regime. While psychiatrists claimed for open care systems and for more transparency of psychiatric practice to the public in the first decades of the twentieth century, psychiatry became a crucial part of NS-health policies after 1933. The psychiatrist’s participation in the largest systematic action to kill mentally ill patients known in history forced them to search for ways to legitimatize the murder program and to integrate it into a therapeutical view of future psychiatry by trying to avoid arbitrariness and assigning research a central importance.


Schizophrenia is considered as a neurodevelopmental disorder with genetic and environmental factors playing a role. Animal models show that developmental hippocampal lesions are causing disconnectivity of the prefrontal cortex. Magnetic resonance imaging and postmortem investigations revealed deficits in the temporoprefrontal neuronal circuit. Decreased oligodendrocyte numbers and expression of oligodendrocyte genes and synaptic proteins may contribute to disturbances of micro- and macro-circuitry in the pathophysiology of the disease. Functional connectivity between cortical areas can be investigated with high temporal resolution using transcranial magnetic stimulation (TMS), electroencephalography (EEG), and magnetoencephalography (MEG). In this review, disconnectivity between different cortical areas in schizophrenia patients is described. The specificity and the neurobiological origin of these connectivity deficits and the relation to the symptom complex of schizophrenia and the glutamatergic and GABAergic system are discussed.


The aim of this dual-isotope SPECT imaging study was to evaluate striatal dopamine transporter (DAT) and D2 receptor availability in first-episode never-treated and haloperidol-treated
schizophrenic patients and whether the availability is associated with psychopathology. Twenty-four inpatients with a first acute schizophrenic episode were enrolled in the study; 12 of these patients were treated with haloperidol for 2 weeks before dual-isotope SPECT was performed, whereas the other 12 patients underwent the SPECT evaluation directly after enrollment. Twelve healthy control persons were also recruited and evaluated with the dual-isotope SPECT protocol. Psychopathology was assessed by the Positive and Negative Syndrome Scale and other scales. D2-radioligand binding did not differ between drug-naive patients and the control group but was significantly lower in the haloperidol-treated group. DAT availability was also significantly lower in the haloperidol patients than in the other two groups and differed significantly between drug-naive, positive-syndrome-type patients and healthy controls. The data obtained with the new dual-isotope SPECT technique reveal a direct effect of haloperidol at the D2 and DAT receptor level.


The history of the German Association for Psychiatry and--after its merger with the Society of German Neurologists and Psychiatrists (Gesellschaft deutscher Neurologen und Psychiater, GDNP) during the period of National Socialism has been subjected to only rudimentary research. The conventionally accepted idea that two independent professional associations were "coordinated" from above and turned into the extended arm of Nazi genetic health policy (Erbgesundheitspolitik) against their will must be reconsidered. This paper asks how the relationship between the GDNP and the Nazi state can be described adequately. Psychiatry and neurology as practice and science, and the biopolicy development dictatorship of National Socialism functioned, so the basic thesis, as "resources for each other" (Mitchell Ash).


The aim of this article is to review how psychotherapy is dispensed to patients in psychiatric treatment and to render the future perspectives of psychotherapy in psychiatric outpatient and inpatient care in Germany. We demonstrate that--according to the currently available data about healthcare providers, allocation of financial resources and curricular regulations--the presently used definition of the term "psychotherapy" is ambiguous. One major problem for the application of psychotherapy in psychiatry is obviously constituted by the dominance of the major guideline therapies ("Richtlinienverfahren") within psychiatric services. Here, guideline therapies do not meet the needs of a significant proportion of acutely, severely and/or chronically ill psychiatric patients and restrain the application of scientifically approved, disorder-oriented and context compliant interventions in psychiatric practice. As a future perspective, we suggest that the training of psychiatrists should impart profound interpersonal skills and provide the competence to offer psychotherapy within a multimodal, modular, and flexible treatment plan on the background of the self-conception of psychiatry as a medical discipline. Moreover, future concepts of psychiatric psychotherapy should promote an evidence-based selection and application of scientifically
approved, disorder-oriented, and integrative treatment methods, which are available in growing number.


The aims of this study were to analyze the presence of gender differences in the phenotypic expression of schizophrenia at the onset of illness and to explore whether these differences determine clinical and functional outcome 2 years after the initiation of treatment. Data from 231 first-episode-psychosis non-substance-dependent patients (156 men and 75 women) participating in a large-scale naturalistic open-label trial with risperidone were recorded at inclusion and months 1, 6, 12, and 24. Men presented a significant earlier age of onset (24.89 years vs. 29.01 years in women), poorer premorbid functioning, and a higher presence of prodromal and baseline negative symptoms. Women were more frequently married or lived with their partner and children and more frequently presented acute stress during the year previous to onset than men. No other significant clinical or functional differences were detected at baseline. The mean dose of antipsychotic treatment was similar for both genders during the study, and no significant differences in UKU scores were found. The number of hospitalizations was similar between groups, and adherence was more frequent among women. At the 2-year follow-up, both groups obtained significant improvements in outcome measures: PANSS, CGI severity, and GAF scores. Significant gender * time interactions were detected for negative and general PANSS subscales, with the improvement being more pronounced for men. However, no differences were detected for the mean scores obtained during the study in any outcome measure, and the final profile was similar for men and women. Our results suggest that although the initial presentation of schizophrenia can differ according to gender, these differences are not sufficient enough to determine differentiated outcome 2 years after the initiation of treatment in non-substance-dependent patients. The influence of gender on the early course of schizophrenia does not seem to be clinically or functionally decisive in this population.


The self-medication hypothesis attempts to explain the extraordinary high levels of cigarette smoking in schizophrenia; patients may smoke in an attempt to reduce their cognitive deficits, symptoms, or the side effects of antipsychotics. In a previous report, we detected beneficial performance in attention and working memory in patients with first-episode psychosis who smoked compared to non-smoking patients soon after stabilization. In the present study, we examine differences in the course of those deficits 12 months after the initiation of antipsychotic treatment. We also explore the association between smoking and symptoms and side effects of medication. Neuropsychological assessments were performed at baseline, month 6 and month 12 using a computerized battery that included measures of sustained attention (Continuous Performance Test CPT-O), selective attention (Stroop interference task) and working memory (CPT-XO). Patients met the criterion of fitting in the same smoking category throughout the study: non-smoker (n = 15; 0 cigarettes/day) and smoker (n = 26; >15 cigarettes/day). The non-smoking patients showed significant cognitive improvements, whereas smoking patients lost their superior baseline performance, which was probably obtained through nicotinic stimulation, at the 6- and 12-month assessments due to a static course of deficits. Smokers did not obtain any cognitive benefit after instauration of treatment and worsen their symptoms over the first year. These results suggest that smoking may constitute a marker of a more severe illness. Smoking was not associated with fewer extrapyramidal side effects. Smoking might
improve attention and working memory to a similarly modest extent as atypical antipsychotics and could reflect an effort to ameliorate these cognitive dysfunctions previous to treatment instauration.


Aim of this paper is to investigate the psychobiological reactions to experimentally induced negative emotional states in active marijuana-dependent smokers and whether changes in emotional reactivity were reversed by prolonged abstinence. Twenty-eight patients were randomly included into group A (fourteen active marijuana-dependent smokers) or group B (fourteen abstinent marijuana-dependent subjects). Emotional response evaluation of group B subjects was assessed after 6 months of abstinence. Fourteen healthy volunteers, matched for age and sex, were used as controls. Psychometric and emotional response evaluations were performed by administering Symptoms Check List-90 and State-Trait Anxiety Inventory Y-1 (STAI). Neutral and unpleasant set of pictures selected from the international affective picture system and the Self-Assessment Manikin procedure (SAM) have been used to determine ratings of pleasure and arousal. Before and after the experimental session, blood samples were collected to determine ACTH and cortisol plasma levels. Active cannabis users displayed significantly higher levels of pleasantness SAM scores and lower levels of arousal SAM scores compared to abstinent cannabis users and controls in response to emotional task. In a close parallel with psychological data, hormonal findings indicate a persistent hyperactivity of hypothalamus-pituitary-adrenal (HPA) axis in cannabis users, particularly among active marijuana smokers, and an impaired hormonal reaction to negative emotions, in comparison with healthy subjects. The capacity of the HPA axis to respond to stressful stimuli/negative emotions seems to be only partially recovered after 6 months of abstinence. Ours findings, although obtained in a small number of subjects, suggest an association between active cannabis use, subjective reduced sensitivity to negative emotions and threat and HPA axis dysfunction.


Magnetic resonance imaging and postmortem studies on schizophrenia provided evidence for compromised myelin integrity and reduced numbers of oligodendrocytes, which may worsen during the disease course. However, it is not clear whether these findings result from disease-inherent oligodendrocyte degeneration or side effects of antipsychotic treatment. Therefore, effects of haloperidol and clozapine on the viability and apoptosis of immature oligodendrocytes (OLN-93 cells, immunopositive for NG2, Olig1, Olig2) have been evaluated in the present study by labeling with propidium iodide and a caspase 3 assay. Given the indications for impaired cerebral energy supply in schizophrenia, a serum and glucose deprivation (SGD) model was chosen in comparison with the basal condition (BC). SGD led to increased necrotic and apoptotic cell death. Haloperidol and clozapine were partially protective in this model and reduced the percentage of propidium iodide-positive cells, while caspase 3 activity was not altered. No significant drug effects were observed under BC. The observed protective effects of haloperidol and clozapine on energy-deprived OLN-93 oligodendrocytes suggest that previously reported reductions in oligodendrocyte density in schizophrenia are rather disease related than a side effect of medication. A new mechanism of antipsychotic action is suggested, which may help to establish new oligodendrocyte-directed therapies of schizophrenia.

Attention-deficit hyperactivity disorder (ADHD) is a common disorder with estimated prevalence of 5% in children and 3.4% in adults. Psychiatric disorders are a frequent concomitant feature. Restless legs syndrome (RLS) may mimic the symptoms of ADHD. The aim of the study is to evaluate whether the presence of RLS predicts occurrence of psychiatric disorders in parents of children with ADHD. Thirty-seven parents of 26 children with ADHD were examined for RLS and for lifetime prevalence rates of psychiatric disorders and personality disorders based on the Structured Clinical Interview for DSM-IV Diagnoses (SCID). Prevalence rates in parents were 29.7% for RLS, 67.6% for Axis I and 40.5% for Axis II disorders. Mothers revealed higher rates for depression, anxiety disorders and ADHD than fathers, whereas personality disorders occurred at higher rates in fathers. The presence of RLS predicted a diagnosis of ADHD (odds ratio (OR) 21.9), agoraphobia (OR = 20.4) and any anxiety disorder (OR = 8.5). Although limited by the small sample size, we found evidence for increased rates of cluster B personality disorders (OR = 59.3) in parents with RLS. All parents of the latter group (100%) reported a positive family history of psychiatric disorders which was not the case in parents without RLS (69.2%) excluding the index children with ADHD. RLS seems to indicate increased vulnerability for psychiatric disorders, i.e., ADHD and anxiety disorders, in a subgroup of parents from ADHD children. Synaptic dysfunction affecting dopaminergic transmission among other transmitter systems may be a common final pathway related to the phenotypic spectrum of ADHD.


This study identified, mapped and treated the clinical features of mentally ill people, who had been isolated and restrained by family and community members as a result of a functional failure of the traditional medical, hospital-based mental health model currently practiced in Indonesia. A 10-month epidemiological population survey was carried out in Karangasem regency of Bali, Indonesia. A total of 404,591 individuals were clinically interviewed, of which 895 individuals with mental health problems were identified, with 23 satisfying criteria of physical restraint and confinement. Of the latter, twenty were males; age range was 19-69 years, all diagnosed by the researchers with schizophrenia-spectrum disorder (ICD-10 diagnostic criteria). Duration of restraint ranged from 3 months to 30 years (mean = 8.1 years, SD = 8.3 years). Through the application of a holistic intervention model, all patients exhibited a remarkable recovery within 19 months of treatment. We conclude that the development of a community-based, culturally sensitive and respectful mental health model can serve as an optimum promoter of positive mental health outcomes.


Due to the rise in the social and economic costs of depression, new antidepressant medication with fewer side effects should be found. Several studies have shown that an association exists between omega-3 polyunsaturated fatty acids (omega-3 PUFAs) and depression. However, this association has not been clear enough in the elderly with mild to moderate depression. Sixty-six inhabitants of Kahrizak Charity Foundation participated in this double-blind, randomized, placebo-controlled study. Each participant was >/= 65 years of age, had a Mini Mental State Exam of >/= 22, and had scores ranging from 5 to 11 on the Geriatric Depression Scale-15 (GDS-15). During the 6 months, the drug
group was treated daily with one gram of fish oil capsule containing 300 mg of both eicosapentaenoic acid and docosahexaenoic acid. No significant differences were noted between the groups in regard to level of education, use of antidepressant drugs, alcohol, tobacco use, history of chronic diseases, age, body mass index (BMI), high-sensitive C-reactive protein (hs-CRP), total cholesterol, and GDS-15 scores at baseline. After adjusting for cholesterol, BMI, and history of thyroid dysfunctions, a statistically significant difference was seen in GDS-15 scores between both groups. Furthermore, treatment with omega-3 PUFAs was clinically more effective in treating depression in comparison with the placebo. In this study, low-dose omega-3 PUFAs had some efficacy in the treatment of mild to moderate depression in elderly participants.


In clinical samples, patients with severe psychiatric disorders are found to have cognitive impairments. Less is known whether this applies to samples derived from the general population. We aimed to study cognitive functioning in a population-based sample comprising individuals with schizophrenia, other non-affective psychoses, bipolar disorders, major depressive disorder, and controls derived from the same population. The current analysis was based on 148 persons with severe mental disorders and 66 control subjects, derived from the Psychoses in Finland study. All subjects were interviewed with SCID, and a neuropsychological test battery was administered. Subjects with schizophrenia had a generalized cognitive impairment (d = 0.43-1.07), while those with other non-affective psychoses were impaired in verbal memory and processing speed (d = 0.43-0.59). Subjects with bipolar disorders were not impaired. Unipolar major depressive disorder associated with slowed processing speed (d = 0.64). Our findings on cognitive impairments in subjects with schizophrenia and other non-affective psychoses derived from the general population support previous findings of a generalized cognitive dysfunction in these subjects. However, our results suggest that subjects with bipolar disorders from non-clinical populations may not have significant cognitive impairments. Our results emphasize the importance of using control samples derived from the same population and studied similarly as those with disorders in evaluating cognitive functioning of subjects with severe mental disorders.


Recent findings in the literature suggest a relation between histidine triad nucleotide-binding protein-1 (HINT1) and psychiatric disorders such as major depression, anxiety, and schizophrenia, although its physiological roles are not completely comprehended. Using Western blot, we compared HINT1 protein expression in the postmortem dorsolateral prefrontal cortex and thalamus of schizophrenia patients and healthy controls for contributing to elucidate the role of HINT1 in schizophrenia pathophysiology. HINT1 was found to be downregulated in the dorsolateral prefrontal cortex and upregulated in the thalamus. Our results combined to previous studies in human samples and preclinical models support the notion that HINT1 must be more explored as a potential target for psychiatric disorders.

Here, we review the cerebrospinal fluid (CSF) candidate markers with regard to their clinical relevance as potential surrogates for disease activity, prognosis assessment, and predictors of treatment response. We searched different online databases such as MEDLINE and EMBASE for studies on schizophrenia and CSF. Initial studies on cerebrospinal fluid in patients with schizophrenia revealed increased brain-blood barrier permeability with elevated total protein content, increased CSF-to-serum ratio for albumin, and intrathecal production of immunoglobulins in subgroups of patients. Analyses of metabolites in CSF suggest alterations within glutamatergic neurotransmission as well as monoamine and cannabinoid metabolism. Decreased levels of brain-derived neurotrophic factor and nerve growth factor in CSF of first-episode patients with schizophrenia reported in recent studies point to a dysregulation of neuroprotective and neurodevelopmental processes. Still, these findings must be considered as non-specific. A more profound characterization of the particular psychopathological profiles, the investigation of patients in the prodromal phase or within the first episode of schizophrenia promoting longitudinal investigations, implementation of different approaches of proteomics, and rigorous adherence to standard procedures based on international CSF guidelines are necessary to improve the quality of CSF studies in schizophrenia, paving the way for identification of syndrome-specific biomarker candidates.


The connection between cholinergic transmission and cognitive performance has been established in behavioural studies. The specific contribution of the muscarinic receptor system on cognitive performance and brain activation, however, has not been evaluated sufficiently. To investigate the specific contribution of the muscarinic transmission on neural correlates of working memory, we examined the effects of scopolamine, an antagonist of the muscarinic receptors, using functional magnetic resonance imaging (fMRI). Fifteen healthy male, non-smoking subjects performed a fMRI scanning session following the application of scopolamine (0.4 mg, i.v.) or saline in a placebo-controlled, repeated measure, pseudo-randomized, single-blind design. Working memory was probed using an n-back task. Compared to placebo, challenging the cholinergic transmission with scopolamine resulted in hypoactivations in parietal, occipital and cerebellar areas and hyperactivations in frontal and prefrontal areas. These alterations are interpreted as compensatory strategies used to account for downregulation due to muscarinic acetylcholine blockade in parietal and cerebral storage systems by increased activation in frontal and prefrontal areas related to working memory rehearsal. Our results further underline the importance of cholinergic transmission to working memory performance and determine the specific contribution of muscarinic transmission on cerebral activation associated with executive functioning.


In recent studies, the glutamate (Glu) level has been quantified using the modified STEAM sequence on 3T MRI. We enrolled 15 healthy volunteers and a group of 51 patients who experienced stroke for the first time and had a good prognosis. The patients with infarction were divided into three groups according to their scores by using the DSM-IV diagnostic criteria for major depressive disorder and the 17-item Hamilton Depression Rating Scale (HDRS). We studied the association between post-stroke depression and (1)H-MRS measurements in unaffected frontal lobes. Single-voxel proton magnetic resonance spectroscopy ((1)H-MRS) was performed to assess N-acetylaspartate/creatine (NAA)/Cr, (Glu)/Cr, choline (Cho)/Cr, and myoinositol (ml)/Cr ratios in stroke patients. The 11
patients (21.5%) who met the criteria for depression and 9 patients (17.6%) who had a high score for HDRS, (>14) but were not depressed, had a significantly higher Glu/Cr ratio than patients who scored <=14 on HDRS and control groups (p < 0.001). No differences were found in NAA/Cr, Cho/Cr, or mI/Cr between the groups after stroke. These findings suggest that post-stroke depression is accompanied by changes in glutamate levels in the frontal lobe.


Elevations of serum homocysteine levels are a consistent finding in alcohol addiction. Serum S100B levels are altered in different neuropsychiatric disorders but not well investigated in alcohol withdrawal syndromes. Because of the close connection of S100B to ACTH and glutamate secretion that both are involved in neurodegeneration and symptoms of alcoholism the relationship of S100B and homocysteine to acute withdrawal variables has been examined. A total of 22 male and 9 female inpatients (mean age 46.9 +/- 9.7 years) with an ICD-10 diagnosis of alcohol addiction without relevant affective comorbidity were examined on admission and after 24, 48, and 120 h during withdrawal. S100B and homocysteine levels in serum were collected, and severity of withdrawal symptoms (AWS-scale), applied withdrawal medication, initial serum ethanol levels and duration of addiction were recorded. Serum S100B and homocysteine levels declined significantly (P < .05) over time. Both levels declined with withdrawal syndrome severity. Females showed a trend to a more intense decline in serum S100B levels compared to males at day 5 (P = .06). Homocysteine levels displayed a negative relationship to applied amount of clomethiazole (P < .05) and correlated with age of onset of addiction. No withdrawal seizures were recorded during the trial. As it is known for homocysteine, S100B revealed to decline rapidly over withdrawal treatment in alcoholism. This effect is more pronounced in female patients. S100B could be of relevance in the neurobiology of alcohol withdrawal syndromes. It may be indirectly related to the level of stress level or glutamatergic activity during alcohol withdrawal.


The field of imaging genetics traditionally studies unidirectional associations between genes, brain functioning, and behavior. In a recent study by Ursini et al. (J Neurosci 31:6692-6698, 2011), imaging genetics methods are combined with epigenetic marks in living human beings. This approach may lead to a new field of imaging epigenetics, providing more mechanistic insight into causal pathways of how gene and environment interact and affect brain development.


Agoraphobia (with and without panic disorder) is a highly prevalent and disabling anxiety disorder. Its neural complexity can be characterized by specific cues in fMRI studies. Therefore, we developed a fMRI paradigm with agoraphobia-specific stimuli. Pictures of potential agoraphobic situations were generated. Twenty-six patients, suffering from panic disorder and agoraphobia, and 22 healthy controls rated the pictures with respect to arousal, valence, and agoraphobia-related anxiety. The 96 pictures, which discriminated best between groups were chosen, split into two parallel sets and supplemented with matched neutral pictures from the International Affective Picture System.
Reliability, criterion, and construct validity of the picture set were determined in a second sample (44 patients, 28 controls). The resulting event-related "Westphal-Paradigm" with cued and uncued pictures was tested in a fMRI pilot study with 16 patients. Internal consistency of the sets was very high; parallelism was given. Positive correlations of picture ratings with Mobility Inventory and Hamilton anxiety scores support construct validity. FMRI data revealed activations in areas associated with the fear circuit including amygdala, insula, and hippocampal areas. Psychometric properties of the Westphal-Paradigm meet necessary quality requirements for further scientific use. The paradigm reliably produces behavioral and fMRI patterns in response to agoraphobia-specific stimuli. To our knowledge, it is the first fMRI paradigm with these properties. This paradigm can be used to further characterize the functional neuroanatomy of panic disorder and agoraphobia and might be useful to contribute data to the differentiation of panic disorder and agoraphobia as related, but conceptually different clinical disorders.


Exercise (EX) and physical activity (PA) have been shown to prevent or delay the onset of several mental disorders and to have therapeutic effects in different groups of psychiatric disorders. This review focuses on studies investigating EX as therapeutic intervention in anxiety disorders, affective disorders, eating disorders, schizophrenia, and substance use disorders. Despite EX being discussed as a potential therapy for several decades, adequately powered randomized, controlled trials are sparse in most disorder groups. Nevertheless, evidence points toward disorder-specific benefits that can be induced by EX/PA. Mechanisms of the therapeutic effects of EX/PA are summarized, including metabolic and physiological as well as psychological aspects. Finally, implications for research and therapeutic practice are illustrated.


Self/other (i.e., internal/external) source monitoring is one of the leading paradigms for the study of hallucinations in schizophrenia. The cognitive processes that underlie hallucinations are theorized to transform self-generated (internal) cognitive events into other-generated (external) cognitive events. These proposed cognitive operations also appear to play a role in producing analogous types of errors in self/other source monitoring, namely a memory bias whereby recalled material that was self-generated is misremembered as other-generated, referred to as an externalization bias. Externalization biases are more frequent in groups of hallucinating schizophrenia patients than in other groups. One source of measurement error that is inherent in the study of the externalization bias is that, even for never-previously viewed items, there is a tendency to guess an external source under conditions of uncertainty. If such guessing takes place in response to self-generated but forgotten items, these guesses will be summed along with true externalization biases in the frequency count of externalizations, producing measurement error. Multinomial modeling is a statistical technique that has been used to estimate the influence of external-source guessing in order to separate it from true externalization bias estimates. However, a number of challenges related to model choice and model validation are involved, and these challenges may render multinomial modeling impractical. We instead recommend analysis of covariance (ANCOVA), or difference score methodology, as an appropriate method for partialling external-source guessing rates (external-source false positives) out of externalization bias rates.

This paper presents gender-related features of Delusional Disorder. It is part of the Halle Delusional Syndromes Study (HADES-Study). All inpatients fulfilling the DSM-IV/ICD-10 criteria of Delusional Disorder/Persistent Delusional Disorder (DD) during a 14-year period were included and followed up for an average of 10.8 years. Gender distribution was almost equal, women became ill significantly later than men, and almost all women had a stable diagnosis-in contrast to men. The great majority of women, at the end of the follow-up period, had an unremitted DD. Women more frequently had low social functioning at admission, but then were more compliant and received more frequently pharmacological medication. There were no differences in the delusional topic and no differences regarding long-term disability and autarky. In spite of previous reports, the HADES-Study found no gender difference in the frequency of DD. However, men tended more frequently to change into schizophrenia and schizoaffective disorder. In these cases, the DD might have been a prodrome of schizophrenia or schizoaffective disorder, which manifests later in life. Although in both female and male DD patients, the majority remained unremitted, almost none of them lost their autarky (independent living). While women more frequently received psychopharmacological medication, their DD was usually found to be unremitted.


Most studies point to an increased prevalence of metabolic syndrome (MS) and an increased risk of coronary heart disease (CHD) in schizophrenia patients with MS. The aims of this study were to compare the prevalence of MS in schizophrenia patients with the general population, to explore the clinical correlates and predictors of MS and to evaluate the risk for CHD within 10 years. Consecutive 319 patients, aged 18-75 years, with a diagnosis of schizophrenia according to the DSM-IV were enrolled. The ATP-III, the ATP-IIIA and the IDF criteria were used to define MS. 10-year risk of CHD events was calculated with the Framingham score. One hundred nine (34.2%) patients met the ATP-III criteria, 118 (37%) the ATP-IIIA and 133 (41.7%) the IDF criteria for MS. Patients with MS were older, had a later onset of illness and an older age at first hospitalization. The prevalence of MS in schizophrenia patients was higher from the general population only within the 20-29 age group. Patients with MS had a higher age and sex-corrected 10-year risk of CHD events. The only predictor of MS was the age of illness onset. In conclusion, countries where the general population prevalence of MS is already too high, schizophrenia patients younger than 30 years of age might be under higher risk of morbidity and mortality related with MS. This study points to the necessity for aggressive interventions to correct MS in schizophrenia as early as possible, within the first 10 years of post detection.


The negative symptoms of schizophrenia have been considered to be a psychiatric form of the frontal lobe syndrome. However, no studies have compared these two disorders at the clinical level. In this study, 12 negative symptom schizophrenic patients and 11 patients with behavioural variant frontotemporal dementia (bv-FTD) were rated for negative symptoms and for occurrence of frontal lobe behaviours in everyday life. They were also rated for speech disorder and were given a series of executive tests. Both patient groups showed positive ratings on negative symptoms and frontal lobe behaviours in daily life; however, the schizophrenic patients had higher negative symptom scores
and the bv-FTD patients had higher carer ratings on frontal behaviours in daily life. Both groups were impaired on the executive tests, but the bv-FTD patients showed significantly greater impairment on verbal fluency and a test requiring inhibition of prepotent responses. A minority of the bv-FTD patients unexpectedly showed speech abnormalities typically associated with schizophrenia. The findings indicate that the negative syndrome in schizophrenia and the frontal lobe syndrome resemble each other clinically in important respects. Some of the differences may be attributable to the additional presence of disinhibition in the frontal lobe syndrome.


Besides the ventral tegmental area and the nucleus accumbens as the most investigated brain reward structures, several reports about the relation between volume and activity of the amygdala and drug-seeking behavior have emphasized the central role of the amygdala in the etiology of addiction. Considering its proposed important role and the limited number of human protein expression studies with amygdala in drug addiction, we performed a human postmortem proteomic analysis of amygdala tissue obtained from 8 opiate addicts and 7 control individuals. Results were validated by Western blot in an independent postmortem replication sample from 12 opiate addicts compared to 12 controls and 12 suicide victims, as a second "control sample". Applying 2D-electrophoresis and MALDI-TOF-MS analysis, we detected alterations of beta-tubulin expression and decreased levels of the heat-shock protein HSP60 in drug addicts. Western blot analysis in the additional sample demonstrated significantly increased alpha- and beta-tubulin concentrations in the amygdala of drug abusers versus controls (P = 0.021, 0.029) and to suicide victims (P = 0.006, 0.002). Our results suggest that cytoskeletal alterations in the amygdala determined by tubulin seem to be involved in the pathophysiology of drug addiction, probably via a relation to neurotransmission and cellular signaling. Moreover, the loss of neuroprotection against stressors by chaperons as HSP60 might also contribute to structural alteration in the brain of drug addicts. Although further studies have to confirm our results, this might be a possible pathway that may increase our understanding of drug addiction.
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