Cognitive Therapy is establishing itself in psychiatry as a powerful treatment for a variety of psychological disorders, including anxiety, depression, eating disorders and schizophrenia. In less severe conditions it can prove as effective as psychotropic medication, while in more severe conditions it can complement drug treatment. Follow up studies suggest that cognitive therapy has a long term effect on relapse in anxiety and depression. Cognitive therapy is a brief, structured, problem focused approach that aims to alleviate symptoms and solve problems, teach coping strategies and prevent relapse through changing underlying beliefs and assumptions. Patients learn to identify and modify unhelpful thoughts and behaviours within a collaborative relationship with the therapist. The general cognitive model as applied to anxiety and depression will be described and a method for conceptualising cases presented. Specific models for panic disorder and schizophrenia workshop will be outlined. A mixture of presentation, video and group discussion will be used to demonstrate the therapy in action and introduce participants to some basic cognitive and behavioural techniques. Empirical evidence for cognitive therapy in psychiatric disorders will be reviewed. Material will be presented in an interactive format. Basic CBT principle will be presented using Powerpoint and illustrated with VHS videotapes. Participants will be encouraged to contribute through experiential exercises and discussion of their own clinical experience.

Tuesday, April 5, 2005

C-17. Educational course: Interpersonal psychotherapy of depression

Course director(s): Torsten Grüttert (Düsseldorf, Germany)
14.15 - 17.45, Hilton - Salon Studer

Among short-term psychotherapies developed for the treatment of depression, IPT by Klerman et al. (1984) is meanwhile one of the most well known approaches. IPT has been controlled in a variety of studies proving efficacy. The interpersonal school of psychiatry (Sullivan) is IPT´s most influencial theoretical backgrood hypothesizing that all psychiatric illnesses (incl. depression and also here the therapy) develop in an interpersonal context: interpersonal problems may contribute to onset and potentially chronicity of (current) depression or/and depressive symptoms may interfere with interpersonal well being. Refering to research on life events, social support, stress and depression etc. the authors defined four problem areas that can be attributed to depression and will be focussed on in IPT: 1) retarded grief, 2) interpersonal conflict, 3) interpersonal role conflict/role transition and 4) interpersonal deficits/isolation. IPT has three parts: Within the introduction period (3-4 sessions) the patient's current depression will be attributed to one (individual) problem area on which will be focused strictly within the main therapy sections. IPT works in a here-and -now framework and connects state and change of depressive symptoms with state and change of interpersonal functioning and well being through therapeutic work. The dual aim of IPT is · symptom remission and · solving of attributed interpersonal problem by promoting patients´ interpersonal skills in and out of sessions. Open and focussed exploration, psychoeducation (patient expert of his illness), the explenation of the sick role (Parsons), assessment of the interpersonal inventory/ interpersonal resources, goal attainment scaling, the definition of patient and therapist role during therapy, the explanation of the IPT concept, the agreement on the problem area and a therapy contract are important parts of introductory sessions in IPT. In the main (3/4-14 sessions) period the patient and therapist work on the agreed focus. The IPT manual describes goals and treatment strategies for each problem area. Clarification, self disclosure, communication analysis, option seeking etc. are main techniques in IPT. During termination period the patient resumes what was learned, what still is left, clarify motivation for booster sessions (maintenance), and learn about prophylaxis and crisis management. This CME course will teach IPT-basics so that course members will e. g. be able to start practicing IPT under supervision. The following aspects will explicitly be focused on: 1) time frame, 2) medical model, 3) dual aims of solving interpersonal problems and symptom remission, 4) interpersonal focus on patient's affective engagement solving current life problems contributing to current depression, 5) specific and general psychotherapeutic techniques and 6) empirical support of IPT. Short role playing is used to train IPT techniques. A comprehensive handout will be available. Background informations about adaptations of IPT concept for depressed adolescents (IPT-A), for bipolar disorder (IPSRT) or group concepts (IPT-G) will be given.

Sunday, April 3, 2005

O-01. Oral presentation: Affective disorders I

Chairperson(s): Giovanni Stanghellini (Florence, Italy), Janusz Rybakowski (Poznan, Poland), Marianne Kastrup (Copenhagen, Denmark)
08.30 - 10.00, Holiday Inn - Room 7

O-01-01

Immediate switching of antidepressant therapy: Results from a clinical trial of duloxetine

M. Wohlreich, C. Mallinckrodt, J. Greist, P. Delgado, L. Driver, J. Watkin, M. Fava. *Eli Lilly and Company, Indianapolis, USA*

Objective: We examined the efficacy and tolerability associated with switching from a selective serotonin reuptake inhibitor (SSRI) or venlafaxine to duloxetine.

Methods: Patients with major depressive disorder entered this open-label study. Patients (N=112) exhibiting suboptimal response or poor tolerability to their current antidepressant were "switched" to duloxetine 60 mg QD without tapering or titration. A comparator group not currently receiving antidepressants ("untreated") were randomized to duloxetine 60 mg QD (N=70). Patients remained on 60 mg QD for 1 week. During the remaining weeks of the study, titration from 60 mg to 90 mg to 120 mg QD was possible. Efficacy measures included the Hamilton Depression Rating Scale – 17 items (HAMD17), Hamilton Anxiety Scale (HAMA), and the Clinical Global Impression of Severity (CGI-S) scale.

Results: The efficacy of duloxetine did not differ significantly between switched and untreated patients initiating duloxetine (mean changes: HAMD17 total score: -13.1 vs. -13.3; HAMA: -10.6 vs. -10.2, CGI-S: -2.2 vs. -2.4, respectively; all p-values >.30). However, the rate of discontinuation due to adverse events among switched patients was significantly lower than that in untreated patients initiating duloxetine (6.3% vs. 18.6%, p=.014). Treatment-

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emergent adverse events occurring in >10% of patients in both groups were nausea, headache, dry mouth, insomnia, diarrhea, and constipation. Patients switched to duloxetine reported significantly lower rates of nausea, anorgasmia, and muscle cramp when compared with untreated patients initiating duloxetine.

Conclusion: In this study, the efficacy of duloxetine in switched patients was very similar to that observed in untreated patients initiating duloxetine therapy. Immediate switching from an SSRI or venlafaxine to duloxetine (60 mg QD) was well tolerated.

O-01-02

Remission during treatment of first vs multiple episode of depression - results of Polish naturalistic study

F. Rybakowski, D. Nawacka, A. Kiejna. *Poznan University of Med. Sci. Psychiatry, Poznan, Poland*

Objective: The aim of the study was to compare treatment results of depression, occurring as the first depressive episode, the second depressive episode or the third or further depressive episode, in terms of obtaining remission in the course of one-year observation. This study was prospective and naturalistic, carried out by 184 Polish psychiatrists in 1999-2000, supported by unrestricted research grant from Servier.

Methods: One-hundred and seventy-nine patients with the first depressive episode (Group I), 170 patients with the second episode (Group II) and 183 patients with the third or further episode of depression (Group III) were compared. Remission was assessed after 6 months and 12 months of observation, and was defined as the score of ≥ 7 points on 17-item Hamilton Depression Rating Scale.

Results: The groups of patients studied did not initially differ as to age, proportion of gender and intensity of depression. The percentages of remission after 6 months of observation in group I, II, and III were: 49%, 41% and 32% and after 12 months 69%, 60% and 50%, respectively.

Conclusion: The results obtained indicate that the proportions of depressed patients who obtain remission during one-year observation are lower than those described in the literature. Furthermore, the course of subsequent depressive episodes is less favourable compared to the first depressive episode. This may have implications regarding duration of pharmacological treatment of depressive episode.

O-01-03

Obtaining complete remission of depression: Geneva outpatients depression study

G. Bondolfi, N. Gervasoni, M. Gex-Fabry, J.-M. Aubry, G. Bertschy. *Hopitaux Universitaires Geneve Psychiatry, Genève, Switzerland*

Objective: We performed a semi-naturalistic study with depressed outpatients to address the issues concerning therapeutic strategies to reach complete remission of a depressive episode. The main objective was to describe the therapeutic pathways of the patients who reach remission using standard operational rules in the decision making process.

Design and method: Outpatients with a diagnosis of depression (ICD10 criteria using the M.I.N.I) of severe intensity (MADRS score 25) were treated with paroxetine (a selective serotonin reuptake inhibitor antidepressant). A decision tree determined the different steps of the treatment, making it possible to reinforce the treatment (dose increase, lithium or T3 addition, switch to an antidepressant belonging to a different class such as venlafaxine or clomipramine) until complete remission is obtained (score 8 with the MADRS at 2 consecutive two weeks interval visits). The plasma level concentrations of the antidepressant were measured for the monitoring of observance

Results: 135 patients were included. 41 (31.3%) reached a complete remission, 17 (12.9%) responded (reduction 50% of the initial MADRS score) without complete remission and 6 (4.6%) were resistant. 84 patients weredrop out cases: 16 (14.5%) stopped their study participation, 12 (9.2%) stopped their study participation and were also noncompliant to drug treatment according to monitoring results, 19 (14.5%) were excluded because of non-compliance, 24 (18.3%) dropped out because of side effects and 13 (9.9%) dropped out for others reasons.

Conclusion: In this study, the rate of complete remission and the rates of drop-out and non compliance confirms previous data from the literature.

O-01-04

Speed-accuracy tradeoff in depression and antidepressant treatment

R. Kalb, M. Dörner. *University Erlangen-Nuremberg Psychiatry, Erlangen, Germany*

Objective: How do the measurement of reaction times and error rates extend our knowledge about the effects of depression and antidepressant treatment on cortical information processing?

Methods: Auditory and visual, left-hand and right-hand, simple and choice reaction tasks have been used to calculate median reaction times, minimal reaction times, and error rates. In a first study the reaction time parameters were correlated with antidepressant doses. In a second study significant differences between medicated, depressive patients and healthy control subjects were investigated.

Results: In the first study, antidepressant doses correlated negatively with reaction times but positively with error rates. In the second study the patients with depression showed increased reaction times but reduced error rates compared to the control subjects.

Conclusion: Depression and antidepressant treatment had opposite effects on minimal reaction times and error rates.

O-01-05

Cognitive function in unipolar depression during the depressive episode and after recovery

E. Biringer, A. Lundervold, K. Stordal, A. Mykletun, J. Egeland, R. Bottlender, A. Lund. *Institute of Clinical Medicine Section of Psychiatry, Bergen, Norway*

Objective: To investigate if and to what extent subjects with unipolar major depression improve cognitively upon remission of depressive symptoms. One field that has been shown to be particularly affected in depression is that of 'executive function'. The field is sometimes referred to as 'frontal' because it is presumed to be linked to functional circuitries that involve the frontal lobe.

Methods: Thirty subjects with diagnoses of major depression according to the DSM-IV were tested twice with neuropsychological tests regarded as measures of executive function. Test re-test interval

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was two years. Patients were completely or partly recovered at re-testing.

Results: A significant correlation between change in Hamilton Depression Rating Scale and a neuropsychological composite scale of change was found. At baseline, the depressed group's mean test performance was 0.55 SD below that of the healthy controls. After complete recovery, the recovered sub-group had improved their performance to merely 0.24 SD below the control group.

Conclusion: Cognitive function improves significantly upon depression recovery. This should be of importance for clinicians who are responsible for patients who experience cognitive problems during the depressive episode.

O-01-06

Cognitive impairment in depression – a clinical follow-up study

K. Frasch, C. Bullacher, R. Kilian, M. Rink, N.-U. Neumann. *BKH Guenzburg Psychiatrie II der Univ. Ulm, Guenzburg, Germany*

Objective: Target of this study is the longitudinal analysis of cognitive impairment in patients with affective disorders in routine psychiatric in- and outpatient treatment.

Methods: In an observational prospective study, major depressive in- and outpatients (ICD-10: F31-F33) were examined at baseline and two follow-ups after one and two years by means of standardized computerized performance tests. The clinical status was determined by use of the HAMD-21, the dosages of psychotropic medication were categorized by an expert rating procedure. Data were analysed by means of random effects regression models including linear time effects and covariates for illness severity, depressive symptoms and type of medication.

Results: At baseline, 107 patients were included in the study, the first follow-up included 62 patients and the second follow-up included 26 patients. Random effects regression models show significant linear improvements in the three cognitive performance subtests. Effects of covariates indicate a negative impact in depressive symptoms and age on different indicators of cognitive performance. The results of two subtests were negatively affected by the dosage of antipsychotic drugs.

Conclusion: Results of the study indicate an improvement of the cognitive performance during routine treatment of affective disorders. In part this improvement is related to the reduction of depressive symptoms but the independent time effect suggests that other aspects of the treatment process are also effective. However, interpretation of data has to take possible learning effects into consideration.

O-01-07

The impact of shared decision making on patients' treatment acceptance, compliance and clinical outcome in primary care of depression

A. Loh, D. Simon, M. Haerter. *University Hospital Freiburg Psychiatry and Psychotherapy, Freiburg, Germany*

Objective: The involvement of patients in the process of medical decision making is a central element to ensure adequate care by increasing compliance and treatment success. The impact of shared decision making in primary care of depression has not been evaluated in detail although depression is highly relevant in primary care.

Methods: In a randomised controlled trial 30 general practitioners documented their clinical management. 486 patients suffering from depression were asked for patient participation in decision making process (Man-Son-Hing's Scale), acceptance of diagnoses and treatment (5 point Likert-Scales) and health status (PHQ). To measure the effects of treatment, clinical data were collected twice within 6 weeks (t1-t2). The shared decision making concept was implemented in the intervention group by physician training, patient information and a decision aid.

Results: Patient participation in decision making (p .000) and patients' acceptance of treatment (p.02) was significant higher in the intervention group. Compliance was higher in the intervention group but failed significance (p.08). Patients with higher participation rates showed higher clinical outcomes (p.04). Significant positive correlations could be assessed between patient participation and patients' acceptance of treatment (p.05), compliance (p.01) and clinical outcome (p.01). Regression analyses showed a significant influence of patient participation on clinical outcome (beta .18) and on patient-physician-concordance (beta .42).

Conclusion: Patients suffering from depression involved in decision making process show higher acceptance of diagnosis and therapy, perform therapeutic tasks to a higher degree and gain more clinical effects than patients not involved in decision making.

O-01-08

Reduced hippocampal volumes associated with the long variant of the serotonin transporter polymorphism in major depression

T. Frodl, B. Bondy, R. Rupprecht, D. Rujescu, M. Reiser, H.-J. Möller, E. Meisenzahl, *LMU Munich Psychiatry, Munich, Germany*

Objective: Substantial evidence supports a role for dysfunction of the serotonin transporter (5-HTT) in the pathogenesis of major depression. Several studies found reciprocal interactions between the 5-HT-system and brain derived neurotrophic factor (BDNF) and glutamate, which are known to modulate or affect hippocampal morphology. The aim of the study was to examine the influence of a polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) on hippocampal volumes in patients with major depression and healthy controls.

Methods: Forty inpatients with a major depression as well as forty age, gender and handedness matched healthy control subjects were examined with high resolution magnetic resonance imaging (MRI). Furthermore, genotyping for the biallelic polymorphism in the promoter region of the serotonin transporter (5-HTTLPR) was performed.

Results: Patients with the L/L genotype had significantly smaller hippocampal gray (left: p=0.003, right: p = 0.013) and white matter (left: p=0.001, right: p=0.002) than L/L controls. No significant differences were found between patients and controls with L/S or S/S genotype. Moreover, within the patient group, the L/L homozygous genotype had significantly smaller hippocampal white matter volumes than the L/S or S/S genotype (p=0.032).

Conclusion: These findings suggest that homozygosity for the L-allele is associated with decreased hippocampal volumes in patients with major depression, but not in healthy controls. A possible explanation may be the interaction between the 5-HT-system and neurotrophic factors as well as excitatory amino neurotransmission, that are hypothesized to affect hippocampal morphology.

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O-01-09

Metabolic changes in frontal lobe white matter of depressive patients assessed by single-voxel proton MRS at 3 Tesla

R. Frey, S. Kasper, E. Moser, S. Gruber, L. Reinfried, H. Nassan-Agha, V. Mlynarik, A. Stadlbauer. *Medical University of Vienna Dept. of Psychiatry, Wien, Austria*

Objectives: In depressives and controls, absolute concentrations of total creatine (creatine + phosphocreatine, Cr), N-acetyl-aspartate (NAA), choline (Cho) and myo-Inositol (mI) were compared in the prefrontal region by means of proton magnetic resonance spectroscopy (1H-MRS).

Methods: Single voxels (2x2x2cm3) in white matter of the left and right prefrontal region were examined (3 Tesla, STEAM, TR/TE/TM = 6000/20/30 ms). Metabolites were quantified (mM/kg). At baseline, 24 drug-free patients with unipolar depression (14 females, 10 males; mean age: 37 ± 12 y; first episode, ICD-10: F32, n=12, drug-naïve; recurrent depression, ICD-10: F33, n=12) were compared to 24 age and sex matched healthy controls. After 4 weeks of therapy with citalopram, changes were analysed in 20 patients.

Results: Compared to controls, depressive patients showed significantly higher Cr concentrations in the left (+ 14%, $p < 0.001$) as well as in the right frontal region (+ 19%, $p < 001$). NAA, Cho and mI were unchanged. Treatment caused a trend towards a decrease of Cr in the left (– 12%; $p = 0.08$) and in the right hemisphere (– 9%; $p = 0.09$) compared to baseline. The differences between the patients' Cr at day 28 and controls were no more significant. Subgroup analyses showed the Cr augmentation at baseline predominantly in responders. The initial Cr augmentation in F32 and in F33 patients was reduced at day 28 only in F32 patients.

Conclusion: The state dependent increase of the Cr concentration indicates bifrontal deviations in the Cr transport or ATP synthesis in unipolar depressive disorder.

O-01-10

Behavioural alternations evoked by chronic psychosocial stress in rats and the antagonism by citalopram

U. Havemann-Reinecke. *Dpt. of Psychiatry and Psycho- therapy, Univ. of Goettingen, Goettingen, Germany*

Objective: A new model of chronic psychosocial stress was developed in rats and the effects of the selective serotonine reuptake inhibitor citalopram were investigated.

Methods: Rats were subjected to daily social defeat for period of 35 days. In parallel animals were treated for 28 days with citalopram (40mg/kg). The drug was administered orally via drinking water. The effective dose was determined by drug monitoring. The animals were evaluated in behavioural tests (measurement of locomotor and exploratory activity, sucrose preference tests and forced swimming test).

Results: Chronically stressed rats showed a decreased motility and exploratory activities, decreased body weight gain, reduced preference to sweet sucrose solution and increased immobility time in the Forced Swim Test. Citalopram treatment diminished these adverse changes. In parallel molecularbiological studies in collaboration with the German Primate Center (N. Abumari, G. Flügge) this chronic-stress procedure was shown to regulate in the raphe nuclei several genes being mainly related to cell proliferation, axonal growth, neuroprotection, synaptic plasticity and neuro-transmission. Citalopram was found to normalize or to enhance the expression of some of those genes.

Conclusion: Chronic social stress induces depressive like symptoms in rats, which can be studied on the behavioural, pharmacological and molecular level. The presented behavioural results provide further evidence that the chronic social stress paradigm is valuable as model for depressive symptoms in rats.

Monday, April 4, 2005

O-04. Oral presentation: Affective disorders II

Chairperson(s): Fritz Hohagen (Lübeck, Germany), Christine Norra (Aachen, Germany)
08.30 - 10.00, Holiday Inn - Room 7

O-04-01

Functional status of patients with acute mania

I. Goetz, C. Reed, H. Grunze, E. Vieta. *Eli Lilly & Co European Health Outcomes, Windlesham, United Kingdom*

Objective: To describe the functional status of patients enrolled in EMBLEM (European Mania in Bipolar Longitudinal Evaluation of Medication study).

Methods: EMBLEM is a 2-year prospective, observational study on the outcomes of pharmacological treatment for mania conducted in 14 European countries. Adult patients with a diagnosis of bipolar disorder are enrolled within the standard course of care as in- or outpatient if they have initiated/changed oral medication (excluding benzodiazepines) for treatment of acute mania. All treatment decisions are at the discretion of the treating psychiatrist. 530 psychiatrists have enrolled 3682 patients between 12/2002 and 06/2004 using the same study methods assessing demographics, psychiatric history, clinical status (CGI-BP, YMRS, HAM-D, Life Chart Method), functional status (relationships, dependants, housing conditions, work, social contacts, Slice of Life items) and pharmacological treatment patterns including tolerability, compliance, and concomitant medication.

Results: Of 3536 eligible patients at baseline 55% were female and the mean (sd) age was 44.6 years (13.4). 27% of patients have attempted suicide at least once previously; 25% have experienced alcohol problems; 41% had no partner and 20% did not participate in any social activities in the previous month. 47% were moderately/severely impaired in their work function, 21% were unable to work. 41% were (very) dissatisfied with their lives.

Conclusion: Patients with acute mania as part of bipolar disorder are severely impaired in their functional well-being. As the biggest naturalistic study so far EMBLEM provides invaluable longitudinal information on both pharmacological treatment and outcomes of bipolar disorder in routine clinical practice.

O-04-02

Short psychoeducation for bipolar patients

A. Erfurth, M. Dobmeier, M. Zechendorff, *BHK Augsburg, Augsburg, Germany*

Objective: Psychoeducation and psychotherapy are of growing importance for the management of bipolar patients. Several controlled studies (e.g. Colom et al. Arch Gen Psychiatry

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