

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 < 0.001). 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

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Objective: A new model of chronic psychosocial stress was developed in rats and the effects of the selective serotonin 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

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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*

2003; 60:402-7) have shown significant treatment results. However, outside of university structures, these programmes are difficult to perform: 21 consecutive modules can barely be performed in a community setting.

Methods: Based on the experiences with short psychoeducative groups for bipolar patients at Münster University Hospital, Cham Day Hospital and at the Bipolar Outpatient Clinic at the Augsburg Hospital, we have developed a short psychoeducation with the following characteristics: (a) 6 weekly meetings, (b) patients can enter the group at any time and (c) continuity: the group can be "used" by the patient as long as he wishes.

Results: Our group therapy is well adapted to the practical needs of community facilities. A manual has been developed by the authors that can be used in different settings.

Conclusion: The authors present a programme that can easily be learned by future trainers and which exhibits high flexibility. Only one of the six modules should be performed by a physician, so that also other professionals (e.g. psychologists, social workers, nurses) and institutions (e.g. local public health departments) can offer this psychoeducational training. It should be the long-term goal to offer group psychoeducation to all European bipolar patients regardless of their place of residence.

O-04-03

Effects of lithium on the HPA axis in patients with unipolar major depression

T. Bschor, D. Ritter, U. Lewitzka, M. Bauer, M. Adli, C. Baethge, M. Uhr, M. Ising. *Jewish Hospital Berlin Dept. of Psychiatry and PT, Berlin, Germany*

Objective: (I) Profound alterations of the hypothalamic-pituitary-adrenocortical (HPA) axis regulation were repeatedly shown in depressed patients. The most sensitive challenge test of the HPA axis, the combined dexamethasone/CRH test (DEX/CRH test), shows an overstimulation of ACTH and cortisol in depressed patients. Under tricyclic antidepressant treatment, a normalization of the HPA axis overdrive was found to precede the clinical improvement. (II) Lithium is a well established drug for the treatment of affective disorders. Yet, its exact mode of action and its effects on the HPA axis are still unknown.

Methods: Three 4-week studies with each 30 acutely depressed patients (unipolar, SCID I confirmed) were conducted. In study 1, patients refractory to a treatment trial with an antidepressant of at least four weeks were treated with lithium augmentation. In study 2 and 3, drug free patients were treated with lithium monotherapy or citalopram monotherapy respectively. Weekly HAM-D ratings were performed. In each study, the DEX/CRH test was conducted right before and four weeks after initiation of the pharmacotherapy.

Results: All three pharmacological strategies showed good antidepressive efficacy. Both lithium monotherapy and lithium augmentation led to a (for most parameters significant) increase in the HPA axis activity. In contrast, citalopram monotherapy resulted in a decrease of the hormone response to the DEX/CRH test.

Conclusion: Lithium has HPA axis activating effects in depressed subjects. This is in line with results of former laboratory and animal studies. Study 3 showed that this effect is not simply related to serotonergic effects. A down-regulation of the HPA axis does not seem to be a necessary prerequisite of an effective antidepressive drug response.

O-04-04

Parental bonding attitudes of bipolar, depressive, and substance dependent subjects as assessed by parent and offspring

Y. Lustenberger, S. Rothen, M. Preisig, F. Ferrero, *UREP DUPA, Prilly, Switzerland*

Objective: The objective of the present paper was to: 1) compare parenting attitudes reported by parents and their children; 2) assess associations between parental mood and substance use disorders and parenting attitudes as reported by both parents and their offspring.

Methods: In a family study on mood and substance use disorders, we collected clinical information on treated probands and their children. The sample included 45 bipolar, 39 depressive, 16 substance dependent and 32 control probands as well as their 174 9 to 17 year-old children. Diagnostic assignment was based on a best estimate procedure including semi-structured interviews, medical records and family history information. Parenting was measured using the Parental Bonding Instrument. Analyses were based on multiple regression models with adjustment for sex and age.

Results: 1) There were significant but only low to moderate correlations between parenting attitudes reported by parents and children. 2) Regarding parenting reported by parents, bipolars described themselves as providing more encouragement of freedom than controls; in contrast, children of depressive probands rated their parents higher on the encouragement of freedom and lower on the denial of autonomy subscales as compared to controls.

Conclusion: Parents and children only partially agree in their judgment of parental attitudes. Children of depressive probands report their parents as less protective than children of controls, whereas their parents do not describe their parenting as different from those of controls.

O-04-05

Phenomenon of loneliness in structure of anxious- depressive disorders of an out-patient level

A. S. Kim, S. M. Karybaeva. *Russia*

Objective: The Phenomenon of loneliness is one of the mechanisms causing evolution and lingering of anxious-depressive disorders. Study the correlation of the level of the phenomenon of loneliness and the intensity of anxiety and depression in structure of affective somatisations.

Methods: We surveyed 74 patients at RCMH, Bishkek city, in the age of 16- 60 years with anxious- depressive somatisations. Clinical, clinical-cwantic, scale UCLA for the evaluation of the level of the loneliness, a Spielberg-Khanin's scale for the evaluation of anxiety, Zung's scale for the evaluation of depression.

Results: Patients with anxious somatisations (panic disorder F41.0, generalized anxious disorder F41.1) 32 persons had the least level of loneliness 37.8 (P <0.01). Patients with somatoform disorders (F45), 42 person, had 44,2 (P <0.01). Patients with somatic depression with prevalence of hypothyroid affect (On Zung 46,2 (P <0.01)) had the last one 57,3 (P <0.01). The change of the level of loneliness depending on duration of the disorder was following: 1 year 30,5 (P <0.01). 1-4 years 37,5 (P <0.01). Over 4 years 58,7 (P <0.01).

Conclusions: - The phenomenon of loneliness is one of clinical-psychological mechanisms in evolution of anxious- depressive disorders. - The phenomenon of loneliness is one of patoplastic

factors in evolution and duration hypothymic affect. - The lingering and resistance of disorders at evidence of functioning hypothymic affect is the mechanism of increasing of the level of loneliness.

O-04-06

Depressive mood and quality of life in patients with chronic heart failure (CHF): Impact of sleep related breathing disorder and cardiac resynchronisation therapy

C. Norra, A.-M. Sinha, E. C. Skobel Erik C. Skobel. *University Hospital Aachen Psychiatry and Psychotherapy, Aachen, Germany*

Objective: Patients with advanced heart failure (NYHA IV) often suffer from severe sleep related breathing disorders (SRBD) like central or obstructive sleep apnea (OSAS) with prediction of enhanced mortality. Still, in stable CHF the influence of moderate SRBD on sleep, quality of life, and mood as well as the effect of cardiac resynchronization therapy (CRT) is not yet established.

Methods: Applying echocardiography, spirometry and ambulatory polygraphy we identified 69 patients with stable CHF (NYHA II-III) either with SRBD (Apnea/Hypopnea-Index: AHI 16-30/h) or without (AHI<5/h) SRBD. Age-matched healthy volunteers and patients with exclusive OSAS served as controls. All participants were evaluated psychometrically for sleep quality (PSQI), mood (BDI) and health related quality of life (SF-36). Furthermore, in patients (24 CHF/SRBD vs. 14 CHF) with conduction disturbances tests were performed before and after (18±6 weeks) implantation of CRT.

Results: As opposed to patients with CHF only, severity of additional moderate SRBD was associated with reduction of sleep quality, quality of life and increase of depressed symptoms. While CRT led to improved myocardial function in all patients, only patients with additional SRBD presented with significant improvement of sleep quality, quality of life, and mood, in correlation with a decrease of AHI: all previous (1/3) symptomatic depressed patients were subjectively non-depressed thereafter.

Conclusion: In CHF, comorbidity with even moderate SRBD worsens quality of sleep and life, and correlates with depressed mood, all of these improved by CRT. - SRBD may represent a risk factor for organic induced (sub-)syndromale depressed states and should be treated accordingly.

O-04-07

Depression and anxiety during the climacteric period - The HUNT-II study

T. T. Haug, A. Mykletun. *Institute of Clinical Medicine Department of Psychiatry, Bergen, Norway*

Objective: The aim of the study was to examine the level of anxiety and depression in relation to menstruation status in a non-clinical population of women

Methods: The women in this study is a sub-sample from the Health Study of Nord-Trøndelag County (HUNT) in Norway were all inhabitants aged 20 years or older were invited to participate. From 1995 to 1997 HUNT sent a Questionnaire covering demographic factors, life-style factors, physical and mental health. Anxiety and depression were self rated by Hospital Anxiety and Depression Scale (HADS).

Results: The sub-sample of women aged 35 to 65 years consisted of 12685 persons. There was a significant increase in scores on HADS from the pre-menopausal period to the peri-

menopausal period, and from the pre-menopausal period to the post-menopausal period. Adjusting for somatic symptoms, life-style factors and somatic diseases did only reduce this association to a minimal degree.

Conclusion: The Level of anxiety and depression is significantly increased during the transition from perimenopause to postmenopause in women in the general population.

O-04-08

The association between eczema, anxiety, and depression: Exploring etiological models

M. K. Fremstad, A. Mykletun. *Alesund Sykehus, Helse-Sunnmø Dep. of Psychiatry, Alesund, Norway*

Objective: The objective of this study is to explore the association between eczema, anxiety and depression in a general population, and to test if there is any empirical support for the suggested explanatory models, involving atopy, gender, symptoms of somatization and hypochondria, and omega-3 fatty acid supplement.

Methods: Information on anxiety, depression, and eczema was obtained from The Health Study of Hordaland County (HUSK). The participants (N= 18777) were aged 41-48 years. Anxiety, and depression were assessed with the Hospital Anxiety and Depression Scale (HADS), which is a validated self-report questionnaire. Information on eczema was obtained by three dichotomous self-rating questions covering eczema of the hand, face, and body. Associations were explored by logistic regression analysis, with stepwise adjustment for the different covariates. Effects were given as odds ratios (OR) with 95% confidence intervals.

Results: Anxiety disorder and depression were significantly associated with eczema in all body areas. Preliminary results indicate that symptoms of somatization and hypochondria explain more than 70% of the association between eczema, anxiety, and depression, while the other covariates only have minor mediating effects.

Conclusion: Somatization, and symptoms of hypochondria seem to explain a substantial part of the association between eczema, anxiety, and depression. The cross-sectional nature of the data, prevent us from drawing fixed conclusions, but as none of the biological, explanatory models seemed to contribute, this report point out the importance of recognizing the interplay between eczema, and psychological factors, with implications for future treatment of these conditions.

O-04-09

Help-seeking behaviour in patients with anxiety disorder and depression

A. Roness, A. Mykletun, A. A. Dahl. *Prof. in Psychiatry Haukeland Universitetssykehus, Bergen, Norway*

Objective: The objective of this study was to investigate help-seeking behaviour among persons with anxiety disorder and depression based on self-rating in a Norwegian population (the HUNT study).

Methods: Of the 92.100 inhabitants aged 20 to 89 years invited, 65.648 (71.3%) took part. Among them 60869 (66.1%) persons delivered valid ratings on HADS, and had answered the requested help for mental problems question.

Results: Among HUNT attenders 13% of those with depression and 25% with anxiety disorders had been help-seekers. Help-seeking was only non-significantly associated with demographic or other variables.

Conclusion: Most persons with anxiety disorder and/or depression in the population had not sought help for their mental disorders, but the disparity between use and need of health service must not be overassessed. Improvement of the help-seeking rate for common mental disorder should have high priority in mental health politics.

O-04-10

Hypericum possibility in Lithuania

B. Burba, A. Gendrolis, O. Jankuviene. *Kaunas Medical University Psychiatry, Kaunas, Lithuania*

Objective: Depression treatment cost took fourth place in 1990 and it is expected to be in the second by 2020. Additional treatment modalities with little risk, credible benefit, and moderate cost could be a useful addition to depression management in primary care settings. This study aims to ascertain the experience and view of Lithuania psychiatrists in relation to St John's Wort (Hypericum) as alternative treatment.

Methods: A questionnaire about alternative treatment generally and the benefits and risk to use St John's Wort for treatment of depression was posted to 238 Lithuania psychiatrist.

Results: 80% of respondents were sceptical, 16% respondents' point of view was neutral and only 4% of psychiatrists attitudes about Hypericum and alternative treatments were positive.

Conclusion: Regarding literature Hypericum reduces about 68% depressive symptoms of mild or moderate depression after 6 weeks treatment, for 51% of females with premenstrual syndrome (PMS) using hypericum extract every day reduces PMS symptoms, 92% reduces wish to cry, 85% mood get better and 71% reduces stress. There are created technologies for Hypericum tincture, Hypericum liquid extract, Hypericum oily extract, Hypericum tea, honey with Hypericum extract preparation for PMS in Drugs technology and Pharmacy organization department, Kaunas Medical University, Lithuania. However practitioners are sceptically set on Hypericum preparations and prescribe them quite rarely in Lithuania yet.

Sunday, April 3, 2005

P-03. Poster session: Affective disorders I

Chairperson(s): Patrice Boyer (Ottawa, Canada), K.N. Fountoulakis (Aretsou, Greece)
11.15 - 12.15, Gasteig - Foyers

P-03-01

Lithium blood level and polarity of recurrence in bipolar disorder

E. Severus, N. Kleindienst, W. Greil, H.-J. Möller. *LMU Munich Psychiatry, Munich, Germany*

Objective: Recently published data on prophylactic lithium might indicate that prophylactic lithium is effective in preventing depression at low doses whereas higher doses might be needed to

prevent manic or mixed states. To systematically test this hypothesis several sources of evidence were exploited.

Methods: We present data from two different types of analyses. First, a systematic review was carried out to test whether depressive recurrences might be more likely to occur in studies with high lithium levels. Second, we carried out more detailed analyses of studies that allowed to relate blood levels to the pole of recurrence (depressed vs. manic or mixed) on an individual basis.

Results: The major result from the systematic review is that the percentage of depressive recurrences (with regard to the total number of recurrences) was significantly higher in studies with a higher range of lithium serum levels. Detailed data from recent large RCTs using lithium as a control treatment are not fully available yet. However, preliminary results do confirm the findings of the systematic review.

Conclusion: If further analyses corroborate the hypothesis that low lithium levels are effective to prevent depressive episodes whereas higher levels are needed to prevent manic or mixed episodes, a more individually adopted prophylaxis with lithium - according to the prior course of the illness - will possibly be feasible in the future.

P-03-02

Are low lithium levels needed to prevent bipolar depression and high lithium levels to prevent mania?

N. Kleindienst, E. Severus, H.-J. Möller, W. Greil. *University of Munich Department of Psychiatry, Munich, Germany*

Objective: A more differentiated use of mood-stabilizers presupposes more detailed knowledge about their spectrum of efficacy. Some recently published data might suggest that prophylactic lithium is effective in preventing depression at lower doses whereas higher doses might be needed to prevent manic episodes. To thoroughly test this hypothesis several sources of evidence were evaluated.

Methods: Data presented in this poster originate from a RCT with a prospective maintenance period of 2.5 years (MAP- study) including 86 bipolar patients (DSM-IV) on lithium monotherapy with regular assessment of both lithium levels and psychopathology. The last lithium level during the euthymic interval was used to predict polarity of the first reappearance of significant symptomatology (depressive vs. manic or mixed).

Results: Depressive recurrences were preceded by significantly lower lithium serum levels than manic recurrences. Detailed analyses implying multivariate analyses with potential confounders fully corroborate this finding. Patients without significant worsening of symptoms had an intermediate serum level (i.e. higher than patients who had to be treated for reappearance of manic or mixed symptoms but lower than patients with reappearance of depressed symptoms).

Conclusion: The results confirm the hypothesis that higher lithium levels are rather related to depressive (not manic or mixed) polarity of recurrence. If substantiated by further analyses that are underway this finding would help to better adjust an individually optimal lithium level. Currently, detailed re-analyses of data are carried out in collaboration with research groups who carried out RCTs implying a lithium group and a systematic review of published lithium studies is in preparation.