Methods: 62 medicated bipolar patients received 14 90-min sessions of our cognitive-psychoeducative group therapy. The patients knowledge of bipolar disorder was assessed before and after the intervention. Additionally the patients rated a feedback questionnaire after the intervention. Comparison of the data before and after the group was made using a paired t-test.

Results: The psychoeducated patients significantly improved their knowledge of bipolar disorder and treatment possibilities. In the feedback questionnaire, they all rated the group as informative and helpful. They also benefited from the discussions in the group and the exchange of useful strategies. They highly recommend the group to other patients.

Conclusion: These preliminary results suggest that psychoeducational interventions on bipolar patients may improve the patients knowledge of the illness. The participants value the intervention as highly informative and helpful.

P-03-14

Bipolar disorder and quality of life

M. Centeno, S. Arranz, A. Rodriguez, M. García, D. Gonyalons. *Hospital de Granollers Psychiatry, Granollers, Spain*

Objective: Bipolar disorder is a disease characterized by alternance of depression and mania or hipomania, usually exists a euthymic period between both episodes. Quality of life (QV) usually is defined as "capacity to work correctly, to enjoy a well-being sensation and to experience with satisfaction social, emotional, physical and intellectual the aspects of the life". Evaluation of patients' QV in different settings is considered at the moment as a nuclear aspect of the medical performance.

Methods: Patient diagnosed of bipolar disorder were selected from different clinical setting, obtaining socio-demographics and clinical data. The euthymic status of the patient was evaluated by the HDRS and the YMSR; and the quality of life was evaluated by SOFAS and QLS-R&B.

Results: The sample was composed by 90 patients. The averages of scales' scores were: YMRS 1, HDRS 2.5, SOFAS 78.3, and all scores from QLS-R&B were below the mean provided by the questionnaire authors. There was a negative correlation between the SOFAS and the YMRS (r = -0,259 and p=0, 01) and the HDRS (r = -0,408 and p=0, 05), and between number of episodes and the QLS-R&B social support (r = 0.276 and p=0, 05). There was a positive correlation between the QLS-R&B physical/ psychological wellbeing and the HDRS (r = 0.216 and p=0, 05).

Conclusion: Patients diagnosed of bipolar disorder have lower quality of life than general population, with higher quality of life as lower number of episodes and lower scores in YMRS and HDRS; and without relation with socio-demographics information.

P-03-16

Cerebral blood flow and neuropsychological assessment in a patient with Cotard's Syndrome

F. Van den Eynde, M. Portzky, F. Jacobs, S. De Saedeleer, K. Audenaert, C. van Heeringen. *University Hosipital Ghent, Gent, Belgium*

Objectives Cotard's syndrome is a rare monothematic delusion, characterized by nihilistic thoughts of being dead or having lost all organs. It occurs within a broad variety of psychiatric pathologies as a psychotic depressive episode and is predominately due to a right hemispheric brain dysfunction. We aimed, firstly, to investigate whether cerebral perfusion abnormalities could be shown in a patient with Cotard's syndrome and secondly to investigate neuropsychological performance of this patient. Methods A 46-year old female patient with a bipolar disorder type I was suffering from a severe case of Cotard's syndrome during a depressive episode. A Single Photon Emission Computed Tomography (99m Tc-Ethyl Cysteine Dimer, ECD) was performed during this depressed period and was repeated 6 weeks later during a hypomanic state. Data were analysed with Statistical Parametric Mapping. A broad neuropsychological test battery was performed by a trained neuropsychologist. Results The neuropsychological data strongly indicate a severe right hemisphere dysfunction in this patient with Cotard's syndrome (e.g. clock drawing test, Rey's complex figure). However, no cerebral regions showing a significantly altered perfusion could be detected in this patient, compared to healthy volunteers. Neither were significant differences in regional cerebral perfusion in the within-subject comparison detected. Conclusion Regardless the presence of severe neuropsychological right hemisphere abnormalities in a case of Cotard's syndrome, no abnormalities in cerebral perfusion patterns were shown. This is in accordance with the literature available on this topic and stress the importance of a neuropsychological evaluation in some patients.

Monday, April 4, 2005

P-10. Poster session: Affective disorders III

Chairperson(s): Filip Rybakowski (Poznan, Poland), Verena Henkel (München, Germany)
18.00 - 19.30, Gasteig - Foyers

P-10-01

In vivo Imaging of the serotonergic neurotransmitter system in an animal model

E. Meisenzahl, G. Schmitt, C. la Fougere, T. Zetzsche, T. Frodl, M. Keck, M. Müller, K. Hahn, H.-J. Möller, S. Dresel. *Psychiatrische Klinik der Ludw, München, Germany*

Serotonin is an essential neurotransmitter for the normal functioning of the CNS. The serotonergic system ist not only important physiologically but also affects other behaviors such as the sleep-awake cycle, modd, appetite, body temperature and depression. Depression has been shown to be associated with abnormal functioning of the serotonergic system. The dysregulation of the serotonergic transmission may be associated with a dysregulation of the serotonin transporter protein (SERT). It is still a matter of controversity if altered SERT density or function is involved. Additionally, the acute and long-term effects of psychopharmacological treatment with antidepressants on the 5HT system are largely unknown. The animal model is the most equivalent approach to analyze in vivo the SERT in depression and during pharmacological challenges. A small animal SPECT-device with ultra high resolution pinhole collimators is used to assess in vivo SERT density and functional changes. Additionally, post mortem analysis is performed. The in-vivo analysis of the CNS of Sprague-Dawley rats is performed by a SPECT protocol using I-123 ADAM. The investigation of the detailed biodistribution and specific binding will be presented.

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P-10-02

Hippocampal and amygdala changes in patients with major depression and healthy controls during a one-year follow-up

T. Frodl, T. Höhne, T. Zetzsche, M. Jäger, R. Bottlender, M. Reiser, H.-J. Möller, E. Meisenzahl. *LMU Munich Psychiatry, Munich, Germany*

Objective: Although the hippocampus has been found to be smaller in patients with depression, prospective longitudinal in vivo studies are necessary to investigate whether depression can result in a further diminution of hippocampal volumes or whether a smaller hippocampal volume predisposes an individual to the development of depression.

Methods: Thirty patients with major depression as well as thirty healthy control subjects matched for age, gender and handedness were examined at admission to hospital and one year later by high resolution magnetic resonance imaging (MRI).

Results: No significant volume changes were observed in patients or controls between baseline and one-year follow-up investigations concerning hippocampal and amygdala volumes. However, the subgroup of patients who were non-remitted at the time of the follow-up investigation showed significantly reduced left and right hippocampal volumes at both baseline and the one-year follow-up as compared to remitted patients. Moreover, the right hippocampal volumes of non-remitted patients were significant smaller as compared to matched healthy controls.

Conclusion: These results do not support that hippocampal volumes diminish during the one-year follow-up period. However, smaller hippocampal volumes may be related to a bad clinical outcome after one year.

P-10-03

Effects of electoconvulsive therapy in major depression measured by diffusion tensor imaging

N. Koutsouleris, T. Schlossbauer, C. Born, M. Reiser, H.-J. Möller, E. M. Meisenzahl. *Ludwig-Maximilians-University Dept. of Psychiatry, Munich, München, Germany*

Over the last few years diffusion tensor imaging (DTI) emerged as a new MR technique in the field of scientific neuroimaging. DTI measurements of the regional and global diffusion of water molecules are thought to be representative of white matter microstructure throughout the human brain. They provide information about the integrity of neural circuitry in a variety of physiological and pathological conditions, such as normal ageing, Alzheimer's disease, schizophrenia and geriatric depression. Diffusion tensors have been used in different scientific approaches: the calculation of Fractional Anisotropy (FA) and Apparent Diffusion Coefficient (ADC) maps from tensor data enables researchers to assess the axonal integrity in vivo. Diffusion tensors may serve as a basis for DTI tractography, an ideal tool for studying the connectivity between cortical regions. In a small recent study using DTI in a regions-of-interest (ROI) approach the authors investigated the effects of Electoconvulsive Therapy (ECT) in geriatric depression. They reported a reduced FA of frontostriatal pathways in the patient group before and diffusion parameters similar to the control group after treatment, thus showing that ECT has a strong impact on white matter tract integrity during the course of repetitive treatments. The longitudinal study design includes a baseline DTI scan of patients diagnosed with major depression according to the DSM IV/ICD-10. criteria which is followed by a second scan after a treatment period of three months. Patients receive a standard protocol of 12 unilateral ECT treatments. Then regional and whole brain ADC and FA maps computed from raw DTI data are analyzed by means of ROI and voxel-based morphometry (VBM) implemented in current software packages like SPM2 and FSL. Additionally, DTI tractography is performed in order to assess white matter integrity in defined axon fiber bundles. For both scans the study comprises a cross-sectional approach that compares the acquired patient data with a group of matched healthy volunteers. We expect the study results to give valuable hints to three important questions: (1) Are there any differences between patients and healty subjects before and after ECT? (2) Does ECT influence the integrity of white matter? (3) Do the cognitive side effects of ECT correlate with changes of FA and ADC in distinct regions of the brain? Preliminary results will be presented.

P-10-04

Brain- mapping in depressions: Antidepressants with the different mechanism of action

E. Grigorieva, A. Dyakonov. *Yaroslavl Stae Medical Academy Department of Psychiatry, Yaroslavl, Russia*

Objective: The objective of the research was a comparative neurophysiological study of action of amytriptyline, tianeptin, fluoxetine and moclobemide in treatment of moderate and severe depressions with the dominant affect of anguish.

Methods: Totally, 94 depressed patients (aged 20-42) were clinically examined. Computer EEG was recorded before the therapy and on its 20-21-th days (amytriptyline n - 22, tianeptin n - 24, fluoxetine n - 29, moclobemide n - 19). Control group consisted of 25 healthy people of the same age.

Results: Brain-mapping of depressed patients showed the zones of "increased" activity in the right temporal fields and those of "decreased" activity in the left temporal fields. All drugs "decreased" activity in the right temporal fields and "increased" activity in the left temporal fields. Specification of fluoxetine and moclobemide action in more significant "increased" activity in the left temporal fields. Another result was in amytriptyline treatment – expansion activation zone on the left temporal, parietal, occipital fields, and "decreased" activity in the left frontal fields. An originality of coaxil action was presence of migrating zones of activation.

Conclusion: All drugs reduce activation right and strengthen activation of the left temporal fields. More appreciable rising of activation of the left temporal field causes the specificity of fluoxetine and moclobemide action. Feature of amytriptyline action was the expansion of a zone of activation from the left temporal field on occipital and parietal fields, at "decreased" of activation in the left frontal field. An originality of coaxil action was presence of migrating zones of activation.

P-10-05

Sham stimulation in TMS: How suitable is a commercial placebo coil?

R. Freudenmann, C. Schönfeldt-Lecuona, A. Thielscher, T. Kammer. *University of Ulm Dept. of Psychiatry, Ulm, Germany*

Objective: Therapeutic interventions of transcranial magnetic stimulation (TMS) still have to be evaluated in clinical trials including an adequate placebo control stimulation. For that purpose

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a few dedicated placebo coils are on the market. We set out to compare subjective effects of such a coil with real stimulation.

Methods: We tested three different application forms of TMS in 9 healthy subjects: real stimulation of the left dorsolateral prefrontal cortex (DLPFC), two wings angled coil position (45°) over the DLPFC, and the Magstim® placebo coil. After each stimulation trial (300 pulses, 0.5 Hz, 130% of the motor threshold) subjects were asked to assess mood changes as well as the subjective effect of the stimulation using a computer based visual analog scale (0-1).

Results: We found a significant difference in the evaluation of stimulation efficacy and local effects on the skin (interaction QUESTION x STIMULATION: $F(26,208)=8.96$, $p < .0001$). Real stimulation revealed highest scores for both rating aspects. Angled stimulation showed intermediate scores, and placebo coil stimulation resulted in lowest scores. No effect of factor STIMULATION was found in the scores reflecting the mood state.

Conclusion: The Magstim® placebo coil can subjectively be identified as less efficient. This finding questions its use as an adequate placebo control in clinical trials. The same holds true for the angled position that is widely used as placebo control. The ideal placebo coil should stimulate the skin in a similar way as the real coil.

P-10-06

Accuracy of a frameless stereotaxic TMS-positioning system

C. Schönfeldt-Lecuona, U. Herwig, T. Kammer, M. Spitzer, R. Freudenmann. *University of Ulm Psychiatry III, Ulm, Germany*

Objective: frameless stereotactical navigation has been used for brain-mapping purposes to precisely guide the magnetic coil to a desired cortical area. The aim of our study was to test the precision of an optically tracked neuronavigation device (Surgical-Tool-Navigator™, STN) in the clinical use of stereotaxic transcranial magnetic stimulation (TMS), since no currently available data regards the accuracy of such devices when combined with TMS.

Methods: In order to estimate the stability of the neuronavigation device, six pre-defined facial landmarks (LM, intern angel of both eyes, the nib of the tragus of both ears, and both lateral parts of the nose wings) were recorded twice: first after the initial registration and second after a TMS treatment. Further, the two sets of coordinates were then compared with respect to each other. The reproducibility of the reference procedure was investigated by double Patient registration with the STN in two consecutive days, and the variance of the recorded LM coordinates was analyzed.

Results: Nine patients were included. Altogether, LM were registered 1728 times (192 measures per subject). The mean Euclidean distance (MED) between the 3D LM positions before and after rTMS was 1.6 mm (when pooling over all LM), and hardly exceeded 1.8 mm (upper bound of the 95% confidence interval). The MED between the LM positions recorded immediately after the reference procedures showed an average deviation of 2.5 mm.

Conclusion: Optically tracked neuronavigation is suitable for accurate stereotaxic TMS, and is very comfortable in its practical use in clinical and experimental settings.

P-10-07

Transcranial magnetic stimulation in motor conversion disorder

C. Schönfeldt-Lecuona, B. J. Connemann, U. Herwig, T. Kammer, R. Freudenmann. *University of Ulm Psychiatry III, Ulm, Germany*

Objective: The neurophysiological mechanisms involved in non-organic paralysis are unclear. Since there is no established standard therapy we investigated the effect of repetitive transcranial magnetic stimulation (rTMS) in four patients suffering from non-organic limb paralysis.

Methods: Within the framework of a treatment trial 4 patients suffering from non-organic limb paralysis were treated over a period of five to twelve weeks with rTMS applied to the contralateral motor cortex. Stimulation frequency was 15 Hz, train length 2 s, inter-train interval 4 s; daily total number of stimuli 4000. Motor function was quantified weekly by an neurological experienced clinician using a 6-point rating scale (0-5, 5 representing normal strength).

Results: Motor function was completely restored in one patient after extended rTMS-intervention; muscular strength was rated 5 (normal). Two patients experienced a marked amelioration (muscular strength was rated 4-5)correlating with rTMS treatment. By contrast, one patient who had been diagnosed as a malingerer did not improve.

Conclusion: Because of the positive correlation between rTMS-intervention and the recovery of the symptoms, we attributed the clinical amelioration to the rTMS and not to the natural course of the illness. Our observations may be taken to suggest that rTMS can influence endogenous processes of movement preparation without disrupting the conscious perception of volition. High-frequency rTMS may have a therapeutic effect in motor conversion disorder and may help elucidate neurophysiological aspects of this condition.

P-10-08

Modulation of cortical excitatory aminoacids by clomipramine treatment in a rat model of depression

N. Kokras, E. Anderzhanova, C. Dalla, K. Antoniou, Z. Papadopoulou Daifoti. *University, Medical School Dept. of Pharmacology, Athens, Greece*

Objective: Strong evidence over the last decade has linked the biogenic amines with the pathophysiology of depression and with the antidepressants' mechanism of action. Though these drugs are affecting different monoamine systems it is possible that all systems may act through a same final common pathway at the postsynaptic transduction level. A probable neurotransmitter in that common pathway is glutamate. We investigated the effect of clomipramine treatment on cortical glutamate and aspartate tissue levels in Flinders Sensitive Line (FSL) of rats, which is regarded as a valid animal model of depression.

Methods: Adult male FSL and controls rats were treated with clomipramine or vehicle for 14 days. Subsequently all animals were sacrificed and the prefrontal cortex was isolated. Tissue glutamate and aspartate levels were assayed using HPLC-ED.

Results: FSL rats presented significantly lower basal cortical glutamate levels than controls ($p=0.05$). Chronic clomipramine treatment caused a significant increase in glutamate levels in FSL ($p=0.03$) but did not alter the glutamate levels in the control rats. Cortical aspartate levels were also significantly lower in vehicle

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treated FSL rats (p=0.01) and clomipramine treatment increased them (p=0.05). However clomipramine treatment caused a significant decrease of aspartate levels in the control rats (p=0.03).

Conclusion: Our results are in accordance with the proposed role of excitatory amino acids in the pathogenesis of depression. Furthermore, our findings suggest the involvement of the excitatory amino acids in the antidepressants´ mechanism of action in prefrontal cortex. Further studies are under way to investigate this concept on different brain regions with various antidepressant agents.

P-10-09

Depressive symptoms in young females abused in childhood: effect of serotonin transporter gene

F. Rybakowski, M. Weglarz, A. Slopien, A. Rajewski, J. Hauser. *Poznan University of Med. Sci. Psychiatry, Poznan, Poland*

Objective: Several lines of evidence point to the role of childhood adversities in pathogenesis of depression. Recent studies indicate, that serotonin transporter (5-HTT) gene may interact with environmental influence, modifying the risk of depression after traumatic experience.

Methods: We recruited 76 females (mean age 21.2 sd. 1.7) from general population. Childhood trauma was assessed with self-report inventory (Child Maltreatment Questionnaire), and depression with Beck Depression Inventory- (BDI). In all subjects 5-HTT gene (short/long polymorphism) was genotyped, and the group was subdivided into subjects homozygous for "short" allele and carrying at least one "long" allele.

Results: In the whole sample, self-reported depression was associated with exposure to trauma in childhood. Depression occurred in 5/51 (9.8%) of non-exposed subjects, and was reported by 11/26 (42.3%) of exposed females. In subjects with at least 1 "long" allele (n=43) depression was observed in 2/27 (7.4%) of participants non-exposed to childhood adversity, and in 5/16 (31.3%) females exposed to traumatic experience (chi-square test: p=0.09). In s/s homozygotes (n=33), depression was observed in 3/23 (13.0%) females non-exposed to traumatic experience and 6/10 (60.0%) subjects reporting childhood trauma (chi-square test: p=0.01).

Conclusion: Association between childhood adversity and self-reported depressive symptoms in non-clinical female population may be more pronounced in subjects homozygous for "short" allele of 5-HTT gene. This group may be particularly vulnerable for depression after early-age traumatic experiences.

P-10-10

Pharmacological therapy of depressions in the primary medical network

Y. L. Rivkina. *Moskau, Russia*

Objective: studying of efficiency of modern antidepressants for therapy of depressive disorders in conditions of a therapeutic site of a territorial polyclinic.

Methods: clinical-psychopathological, clinical-pharmacological.

Results: 120 patients (age from 18 till 55 years, from them 113 women and 7 men) of territorial polyclinics with depressive disorders (F32 – 38 persons, F33 – 25 persons, F41 – 29 persons, F34.0 – 9 persons, F34.1 – 19 persons) are surveyed. At the expressed depression of 15 and more points on a scale of depression of Hamilton, the rate of monotherapy (not less than four weeks) with coaxil (n=63) in a doze 12,5-37, 5 mg to day, or with fluoxetine (n=31) in a doze of 20 mg day, or with Zoloft (n=25) in a doze of 25 mg day. During treatment the essential reduction of depressive semiology, decrease(reduction) in parameters of used scales that testifies to efficiency of all three preparations is marked. It is necessary to note more expressed influence of coaxil on a reduction somatic anxiety components, fluoxetine on a reduction of mental components. At therapy with Zoloft antidepressive and sedative effects are most expressed.

Conclusion: high efficiency and safety of coaxil, Zoloft and fluoxetine is confirmed at therapy of depressive disorders in conditions of territorial polyclinics. The reduction of an accompanying somatic pathology and improvement of social functioning that is especially important for working patients is in most cases revealed.

P-10-11

Atypical depression: Is there still evidence for superiority of MAO-inhibitors?

V. Henkel, R. Mergl, U. Hegerl, *LMU München Psychiatry, München, Germany*

Objective: The concept of atypical depression is sophisticated in its combination of unusual depressive symptoms and special personality features (increased sensitivity to rejection in interpersonal relationships). Moreover, the origin of the concept is based on treatment implications (superiority of MAO-inhibitors). According to several studies about 30% of depressive outpatients may meet DSM criteria for atypical depression. Therefore, atypical depression deserves special consideration. In this context, we were interested in the evidence for a concept of atypical depression as a depressive subtype that is preferentially responsive to MAOI-treatment.

Methods: We conducted a meta-analysis in the indication atypical depression according to DSM-III research criteria or DSM-IV criteria, respectively. Studies included into the analysis had to meet several criteria, especially a double-blind, controlled condition as well as a sufficient sample size (N>40).

Results: Our results contrast an effect size of 0.497 for comparison for MAOIs versus placebo with an effect size of 0.095 for a comparison of MAOIs versus SSRIs. The effect size MAOIs versus tricyclics was 0.269.

Conclusion: MAOIs, but also SSRIs, may be more effective for atypical major depressive disorder than are tricyclic antidepressants. In addition to efficacy aspects, treatment decisions should be based on side effect issues. Most clinical research had been conducted on traditional MAOIs (e.g. phenelzine). For treatment guidelines more studies testing the more recently developed reversible MAOIs with a preferable safety profile (e.g. moclobemide) would be helpful.

P-10-12

Treatment of atypical depression in primary care

V. Henkel, R. Mergl, J. C. Coyne, A.-K. Allgaier, M. Hautzinger, R. Kohnen, H.-J. Möller, U. Hegerl, *LMU München Psychiatry, München, Germany*

Objective: Many depressed primary care outpatients suffer from atypical features, complicating recognition and treatment decisions. This paper examines the efficacy of different

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antidepressant treatment strategies in depressed patients with atypical features and with a level of severity more consistent with what occurs in primary care than has been the case with past trials.

Methods: This study was originally designed as a partial patient preference randomized controlled trial (five arms). However, the number of patients with atypical depression opting to select their own treatment was too limited for full comparison. We therefore conducted a post-hoc analysis of the remaining four arms. The present analyses involve a double-blind comparison of sertraline versus placebo and a single-blind comparison between cognitive-behavioral therapy (CBT) versus a non-specific psychotherapeutic group strategy (NPG), with primary efficacy endpoints the Inventory of Depressive Symptomatology (IDSC) and Hamilton Depression Scale (HAMD).

Results: Using an intent-to-treat strategy and LOCF conducted separately for the subgroup of 95 depressed patients with atypical features, the overall decrease on the IDSC scale (and HAMD) was greater after CBT compared to NPG: p=0.02 (p=0.03 for HAMD). The difference between SSRI versus placebo was not significant: p=0.44 (p=0.72 for HAMD). Treatments were equally well tolerated.

Conclusion: It is noteworthy that too few patients opted for selecting their treatment to include the patient preference condition in the formal analysis. The promise of patient preference designs remains to be demonstrated. Results suggest that acute treatment with CBT may be an effective alternative to an unspecific psychotherapeutic approach in the treatment of mildly depressed patients with atypical features. Although SSRI was not superior to placebo, it would be premature to rule it out as efficacious in atypical depression. It is noteworthy that this study included many patients with mild major depression who would have been excluded from past trials.

P-10-13

Efficacy and tolerability of duloxetine: Comparison of 30mg QD and 60 mg QD starting doses

M. Wohlreich, D. Dunner, C. Mallinckrodt, W. Estergard, J. Watkin, M. Fava. *Eli Lilly and Company, Indianapolis, USA*

Objective: Clinical consequences associated with alternative starting duloxetine doses are examined.

Methods: Patients with major depressive disorder were randomized to open-label duloxetine 30mg (n=67) or 60mg QD (n=70) for one week. After one week, the 30mg group had their dose increased to 60mg. During the remainder of the 12-week study, titration from 60mg to 90mg to 120mg QD was possible. Measures included HAMD17, Hamilton Anxiety Scale, Clinical Global Impression of Severity, discontinuation rates, and treatment-emergent adverse events.

Results: At week one, there were some transitory differences in secondary efficacy outcomes among patients starting at 30mg compared with the 60mg group. However, from Week 4 onward, both treatment groups showed essentially equal magnitudes of improvement on all efficacy measures. The rate of discontinuation due to adverse events did not differ significantly between treatment groups, but was rically lower for patients starting at 30mg QD (13.4%) vs. 60mg QD (18.6%). In the first week of therapy, the 30mg group had a significantly lower rate of nausea compared with the 60mg group (16.4% vs. 32.9%, respectively; p=.030). Over the 12-week acute therapy phase, patients starting at 30mg had a slightly higher overall rate of adverse events, but a significantly lower rate of nausea (p=.047), compared with patients initiated at 60mg.

Conclusion: These results support the recommendation of 60mg QD as the target duloxetine dose. However, 30mg QD for one week followed by escalation to 60mg QD may reduce certain adverse events, while producing only a transitory impact on efficacy compared with starting at 60mg QD.

P-10-14

Daily measurements elucidate effects of initial dosing of duloxetine on emotional and painful physical symptoms of depression

M. Wohlreich, J. Mundt, C. Mallinckrodt, A. Andorn, J. Greist, L. Arnold, M. Fava, H. Moore. *Eli Lilly and Company, Indianapolis, USA*

Objective: Compare tolerability and timing of onset of efficacy for duloxetine during the first week of treatment.

Methods: Patients (N=112) exhibiting suboptimal response or poor tolerability to their current antidepressant were "switched" to open-label duloxetine 60mg QD. Comparators not currently receiving antidepressants ("untreated") were randomized to duloxetine 60mg QD (N=70) or 30mg QD (N=67). Patients reported daily an adapted Visual Analog Scale for pain and Patient Global Impression of Improvement using Interactive Voice Response.

Results: Untreated patients started at 60mg reported significantly greater improvement vs. 30mg in shoulder and back pain on day one (D1), pain while awake (D3), global emotional improvement (D5), and global physical improvement (D7). Switch patients (started on 60mg) reported significantly greater improvement than untreated patients started on 30mg in pain while awake and back pain by days 3 and 4, respectively. Although 30mg untreated and 60mg switch patients reported significantly less nausea (16.4%, 15.2%) than 60mg untreated patients (32.9%), no significant differences occurred between groups in discontinuation due to nausea or other adverse events.

Conclusion: A 60mg QD dose demonstrated efficacy onset within 1 week, with improvement superior to 30mg QD as early as day one. Untreated patients on 30mg and patients switching directly from an SSRI reported less nausea, suggesting greater initial tolerability.

P-10-15

Duloxetine vs. placebo in the treatment of elderly patients with MDD

J. Raskin, C. Wiltse, J. Dinkel, A. Siegal, J. Sheikh, J. Xu, B. Rotz, R. Mohs. *Eli Lilly and Company, Indianapolis, USA*

Objective: To compare the effect of duloxetine vs. placebo on cognition in elderly MDD patients.

Methods: Patients were at least 65 years old, with median age of 72 (65-89). Patients were randomized to duloxetine 60 mg once daily (n=207) or placebo (n=104) for 8 weeks. The primary outcome measure was a prespecified composite cognitive score based on 5 cognitive tests that measured verbal learning and memory, selective attention, and executive functioning. Secondary measures included the Geriatric Depression Scale (GDS), HAMD17, Visual Analog Scale (VAS) for pain, CGI-Severity, and SF-36.

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Results: Duloxetine demonstrated significantly greater improvement in the cognitive composite score vs. placebo (least squares mean change from baseline to endpoint of 1.95 vs. 0.76, p=0.013). Duloxetine showed significantly greater reductions in both HAMD17 and GDS scores. Duloxetine HAMD17 response and remission rates were approximately twice those of placebo. Duloxetine demonstrated greater improvement vs. placebo on CGI-severity, VAS for back pain and time in pain while awake. Discontinuation rates due to adverse events were similar for duloxetine and placebo (9.7% vs 8.7%). Significantly more placebo than duloxetine patients discontinued due to lack of efficacy (9.6% vs 2.9%). Common treatment-emergent adverse events included dry mouth, nausea, constipation, dizziness, diarrhea, fatigue and somnolence. Rates of discontinuation-emergent adverse events were similar for duloxetine and placebo (14.2% vs 10.0%).

Conclusion: Duloxetine improved cognition, depression, and some pain measures significantly compared to placebo, and was well-tolerated in elderly MDD patients.

P-10-16

Global benefit-risk evaluation for the treatment of major depressive disorder with duloxetine: results from six pooled placebo- and ssri-controlled clinical trials

D. Perahia, Y. Lu-Pritchett, R. Tamura, M. Detke, D. D'Souza, P. Tran. *Eli Lilly and Company, Indianapolis, USA*

Objective: Evaluate the treatment of major depressive disorder (MDD) with duloxetine, versus selective serotonin reuptake inhibitors (SSRIs) and placebo, using the global benefit-risk method.

Methods: Six placebo- and SSRI-controlled studies of duloxetine were pooled for this evaluation. In the pooled database, patients meeting DSM-IV criteria for MDD received placebo, duloxetine, or SSRI for 8 weeks. Benefit was defined by HAMD17 total ≤ 7 at endpoint, and risks were classified by the status of treatment-emergent adverse events (AEs). The linear and log ratio GBR scores were computed using a weight function. The between-group differences in linear and log ratio GBR scores were evaluated using Z-tests.

Results: Treatment with duloxetine resulted in a higher remission rate than with SSRIs, and was superior to placebo. The percentages of patients having at least one AE were comparable between two active treatments. Using GBR analysis for all randomized patients, both linear and log ratio statistics demonstrated an advantage of duloxetine over SSRI and placebo. In patients with baseline HAMD17 total ≥ 19, significant superiority of duloxetine over SSRI was observed for linear (p=0.016) and log ratio (p=0.019) GBR scores. The superiority over placebo was also observed for both GBR scores (p<0.001). The advantage of SSRI over placebo was marginally significant for linear (p=0.051) and log ratio (p=0.020) scores.

Conclusion: When considering benefits and risks together, duloxetine outweighed SSRI and placebo in the treatment of MDD. The GBR method provides a novel approach where different therapies can be compared from a consolidated benefit-risk point of view.

P-10-17

Case study on the effect of quetiapine (Seroquel) on the symptoms

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Objective: The psychopathological symptoms of depressive patients often include restricted thinking, together with more or less marked and ceaseless occupation with thoughts with depressive content (rumination). The object of this case study is the investigation of the effect of concomitant medication with the antipsychotic drug quetiapine (Seroquel) on those target symptoms.

Methods: 6 in-patients suffering from depression (5m/1f), aged 38-58 years (M=45.7), with a severe depressive episode (DSM-IV:296.2 or 296.3)and the symptoms "restricted thinking" and "rumination" in accordance with the AMDP criteria were consecutively enrolled in this case study. In addition to antidepressive medication, they were given concomitant treatment with quetiapine (target dose 300mg/d) for the duration of 4-12 weeks (M=7,5). All patients were submittet to a weekly rating with the AMDP Manual, Rumination on Sadness-Scale (RSS), Hamilton Depression Rating Scale (HDRS) and the Beck Depression Inventory (BDI). In addition, extrapyramidal symptoms, serum prolactin concentration and body weight were recorded weekly.

Results: 4 of 6 patients responded well to quetiapine, with respect to reductions in the RSS score and in the AMDP characteristics "rumination" and "restricted thought". The response was inadequate with two patients.

Conclusion: Concomitant medication with quetiapine as a complement to antidepressive treatment can contribute to a remission in psychopathological symptoms. The results of this pilot study should encourage the performance of future studies, dealing with the specific effect of quetiapine with different antidepressive comedications.

P-10-18

Alteration of DHEA-S level during the tianeptine treatment

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Objective: Dehydroepiandrosterone sulfate (DHEAS) is a circulating steroid, produced in the adrenals and in the brain, with different important neurophysiological functions. DHEAS has been less extensively studied in depressed patients, than cortisol. There is only limited information about the effect of antidepressants on the DHEAS level. The aim of the study was to investigate DHEAS level in depressed patients with tianeptine treatment.

Methods: There were examined 27 patients with depressive episode (F 32.2). Patients had antidepressant treatment of tianeptine during three weeks in the average dose of 37,5 mg per day. Depressive symptoms were evaluated by the Hamilton Depression Scale (HDS). Blood samples for DHEAS measurement were drawn two times: before tianeptine treatment, and on 21 day after. Serum DHEAS level was measured using immune-enzyme method.

Results: There was a negative correlation between DHEAS level and score by the HDS before treatment (r = - 0,47, p=0,037). 15 patients had shown decrease of DHEAS level (0,7±0,2 mkg/ml) in comparison with normal value (2,4±0,9 mkg/ml). DHEAS level of these patients significantly increased on the 21st day of therapy (1,3±0,2 mkg/ml, p=0,03). Increase in DHEA-S level was correlated with improvement in depressive symptoms.

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Conclusion: Decreased DHEAS level may be the one of endocrine markers of depressive illness and symptom severity. Our results show that changes in DHEA-S serum concentration during antidepressant treatment correlate with improvement depressive symptoms.

P-10-19

Metyrapone as additive treatment in major depression: A double-blind and placebo-controlled trial

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Objective: Inhibitors of steroid-synthesis have been reported to exert antidepressive effects. The hypothesis was tested whether addition of metyrapone to standard antidepressants induces a more rapid, more efficacious and sustained treatment response in Major Depression.

Methods: 63 in-patients with a DSM-IV diagnosis of Major Depression and a baseline score ≥ 18 points on the Hamilton Rating Scale for Depression were randomly allocated to two treatment groups receiving either placebo or metyrapone receiving (1g/die) metyrapone for the first 3 weeks during a 5 week treatment with standard serotonergic antidepressants in a double-blind design.

Results: Primary outcome criteria were number of responders, and time to onset-of-action. The number of responders was considered twice after 3 and 5 weeks. Treatment response was defined as a 30% and 50% reduction from baseline HamD-17. sum-scores, respectively. Onset-of-action was defined as the time-point of a at least 20% reduction from baseline HamD-21. sum-scores. Using intent-to-treat analysis, a higher proportion of patients receiving metyrapone showed a positive treatment response at day 21 (23 of 33 patients) and also at day 35 (19 of 33 patients) compared to placebo (day 21: 13 of 30 patients; Fisher's exact p=0.031; day 35: 10 of 30 patients; Fisher's exact p=0.047). The clinical course of patients treated with metyrapone showed an earlier onset-of-action (Kaplan-Meier analysis; log-rank test p< .006). The treatment was well tolerated.

Conclusion: Metyrapone is an effective adjunct in the treatment of major depression accelerating the onset of antidepressant action.

Reference

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P-10-20

Quality of life and side effects of pharmacological treatment in patients with affective disorders

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Objective: The aim of study was to evaluate severity of side effects of antidepressant treatment in patients with affective disorders and to assess their impact on quality of life.

Methods: 52 patients with affective disorders were included into the study. 29 patients were in psychiatric hospital, and 23 treated at the Outpatients Clinic. Quality of life was assessed using WHOQOL Bref, side effects (SEf) using UKU side effects rating scale for patients and severity of depressive symptoms were evaluated by Beck Depression Inventory.

Results: Global score of WHOQOL of the patients was negatively influenced by depression intensity and by Psychiatric, Neurological SEf and several other SEf. General perception of quality of life correlated with concentration difficulties, memory impairment, emotional indifference, neurological SEf, reduced sexual desire. Women had more pronounced increased dream activity, akathisia, constipation and reduced sexual desire and scored significantly worse in Psychological domain of WHOQOL comparing to men. Male patients had significantly higher level of sleepiness score. In depressed patients significantly higher levels of Psychiatric SEf, of Neurological SEf, higher scores of such items as: disturbances of accomodation, palpitations/tachycardia, photo-sensitisation, weight loss and reduced sexual desire. Non-depressed patients had only higher scores in weight gain item. Younger patients scored significantly worse in global quality of life of WHOQOL and had significantly more concentration difficulties, emotional indifference, hypokinesia/ akinesia, orthostatic dizziness, and weight loss items.Side effects significantly impair the quality of life of affective patients. Age- and gender differences in the side effects of treatment of affective disorders were also observed.

Conclusion: Side effects significantly impair the quality of life of affective patients. Age- and gender differences in the side effects of treatment of affective disorders were also observed.

P-10-21

Dysphoria and mixed states: An empirical study

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Mixed affective states are heterogeneous clinical entities difficult to define precisely. The stringent actual DSM IV criteria are often unsatisfactory for clinical use. Recent and less recent studies lend support to largerbroader definitions of mixed states, such as mixed manic states (a full manic episode associated with a few depressive symptoms) and depressive mixed state (a full depressive episode with a few manic symptoms). Dysphoria, defined as a syndrome which that includes irritability, inner tension, hostility and aggressiveness, is frequently associated to with mixed states. The question of the nature of dysphoria is stillremains a debated issue: is-it a third psychopathological dimension which is independent of the two other dimensions (depression and mania) or the result of the mixing of these two dimensions ? Using a modified version of the Mini International Neuropsychiatric Interview (modifications to that allow the evaluation assessment of dysphoria and the subtyping of mixed states) we have evaluated the presence of dysphoria among 165 inpatients presenting a major depressive or/ and a manic episode. To document the strength of the association between mixed states and dysphoria we have then compared the prevalence of dysphoria among the subgroups of non-mixed depressive, mixed depressive, full mixed (DSM IV narrow definition), mixed manic and non-mixed manic patients according to the nosography our group has proposed (Dayer et al, Bipolar Disorders, 2000). The prevalence wasDysphoria was present in 24.5, 75.6, 73.3, 70.0 and 20.0% of patients, respectively. Then cConsidering the hypothesis that dysphoria could be a marker of mixed states, we also examined the relationship between the number of symptoms of the opposite dimension (i.e. the number of manic symptoms associated to a full depressive episode and vice-versa) and the prevalence of dysphoria to discuss the question of the diagnostic threshold of for mixed states.

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P-10-22

Neurocognitive differences between female and male with major depression

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Epidemiologic data indicate that MD is approximately twice as common in women as in men. The biological hypotheses have been proposed to explain the predominance of MD in women attributes the sex difference in brain structure and function between men and women. Little is known about the effects of gender differences on cognition in depression. The objective of the study was to compare cognitive function between female and male patients suffering from DSM IV. major depressive episode. We hypothesized that both patient groups will show some gender-specific neurocognitive functioning. The neuropsychological battery included tests that assessed attention, verbal memory, non verbal memory, working memory, executive function. Results showed that females had better recalling memory as compared to men. There was a significant difference, males attained lower verbal memory scores as compared to females. While reproducing from memory the performance of both females and males was worse in comparison to normative data. When compared the colour identification period in patient group with the normative data obtained from generally accepted studies, it was observed that depressed group took a significantly longer period to identify colours. For measures visual scanning ability and speed attention there were significant differences between the patient group and standard subjects, women performed somewhat faster than men. The findings of this study suggest that although global cognitive impairment is absent in major depressive episode, deficit in most of the specific domains are present. Most individual test score differences were found within the memory and executive functioning domains, where depressed males typically were most impaired.

P-10-23

Mood disorders and their treatment in patients with epilepsy

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Objective: Mood disorders in patients with epilepsy are frequently not diagnosed and not treated. Because of the high prevalence of depression and the resulting high suicide rate, precise diagnosis and effective therapy are very important.

Methods: A review of the literature is given

Results: Frequently, the clinical pictures of depressive syndromes in epileptics do not correspond with those described in operationalized classification systems such as ICD-10. or DSM IV. The incidence of depressive disorders in epileptics is estimated in the literature to be 30-70%. Multifactorial pathogenetic models include the type of seizures, the location of the epileptic focus, and neurotransmitter dysfunctions, as well as hereditary and psychosocial influences, and negative psychotropic effects of antiepileptic drugs (AEDs).

Conclusion: Despite an insufficient number of available controlled studies, based on the current data, treatment with the newer serotonergic antidepressants can be recommended for patients with epilepsy.Recommendations for therapy are given.

P-10-24

Comparison among measures of depression: Reliability, validity, relationship to anxiety and personality and the role of age and life events

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Objective: During the last decades, several scales assessing depressive symptoms emerged, however there are only a few studies comparing them in terms of reliability and validity.

Methods: The study sample included 40 depressed patients 29.65 ± 9.38 years old, and 120 normal comparison subjects 27.23 ± 10.62 years old. Clinical Diagnosis was reached by consensus of two examiners with the use of the SCAN v.2.0. The depressive scales applied and standardized were the CES-D, ZDRS, BDI-I, and the KSQ. Also, the STAI, the Life Events scale (Holms and Rahe), and the EPQ were administered. The analysis included the comparison of psychometric properties and the use of Pearson correlation coefficient and factor analysis.

Results: The results suggest that all scales correlated with anxiety measurements, sociodemographic variables, personality dimensions and non-significant indices to a similar extend. However, the MDI performed somewhat better, while the ZDRS had a very low internal consistency.

Conclusion: The comparison of several depressive scales provided no impressive results on the superiority or inferiority of a specific scale on the others.

P-10-25

Clinical, neurobiological and psychometric differences between early and late onset depressive illness

K.N. Fountoulakis. *Aretsou, Greece*

Tuesday, April 5, 2005

P-12. Poster session: Affective disorders II

Chairperson(s): Jules Angst (Zürich, Switzerland), Eduard Vieta (Barcelona, Spain)
11.15 - 12.15, Gasteig - Foyers

P-12-01

Olanzapine/fluoxetine and olanzapine treatment for bipolar depression: Open-label continuation in rapid cycling patients

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Objective: Olanzapine/fluoxetine combination (OFC) has demonstrated efficacy in treatment of bipolar depression. This secondary analysis of patients with a history of rapid cycling (RC) examines the efficacy of OFC and olanzapine (OLZ) during a 6-month open-label (O-L) extension.

Methods: 833 subjects with an index depressive episode enrolled in an 8-week, double-blind, randomized trial with 315 RC patients receiving OFC (n=37), OLZ (n=140), or placebo (n=138). Patients achieving remission (MADRS≤8; YMRS≤12) entered O-

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