

particularly respiratory distress; however, the quality of the available evidence is insufficient.

**Methods:** Outcomes of neonates whose mothers used SSRIs in late pregnancy (N=83), used SSRIs only in early pregnancy (N=36), or did not use SSRIs during pregnancy (N=137) were compared. All mothers were patients at a tertiary care reproductive mental health clinic. Data were abstracted from both maternal and infant hospital charts.

**Results:** No significant differences between groups were found in frequency of respiratory distress, tachycardia, admission to neonatal intensive care unit, or irritability. Birth weight differed significantly between the three groups ( $p < 0.05$ ), and post-hoc analysis revealed significant differences between infants exposed in early pregnancy (Mean wt.: 3286g) and unexposed infants (Mean wt.: 3527g); however, multiple regression revealed no effects of SSRI exposure after correction for gestational age. APGAR scores at one minute were significantly lower in infants exposed to SSRIs at term (Mean: 7.98) than control infants (Mean: 8.38,  $p < 0.05$ ). At five minutes, the difference between these two groups was no longer significant. The same pattern of results was observed when only mothers with significant symptoms of depression (Edinburgh Postnatal Depression Scale scores  $> 11$ ) were considered.

**Conclusions:** These findings are limited by a modest sample size and retrospective design. However, they do not support the existence of a neonatal withdrawal/discontinuation syndrome associated with maternal use of SSRIs in late pregnancy. Additional research is urgently required to aid decision making in treating pregnant women with depression.

Tuesday, April 5, 2005

## P-15. Poster session: Affective disorders IV

*Chairperson(s):* Siegfried Kasper (Wien, Austria),  
Jean-Pierre Olie (Paris Cedex 14, France)  
18.00 - 19.30, Gasteig - Foyers

### P-15-01

Escitalopram in the treatment of severe depression

S. Kasper, P. Ninan, D. Ventura, J. Wang. *Medizinische Universität Allgem. Psychiatrie, Wien, Austria*

**Objective:** Escitalopram is the most selective serotonin reuptake inhibitor (SSRI) antidepressant, and has been shown to be more effective than citalopram, another SSRI, in the treatment of severe major depressive disorder (MDD). To determine prospectively the effect of escitalopram in the treatment of severe MDD.

**Methods:** Patients with severe MDD (mean baseline 24-item Hamilton Depression Rating Scale [HAMD] score=30) were randomly assigned to 8 weeks of double-blind treatment with 10-20 mg/day escitalopram (N=147) or placebo (N=153). Efficacy assessments included Montgomery-Åsberg Depression Rating Scale (MADRS; primary efficacy measure), HAMD, and Clinical Global Impression (CGI) scales. Response was prospectively defined in three ways: at least a 50% decrease in MADRS, or in HAMD total scores, or CGI-I  $\leq 2$ . Tolerability was assessed on the basis of adverse events (AEs).

**Results:** Overall, 82% of patients completed the trial. For LOCF analyses, escitalopram treatment led to significant ( $p < 0.05$ )

improvement versus placebo by week 2 in HAMD scores, and by week 4 in MADRS and CGI-I scores; statistically significant improvement compared with placebo was maintained at all subsequent visits. Approximately half of escitalopram treated patients (49-52%) at endpoint (LOCF) were responders, according to each definition, and these rates were significantly superior to placebo treatment (30-38%;  $p < 0.05$ ). Incidence of AEs was similar to those reported previously for escitalopram treatment. Discontinuation rates due to AEs were low (6% escitalopram, 0% placebo).

**Conclusion:** Escitalopram is an effective and well-tolerated treatment of severe major depression.

### P-15-02

The efficacy and tolerability of escitalopram in depressed patients with or without concomitant anxiety

J.-P. Olie, B. Tonnoir, I. Florea. *Centre Hospitalier Sainte-Anne, Paris Cedex 14, France*

**Objective:** This was an open multicentre prospective study assessing the efficacy and tolerability of escitalopram in depressed patients with or without concomitant anxiety.

**Methods:** Escitalopram 10 to 20mg/day was administered over a 12-week treatment period in patients retrospectively divided into 3 groups according to their level of anxiety determined by HAM-A total score at baseline

**Results:** 649 out of 790 patients completed the study. At baseline, the mean MADRS total score was 31.5 (increasing as the HAM-A total score increased) and improved to 10.5 (OC) [12.4 (LOCF)] at endpoint. The mean HAM-A total score at baseline was 25.6, which improved to 9.0 (OC) [10.8 (LOCF)] at endpoint. There was no apparent effect on response to treatment of the presence or absence of anxiety, of the presence of one or more anxiety disorder at baseline, or of the type of anxiety disorder present. However, the therapeutic effect on anxiety (assessed by HAM-A) was slightly increased, while the therapeutic effect on depressive symptoms (assessed by MADRS) was slightly reduced, when either the severity of baseline anxiety or the number of comorbid anxiety disorders were high, suggesting a strong anxiolytic effect. 251 patients (32%) had adverse events (AEs). The AEs that occurred most frequently were nausea in 67 patients (8%) and headache in 38 patients (5%); 61 patients (8%) discontinued due to AEs.

**Conclusion:** Escitalopram was effective at reducing symptoms of depression in patients with or without comorbid anxiety over the 12-week treatment period and was well tolerated.

### P-15-03

A comparison of escitalopram and mirtazapine and placebo on driving performance, psychomotor performance and cognitive function in healthy subjects

S. Langer, M. Wingen, H. Andersen, J. Bothmer, J. Ramaekers. *Lundbeck GmbH Clinical Research, Hamburg, Germany*

**Objective:** Some antidepressant drugs are known to produce side effects like drowsiness and sedation, which may impair psychomotor functioning. Consequently, antidepressants may have an impact on everyday safety, including driving. The objective of this study was to evaluate the effect of escitalopram (10-20mg/day) and mirtazapine (30-45mg/day) in healthy subjects, primarily on driving performance

using the standard deviation of lateral position (SDLP) during a road-tracking test, and secondarily on psychomotor and cognitive function.

**Methods:** A total of 19 healthy subjects were enrolled in a randomised, double blind, placebo-controlled, multiple-dose, 3-way crossover trial. Each treatment period lasted for 15 days and was separated from the next period by a washout period of at least 13 days. On Day 2, reflecting the acute phase, a highway road-tracking test was performed. The tests were performed 12–16h after drug intake.

**Results:** Treatment differences were most visible in the acute phase, in which subjects treated with 30mg mirtazapine performed statistically significantly less well in the road-tracking test than those treated with 10 mg escitalopram (3.54; CI95% 1.84, 5.23;  $p < 0.001$ ) or placebo (3.77; CI95% 2.04, 5.50;  $p < 0.001$ ). The difference in driving performance between escitalopram and the placebo group was not statistically significant (0.23; CI95% -1.49, 1.96;  $p = 0.79$ ). A Divided Attention Task revealed a significantly increased tracking error of 30mg mirtazapine in the acute phase compared to 10mg escitalopram and placebo.

**Conclusion:** While mirtazapine (30mg/day) significantly impaired driving performance and tracking error in healthy subjects during the acute treatment phase, escitalopram treatment (10–20mg/day) did not affect driving performance or psychomotor and cognitive function throughout treatment.

### P-15-04

The effect of escitalopram versus sertraline versus duloxetine on CYP 2D6 function

T. Burt, S. Preskorn, A. Klick Davis, M. Ramadan, B. Baker, K. Omo, M. Erickson, M. Erickson, T. Burt. *Pfizer Inc., New York, USA*

**Objective:** Learn the differential effects of three antidepressants on the functional activity of the cytochrome P450 enzyme 2D6 as reflect by changes in the metabolism and clearance of metoprolol.

**Methods:** Hypothesis: Sertraline will have less in vivo effect on the functional activity of the cytochrome P450 (CYP) drug metabolizing enzyme 2D6 than does either duloxetine or escitalopram.

**Methods:** Single dose pharmacokinetics of metoprolol, a model CYP 2D6 substrate-drug, was measured before and after 17 days of treatment with duloxetine 60 mg/day, escitalopram 20 mg/day, or sertraline 100 mg/day in young healthy male and female volunteers (15 – 20 individuals in each treatment condition). The metoprolol outcome measures were change in peak plasma levels ( $C_{max}$ ), area under the plasma concentration – time curve (AUC), and clearance. These results were tested using analysis of covariance (two-tailed) taking into account the following patient data as indicated: height, weight, and body mass index.

**Results:** Escitalopram in comparison to sertraline produced a greater increase in  $C_{max}$  (1.945 versus 1.277, respectively,  $p < 0.01$ ) and AUC (1.995 versus 1.428, respectively,  $p, 0.05$ ). The reduction in clearance trended in the same direction but was not statistically significant. The duloxetine samples are being assayed now. Hence, duloxetine results are not available now but will be at the time of the meeting.

**Conclusion:** Under steady state dosing conditions, escitalopram 20 mg/day produced a greater in vivo inhibition of CYP 2D6 than did sertraline 100 mg/day. The results for duloxetine 60 mg/day are pending.

### P-15-05

Depression and sleep disturbance: the effect of escitalopram

M. Lader, E. Reine, H. F. Andersen. *Institute of Psychiatry Psychiatry, London, United Kingdom*

**Objective:** More than 80% of patients in primary care complaining of sleep disturbances are suffering from depression. In the present paper, the effect of treatment with escitalopram, the most selective serotonin reuptake inhibitor, on sleep disturbance was analysed in patients with major depressive disorder (MDD).

**Methods:** The results from three separate 8-week, randomised, double-blind, placebo-controlled studies in MDD, in which citalopram was the active reference, were pooled and the Montgomery-Åsberg Depression Rating Scale (MADRS) item 4 (reduced sleep) scores were analysed

**Results:** There was a significant improvement for escitalopram-treated patients ( $n=520$ ) in the MADRS item 4 scores at Weeks 6 and 8 versus placebo ( $n=398$ ;  $p < 0.01$ ), and at Weeks 4, 6 and 8 ( $n=403$ ;  $p < 0.05$ ) versus citalopram. Escitalopram-treated patients ( $n=254$ ) with more severe sleep disturbances (MADRS item 4 score 4) showed statistically significant improvement of MADRS item 4 at Weeks 4, 6, and 8 compared with patients treated with placebo ( $n=191$ ;  $p < 0.05$ ) or citalopram ( $n=193$ ;  $p < 0.01$ ). These patients also showed significant and clinically relevant improvement in MADRS total scores after escitalopram treatment versus citalopram at Weeks 1, 4, 6 and 8 (observed cases) and endpoint (-2.45) and statistical significance in favour of escitalopram versus placebo treatment was found at all visits, including endpoint (-4.2).

**Conclusion:** Escitalopram shows a significant beneficial effect compared with placebo or citalopram in reducing sleep disturbance in patients suffering from MDD.

### P-15-06

The tolerability and safety of Bupropion XL versus Escitalopram in the treatment of major depressive disorder

J. Horrigan, D. Wightman, J. Modell. *GlaxoSmithKline Neurosciences MDC, Research Triangle Park, NC, USA*

**Objective:** This study examined the comparative tolerability and safety of two newer antidepressants, the once-daily formulation of bupropion (bupropion XL) and escitalopram, in outpatients with major depressive disorder (MDD).

**Methods:** 420 outpatients with moderate to severe MDD were randomized in a 1:1:1 manner to placebo, bupropion XL or escitalopram in this double-blind study with an 8 week treatment period. Subjects were evaluated on a weekly or biweekly basis during the study with investigator- and self-rated instruments for depressive symptoms as well as sexual functioning, coupled with questioning about treatment-emergent adverse events.

**Results:** Adverse events triggered premature discontinuation in the following proportion of patients: placebo 5%, bupropion XL 3%, and escitalopram 5%. The following adverse events occurred with an incidence of at least 5% on drug and at a rate  $> 1.5X$  the rate observed with placebo. For bupropion XL: nausea, dry mouth, insomnia, nasopharyngitis, and constipation; for escitalopram: dry mouth, insomnia, diarrhea, decreased appetite, and somnolence. In addition, sexual functioning inventories indicated that the escitalopram group typically experienced twice the level of sexual

dysfunction as compared to the bupropion XL and placebo groups by the end of treatment.

**Conclusion:** Both bupropion XL and escitalopram were generally well-tolerated. However, significant differences were noted between bupropion XL and escitalopram with regard to treatment-associated sexual dysfunction, beginning at the end of the first week of treatment. Sexual side effects may contribute to premature discontinuation of antidepressant medication treatment.

### P-15-07

Treating mood disorders during pregnancy: safety considerations

M. Eberhard-Gran. *Norwegian Institute of Public Health, Norway*

**Objective:** Mood disorders in pregnancy may have negative effect on self care and pregnancy outcome which affects the mother directly and the child indirectly. Thus, some women may require pharmacological treatment. Pharmacotherapy of mood disorders during pregnancy implies specific considerations. This paper presents an updated review of available studies on treatment of mood disorders and present knowledge on teratogenicity, neonatal effects and long-term neurobehavioral effects for the different psychotropic drugs.

**Methods:** Identification of relevant literature was conducted using Medline, EMBASE and the Science Citation Index Expanded (ISI) (1966 until March 2004). This review includes treatment with selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), other antidepressants, benzodiazepines, lithium, carbamazepine/valproic acid, lamotrigine, and novel antipsychotics.

**Results:** SSRIs and TCAs have not been associated with increased risk of major malformations. However, poor neonatal adaptation has been described. Benzodiazepines used in first trimester have been associated with orofacial clefts. Mood stabilizers such as lithium, carbamazepine and valproic acid are associated with increased risk of fetal malformations. Both benzodiazepines and lithium may cause adaptation problems in the newborn. In utero exposure to novel antipsychotics has not been associated with congenital malformations, however, the data is still limited. The knowledge about long-term neurobehavioral effects in the offspring is still limited for all agents and requires further investigation.

**Conclusion:** The existing knowledge on the consequences of use of antidepressants during pregnancy suffers from lack of results from randomized controlled trials. Most of the observational studies can be criticized for inadequate design such as small sample sizes, short follow-up times, and lack of control for confounding factors. Systematic research is needed to gain knowledge on the effects of in utero antidepressant exposure on child development. Possible adverse effects of fetal exposure must be balanced against adverse effects of untreated maternal mood disorder.

### P-15-08

Postnatal depression- does it exist as a specific entity?

M. Eberhard-Gran. *Norwegian Institute of Public Health, Norway*

**Objective:** The aim of the study was to study if postpartum women are at increased risk of depression. The second aim was to study the risk factors of depression in postpartum women as compared with non-postpartum women.

**Methods:** A population based questionnaire study was performed among women 18-40 years in two municipalities in

Norway in 1998-1999. 2730 women were included, of whom 416 in the postpartum period. Two different mental health-screening instruments were included in the questionnaires, the Edinburgh Postnatal Depression Scale (EPDS) and the Hopkins Symptom Check List 25-items version (SCL-25).

**Results:** The prevalence of depression (EPDS >10) was higher in non-postpartum as compared to postpartum women. High scores on the life event scale, a history of depression and a poor relationship to the partner were associated with depression in both postpartum women and non-postpartum women. When controlling for the identified risk factors of depression the odds-ratio for depression (EPDS >10) for being in the postpartum period was 1.6 (95% CI: 1.0-2.6).

**Conclusion:** The risk of depression was slightly increased in the postpartum period, when controlling for the uneven distribution of risk factors. The risk factors for depression were mainly the same among postpartum women as compared with non-postpartum women, suggesting that the etiology does not differ much. We found only modest evidence of an association between depression and the postpartum.

### P-15-09

The European Alliance Against Depression - EAAD

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**Objective:** The "European Alliance Against Depression (EAAD)" is an international network targeting at the problems of affective disorders and suicidality. EAAD provides a concept and instruments for a community-based intervention programme targeting at an improvement of care for affected persons and their relatives.

**Methods:** The intervention programme takes place on four different levels complementary to each other: · Co-operation with general practitioners (e.g. workshops, screening tools, videos) · Public relations campaign (e.g. posters, leaflets, information brochures, several public events) · Community facilitators (e.g. training for priests, policemen, geriatric caregivers) · High risk groups and self-help The evaluation of the network's activities will be based on commonly defined indicators such as e.g. suicides, suicide attempts or surveys).

**Results:** Up to now several EAAD-partners already initiated intervention programmes in their regions, produced information material or adapted training concepts to local requirements. A common catalogue of available campaign material ranging from posters and placards over training concepts to leaflets and flyers has been compiled as well. A common website ([www.eaad.net](http://www.eaad.net)) informs about the project and serves as platform for information exchange among the partners.

**Conclusion:** During the actual and next stages of the project more and more regions will conduct regional intervention programmes based on the common four level concept. The EAAD network helps to reduce redundancies and contributes to a more effective usage of already available concepts and instruments. In the future the EAAD concept may also be applicable for a broader focus targeting at other mental health problems.

### P-15-10

Depression guidelines: how useful are they to the clinician?

M. Livingston. *Southern General Hospital Dept. of Psychiatry, Glasgow, United Kingdom*

**Objective:** To review recently published depression management guidelines in order to assess their utility.

**Methods:** Depression affects 7% of the population per annum and WHO predicts it will soon become the second most common cause of disability in the world. The detection and treatment of depression is therefore of the utmost importance. We evaluated recently published depression such as those from the World Federation of Biological Psychiatrists, the British Association for Psychopharmacology and the England Wales National Institute for Clinical Excellence (NICE) to see whether the advice offered was reasonably consistent across guidelines, reliable, valid, and of practical utility to the clinician.

**Results:** Consistency was achieved in much of the advice offered by the guidelines, principally because guidelines mainly use a similar, systematic approach to their literature search. Reliability, validity, and utility depend essentially on whether the diagnostic systems, which provide the entry criteria for the RCTs evaluated in guideline formulation, are reliable and valid means in diagnosing depression.

**Conclusion:** The guidelines offer reliable advice on the management of more severe depressive disorders. In the absence of a biological validation criterion for diagnosing depression, there is less certainty about distinguishing pathological from non-pathological depressive symptomatology and hence the management of patients with milder depressive syndromes.

### P-15-11

Do past life change events still have an impact on post-MI depression in the PTCA era?

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**Objective:** Evaluate the influence of last year life change events on the development of depressive symptoms post-myocardial infarction (MI) in a population submitted to percutaneous transluminal coronary angioplasty (PTCA).

**Methods:** 20 consecutive inpatients at the Coronary Intensive Care Unit, with MI diagnosis, were prospectively evaluated during the first week and in a month. Psychiatric diagnosis was established using DSM-IV criteria. Patients were separated in two groups according to Life Change Events Scale (LCE) (Holmes and Rahe, 1967) using a cut-off point of 200. The total scores of Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) were compared in the two groups. Fisher test or ANOVA were used for statistical analysis.

**Results:** On the first evaluation no significant results were found. At second evaluation the group of patients with LCE had at least one depressive symptom ( $p < 0.05$ ), higher BDI ( $p < 0.01$ ), HAM-D ( $p < 0.05$ ) and HAM-A ( $p < 0.05$ ) scores. No patient met criteria for major depressive episode on both evaluations.

**Conclusion:** LCE influence the development of depressive symptoms in post-MI patients probably by a cumulative effect of stress. Although these findings were stated by several past studies (Carney et al, 1997), this is the first study using only PTCA patients. These patients may have different characteristics from those of previous studies (PTCA improves morbidity and mortality and reduces the stress associated with MI). These are preliminary results that need to be confirmed by future increased in our sample.

### P-15-12

Dimensions of response styles in a unipolar depressive and in a population based sample

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**Objective:** To examine components of the Response Styles Questionnaire (RSQ, Nolen-Hoeksema, 1991) for assessing response styles to cope with depression and the relationship between these factors and gender, depression severity, and related constructs.

**Methods:** 91 unipolar depressive patients after discharge from inpatient treatment and 91 age and gender matched untreated individuals from the Mannheim population (each with 49,5% women) filled in questionnaires to assess response styles (RSQ), action orientation (HAKEMP), and dysfunctional and functional self-consciousness (DFS). Additionally assessed was depression severity (FDD-DSM-IV, MADRS).

**Results:** Using a principal component analysis the RSQ yielded four factors: Symptom Focussing (accounting for 20.9% of the total variance), Distraction (14.9%), Self-Isolation (10.7%) and Reflection (7.6%). Analyses of variance revealed no gender differences though effects of sample membership for Symptom Focussing, Distraction, and Self-Isolation. The cross-product terms (sex x membership) were non-significant. Symptom Focussing and Self-Isolation were negatively associated with functional self-consciousness and action orientation, and positively with dysfunctional self-consciousness while Distraction showed opposite relationships with these variables. Symptom Focussing, Distraction and Self-Isolation were also associated with depression severity while Reflection was not.

**Conclusion:** Our results suggest that the responses to the RSQ are best represented by a four-factor-solution. Of interest is the fact that not all components of the RSQ are associated with depression severity and the mentioned related constructs. In a next step we will assess the predictive value of these factors regarding the prospective course of depression.

### P-15-13

EPID - Epidemiology of depression in Slovakia: Recurrence of depression in connection to socio-demographic factors

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**Objectives:** EPID was first psychiatric epidemiological study on adult population of inhabitants in Slovak Republic and was focused on depressive disorders.

**Methods:** Quota sample consisted of 1212 participants. The main diagnostic tool to gather data on 6-month prevalence of depression was MINI (Mini International Neuropsychiatric Interview), similarly as in DEPRES study conducted in 6 EU countries. Supplementary shortened version of Beck Depression Inventory was used to get picture of „actual depression“.

**Results:** Generally we found high prevalence of depression (MINI) in together 40,9% of sample (12,8% for Major Depression according to MINI). Participants with positive diagnosis (MINI) were asked whether they suffered similar difficulties in the past. We found recurrence of depression in 56% participants diagnosed by MINI. Significant differences in percentage of reported recurrence were in three forms of depression by MINI (47% of participants with Minor Depression, 54% with Depressive



Symptoms and 64% with Major depression). Women had repeated depressive symptoms significantly more often than men (27% to 17%). Single participants and participants living outside family had significantly higher recurrence of depression. Recurrence of depression was also significantly higher in widowed. Although according to employment grouping of sample unemployment participants were found more often depressed, they had the lowest rate of recurrence. The study had not found nor link between recurrence and age groups, nor recurrence and nationality of inhabitants (Slovakian, Hungarian), recurrence and urban/rural characteristic nor the relation between recurrence and education of participants. Conclusions: Depressive disorders are clearly recurrent disorders. Relations between rous socio-demographic characteristics and recurrence of depression are discussed.

### P-15-14

Group treatment for depression in mothers of young infants: A controlled study

U. Frisch, M. Hofecker Fallahpour, P. Ley, C. Neuhofer Katz, R.-D. Stieglitz, A. Riecher-Rössler. *Universitätsspital Abt. Psychiatrie, Basel, Switzerland*

**Objective:** To evaluate the efficacy of a manualized group psychotherapy intervention for mothers of infants suffering from depression. The group therapy specifically adjusted to the needs of depressed mothers was developed in Basel and was now compared to individual therapy-as-usual.

**Methods:** The group program which consisted of 12 group sessions and 1 couple session was administered in 5 consecutive groups to 31 participants. The main therapeutic method used was cognitive behavioral therapy (CBT). Antidepressants were administered if necessary. In a second step a control group of 21 participants receiving individual therapy-as-usual has now been evaluated and compared to the specific treatment group in a pre-post-design using BDI, SCL-90-R and other scales. Symptom reduction and other outcome variables such as quality of marriage and impact on the mother-infant relationship, were determined.

**Results:** Both treatment group and control group showed significant improvement of depression, there was no significant difference between the two treatment strategies. However differences were seen in acceptance, satisfaction with treatment as well as in terms of treatment costs. Furthermore there was a trend to less group patients being in need of antidepressive medication at the same time. Group therapy also showed a tendency for a better improvement of aggressivity.

**Conclusion:** This newly conceptualized group therapy proved to be efficacious and effective. The performance of the treatment program is facilitated by a specifically developed manual.

### P-15-15

Outpatient Electroconvulsive Therapy

S. Barrio, J. Carton, A. Sanchez, L. Perez, T. Piza, J. I. Andonegui. *Donostia-San Sebastian, Spain*

**Objective:** Description of the characteristics of the patients submitted to outpatient electroconvulsive therapy (ECT) during a period of one year, revising indications, modalities of application and side effects in order to design a protocol for maintenance ECT.

**Methods:** We carried out an observational and retrospective study with a sample of twelve patients submitted to outpatient ECT

during a period of one year. Some of the included variants were as follows: · Demographic variables (sex, age, etc..) · Clinical variables (diagnosis, non psychiatric comorbidity, pharmacologic treatment, previous ECT, side effects, ...) ECT modality: - Index. - Consolidation (number of sessions) - Maintenance (frequency).

**Results:** Up to the present moment a sample of 12 patients have been obtained. The majority of patients are middle – aged, from an area relatively near to the hospital, diagnosed of affective disorder, with pharmacological treatment associated and that have received ECT previously in a vast majority. We haven't observed important side effects. According to the modality of ECT received we have found differences in the patients' clinical course.

**Conclusion:** Still it is not possible to make a conclusion as we are still analysing the results.

### P-15-16

Psychopathological and somatic comorbidity in major depressive disorders

D. Vasile, M. Gheorghe, O. Vasiliu, E. Lungut. *Central Military Hospital Department of Psychiatry, Bucharest, Romania*

**Objective:** To evaluate the frequency of (1) somatic diseases, (2) personality disorders and (3) alcohol related disorders that have been diagnosed simultaneously with a major depressive disorder. Depressive disorders often associate a psychological or somatic dysfunction, the result being that many cases considered „treatment resistant” are, in fact, the result of a „silent”, undiagnosed, disorder.

**Methods:** Our study group consisted in 40 patients, 28 male and 12 female, diagnosed with major depressive disorder, presenting more than two previous admissions for major depressive episodes (DSM IV TR), medium age 42.8 years. We evaluated their psychiatric status using HAM-D, SCID, CAGE and AUDIT. A thoroughly somatic examination was performed, as well as blood (including GGT) and urine analyses, ECG and EEG. An interdisciplinary team, including an internist and a neurologist, analysed the results.

**Results:** We have found a high incidence of somatic comorbidity (35%), personality disorders (59%) or both (22%) in depressed patients. The most frequently assessed somatic diseases were cardiovascular dysfunctions, cerebral organic syndroms, thyroid pathologies, malignant tumors. Personality disorders were mainly cluster C, dependent and avoidant, in particular and cluster B, borderline and histrionic personality disorders. An important degree of comorbidity (32%) was evidenced between alcohol related disorders and depression.

**Conclusion:** The importance of a comprehensive evaluation in depressive patients can not be overestimated. Such an evaluation should include an interdisciplinary assessment of both organic and psychiatric comorbidities.

### P-15-17

The impact of sexual dysfunctions on mood and quality of life in patients with diabetes

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**Objective:** Diabetes is the most prevalent chronic disease and more than 30% patients with diabetes suffer from depression. Both depression and diabetes cause sexual dysfunctions. The aim of the study was the evaluation of prevalence and types of sexual

dysfunctions, severity of depressive symptoms and their influence on quality of life in patients with diabetes.

**Methods:** We evaluated 21 diabetics (16 women, 5 men, age 51+/- 11,9 yrs.) and twenty two age- and sex- matched healthy controls. Eight patients were on hypoglycaemic drugs, 13 - on insulin. All subjects were involved within last 12 months. We used semi-structured questionnaire concerning diabetes course and sexual life, Beck Depression Inventory (BDI), WHO Quality of Life Questionnaire Bref, and UKU side effects scale to estimate sexual complaints.

**Results:** Diabetics had significantly lower global quality of life, they score less in physical domain as well. Their sexual desire score was decreased comparing to control group, and they had lower number of orgasms. There was a correlation between global estimation of quality of life and diabetes duration, and a correlation between global assessment of quality of life and type of prescribed medication (insulin vs oral drugs)- patients on insulin reported worse quality of life. Women on insulin complained of pain during sexual intercourse. There was no correlation between duration of diabetes and sexual dysfunctions.

**Conclusion:** Almost half of diabetics reported sexual dysfunctions influencing their quality of life. Preventive medical care for the diabetic population may reduce the risk of sexual dysfunction and improve their quality of life.

### P-15-18

Prevalence of depression among hemodialysis patients: Analysis of possible factors related to depression

V. Popovic, J. Popovic, A. Jovanovic, N. Dimkovic. *Institute for Psychiatry Clinical Centre of Serbia, Belgrade, Serbia + Montenegro*

**Objectives:** Depression affects a substantial number of hemodialysis (HD) patients. It is an important psychiatric problem that could influence their morbidity and mortality. The aim of this study was to assess the prevalence of depression in HD population and analyze and identify possible clinical and psychosocial factors related to it. **Methods:** All patients (free of intercurrent disease, without psychiatric diagnosis) enrolled in chronic HD program for more than one year were assessed using the Beck Depression Inventory (BDI). Their demographic characteristics, HD duration, education level, marital status, stages of rehabilitation, laboratory factors (albumin, hemoglobin, cholesterol and phosphorus), erythropoietin use and comorbid conditions were observed. **Results:** The total of 111 patients (49 female and 62 male) were studied. Their mean age was 54 years (range 25–78), and mean HD duration 87 months (range 12–279). The mean BDI score for the entire study group was 15. According to BDI, 69% of the subjects were depressive (BDI score 10 or more). Depression scores were significantly higher in females (19 vs. 12). Non-depressive subjects (BDI score less than 10) had significantly lower phosphorus in comparison to those who were depressive according to BDI. There was significant but weak correlation (-.248) between hemoglobin and BDI score. The patients's age, duration of HD, albumin, cholesterol, marital status, education levels, comorbidities or stages of rehabilitation were not of significant influence on depression. **Conclusions:** High prevalence of depression in HD patients stresses the importance of early identification, evaluation and treatment in order to improve their quality of life.

### P-15-19

Modafinil Treatment of Depressive Symptoms Pre- and Post-Cardiac Transplant: Case Report

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**Objective:** When severe co-morbid medical illnesses are present, treatment of depression is clinically challenging. Rapid resolution of depressive symptoms is necessary to minimize morbidity/mortality. Psychostimulants, such as methylphenidate, are especially effective, but may have untoward adverse effects (AEs). The novel psychostimulant modafinil is FDA-approved for treating daytime sleepiness associated with narcolepsy, sleep apnea/hypopnea syndrome, and shift work sleep disorder. Off-label uses include adjunctive/monotherapy treatment of depression, cognitive enhancement, and treatment of sedation/fatigue associated with multiple medical illnesses. Modafinil has limited AEs without abuse potential. This paper addresses modafinil treatment of depression pre/post cardiac transplant.

**Methods:** Case analysis with literature review.

**Results:** 68-year-old male presented with acute myocardial infarction. Cardiac catheterization revealed severe 3-vessel coronary artery disease requiring intra-aortic balloon pump and left ventricular assist device (LVAD) pending heart transplant. Following LVAD placement, he suffered mental status deterioration consistent with delirium and mood disorder secondary to a general medical condition. There was limited response to combined olanzapine, trazodone, and low dosage SSRIs. Appetite, energy and motivation remained impaired. Depression threatened his ability to survive and recover from heart transplant. Modafinil 100 mgqd was initiated. Within days he exhibited dramatic improvement: more spontaneous behavior, broader range of affect, improved appetite, increased energy and engagement in his treatment. No systemic AEs were noted with modafinil. In the post-transplant period, modafinil was discontinued; he again developed a mood disorder that resolved with re-initiation of modafinil.

**Conclusion:** The on-off-on response exhibited suggests clinical utility of modafinil in patients with severe cardiac compromise, including transplant patients.

### P-15-20

Prevalence depressive disorder with inpatients in poststroke period in neurologic clinic

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**Objective:** The prevalence of depressive disorders (DD) with inpatients in poststroke period (PSP) was investigated.

**Methods:** A random sampling of 130 apoplectic in-patients after stroke were investigated. 29 male (mean age 53,9±7,8) and 36 female (mean age 57,6±8,1). In accordance with the research objectives 130 patients with cerebral ischemic stroke were investigated. (65 males, 65 females). Comorbid depressive disorders were detected in 65 patients (29 males, 36 females). Diagnostics of the stroke and comorbid (DD) was performed taking into consideration ICD-10. criteria for strokes and depressive disorders). For diagnostics of the clinical depression BDI was also used. In the group of patients with DD the figure was 24.95

**Results:** The prevalence of minor and major depression made up total 50% in early and late post-stroke periods. With 50.8% patients DD preceded the stroke. In 41.5% cases depression developed during the acute period of stroke. In 7.7% cases DD developed during the late post-stroke period. Mild depression episode (DE) was marked in 41 patients (63.1%) with stroke, moderate DE in 14 patients (21.5%), severe DE in 10 persons (15.4%).

**Conclusion:** High prevalence of DD in PSP speaks for the necessity to introduce the study of its diagnostics and therapy to neurologists. This problem in Russia can be solved by the introduction of the educational program WPA/PTD “Depression Disorders in Neurology”.

### P-15-21

Social functioning and quality of life under depressive disorders

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**Objective:** Study of the indexes of social adaptation with depressive disorders (DD) patients before therapy.

**Methods:** 72 depressive inpatients (28 male, 44 female; mean age 39±6.2) were to be a random sampling. BDI, SASS [1] and their interconnections were studied. Diagnostics with the use of RDC of ICD-10. was conducted.

**Results:** The level of satisfaction with leisure was in inverse proportion to the pronounced level of DD according to BDI ( $r = -0.46$ ;  $P < 0.05$ ). Dissatisfaction with the feeling of losing control over one's life was also connected with depression ( $r = -0.46$ ;  $P < 0.05$ ). The indicators of DD according to BDI determined: loss of satisfaction with one's work ( $r = -0.41$ ;  $P < 0.05$ ); decline of communicative activity ( $r = -0.38$ ;  $P < 0.05$ ); narrowing of social sphere ( $r = -0.36$ ;  $P < 0.05$ ); negative evaluation of ones relations with other people ( $r = -0.34$ ;  $p < 0.05$ ). DD also influences: reduction of searching activities and interest for different information: cultural, technical, scientific, etc. ( $r = -0.35$ ;  $p < 0.05$ ); dissatisfaction with the quality of free time ( $r = -0.32$ ;  $P < 0.05$ ); reduction of ability to manage one's own finances and incomes ( $r = -0.31$ ;  $P < 0.05$ ), difficulties in formulating one's own opinion ( $r = -0.30$ ;  $P < 0.05$ ).

**Conclusion:** Indexes of social functioning and quality of life SASS reflect DD symptoms and relevant ties with BDI.

### P-15-22

Why is the involuntional depression in the female destiny?

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**Objective:** The involuntional age brings about new redeployment of libidinous cathexes in relation to both objects and self-representations, through the processes of de-cathexis and recathexis. This paper represents a metapsychological study on the psychodynamics of the depressive decompensation in women in the involution and it is based on two fundamental theses: 1. CENTRAL TRAUMA IS THE DISAPPOINTMENT IN CORPOREAL SELF. (Such disappointments are an attack to the self-respect, resulting in anxiety and depressiveness) 2. Acceptance of new developmental requests of the involuntional age is made difficult by two genetic factors of the early structuring imminent to women: a) NARCISISTIC LIBIDO IS SHIFTED TO THE ENTIRE BODY («Due to the lack of penis»). (Thus, regressive

motions in women are more closely related to the earliest structuring strata, when the corporeal self has been the primary material of the formation of self-images.) b) EARLY FORMATION OF EGO IDEAL (Powerful reproachful introjections and shame problems destruct self-respect and consequently, contents of the depressive position are established.)

### P-15-23

Increased risk of Parkinson's disease in patients treated for affective disorders?

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**Objective:** Patients with Parkinson's disease experience increased rates of depression. Recent data suggest that the opposite might as well be the case. To compare the risk for persons who purchased antidepressants or lithium of subsequently purchasing anti-parkinsonian drugs with the risk for two control-groups

**Methods:** An observational cohort study with linkage of nationwide registers covering 100% of the prescribed antidepressants, lithium, anti-diabetic drugs and anti-parkinsonian drugs in Denmark from 1995-1999. All persons who purchased antidepressants, lithium or anti-diabetic drugs (=first control-group) and subsequently purchased anti-parkinsonian drugs were included. A second control-group was selected randomly among the general population. In total 390,530 persons purchased antidepressants or lithium and 114,639 purchased antidiabetic drugs. The random sample comprised 788,620 persons who didn't purchase any study drugs.

**Results:** Persons who purchased antidepressants or lithium had greater risk of subsequently purchasing anti-parkinsonian drugs compared to persons who purchased antidiabetic drugs or persons who didn't purchase any of these drugs. The associations were most pronounced for men. Significant interactions were found of age and exposure status ( $\chi^2 = 45.47$ ,  $df = 6$ ,  $P < 0.001$ ) and gender and exposure status ( $\chi^2 = 108.85$ ,  $df = 3$ ,  $P < 0.001$ ).

**Conclusion:** Patients with depressive / anxiety disorders and patients with bipolar disorder are at increased risk of developing Parkinson's disease.

### P-15-24

Effect on mood after subthalamic stimulation in Parkinson disease

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**Objective:** Several cases of transient acute depression or manic symptoms are reported in the literature after bilateral subthalamic nucleus (STN) deep brain stimulation in patients with Parkinson's disease. These are case reports. We have few data about their frequency or cause. Different hypothesis involve premorbid personality disorders or thymic past history. Another hypothesis involve subthalamic nucleus. The inhibition of this structure is associated with behavioral disorders. Its relations to the limbic system and the frontal cortex are suspected to be involved.

**Methods:** We elaborated a one year prospective study to evaluate mood disorders frequency and physiological mechanisms of 20 Parkinsonian patients treated by bilateral STN stimulation. We enrolled in our sample the 20 first consecutive Parkinsonians who were selected to be operated. Evaluation consist of pre and

post-operative psychiatric interview and scales: Montgomery and Asberg Depression Rating Scale (MADRS), Mini International Neuropsychiatric Inventory (MINI), Scale Inventory Personality Disorder (SIPD), Mania Assessment Scale (Bech), Assessment of Depression (Beck), Apathic scale and neuropsychological tests.

**Results:** After six months, among 12 operated patients, temporary results show one case of hypomania with behavioral disorder (DSM-IV criteria disorder). This patient, without thymic history, presented a paranoid personality disorder. Using tools, we did not identified in the others 11 patients, acute depression or manic symptoms.

**Conclusion:** Data are still being analysed, but this case draw our attention to the effects of STN stimulation on mood and behavioural disorders and to the importance of the psychiatric follow-up.

Monday, April 4, 2005

### LS-03. Satellite symposium: Implication of serotonergic and melatonergic systems: New perspectives for the treatment of depression

Supported by an unrestricted educational grant from Servier

*Chairperson(s):* Mario Maj (Naples, Italy), Dieter Naber (Hamburg, Germany)

12.30 - 14.00, Gasteig - Carl-Orff Hall

#### Introduction

M. Maj *University of Naples of SUN Dept. of Psychiatry, Naples, Italy*

#### LS-03-01

Biological rhythm disturbances in mood disorders

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The clinical observations of diurnal variation of mood and early morning awakening in depression are incorporated into the established diagnostic systems. Not only is sleep disturbed, but many circadian rhythms in depressive patients are abnormal: earlier in timing, diminished in amplitude, or of greater variability. Whether these disturbances are of etiologic significance for the role of circadian rhythms in mood disorders (are there allelic mutations in "circadian clock"– or "sleep"-related genes in depression?), or whether they are a consequence of altered behavior is not yet clear. Genetic vulnerability and stress influence circadian rhythms and sleep patterns, leading to the symptoms characteristic of affective disorders. Circadian regulation interacts with, and is determined by, neurotransmitter function; for example, the highest concentrations of CNS serotonin are found in the biological clock in the suprachiasmatic nucleus. CNS serotonin turnover undergoes marked circadian and seasonal rhythmicity, and is rapidly stimulated by light exposure. This links the important role of light as a zeitgeber or synchronizer of the circadian system to the role of serotonin in mood disorders. Zeitgebers ensure stable phase relationships between internal and external time, which is crucial for a stable mood state. Melatonin is also a zeitgeber for the

circadian system. The specific pharmacological profile of agomelatine, as an agonist of melatonergic MT1 and MT2 receptors with 5-HT2C receptor antagonist properties, uniquely combines zeitgeber with neurotransmitter regulation properties, with evolving evidence for robust antidepressant efficacy. New to neuropharmacology is the zeitgeber aspect, providing innovative perspectives for drug development.

#### LS-03-02

Insights into the pharmacology of agomelatine: The first melatonergic antidepressant

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Depressive disorders represent a collection of psychological, physiological and behavioral symptoms whose frequency and chronicity together constitute a recognizable clinical condition. Despite extensive investigations, the exact neurobiological processes leading to depression and the mechanisms responsible for the therapeutic effects of antidepressant drugs are not completely understood. Limitations of current antidepressant medications such as the delay before there is a therapeutic response, a substantial rate of nonresponders, and bothersome side-effect profiles, merit the exploration of all plausible agents with novel antidepressant mechanisms of action. The well-established clinical finding that depressive disorders are often associated with desynchronization of internal rhythms has stimulated the idea that resetting normal circadian rhythms may have antidepressant potential. Initial attempts to prove an antidepressant activity for the powerful endogenous synchronizer melatonin were not successful. However, recent experiments using the novel melatonin receptor agonist agomelatine (S 20098; N[2-(7-methoxy-1-naphthyl)ethyl]acetamide) revealed clear antidepressant-like effects in a wide variety of rodent and non-rodent models. In vitro binding studies revealed that agomelatine is a high affinity agonist at both the melatonin MT1 and MT2 receptor types. In addition, these studies revealed that agomelatine - but not melatonin - blocks with high affinity 5-HT2C receptors. Interestingly, antagonism of 5-HT2C receptors is reported for various established antidepressant compounds. Therefore, one may assume that the agonistic activity at the melatonin receptors with blockade of 5-HT2C receptors probably contributes to the rapid onset and the efficacy of this novel compound at least in animal models for depression.

#### LS-03-03

Antidepressant efficacy of agomelatine: Clinical implications

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Agomelatine is a new antidepressant with a unique mechanism of action. It is the first melatonergic (MT1 and MT2 receptor) agonist antidepressant. Its antidepressant efficacy was demonstrated in a range of clinical trials. Due to its mechanism of action, agomelatine was proven to have special advantages in improving sleep and anxiety, without being sedative and affecting vigilance. In a multicenter, placebo-controlled, dose-ranging study over 8 weeks, agomelatine was shown to be an effective antidepressant at a dose of 25 mg once daily, by reducing the initial HAMD score to a similar extent to that of paroxetine (HAMD scale: 2.57 point difference between agomelatine and placebo;  $P < 0.05$ ). In 2 studies in an adult population aged 18 to 65, agomelatine 25 mg was