

the Dissociative Experiences Scale (Bernstein and Putnam, 1986) to 90 subjects (30 in each sample): depressive patients, alcoholic patients and normal controls. Three types of dissociative experiences were examined: amnesia, depersonalisations/desrealization and absorption. The highest levels were found in the depressive and alcoholic patients (scores - 28.41 and 27.11) compared with normal controls (score - 4.12). In the alcoholic sample there is a predominance of absorption experiences (35.22). On the other hand, in depressive patients depersonalization/desrealization is the main type of dissociative experiences. Data will be analyzed taking into account phenomenological aspects of affective pathology.

### P02.224

#### ANTIDEPRESSANT EVOKED ALTERATIONS OF TRANSMEMBRANE CELL SIGNALLING

H. Kovářů<sup>1</sup>\*, A. Fišerová<sup>2</sup>, F. Kovářů<sup>3</sup>, Z. Fišar<sup>1</sup>, V. Lisá<sup>4</sup>, I. Malbohan<sup>1</sup>. <sup>1</sup>Charles Univ., 1<sup>st</sup> Fac. Med.; <sup>2</sup>Inst. Microbiol., CAS; <sup>3</sup>Univ. Veter. Pharm. Sci.; <sup>4</sup>Inst. Physiol., CAS, Prague and Brno, Czech Rep.

This study examines suggestion, that signal transducing heterotrimeric GTP-binding (G) proteins may be involved in postreceptor effects of antidepressants (AD) as well as in pathophysiology of depressive disorders. We performed analyses in vitro using C6 glioma (astrocytoma) cell line as model of postsynaptic changes and human natural killer (NK) lymphocytes, effector cells of natural immunity. We studied levels of main subtypes of alpha subunits of G proteins - G $\alpha$ (s) and G $\alpha$ q/11, which were estimated by immunochemical techniques in cholate extracts of membranes (1, 2). Attention was focused on SSRI (selective serotonin reuptake inhibitor) sertraline and fluoxetine in comparison with mirtazapine, NaSSA (noradrenergic and specific serotonine AD). We demonstrated AD dependent changes in G $\alpha$  subunit profiles: sertraline affected decrease of G $\alpha$ (s) subunit with effector adenylyl cyclase, fluoxetine influenced decrease of G $\alpha$ q/11 with effector phospholipase C. Results are supported by levels 1, 4, 5 IP<sub>3</sub>, 2<sup>nd</sup> messenger released by phospholipase C. Mirtazapine affected both inhibition of G $\alpha$ (s) and elevation of G $\alpha$ q/11 subunit levels. If depressive disorders are associated with abnormal transduction mechanisms, then results can indicate postreceptor changes affected by individual ADs according their pharmacological action.

Supported by grants GA ČR 310/98/0347, GAUK 143/97C, Int. Scientif. Progr. CEZ: J 16/98: 161700001 FVL VFU Brno.

(1) Kovářů et al. Proc Royal Micr. Soc., 1997, Pt2: 123.

(2) Kovářů et al. Acta Vet. Brno, 1998, 67: 15-20.

### P02.225

#### WISCONSIN CARD SORTING TEST PERFORMANCE IN SUBCLINICAL OBSESSIVE-COMPULSIVE SUBJECTS: RELATION TO SYMPTOM DIMENSIONS

D. Mataix-Cols, M. Aleu, C. Junqué, M. Sánchez-Turet\*. *Department of Psychiatry and Clinical Psychobiology, University of Barcelona, Catalonia, Spain*

**Objective:** To investigate the relation of factor-analyzed symptom dimensions of Obsessive-Compulsive Disorder (OCD) to neuropsychological performance in a psychometrically-defined subclinical OC sample.

**Method:** Twenty-five subclinical OC subjects scoring higher than 1SD above the mean on the Spanish version of the Padua Inventory (PI), and 27 non-OC controls with PI scores around

the mean, were selected from an initial pool of 476 undergraduates. All subjects were administered a computerized version of the Wisconsin Card Sorting Test (WCST), the Raven's Advanced Progressive Matrices, and measures of psychological state (anxiety and depression).

**Results:** After controlling for anxiety and depression scores, the groups did not differ on any of the WCST indices. Multiple regression analyses showed that the "Washing" dimension of the PI had strong positive and significant partial correlations with WCST total errors ( $R^2 = 0.33$ ; Beta = 0.57;  $p = 0.002$ ), perseverative errors ( $R^2 = 0.25$ ; Beta = 0.50;  $p = 0.01$ ), and non perseverative errors ( $R^2 = 0.39$ ; Beta = 0.63;  $p = 0.0007$ ). This dimension was also negatively correlated with the number of categories completed ( $R^2 = 0.26$ ; Beta = -0.50;  $p = 0.009$ ). No significant correlations were observed within the control group.

**Discussion:** The composition of the samples studied (i.e. the presence of particular symptom subtypes of OCD) might in part explain the inconsistencies of the previous neuropsychological findings in OCD. These results need to be replicated in a clinical OCD sample.

### P02.226

#### PSYCHOTROPIC TREATMENT AND WEIGHT GAIN

S. Stella\*, A. Ravera, F. De Santis, C. Persichella, N. Gosio, C. Rizzoli. *Mental Health Department, Azienda U.S.L. Bologna, V. dello Scalo, 23, Bologna, Italy*

From clinical psychiatric experience emerges that the use of psychotropic medication is often associated with weight gain. While an undesired weight increase is a documented side effect of psychotropic drug use, the possible mechanisms for this effect are poorly understood. Certainly this effect has important implications in the patient management. The weight gain compromises medication compliance. This would increase the likelihood of relapse, the cost of the treatment compared with the benefits and would negatively affect the relationship with the patient and result with a retirement in the self. One the aspects directly to the above mentioned is a decrease of self esteem and an emotional flatterer. Therefore any kind of pharmacological therapy resumption is deeply compromised. Our clinical experience too has highlighted all these aspects and has motivated us to make a review on this argument. First of all we reviewed the physio-chemical mechanisms which regulate the feelings of hunger and repletion. Therefore the analysis of the use of the new molecules has highlighted the responsibility scales for weight gain due to the various psychotropic drugs according to the categories. Afterwards we analysed the strategies to prevent or minimize this problem. At last we have reported our experience carried out in a Mental Health Department with an associated Territorial Day Hospital.

### P02.227

#### COMPARISON OF THE CORONARY HEART DISEASE RISK FACTOR PROFILE OF RISPERIDONE VS OLANZAPINE TREATED PATIENTS

R.H. Bouchard\*, J. Villeneuve, N. Alméras<sup>1</sup>, I. Simoneau, M.F. Demers, C. Cadrin, M.A. Roy, J.P. Mottard, J.P. Després<sup>1</sup>. *Polyclinique Sainte-Anne, Québec; <sup>1</sup>Centre de Recherche sur les Maladies Lipidiques, Québec, Canada*

**Background:** Weight gain is commonly observed among atypical neuroleptics treated patients and may represent a health hazard if associated with metabolic alterations predictive of an increase risk

of coronary heart disease (CHD). Whether atypical neuroleptics differ regarding their impact on the CHD risk profile is not known.

**Study Design:** We conducted a cross-sectional, multicenter study to compare morphological indices of obesity, adipose tissue distribution and a full fasting metabolic risk profile in patients receiving either risperidone (RP) or olanzapine (OLZ). Inclusion criteria included drug exposition for 6 to 42 months. Exclusion criteria, among others, were previous exposition to atypicals, treatment with drugs altering blood pressure, plasma lipids, insulin and body weight. Anthropometric measurements, laboratory and psychiatric assessments were completed.

**Results:** Preliminary results on 44/120 subjects were analysed. Mean duration of treatment was  $17.4 \pm 8.8$  months for RP and  $17.9 \pm 8.1$  months for OLZ ( $p = \text{NS}$ ). OLZ-treated subjects had significantly higher plasma triglyceride level ( $2.1 \pm 1.3$  for OLZ vs  $1.3 \pm 0.7$  for RP,  $p < 0.01$ ), higher cholesterol/HDL-cholesterol ratio ( $5.3 \pm 1.7$  for OLZ vs  $4.3 \pm 1.4$  for RP,  $p < 0.06$ ) and lower HDL-cholesterol level ( $0.95 \pm 0.2$  for OLZ vs  $1.06 \pm 0.2$  for RP,  $p < 0.08$ ). Finally, 32% of OLZ-treated patients presented the atherogenic metabolic triad (hyperinsulinemia, elevated apo-B, small dense LDL) as opposed to 5% in RP-treated patients.

**Conclusion:** This interim analysis suggests that OLZ-treated patients are characterized by a deteriorated metabolic risk profile compared to RP-treated patients. These results raise concerns about the potentially deleterious effects of OLZ therapy on cardiovascular health.

## P02.228

### SEXUAL DYSFUNCTION BURDEN IN A 24-WEEK STUDY OF SSRIS IN DEPRESSED PATIENTS

L. Ekselius\*, H. Agren, A. Aberg-Wistedt. *Neuroscience, Psychiatry Department, University Hospital, Uppsala, Sweden*

**Background:** Secondary pharmacological characteristics among SSRIs may result in differing potential to induce/alleviate sexual dysfunction.

**Objective:** Examine adverse sexual experiences systematically recorded during a 24-week, prospective, randomized study comparing sertraline and paroxetine (mean daily doses completers 83.0 mg, 27.8 mg, respectively) in the treatment of depressed outpatients.

**Methods:** UKU symptom checklist recorded and quantitated adverse sexual effects experienced by patients receiving sertraline ( $n = 176$ ) or paroxetine ( $n = 177$ ). The interviewer rated UKU assesses increased sexual desire, decreased sexual desire, orgasm dysfunction, ejaculatory dysfunction, and erectile dysfunction: 0 = absent, 1 = mild, 2 = moderate, 3 = severe). The burden score is sum of 5 items for males and sum of 3 applicable items multiplied by 5/3 for females.

**Results:** Mean baseline burden scores for sertraline and paroxetine groups, respectively, were 2.2 and 2.2 ( $p = 0.969$ ). Scores in sertraline and paroxetine groups, respectively, changed by 0.0 and +0.5 at week 6 ( $p = 0.105$ ), -0.4 and +0.2 at week 12 ( $p = 0.035$ ), -0.8 and -0.2 at week 24 ( $p = 0.120$ ), and -0.6 and -0.1 at study endpoint ( $p = 0.050$ ). Analysis by gender revealed a statistically significant difference between treatments amongst female, but not among male, patients.

**Conclusions:** The potential to induce or alleviate sexual dysfunction in depressed patients may differ significantly between sertraline and paroxetine.

## P02.229

### A PLACEBO-CONTROLLED STUDY OF SERTRALINE IN GENERALIZED SOCIAL PHOBIA

M. Van Ameringen\*, R. Swinson, J.R. Walker, R.M. Lane. *McMasters University Medical Center, Hamilton, Ontario, Canada*

**Objective:** To evaluate the efficacy, safety, and tolerability of sertraline, a selective serotonin reuptake inhibitor, in the treatment of generalized social phobia.

**Method:** Following a 1-week, single-blind, placebo run-in, 206 adult outpatients with generalized social phobia from 10 Canadian centers were randomized to 20 weeks of double-blind treatment with sertraline or placebo in a 2:1 ratio. The initial daily dosage of sertraline was 50 mg with increases of 50 mg/day every 3 weeks permitted after the fourth week of treatment (flexible dosing to a maximum of 200 mg/day). Primary efficacy assessments were the percentage of patients much or very much improved on the Clinical Global Impression of Improvement (CGI-I) scale, and the mean total score baseline to endpoint change on the social phobia subscale of the Marks Fear Questionnaire and the Duke Brief Social Phobia Scale (BSPS).

**Preliminary Results:** 71 (53%) of 134 persons receiving sertraline and 20 (29%) of 69 persons receiving placebo were CGI-I responders at the end of treatment ( $p < 0.001$ ). Mean Marks Fear Questionnaire social phobia subscale and BSPS total score were reduced by 32.5% and 34.8% in the sertraline group and 8.6% and 16.7% in the placebo group ( $p < 0.005$ ), respectively. Sertraline-treated patients also evidenced significant improvements relative to patients receiving placebo on all secondary efficacy parameters and on social/leisure functioning and mental health dimensions of quality of life assessments ( $p < 0.05$ ). Overall, sertraline was well tolerated.

**Conclusions:** This study demonstrated sertraline to be an effective treatment for generalized social phobia. Future research should assess whether improvements may be maintained or further improved by either continued treatment or by augmentation with specific cognitive-behavioral techniques.

## P02.230

### SERTRALINE VERSUS IMIPRAMINE IN NON-MELANCHOLIC DEPRESSION

E. Baca\*, M. Gonzalez de Chavez, M. Garcia-Toro, F. Perez-Arnau, A. Rivera, B. Penasa, S. Olivares, J. Espejo, A. Porras, R. Lane. *Clinica Puerta de Hierro, Dept. of Psychiatry, Madrid, Spain*

**Objective:** To compare the acute treatment efficacy, tolerability, and effects on health related quality of life of sertraline (50–200 mg/day) and imipramine (75–225 mg/day) in outpatients with non-melancholic depression.

**Method:** In an open, parallel-group design, 116 patients were randomized to receive sertraline and 123 to imipramine for 8-weeks. The initial daily dose was sertraline 50 mg/day or imipramine 75 mg/day with increases in increments of 50 mg/day allowed at 2-week intervals.

**Results:** There were statistically significantly greater improvements in favour of sertraline on depressive and anxiety symptom reduction, response and remission on all scales from week 4 onwards (ITT, LOCF). In the sertraline and imipramine groups, respectively, baseline HAM-D<sub>21</sub> scores of 24.9 and 24.4 were reduced to 10.3 and 13.4 ( $p = 0.011$ ). Proportions of sertraline and imipramine patients with reduction of HAM-D<sub>21</sub> score  $\geq 50\%$ , and HAM-D<sub>21</sub>  $\leq 8$  were 69% versus 54% ( $p = 0.016$ ), and 51% versus 38% ( $p = 0.041$ ), respectively. In sertraline and imipramine groups, respectively, baseline HAMA scores of 21.8 and 21.9 were reduced