

were much less than those of the control drug, amitriptyline, at a dose of 75 mg. In three of the ten studies there was evidence that paroxetine could cause slight psychomotor enhancement indicated, for example, by increased threshold on critical flicker fusion test.

In summary; No adverse effects of paroxetine are apparent at the dose of 20 mg./day, although minor impairments can be identified at 40 mg./day. An overview of the data indicates that at the standard therapeutic dose of 20 mg./day, paroxetine has no psychomotor or behavioural toxicity.

## SOCIAL FACTORS IN SUICIDE

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**Background:** The study objective was to investigate the age-related variation of social factors in suicide.

**Method:** Age-related variation in marital status, living arrangements, activity in working life and social interaction factors were investigated in an entire 12-month suicide population in Finland ( $N = 1.067$ ); the findings in suicide were compared with appropriate census data.

**Results:** Several social factors varied across age groups among suicides, with some age-related sex differences. Compared with the general population, the suicides were more commonly never married (especially males aged 30–39 years), divorced, and widowed (especially females aged 60–69 years); living alone was more frequent among the suicides, as was living with parents among male suicides aged 25–39 years. A history of psychiatric hospitalization was especially common among young male suicides who had never married or were living with parents. Living alone was particularly frequent among middle-aged male suicides who had misused alcohol.

**Conclusions:** While most of the age-related variation in social factors found in suicide seems to parallel the natural variation of these factors in the general population, the results suggest that some social findings in suicide might be related to the victims' psychopathology and excessive alcohol use.

## TREATMENT OF MODERATELY OR SEVERELY DEPRESSED PATIENTS WITH NEW ANTIDEPRESSANT MIRTAZAPINE

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Antidepressant treatment is recommended as the first-line therapy for moderately or severely depressed patients. Mirtazapine is a potent antagonist of  $\alpha_2$  adrenoceptors, 5-HT<sub>2</sub> and 5-HT<sub>3</sub> serotonin receptors, while it does not block 5-HT<sub>1A</sub> receptors. Its antagonism of pre-synaptic  $\alpha_2$  adrenoceptors is the mechanism whereby mirtazapine enhances the release of noradrenaline. The enhanced release of noradrenaline causes stimulation of 5-HT cell firing and 5-HT release through activation of  $\alpha_1$  adrenoceptors on serotonergic soma and/or dendrites. Hence mirtazapine enhances both noradrenergic and serotonergic neurotransmission, and it can be best described as noradrenergic and specific serotonergic antidepressant (NaSSA). This mode of action may be accounted for its high efficacy in the treatment of depressed patients, including severely depressed (17-item HAMD scores at baseline  $\geq 25$ ). To assess the efficacy of mirtazapine in the treatment of patients with a DSM III diagnosis of a Major Depressive Episode (single or recurrent), an analysis was performed on pooled data from subgroups of moderately or severely depressed patients participating either in the placebo-

amitriptyline-controlled studies of mirtazapine. The patients were stratified according to their total 17-item HAMD scores at baseline: scores of 18–24 were indicative of moderate depression; at least 25 of severe depression. In the subgroup present with moderate depression, significantly larger reduction from baseline were present in the mirtazapine group compared to placebo group ( $p \leq 0.01$ ). Matching results were obtained in the analysis of the severely depressed patients: reductions from baseline during treatment with mirtazapine were statistically and clinically significantly larger than with placebo ( $p \leq 0.01$ ). In pooled data analysis comparing mirtazapine with amitriptyline, equivalent reductions from baseline were found both for the moderately depressed group and severely depressed group of patients. These results demonstrate that mirtazapine is effective in the treatment of both moderately and severely depressed patients.

## NEUROENDOCRINOLOGICAL REACTION TO THE TRYPTOPHAN-DEPLETION-TEST IN PATIENTS WITH SEASONAL AFFECTIVE DISORDER WHO RESPONDED TO LIGHT THERAPY

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Some studies describe hormonal dysregulations during episodes of depression, which disappear with remission. Further investigations were able to describe a reduction of brain serotonin activity. Tryptophan-Depletion (TD) induced by ingestion of a tryptophan-free amino acid drink lowers serotonergic function and has been shown to induce symptoms of depression. Therefore we studied hormonal and psychometric reactions to TD in a double-blind placebo-controlled balanced cross-over design in 12 drug-free patients with seasonal affective disorder (SAD). Patients were in stable remission induced by light therapy. Blood samples were obtained one day and 30 minutes before as well as 5 and 7 hours after TD. After TD we found a significant increase in Hamilton Score ( $p < 0.01$ ) and a significant decrease of total ( $p < 0.001$ ) and free tryptophan ( $p < 0.001$ ). During TD and placebo mean plasma concentration of prolactin raised statistically non-significant, while TD was tended to be combined with higher concentrations. Cortisol plasma concentration fell statistically significant during TD (8 a.m.:2 pm  $p < 0.05$ ; 8 a.m.:4 p.m.  $p < 0.05$ ) and tryptophan administration TD (8 a.m.:2 pm  $p < 0.005$ ; 8 a.m.:4 p.m.  $p < 0.005$ ). Concentrations were statistically higher in TD compared to placebo (2 p.m.  $p < 0.05$ ; 4 p.m.  $p < 0.001$ ). Changes of TSH, T3 and T4 were of no clear relation with regard to TD or control testing. Conclusively our results indicate that TD might influence neurohormonal systems as well as the serotonergic system. Moreover during TD we were able to describe a coincidence of depressive symptoms, a decrease in plasma cortisol level and a raise in prolactin concentration.

## PROLACTIN SECRETION IN DEPRESSIVE ILLNESS AND HEALTHY CONTROLS AS A RESPONSE TO THE CITALOPRAM-CHALLENGE-TEST (CCT)

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The Citalopram-Challenge-Test (CCT) is one approach to investigate the reactivity of the serotonergic neurotransmitter system, which is thought to be downregulated in depression. Citalopram, a substance inhibiting serotonin reuptake, leads to an immediate secretion of prolactin in normals. Our study is designed to describe differences in prolactin and cortisol to the CCT. 12 patients, meeting criteria vor

major depression according to DSM VI, and 12 healthy controls were enrolled in this investigation. CCT was performed in a double-blind design with all subjects receiving a dosage of 10 mg, 20 mg citalopram and placebo. At 08.00 a.m. Citalopram in 100 ml NaCl or mere NaCl were infused over 15 minutes. Blood samples (-1 up to +6) for hormonal measurements were drawn from 7.30 a.m. until 10.00 in intervals of 15 minutes and samples -2 to 0 were used for baseline estimation. Hormone secretion was estimate by calculating the area under the curve. Side effects were rare and more often in controls. Predominant were nausea, and feelings of inner restlessness. CCT was interrupted in two cases because of mild akathisia. 90 minutes after citalopram infusion we detected a secretion peak in normals. In healthy subjects (mean AUC: 1637 ng/ml\*90 min) compared to patients (mean AUC: 408 ng/ml\*90 min) the total secretion of prolactin in depressive illness was blunted. Hormonal section after stimulation with 10 mg citalopram did not differ from hormonal secretion after application of placebo. Although our results show differences of the serotonergic reactivity in patients and healthy subjects it remains to clarify if other neurohormonal systems are attached, too, which also might influence the changes in prolactin secretion we found. Besides these points of interest this study indicates that a stimulation with 20 mg citalopram might be useful to describe a disturbance of serotonergic neurotransmitter system in depression.

#### Therapiestandards in der Depressionsbehandlung in Österreich — Eine Umfrage

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In einer pharmakoepidemiologischen Untersuchung zur Behandlung der Depression in Österreich wurde an 455 Psychiater und Neurologen ein 17 Punkte umfassender Fragebogen versandt. Dieser richtete sein Augenmerk auf die bevorzugten Behandlungsstrategien bei akuten depressiven Episoden sowie die Behandlungsgewohnheiten in der Phasenprophylaxe. Drei Fragen erfassten die berufliche Situation der Befragten.

Nach zweimaliger Aussendung konnten 266 Fragebögen (57.8%) ausgewertet werden. Etwa die Hälfte (47.5%) der Befragten kombinieren in der Akutbehandlung der Depression Psychotherapie und Psychopharmaka. Als orale Medikation wurden Citalopram (34.2%) und Amitriptyline (26.7%) am häufigsten genannt. Die mittlere Tagesdosis für Citalopram wurde mit 27 mg, die für Amitriptylin mit 106 mg angegeben. Die mittlere Behandlungsdauer für eine depressive Episode errechnete sich mit 24.7 Tagen.

In der Phasenprophylaxe werden Lithiumpräparate am häufigsten, gefolgt von Antidepressiva und Carbamazepin verwendet. Die Frage nach der Dauer einer prophylaktischen Medikation ergab einen Mittelwert von 211.9 Tagen.

Bei den erhobenen Ergebnissen fallen breite Streuungen bei nahezu allen Fragen ins Auge, insgesamt wird wohl in zu niedriger Dosierung und sowohl im akuten wie auch im prophylaktischen Bereich zu kurz behandelt. Die Erarbeitung von Therapiestandards in der Behandlung der Depression sowie deren Verbreitung stellt eine wichtige Aufgabe dar.

#### Factors associated with multiple admissions to a public psychiatric hospital

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Early identification of the types of psychiatric patients who are likely

to be readmitted is necessary to allow for planning and implementing a program in ambulatory care to prevent rehospitalizations.

The authors attempted to identify the psychiatric and social factors associated with multiple admissions, especially for psychotic patients.

Demographic and diagnostic information (based on the DSM-III-R) were collected in a computerized case register for all patients admitted in the only psychiatric hospital of Geneva. Patients with at least three admissions within a time span of one year were compared to a control group of the total clinic population.

In the year 1994, 1579 patients were hospitalized, 284 patients (18%) were readmitted for the third time or more. The principal diagnoses were psychosis (26%), affective disorders (27%) and substance abuse (20%). The psychotic patients were significantly more readmitted than other patients (26% vs 15%).

The factors associated with multiple admissions for psychotic patients were a diagnosis of schizophrenia, a longer length of illness, the female gender, a younger age, a secondary diagnosis on axis 1 and a worst psychosocial adjustment during the past year. These results emphasize the usefulness of a computerized psychiatric case register even if some improvements could allow more comprehensive clinical studies.

#### A Double-blind comparison of the efficacy and safety of paroxetine and imipramine in the treatment of depression with dementia

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**Aim:** To compare the efficacy of paroxetine and imipramine in the treatment of depression associated with dementia.

**Methods:** 198 patients (mean age 76.6 yr) with dementia and significant depressive symptoms were randomised, double-blind, to receive paroxetine (20–40 mg/day) or imipramine (50–100 mg/day) for 8 weeks. Primary efficacy criteria were the change from baseline to endpoint in Montgomery-Asberg Depression Rating Scale (MADRS) total score and in Clinical Global Impression (CGI) severity of illness total score. Secondary efficacy variables were Carer global rating and CGI global improvement score together with the CGI severity of illness, Cornell scale for depression in dementia, Folstein mini-mental state evaluation and Gottfries, Bräne, Steen Scale for dementia.

**Results:** No significant differences were observed between the paroxetine and imipramine groups in terms of either mean change from baseline in MADRS score (-12.6 and -11.8, respectively,  $p = 0.662$ ) or CGI severity of illness score (-1.3 and -1.3, respectively,  $p = 0.996$ ), at endpoint. No statistically significant differences between any secondary efficacy variables were observed, with the exception of the Cornell Rating Scale, where a significant difference in change from baseline score was observed at weeks 4 and 8 in favour of paroxetine ( $p = 0.047$  and  $p = 0.049$ , respectively). The most frequently reported adverse events were trauma (10.1%) and somnolence (8.1%) in paroxetine-treated patients and trauma (11.1%) and dry mouth (10.1%) in imipramine-treated patients. Paroxetine and imipramine showed similar efficacy, with little evidence of difference between them in the treatment of patients with depression associated with dementia.