items. Comparative scores and profiles on the other psychopathological measures e.g. Scl-90-R, GHQ-30 and PSE (10, item) supported validation. Some items were more sensitive to change over time.

Conclusion: Practical and comparative ratings encompassing grief, and with numerical scoring for use in any circumstances (and to monitor change) can aid comparative studies of bereavement.

MELATONIN SECRETION IN SEASONAL AFFECTIVE DISORDER

T. Partonen, J. Lönnqvist. *Department of Mental Health, National Public Health Institute, Mannerheimintie 160, FIN-00300 Helsinki, Finland*

Background. Seasonal affective disorder (SAD) has been related to abnormal melatonin metabolism and treated with exposure to artificial light for 3–6 hours a day. Our objectives were to test the following hypotheses on SAD patients: there would be, first, phase and amplitude abnormalities in the circadian rhythm of melatonin secretion; second, abnormalities in the onset and offset timing of melatonin secretion; and third, abnormal suppression of melatonin levels by light.

Method. The diagnosis was assessed with the Diagnostic and Statistical Manual of Mental Disorders (III-R/IV). All patients suffered from winter SAD and were drug-free. Samples of saliva were collected from 12 patients every other hour for 24 hours, waking the patient at night, from 16 patients and 13 healthy controls every hour between 20.00 and 24.00 hours as well as 06.00 and 08.00 hours, and from 11 patients and 10 healthy controls at 22.00 and 23.00 hours respectively. On light tests, the subjects were exposed to fluorescent light of 3300 lux at 22.00 hours for 5 minutes and 1 hour respectively during two consecutive evenings. We expected that only the latter would lead to the suppression. The subjects were treated with equal light for 1 hour for 5 mornings, for 1 hour for 14 mornings, and for 1/2 hour for 14 evenings respectively in winter. The second and third protocols were repeated in summer, without exposing the subjects to light.

The samples of saliva were collected in a dark room, thereafter immediately frozen until analysed for melatonin by radioimmunoassay. The best fitting cosinor function was adjusted to the circadian data by using the least squares method. The subjects rated their level of subjective sleepiness with the Stanford Sleepiness Scale and with the Visual Analogue Scale simultaneously with the collection of the samples in each experiment.

Results. There was no significant difference in the mean levels of melatonin or the suppression of melatonin levels in saliva by light between the patients and controls. The treatment with morning light as well as the first light test reduced significantly more the evening level of subjective sleepiness in the patients than in the controls. This reduction correlated with the clinical improvement in the former experiment but was not associated with the change in melatonin secretion in either experiment. In spite of the good antidepressive response observed among the patients, bright light treatment did not result in any significant change in the phase or the amplitude of the circadian rhythm of melatonin secretion, the mean or peak evening and morning melatonin concentrations, or the degree of suppression of melatonin levels by light.

Conclusions. We suggest against the melatonin hypothesis that the antidepressive effect of bright light treatment is not explained by abnormal melatonin secretion or excessive sensitivity to light among SAD patients. The effect of light on mechanisms regulating the level of sleepiness deserves further study. In addition, the duration of exposure to light required daily for effective treatment is shorter than claimed in the literature.

NR16. Psychopharmacology of affective disorders

Chairmen: C Thompson, K Abel

A COMPARISON OF PAROXETINE AND IMIPRAMINE IN SIX MONTHS CONTINUATION THERAPY POST ECT

P. Bech, L. Lauritzen, K. Odgaard, L. Clemmensen, M. Lund, J. Ohrström, C. Black. *Frederiksborg General Hospital, Department of Psychiatry, DK-3400 Hillerød, Denmark*

The results to be presented are part of a comprehensive study [1] including psychopathological structure analysis and placebo treatment of the subgroup of patients with electrocardiological impairments in whom imipramine was contraindicated.

In total 27 patients were randomized to paroxetine in a dose of 30 mg daily and 25 patients to imipramine in a dose of 150 mg daily. No difference between the two groups of patients was found concerning age (mean: 60 years), sex, co-morbid medical disorders (about 30%), number of ECT treatments (mean 11) or duration of convulsions (mean 46 seconds).

In the post ECT or 6 months continuation phase, paroxetine was significantly more effective than imipramine. Thus, 12% of the patients relapsed in the paroxetine treated group and 30% relapsed in the imipramine treated group ($P < 0.05$). In comparison 65% of the patients relapsed in the placebo treated group. It should be emphasized that the mean dose of imipramine in the continuation phase was 140 mg daily leading to plasma concentrations of 448 nmol/l of imipramine and desipramine.

It was not possible clinically to increase the imipramine dose due to intolerable side-effects. However, no difference in plasma levels was obtained between patients who relapsed and patients not relapsing, either in the imipramine nor in the paroxetine treated groups.

In conclusion, paroxetine was found superior to imipramine in relapse prevention after ECT therapy of major depression.

[1] Lauritzen L et al, Acta Psychiatr Scand 1996 (in press).

PHARMACOLOGICAL EVIDENCE THAT DEPRESSIVE SYMPTOMS DO NOT SHARE A COMMON SEROTONERGIC MECHANISM ACROSS DIAGNOSES

A.J. Cleare, K.M. Abel, V. O'Keane. *Department of Psychological Medicine, Institute of Psychiatry, London*

It has recently been suggested by Van Praag (1990) that there may be psychopathological dimensions, such as depressive symptomatology, which share common biological correlates independent of psychiatric diagnosis. We investigated this possibility in patients with major depression (n = 19), schizophrenia (n = 13) and depression secondary to hypothyroidism (n = 10). Subjects underwent assessment with the 17-item Hamilton Rating Scale for Depression and the Montgomery-Asberg Depression Rating Scale in order to obtain a dimensional measure of depressive symptoms. Central serotonergic function was assessed using the prolactin and cortisol (CORT) responses to d-fenfluramine, a specific serotonin (5-HT) releasing agent. Healthy, non-depressed matched control subjects were included in the analyses to correct for age, sex, weight and menstrual cycle phase. Depressive symptoms in major depression ($r = -0.53$, $P = 0.01$) and hypothyroidism ($r = -0.73$, $P = 0.003$) were inversely related to CORT responses. In contrast, depressive symptoms in schizophrenia were positively related to CORT responses ($r = 0.62$, $P = 0.03$).

https://doi.org/10.1016/0924-9338(96)88891-2 Published online by Cambridge University Press

There was no overall relationship between depressive symptomatology and serotonergic function across diagnoses. We conclude that a) depressive symptoms in major depression and organic depression are associated with reduced central 5-HT function, while those in schizophrenia are associated with increased 5-HT function; and b) depression may not have a common serotonergic neurobiological origin across diagnosis.

[1] Van Praag HM, Kahn RS, Asnis GM, et al (1987). Denosologization of biological psychiatry or the specificity of 5-HT disturbances in psychiatric disorders. J Affect Disord.; 13: 1–8.

LITHIUM AND SEROTONIN REUPTAKE INHIBITORS; THERAPEUTIC OR TOXIC?

C. Hawley, S. Quick, B. Starr, S. McPhee, T. Sivakumaran. *Hertfordshire Neuroscience Research Group, University of Hertfordshire, Hertfordshire, AL10 9AB, England*

The aim of this presentation is to review all available data on the safety, tolerability and effectiveness of lithium in combination with serotonin specific reuptake inhibitors in the treatment of Major Depression.

All published reports, including case reports, uncontrolled series and controlled studies, regarding coadministration of lithium and SSRIs were identified for the purpose of the review. Reports made to CSM and to pharmaceutical manufacturers were also considered.

The data were not suitable for meta analysis. Although case reports suggest that toxicity may occur the data from systematic studies, although largely open and uncontrolled, indicate a benign adverse event profile with little risk of serious events. Based upon 90 evaluable cases, the most frequent adverse events appear to be tremor, nausea or vomiting and somnolence. Evidence for efficacy of the lithium add-on strategy rests upon one small placebo controlled study (n = 15). Data from the uncontrolled studies is not incompatible with this but must be interpreted cautiously.

The interpretation of the currently available data is, on balance, that i) lithium add on to SSRIs is an efficacious strategy for the treatment of refractory Major Depression, ii) the combination is associated with an increase in the number of adverse events but these are seldom severe or serious, iii) serious toxicity is an uncommon occurrence. There is sufficient data to justify a large placebo controlled study to evaluate efficacy and tolerability.

'SEROTONERGIC AUTORECEPTOR BLOCKADE IN THE REDUCTION OF ANTIDEPRESSANT LATENCY: A CONTROLLED TRIAL'

María B. Tomé, Rosarii Harte, Michael T. Isaac. *Lewisham and Guy's Mental Health NHS Trust, London, UK; Department of Psychological Medicine, UMDS (Guy's Campus), London, UK*

Objective: To study augmentation of the antidepressant paroxetine with pindolol, a $5HT_{1A}$ autoreceptor blocker. Open studies suggest that, for SSRI antidepressants, the two-to three-week latency of antidepressant effect may be reduced if pindolol is taken simultaneously.

Method: Double blind, randomised, placebo controlled trial. All patients (n = 80; mean age 36 [range 19–65]; asthma, diabetes, cardio-pulmonary disease *excluded*) met criteria for major depression and received paroxetine (20 mg *o.d.*) plus, randomly, either pindolol (2.5 mg *t.d.s.*) or placebo. Assessment: days 4, 7, 10, 14, 21, 28, 42, using clinical measures, the Montgomery-Åsberg Depression Rating Scale [MADRS] and the Beck Depression Inventory. Patients are followed up for six months, allowing assessment of long term safety, tolerability and optimal dosage regimes, and subsequent service usage.

Results: Compared with day 0, 20% of *all subjects* showed a fall in MADRS score > 50% by day 4. By day 7, 30%, and on day 10, 40% of the patients scored > 50%, rising to 48% at day 14. On days 21, 28 and 42, 52%, 56% and 70% of patients registered a fall in MADRS score > 50%. Other measures showed comparable changes.

Conclusions: The markedly reduced latency of antidepressant effects has considerable implications for the future management of depression, and may have an impact on admission for and suicide rates. Larger multi-centre trials are warranted if the breaking of the blind has shown that these results are due to pindolol augmentation of paroxetine.

PROSPECTIVE STUDY OF THE EFFECTS OF INTERRUPTING ANTIDEPRESSANTS

I. Mourad, M. Lejoyeux, J. Adès. *Department of Psychiatry, Hopital Louis Mourier, 92700 Colombes, France; Department of Psychiatry, Hopital Bichat-Claude Bernard, 75877 Paris Cédex 18, France*

Antidepressant withdrawal symptoms, following discontinuation of antidepressants, include general somatic distress (flu-like syndromes, gastro-intestinal disturbances,), anxiety, sleep disturbances, movement disorder and manic reactions. Since most of the data come from case reports and retrospective study, it appeared to us of interest to assess, in a prospective manner, the effects of the withdrawal from tricyclic antidepressants and selective serotonin reuptake inhibitiors (SSRIs) in 16 patients answering to DSM-III-R criteria of major depressive episode.

All patients were hospitalized and a change of antidepressant treatment had been decided. Patients were assessed twice, just before the drug interruption and three days later. Clinical instruments were MADRS, Hamilton Anxiety Rating Scale, and the Scale for evaluation of benzodiazepine withdrawal symptoms which had been modified for the purpose of this study. We added two questions about gastro-intestinal symptoms often present in the case reports of antidepressant withdrawal.

87.5% of the patients presented symptoms following the withdrawal. Most frequent signs were anxiety (31%), irritability and jitteriness (25%), sleep disorders (19%), pain and contractions (20%), arousal and decrease in anergia (19%). Our results do not permit to establish a comparison between the rates of withdrawal syndrome induced by SSRIs and tricyclic antidepressants. They confirm the high frequency of withdrawal manifestations when antidepressant therapy is interrupted. Our results also stress the importance of the prevention of the withdrawal syndrome by a slow tapering of antidepressant dosage.

EVALUATION OF STRATEGIES IN THERAPY-RESISTANT DEPRESSION

G. Lenz, U. Bailer, M. Serim. *Allgemeines Krankenhaus, Department of Psychiatry, University of Vienna, Währinger Gürtel 18–20, A-1090 Vienna, Austria*

An evaluation of the first 73 patients who had attended our outpatient-clinic for therapy resistant depression revealed that only 41% (N = 30) fulfilled criteria for therapy resistant depression. 27 of these patients were followed up 3 months later and efficacy of therapy strategies were evaluated with HAMD and CGI.

6 patients were considered to be full responder (HAMD $\leq$ 6), 8 partial responder and 13 non responder.

There was no statistical significant difference between non responder and responder/partial responder before start of treatment strategies in age, sex, diagnosis, comorbidity on axis 1 or 2 (DSM-