start of adequate drug treatment is a predictor of the persistence of symptoms in major depression. The aim of this study is to examine the 'no-treatment interval' variable in a group of patients undergoing first admission to two Dublin Psychiatric Hospitals, using time to remission as a measure of outcome.

Consecutive admissions to two Dublin Psychiatric Hospitals were screened. Those patients meeting International Classification of Diseases-9 (I.C.D.-9) criteria for major depression undergoing their first psychiatric admission were entered in the study. Patients with organic brain disease or those unable to give consent were excluded from the study. A cohort of 100 patients was established. Details of the index episode were obtained using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN). The 'no-treatment interval' was defined as the duration between onset of the episode and the commencement of 75 mg per day of tricyclic antidepressant or equivalent. The 17 item Hamilton Rating Scale for Depression (H.D.R.S.-17) was preformed on admission, fortnightly during the admission, and three and nine months post discharge. Remission was defined as H.D.R.S.-17 < 8 for at least 2 weeks.

21 of 100 patients were excluded because of inability to date onset of episode or onset of adequate treatment, or failure to complete the study. The excluded group did not differ significantly on clinical or sociodemographic variables from the final group of 79. This final group consisted of 45 (57%) women, 34 (43%) men. The age range was 18–77, mean 41.4 (s.d 14.4) years. The 'no-treatment interval' range was 2 days to 25 months, mean 14.7 (s.d 16.5) weeks. X^2 (Chi-square) distribution showed a significant relationship between 'no-treatment interval' and time to remission ($X^2 = 5.29$. $X^2a = 3.84$, $a = 0.25$). There was no significant relationship between age, sex and social class and time to remission.

The findings of this study support the proposal that the duration of the 'no-treatment interval' is a predictor of the outcome of major depression. This underlines the importance of early and adequate treatment of depression in primary care.

β-ENDORPHIN AND IMMUNODYSFUNCTION IN DEPRESSION AND ANXIETY DISORDERS

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Objectives: To assess cell-mediated immunity in depression and anxiety disorders and to elucidate whether immunodysfunction might be related to a high opioid activity.

Methods: In a prospective study of patients with major depression (n = 34) or anxiety disorders (n = 21), cellular immunity tests, the *in vitro* effects of naloxone on monocytes, and the plasma levels of β-endorphin were investigated. Peripheral blood mononuclear cells and some monocyte parameters were determined by flow cytometry. Natural killer (NK) cell activity was studied by cytotoxicity using the K-562 cell line, γ-interferon production by a standard bioassay, monocytic phagocytosis by ingestion of *Candida Albicans* and latex, and blastogenesis by stimulation with phytohaemaglutinin.

Results: In most patients from both groups it was observed: 1) a dysfunction of monocytes, characterized by a marked reduction in the number of these cells that ingest particles and express cytoskeletal intermediate filaments and surface structures (CR1 receptors and HLA-DR antigens); 2) a monocytosis that was not able to normalize the count of normally functioning monocytes; 3) *in vitro* correction of the monocyte alterations with naloxone; 4) normal concentrations of T lymphocytes and CD4 and CD8 populations; 5) decrease in NK cell number and activity; 6) normal synthesis of γ-interferon; and 7) energy to candidin and tuberculin and a diminished lectin-induced blastogenesis. Some of these immune changes correlated closely with plasma levels of β-endorphin, which were abnormally high in all the cases.

Conclusion: A naloxone-reversible monocyte dysfunction, associated to alterations both in NK count and function and in cell-mediated hypersensitivity, was related to high circulating concentrations of β-endorphin.

IN VIVO BRAIN PET RESPONSES AND NEUROENDOCRINE ALTERATIONS FOLLOWING SEROTONIN RELEASE IN DEPRESSED PATIENTS VERSUS HEALTHY CONTROLS

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The indoleamine hypothesis of depression proposes that major depression is due to a deficiency of available serotonin or subsensitivity of key serotonin receptors in relevant brain regions. We and others have reported results from the serotonin-releasing fenfluramine challenge test which demonstrate a blunted serotonin-mediated prolactin (PRL) response to d-I fenfluramine (FEN) in depressed patients compared with normal controls. The limitations of such results are that these studies only assess hypothalmic neural pathways and do not inform us about where in the brain such serotonin changes occur.

We have recently described a methodology for visualizing *in vivo* regional brain responses to serotonin release with positron emission tomography (PET) by comparing regional brain glucose metabolism after administration of FEN, relative to placebo. We now report on differences between the neuroendocrine responses to FEN and regional brain metabolic responses (rCMRglu) following FEN in 11 patients with an untreated major depressive episode versus 6 healthy controls.

The PRL response to FEN did not distinguish between groups. However, several statistically highly significant prefrontal cortical areas of increase in rCMRglu were seen in healthy controls, whereas no significant increases or decreases in regional glucose metabolism were seen in patients. No overlap was seen in degree of response in patients compared to controls.

These results provide direct *in vivo* support for the indoleamine hypothesis of depression, and are a further step towards visualization of brain regions associated with neurotransmitter alterations that may underlie major depression.

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DEVELOPMENT OF THE COMPREHENSIVE DESCRIPTIVE AND SEVERITY SCALE OF BEREAVEMENT: THE STARDUST BEREAVEMENT SCALE

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Objective: Despite the extensive literature on bereavement, there is a scarity of Comparatative Clinical Data on grief responses whether normal or abnormal. The aim here is to design and validate an easily administered and comprehensive scale of grief.

Method: In the course of studying the effects of a mam made disaster the opportunity arose of sampling the vast majority of bereaved family members (N = 147). A literature Review narrowed the emotional and behavioural responses to 32 items. These were rated in analogue form over a two year time span and provided qualitative and quantitative measures of grief.

Results: The items and ratings were easily understood and quantified by the bereaved. Factor analysis supported hamageneity of the

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

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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

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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

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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 ($r = 0.62$, $P = 0.03$).

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