NR15. Bereavement; Biological and treatment issues in affective disorders — I

Chairmen: G Stein, D Raven

THE MELBOURNE FAMILY GRIEF STUDY: PERCEPTIONS OF FAMILY FUNCTIONING IN BEREAVEMENT

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Objective: Our aim was to identify patterns of family functioning in the adult family following the death of a parent.

Method: 115 families (670 individual responses) assessed at 6 weeks (T1), 6 (T2) and 13 (T3) months after the death of a parent completed measures of family functioning, grief, psychological state and social adjustment. Cluster analytic methods were applied to develop a typology of perceptions of family functioning during bereavement.

Results: Five classes emerged using dimensions of cohesiveness, conflict and expressiveness from the Family Environment Scale (FES). One third of families were named *supportive* for their high cohesion; a quarter *resolved conflict* effectively. Two classes were dysfunctional: *hostile* families were distinguished by high conflict, low cohesion and poor expressiveness, while *sullen* families had more moderate limitations in these three areas; they declined in frequency from 30% at T1 to 15% at T3. The remaining class, termed *intermediate* (one fifth), exhibited midrange cohesiveness, low control (FES) and low achievement orientation (FES). The typology at T1 predicted those at T2 & T3. There were no age or gender differences, but offspring were over-represented in the hostile cluster.

Conclusion: Family types can be identified enabling at risk families to be helped to prevent complications of grief. Screening with the Family Relationship Index (FES) would facilitate such a family-centered approach.

TRANSCRANIAL MAGNETIC STIMULATION A NEW THERAPEUTIC APPROACH TO THE TREATMENT OF DEPRESSIVE ILLNESS

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Transcranial magnetic stimulation (TMS) is a well established diagnostic probe in neurological practice. The increasing knowledge of biological mechanisms in electroconvulsive therapy (ECT) made an obvious case to study the applicability of TMS as a therapeutic tool in psychiatric conditions. (George 1994, Zyss 1994).

Based on the results of our pilot study (Koppi et al 1996) showing a possible antidepressive effect of TMS, we conducted a controlled clinical trial on patients affected by major depression (DSM III R), undergoing TMS as an add on Therapy to standardized antidepressive medication. We compared randomising 2 groups: group 1 (n = 12) was treated with TMS and antidepressants, while group 2 (n = 12) underwent only antidepressive medication.

The groups were comparable in demograhic data, course and duration of index episode and diagnostic criteria for major depression. TMS was applied over a period of ten days dayly in the morning.

Precentral, prefrontal, temporal and parietal regions were stimulated bilaterally with a max. of 1.9 Tesla. The onset of treatment usponsivity was measured by HRS-D 21. Already after the third ad on TMS session a statistically relevant remission of depressive symptoms occured in the patients of group 1 (p = 0.003). This statistical difference between the groups becomes even more evident on the last day of the study p = 0.001 (Wicoxon).

These results confirm the hypothesis, that TMS probably works even as an antidepressive therapeutic tool. Further the TMS doesn't show marked or even serious side effects.

ELECTROPHYSIOLOGICAL CORRELATES OF IMPAIRMENT OF IMAGINABILITY IN DEPRESSIVE PATIENTS

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Research has shown depressive individuals to be impaired at various stages of cognitive information processing, but most mechanisms of these deficits are still not clear. Concerning recognition memory, impairment could be related to changes of working memory capacity itself or to changes of other kinds of processes facilitating these types of memory or recognition processes. Thus, it is well known that emotional processing, learning and retrieval strategies or other stimulus-related factors like the semantic or emotional content of a stimulus, as well as the extent of abstraction or imaginability related to the stimuli, may influence memory performance. To investigate the influence of imaginability of words on recognition processes and the factors of recognition memory impairment in depressive patients, we made use of an Event-Related Potential (ERP)-paradigm. In this type of continuous word recognition experiment brain responses to repeated items which are successfully recognized are characterized by more positive waveforms of the ERPs.

In the present experiment, words were classified according to their imaginability ("high", e.g. rose; "low", e.g. future) and were presented visually with some words being repeated. The subjects had to decide whether a given item had been presented for the first time ("new" word) or the second time ("old" word). The ERPs for the correctly detected "old" words showed an increased positivity beginning approximately 250 ms post stimulus. This "old/new-effect" (e.g., Rugg et al. 1995) was sensitive to the different word imaginability in the normal controls (the high imaginability words showed a pronounced old/new-difference), but the non-medicated depressive patients (DSM-III-R:296.2X and 296.3X; HAMD-score: 17–24; n = 12) appeared to show a much smaller old/new-effect and no significant difference between the "high" and "low" imaginability words. These findings support the hypothesis that depressive patients show an impairment of imaginability of words which influences recognition processes.

TIME TO REMISSION IN MAJOR DEPRESSION. IS THERE A LINK BETWEEN 'NO-TREATMENT INTERVAL' AND OUTCOME?

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The literature on the prediction of the course of depression has suggested several variables which influence outcome. Theses include duration and severity of the index episode, number of previous episodes of illness, family history of affective illness, number of negative life events and level of premorbial neuroticism. More recently it has been proposed that the interval between onset of episode and the

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.

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