We have been carrying out a series of studies into this problem. In this presentation questions will be addressed about the nature of outcomes after acute treatment and factors contributing to them. In a prospective longitudinal study, predominantly of inpatients, remission below major depression was achieved within 15 months in all but 6%. However, 40% relapsed in the next 15 months. An important finding was the presence of residual symptoms reaching 8 or more on the Hamilton Scale in 29% of remitted subjects, 78% of whom subsequently relapsed. Residual symptoms are an important outcome in depression which has received insufficient attention. In a second follow up study at 18 months of a new sample, aftercare received following discharge from hospital has been examined. Data obtained include full details of medication prescribed and taken, all other forms of treatment and care, compliance, attitudes and satisfaction.

FUNCTIONAL PSYCHOPATHOLOGY AND THE DIAGNOSTIC PROCESS IN PSYCHIATRY

H.M. van Praag. *Academic Psychiatric Centre, University of Limburg, P.O. Box 616, 6200MD Maastricht, The Netherlands*

Functional psychopathology is an important though greatly neglected and underdeveloped component of the diagnostic process in psychiatry. The functional approach provides a much more precise and detailed picture of the psychopathology of a given patient than nosological and syndromal diagnoses can. Moreover, in this manner the unsurmountable problems caused by comorbidity in defining a mental condition, can be circumvented. Since many psychological dysfunctions are measurable, often in truly quantitative terms, functional psychopathology provides psychiatric diagnosing with a solid scientific foundation.

Functional psychopathology of a psychiatric condition is a prerequisite for, what I have called "verticalisation" of psychopathological phenomena, while "verticalisation", in its turn, is a prerequisite to target biological and psychopathological research much more accurately than has been possible so far.

Finally, the functional approach provides an opportunity to investigate the relative merits of the nosological disease model and the reaction form model of mental disorders for biological research in psychiatry. The latter model has been disregarded for a long time; I would rather say, for too long.

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[2] Van Praag, H.M. (1996) Over the mainstream — Diagnostic Requirements for Biological Psychiatric Research, Eur. Psychiatry, submitted.

S30. Gender and dementia

Chairman: L Whalley

OESTROGEN MAY AFFECT MOOD AND MENTAL STATE BY AN ACTION ON SEROTONIN$_{2A}$ RECEPTORS AND SEROTONIN TRANSPORTER

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Oestrogen exerts profound effects on mood and mental state. Low levels of oestrogen in women are associated with postmenopausal depression, postnatal depression and the depressive symptoms of the premenstrual syndrome. Sex differences in schizophrenia may also be related to oestrogen. Previous studies have shown that oestrogen stimulates a significant increase in dopamine$_2$ (D_2) receptors in the striatum and we have now shown that in the rat oestrogen stimulates a significant increase in the density of 5-hydroxytryptamine$_{2A}$ (5-HT$_{2A}$) binding sites in anterior frontal, cingulate and primary olfactory cortex and in the nucleus accumbens, areas of the brain concerned with the control of mood, mental state, cognition, emotion and behaviour. Our investigations have also demonstrated that oestrogen stimulates a relatively massive increase in the concentration of the serotonin transporter mRNA in dorsal raphe nucleus and that this corresponds with an increase in serotonin transporter binding sites in this nucleus as well as other areas of the rat brain concerned with behaviour. These findings provide a possible neuropharmacological explanation for the effect of oestrogen on mood and mental state, and the efficacy of oestrogen therapy or 5-HT uptake blockers, such as fluoxetine ("Prozac"), in treating major depression and the depressive symptoms of the premenstrual syndrome. Our findings also suggest that the psychoprotective effects of oestrogen in schizophrenia may be mediated by 5-HT$_{2A}$ as well as D_2 receptors.

Further molecular pharmacological studies are in progress to determine the precise mechanism of action of oestrogen, and neuroimaging studies are being carried out to determine whether oestrogen has similar effects on the serotonin transporter in the human brain.

S31. The long-term outcome of psychiatric disorders

Chairmen: J Angst, C Duggan

SUICIDE IN YOUNG SCHIZOPHRENIC PATIENTS, A CASE CONTROL STUDY

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Schizophrenia is a life-shortening disease and suicide turns out to be the major cause of death. The aim of our study is to identify possible risk factors for suicide in young schizophrenic patients.

We studied a large cohort of 870 DSM-III-R young schizophrenic patients (Age < 30 at index admission), consecutively admitted between 1973 and 1992. The mean duration of follow-up was 11 years and all patients were located. We adapted a matched case control design with matching for: sex, age and subtype. Lifetime psychiatric history was obtained for both cases and controls.

At follow-up 7.2% (N = 63) of all patients committed successful suicide, this is 9.1% for males and 4.2% for female patients. The S.M.R. for suicide is 39.7. 81% used a high-lethal mean and 52% died during an inpatient stay. 77% of the suicides were male. The mean age of suicide was 28.5 years.

Major risk factors are: N admissions > 4 ($p < 0.000$); short duration hospital stay ($p < 0.000$); past suicidal behaviour ($p < 0.000$) and attempts ($p < 0.000$); negative attitude towards treatment, fugues ($p < 0.000$), acting-out ($p < 0.000$), non compliance ($p < 0.000$); major loss ($p < 0.000$); psychosis ($p < 0.000$); depression ($p < 0.000$). Other risk factors are: IQ > 100; discharge against advice; use of antidepressants; living alone at index admission; residential psychiatric care. Odds Ratios are calculated for every risk factor.

Based on these risk factors we developed hypothesis on suicidal

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behaviour in schizophrenic patients and possible interventions. These include: discussion of suicidality in treatment, psycho-education, continuity of care, work on grief and losses, attention to suffering and not only symptoms, adapted living — and work environment, adequate treatment of psychosis and depression.

LONG-TERM OUTCOME OF SCHIZOPHRENIA

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The WHO International Study of the Determinants of Outcome of Severe Mental Disorders (DOSNMeD) identified inception cohorts of psychotic patients in ten countries including both 'developing' and 'developed' cultural settings. The International Study of Schizophrenia (ISoS) is a 13 year WHO co-ordinated follow-up of these and similar samples. We report data from the UK (Nottingham) field center. Ninety-six percent of the original psychosis cohort (n = 99) were traced to residence or point of death (n = 9). None were found homeless or in prison and only two patients were in residential accommodation. Of those assigned a project diagnosis of schizophrenia at onset, 55% showed good or fair social functioning and over 50% were free of psychotic symptoms over the last two years. However, only 17% of the cohort were alive, completely free of symptoms and receiving no treatment. Predictors of long-term outcome were early (2 yr) course type, female gender, age, marital status and acuteness of onset, accounting for over 40% of variance in disability and symptoms. Analysis of course types produced no evidence of progressive deterioration or amelioration, and there was no evidence of 'late recovery' at this stage of follow-up. These findings will be compared and contrasted with preliminary data from other ISoS collaborating centers.

PREDICTORS OF LONG-TERM COURSE IN DEPRESSIVE ILLNESS

Alan Lee. *University Department of Psychiatry, Queen's Medical Centre, Nottingham, NG7 2UH, England and The Institute of Psychiatry, London*

In 1988 we published an 18 year outcome study of depressed inpatients from the Maudsley Hospital, London. 89 consecutive admissions with primary major depressive episodes had been prospectively ascertained and interviewed by R E Kendell in 1965–66. Follow-up was by a trained psychiatrist using standardised instruments who interviewed 94% of the survivors, and was blind to the index data. Over one third suffered unnatural death or severe chronic distress and handicap. Less than one fifth of the survivors had remained well. Similar results from other modern follow-up studies have led to a new focus on the long-term risks of a severe depressive illness. Since depressive disorders are common whilst resources are limited, there is an urgent need to predict at an early stage which patients will develop recurrent, resistant and complicated illnesses, to aid the targeting of preventative strategies.

We have now completed a family study of the Maudsley series. A trained psychiatrist blind to all proband data has used standardised interviews to determine the psychiatric histories of 519 first degree relatives. We present the results of this study together with predictors derived from the index admission. Three predictors of poor global outcome have emerged. 1) A family history of in-patient treatment for depressive disorder, a psychotic episode, or suicide. 2) High (psychotic) scores on Kendell's neurotic-psychotic index, or DSM III melancholia. 3) High neuroticism scores on recovery.

Family history was a strong predictor. Of 24 patients with a family history, none had a good outcome and 20 (83%) were readmitted. The three predictive factors together were multiplicative, so that patients with a family history, and melancholia, and high neuroticism were 15 times more likely to have a very poor outcome.

We have found risk factors in each of the domains of family history, phenomenology and personality. Their predictive power over 18 years, despite many intervening variables, is strong evidence for their importance in causal models. They await replication, but are clinically useful hypotheses to help target biomedical and cognitive prophylaxis.

LONG-TERM PROGNOSIS OF UNI- AND BIPOLAR DISORDERS

A. Marneros, A. Deister, A. Rohde. *Psychiatric Hospital of Martin-Luther-University Halle-Wittenberg, 06097 Halle, Germany*

A dichotomy of schizoaffective disorders into unipolar and bipolar schizoaffective disorders, analogous to the dichotomy of unipolar and bipolar affective disorders, seems to be justified in that the differences between the former resemble those between the latter. The most important differences between unipolar and bipolar schizoaffective disorders were found regarding gender, premorbid personality, occupation at onset, social class at onset, number and frequency of episodes and cycles, mean length of cycles, length of intervals and inactivity period. Unipolar affective disorders differ from bipolar affective disorders in the following parameters: age at onset, occupation at onset, premorbid personality, stable heterosexual relationship, family members with schizophrenia, frequency of long-lasting preepisodic alterations, number and frequency of episodes of illness, mean length of cycles and length of intervals. The most important differences between the unipolar forms of the two disorders (affective and schizoaffective) were in age at first manifestation, which was lower in unipolar schizoaffective patients than in unipolar affective patients, and in outcome, more favourable in the unipolar affective than in the unipolar schizoaffective disorders. Between the bipolar forms of the two disorders (affective and schizoaffective) only small differences were found, regarding some more favourable social aspects of outcome. Building a voluminous group of unipolar disorders and a voluminous group of bipolar disorders similarities and differences remain stable, as between the unipolar and bipolar forms of affective and schizoaffective disorders separately.

A THIRTY YEAR FOLLOW-UP OF THE NEWCASTLE AFFECTIVE DISORDERS COHORT

Jan Scott, Mary Jane Tacchi, Alan Kerr. *University Department of Psychiatry, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, England*

A sample of 154 patients with affective and anxiety disorders who were admitted to Newcastle psychiatric units between 1963–5 was followed-up by an independent assessor, blind to the original diagnosis, at 30 years. No data was available on 12 patients and only limited follow-up information was available on 16 survivors. Of the other 126 patients it was possible to assess survival rates, outcome according to Lee and Murray's criteria (1988) and change in diagnosis over time. Five diagnostic subgroups had been identified originally: reactive depression (n = 42); endogenous depression (n = 30); phobic anxiety depersonalisation syndrome (n = 40); simple anxiety (n = 16); and other diagnoses (n = 14). At thirty years, 46% sample survived with the lowest survival rate (20%) in endogenous depressives and the highest (65%) in the phobic anxiety depersonalisation syndrome group. Only 10% sample had a very good outcome according to Lee and Murray's criteria. Few of the depressives were rediagnosed during the follow-up, but the majority of individuals with phobic anxiety depersonalisation syndrome went on to experience at least one episode of major depression.