THE HYPOTHALAMUS OF DEPRESSED PATIENTS

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Several systems in the human hypothalamus and its afferents (e.g. the locus coeruleus) appear to be involved in the pathophysiology of mood disorders. Abnormalities of biological rhythms and the effectiveness of light therapy in depression suggest that the suprachiasmatic nucleus (SCN), the clock of the brain, may be involved in the pathophysiology of depression. Increased activity of corticotropin releasing hormone (CRH) neurons has not only been implicated in the non-suppression of the dexamethasone suppression test, but also in symptoms of depression.

We recently determined the activity state of these peptidergic systems in the hypothalamus of patients with a mood disorder and found no differences in the number of vasopressin (AVP) and vasoactive intestinal polypeptide (VIP) neurons in the SCN, only the nuclear diameter of the VIP neurons was smaller in depressed patients, suggesting a possible disorder of the entrainment system.

An increase was found in AVP-, oxytocin- and CRH neuron numbers in the paraventricular nucleus (PVN) as compared to matched control subjects. Also an increase was found in CRH-mRNA and AVP colocalization in CRH neurons in the PVN. These data are interpreted as activation of the oxytocin, AVP and CRH neurons in the PVN, that may, because of their central effects, be related to symptoms of mood disorders.

At present we are testing the involvement of the hypothalamus and the locus coeruleus, that innervates the PVN, in the pathophysiology of mood disorders by comparing Alzheimer's disease patients with and without depression. No differences were observed in the number of pigmented noradrenergic neurons in the locus coeruleus.

Brain material was provided by the Netherlands Brain Bank (coordinator Dr. R. Ravid).

THE DISRUPTION OF CORTICOSTEROID FEEDBACK IN CHRONIC STRESS

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Exogenous administration of corticosteroids results in a reduction in adrenal corticosterone secretion, pituitary ACTH release and pituitary POMC mRNA and hypothalamic CRH and AVP mRNAs. Chronic stress also results in increased plasma corticosteroids — but despite this, there is activation rather than suppression of the HPA axis. There is therefore a relative insensitivity to corticosteroid feedback. Further investigation of the hypothalamic response to chronic stressors suggests that the chronic activation of pituitary ACTH secretion is achieved by increased synthesis and release of arginine vasopressin rather than CRH from the hypothalamus. Indeed CRH is actually suppressed in the three models of chronic stress which we have studied

ALTERED HYPOTHALAMIC-PITUITARY-ADRENOCORTICAL REGULATION IN INDIVIDUALS AT HIGH FAMILIAL RISK FOR AFFECTIVE DISORDERS

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A frequent sign of major depression is a disturbance of the hypothalamic-pituitary-adrenocortical (HPA) system. It is reflected by an increase in the secretion of cortisol and adrenocorticotropin (ACTH), a relative refractoriness of ACTH and cortisol to the suppressive effect of dexamethasone (DEX) and a blunted ACTH response to corticotropin-releasing hormone (CRH).

The dexamethasone suppression test is one of the most frequently used neuroendocrine tests to assess HPA-system function in depression, but its sensitivity is low. It has therefore been refined by combining it with a human CRH challenge. After pretreatment with 1.5 mg DEX (2300 h) followed by stimulation with 100 μg CRH at 1500 h the next day depressed patients show an increased ACTH and cortisol release. The level of this effect is dependent on the DEX dose in both patients and controls. In a recent dosage study with the DEX-CRH test (DEX pretreatment 0.75 mg; 1.5 mg; 3.0 mg) we found a linear dose-dependent ACTH and cortisol response, with higher ACTH and cortisol levels in depressed patients than in control subjects in comparable dosage groups. This suggests that the pathological DEX-CRH-test reflects a decreased central glucocorticoid receptor capacity in depression. The mechanism underlying is long-lasting disturbance of the HPA-system remains still unclear. Either early stressful life events or a genetically transmitted risk factor could play a major role. If the latter is the case this HPA disturbance could possibly be observed in healthy individuals with a high genetic risk for psychiatric disorders. Such genetic risk is likely among people with a first-degree relative who has a mood disorder.

Using rigid psychodiagnostic techniques, we screened 431 consecutively admitted inpatients with depression and identified 35 families with one or more high-risk probands. The results of the DEX-CRH test showed that the group of DEX-pretreated (1.5 mg; 2300 h) high-risk probands released more cortisol after stimulation with human CRH (100 μg; 1500 h the next day) than a control group, but less than a group of patients with an acute major depressive episode. A linear discriminant analysis identified 32% of the high-risk probands as showing cortisol response patterns indistinguishable from those of the depressed patients.

These findings support our hypothesis that a genetically transmitted risk factor reflected by a decreased corticosteroid receptor capacity leads to an HPA feedback disturbance that renders the at-risk individuals susceptible to developing an affective disorder.

S4. WHO ICD-10: Evaluation and evolution

Chairmen: JE Cooper, N Sartorius

VALIDITY STUDIES

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A classic paper, written by late Eli Robins and Sam Guze in 1970 — "Establishment of Diagnostic Validity in Psychiatric Illness: its Application to Schizophrenia" — cuts the Gordian knot of semantic wrangles about "disease entities" in psychiatry, by demanding that diagnostic concepts have construct validity. This required validators external to the defining criteria. The St. Louis pioneers grouped all the possible validators under three headings:

Concurrent validators (clinical features and biological measurements made during the episode)

Antecedent validators (demographic and genetic factors, personality and precipitating events)

Predictive validators (diagnostic consistency over time, deterioration, recurrences and response to treatment).

In this paper, the success of their strategy is reviewed, 25 years

later, in relation to subsequent research on schizophrenia, and certain other concepts — cycloid, paranoid, puerperal and psychogenic psychosis.

ICD-10, EXPERIENCES IN WESTERN EUROPE

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Since the beginning of 1994, an increasing number of Western European countries officially have taken ICD-10 in use, and in other countries preparing to do so, extensive introduction and training in use of the psychiatric part of ICD-10 has taken place. In this way, experience with the use of ICD-10 has amounted. As expected, the use of ICD-10, Chapter V has contributed to increased diagnostic reliability leading to improved professional training and heightened quality of diagnosis and treatment in psychiatry. Following a short period of transition, the ICD-10 has been found easy to use, and adequate for the majority of the disorders met in the psychiatric in- and out-patient clinics. Some Western European countries still adhere to the DSM-system, in case the latest revision, DSM-IV, which, in spite of many and profound differences in practice, for the main categories overlap with ICD-10 in most cases. Further experiences including validity studies comparing the two systems will help to point out categories to be considered for the next revision.

INTRODUCTION TO THE ICD-10 COURSE

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The ICD-10 chapter dealing with mental disorders has been produced through an intensive process of collaboration between experts in more than 30 countries. The proposals have been translated into numerous languages and tested worldwide. The process of production of the ICD-10 Chapter V have probably been the largest international collaborative project ever.

The presentation will give a brief description of the process and of its main products, thus serving as an introduction for the course.

EXPERIENCES IN CENTRAL AND EASTERN EUROPE

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First information regarding the progress in cooperation between psychiatrists of the former "Eastern Block" and their western colleagues was given at the 6th AEP Congress in Barcelona, 1992. Authors have continued in their efforts to create the basic semantic tool compatible enough with the western psychiatrists in the sphere of the psychiatric classification. E.g. special courses on ICD-10 and DSM-IV classifications have been organized in Czech Republic and the basic materials of WHO have been translated into Czech. Authors have contacted actually Psychiatric Associations of the Central and some Eastern European countries to reach basic information about their experiences in the application into the practice the new psychiatric classification. The changes of information has been valuable in many cases. The main common problem seems to be difficulties in the development of informational systems which could be sufficient enough to link Eastern and Western informational data bases. The creating of these systems depends first of all on the economical possibilities. Even if the macroeconomical data could give evidences of the substantial changes and improvements, the health systems in the countries of the former "Eastern Block" have suffered from radical reduction of financial meets actually. In spite of these problems, first successful steps have been achieved in the mutual cooperation thanks to the help of the WHO Division of Mental Health, WPA and many institutions and colleagues of the West European countries, U.S.A., Canada and others.

S5. New developments in child and adolescent psychiatry

Chairmen: M Schmidt, RC Harrington

THE OUTCOME OF HOME-TREATMENT COMPARED TO INPATIENT TREATMENT OF CHILDREN WITH PSYCHIATRIC DISORDERS

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Earlier studies have demonstrated that home-treatment and inpatient treatment of psychiatric disorders in children and adolescents is comparable with regard to the outcome of psychopathological, behavioural and psychosocial factors. The aim of the present study is to replicate these treatment effects when home-treatment is performed by a registered nurse with special experience in child and adolescent psychiatry supervised by a child and adolescent psychiatrist. In the home-treatment group children aged 6 to 16 years with need of inpatient treatment are treated two times a week for three months. Control group is an inpatient treated sample of children matched for age, sex, diagnosis, severity of disorder, and psychosocial background. Treatment evaluation includes multi-modal assessments by patient, parents and therapist (self rating scales, structured interviews, performance tests) before, during and after treatment. Treatment effects are evaluated by comparing the home-treatment group with the control group. Furthermore long-term effects will be assessed one year after the end of the treatment. Results are reported for 40 children of each group. Preliminary results reveal that home-treatment is as effective as inpatient treatment and that the effects of the home-treatment are long-lasting.

EARLY ONSET BULIMIA NERVOSA: LIFE EVENTS, DEPRESSIVE FEATURES AND TWO-YEAR FOLLOW-UP

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Typically, bulimia nervosa (BN) begins around 18 years of age and is thought to be related to difficulties in autonomisation and separation from family.

In a French multicenter study including 358 consecutive female outpatients with a DSM-IV diagnosis of BN, 69 subjects (19%) had had onset of their disorder between 10 and 15 years of age. At time of evaluation, they were aged 15 to 46 years.

Compared to patients with a classical late adolescent onset of BN, those with early onset came more often from disrupted families, they had an earlier age of menarche and reported more often a pronounced weight gain at puberty. Other factors cited as possible precipitating events included death of a parent or grandparent, conflict with parents, somatic illness of a parent, change in family composition, and difficulty adjusting to a new school.

At time of evaluation, patients with early onset BN had relatively less severe eating symptoms but more frequent impulsive disrupted

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