randomised trial data are not compelling and there are no controlled studies with newer anti-depressant agents such as SSRIs. There has been recent interest in the augmenting action of pindolol, because animal experimental studies suggest that certain β-adrenoceptor antagonists can enhance the effects of SSRIs on serotonin neurotransmission through 5-HT1A autoreceptor blockade. However, clinical data from controlled trials are not encouraging and PET imaging indicates that the dose of pindolol generally employed in SSRI augmentation studies (7.5mg daily) is probably insufficient to occupy human 5-HT1A receptors. Recently atypical antipsychotic drugs have been used as SSRI augmenting agents with olanzapine producing clinically useful effects in one small controlled trial.

IS01.3

An overview of the antidepressant properties of transcranial magnetic stimulation

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The possibility of focal and noninvasive stimulation of the brain has been an appealing vision that for a couple of years seems to be realized: Repetitive Transcranial magnetic stimulation (rTMS) holds promise as a tool to study localization of function, connectivity of brain regions, and pathophysiology of neuro-psychiatric disorders. Transcranial magnetic stimulation involves placing an electromagnetic coil on the scalp. High-intensity cur-rent is rapidly turned on and off in the coil through the discharge of capacitors. This produces a time-varying magnetic field that lasts for about 100 to 200 microseconds. The magnetic field typically has a strength of about 2 Tesla (40 000 times the earth's magnetic field, or about the same intensity as the static magnetic field used in clinical magnetic resonance imaging).

This technique has been used in Neurology as an investigative tool for more than a decade, but as potential effects on mood have become apparent, interest has grown in its use in treatment and assessment of major depression. Since the technique is non-invasive and can be applied to a non-anesthetized patient it would be extremely promising as an antidepressant modality, since other methods of therapeutic brain stimulation such as electroconvulsive therapy (ECT) are much more invasive.

IS01.4

Vagus nerve stimulation: a potential new treatment for treatment resistant depression?

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Because of the fact that up to 20 % of depressed patients do not respond to the currently available therapies, new treatment options are desirable.

Subjective observations from treatment of patients with epilepsy leaded to the idea that vagus nerv stimulation (VNS) has antidepressive effects. Although the basic mechanism of action of VNS is unknown, both clinical and animal studies indicate a mechanism that is likely to affect the same neurotransmitter systems that are thought to be involved in depression. Furthermore PET scan data showed modulations of cerebral blood flow in humans in key brain structures for depression. An american randomized open-label trial study with 30 patients confirmed these first suggestions and demonstrated a 40% response rate.

We now investigate the first treatment refractory depressed patients in Europe in an open label, non-randomized multi-center study. In addition to weekly psychopathometric ratings we investigate the reactivity of the HPA system using the combined dex/CRH test and the cerebral perfusion performing HMPAO-SPECTs after one and after four weeks of stimulation for monitoring neurobiological parameters of depression under VNS treatment. Preliminary data will be presented.

S01. Major European research networks on schizophrenia

Chairs: W. Gaebel (D), H.-J. Möller (D)

S01.1

The German Network Research on Schizophrenia

W. Gaebel*, W. Wölwer. *Department of Psychiatry, University of Düsseldorf, Germany*

The German Research Network On Schizophrenia is one of three psychiatric "Competence Networks" funded by the German Ministry of Education and Research in order to improve the horizontal and vertical collaboration between research institutions and the psychiatric care system. The schizophrenia network is organized, with respect to illness development, into two main "Project Networks" (PN), focussing primarily on the treatment and need for care in the prodromal phase preceeding the first episode (PN I), and after first hospitalization (PN II). In total, about 30 research projects aim at the improvement of early detection and intervention (PN I), or at the optimization of acute and long-term treatment, especially in first episode patients, including rehabilitation strategies, especially in patients with residual symptoms (PN II). Furthermore, there is a "Special Network" on molecular genetics, together with several more general projects on health economy, fighting stigma and discrimination, postgraduate training, quality assurance, and methodology. More than 20 psychiatric university departments, 14 state hospitals, six psychiatric and primary care networks, and further organizations like self-help associations of relatives collaborate in the network.

S01.2

The Swedish HUBIN Project on Schizophrenia

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The HUBIN (Human Brain Informatics) project is a national interdisciplinary collaborative effort to explore genetic and environmental mechanisms involved in the etiology and pathophysiology in Swedish patients with schizophrenia. Two different subject materials are used in this approach. The first is a case-control material of subjects from the Stockholm area. The second is a unique Swedish material of sib-pairs with schizophrenia. Standard electronic protocols are used to determine, (1) perinatal risk factors from birth records, (2) phenotypic characteristics of the disorder,

https://doi.org/10.1016/S0924-9338(02)80018-9 Published online by Cambridge University Press

(3) quantitative structural MRI brain volumes and (4) DNA characteristics from blood samples. Currently about 400 case-controls and 150 out of 700 potential sib-pair families have been investigated. Coded data are transferred to an IBM DB2 relational database suitable for multivariate and data mining exercises. Preliminary analyses of data indicate relationships between diagnosis and genes regulating monoaminergic pathways and specific chromosomal regions. MRI data indicate possible subgroups among patients with schizophrenia with reductions of white and gray cerebral volumes and vermian lobules. When further expanded, the HUBIN database will allow the validation of previous and new hypotheses concerning etiopathological aberrations among patients with schizophrenia.

S01.3

The Italian Network for Research on Deficit Schizophrenia

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The concept of "deficit schizophrenia" (DS) was introduced to identify a relatively homogeneous subgroup of subjects with a diagnosis of schizophrenia characterized by the presence of enduring, primary negative symptoms.

A large multicenter study was carried out in Italy to test the hypothesis that DS represent a disease different from nondeficit schizophrenia (NDS) by integrating historical, clinical, neuropsychological, neuromorphological and genetic data.

DS had less hostility, grandiosity and disorganized behavior than NDS subjects and a comparable severity of positive symptoms. They were characterized by a poorer premorbid adjustment during childhood and early adolescence, and were more impaired on general cognitive abilities. The deficit state was associated with an impairment of sequencing of complex motor acts.

Data analyzed so far confirm the pattern of historical, psychopathological and neuropsychological impairment previously reported in DS vs. NDS patients and, together with preliminary neuromorphological findings, seem to rule out the possibility that DS just represent the most severe form of the disease.

S01.4

European First Episode Schizophrenia Trial (EUFEST)

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The atypical antipsychotics have been shown to be at least as effective in treating and preventing recurrence of psychosis in schizophrenia without the concomitant emergence of these side effects. However, studies examining drug effects are usually conducted in highly selected samples, excluding patients with dual diagnoses (often drug use). Furthermore, the attrition rate in most of these studies is extremely high, which may be due to the double-blind nature of many of the designs. Thus the generalizability of the studies assessing the efficacy of the newer, atypical antipsychotics is limited at best. It has been argued that the beneficial effects of the new antipsychotics would fail to materialize when compared with low dose use of typical antipsychotics in (medication-naive) schizophrenic patients. This European study will compare the one year outcome after treatment with various atypical antipsychotic medications (amisulpride, olanzapine, quetiapine) with that of a low dose (1–4 mg/day) of haloperidol, as measured by duration of retention to allocated treatment. The study will be conducted in more than 10 European countries involving over 30 sites.

S02. Helplessness and stress related disorders

Chairs: H.-J. Möller (D), F.A. Henn (D)

S02.1

Loss of control and depression

H.-J. Möller*. *Department of Psychiatry, University of Munich, Germany*

The concept of hopelessness/helplessness, focussing primarily on loss of control, might be an important interface between subjective experience of psychosocial stressors and the outcome in terms of depression or suicidal behaviour.

Life event research, which was very common in the last two decades, has demonstrated that different kinds of stressful life events are related to depression and suicidal behaviour indicating that apparently the quantitative amount of stressful life events is more important than specific "depression-related" stressors, a position that was formerly proposed particularly by psycho-dynamic therapists. Nevertheless, also life event research has demonstrated that different life events can have a different meaning for each individual patient. However, it must be underlined that not all people who have experienced a heavy life event burden react in such a way, but apparently genetic dispositions, personality traits, biographical experiences, coping patterns and social support are of importance in a complex theoretical model. In this model the construct of hopelessness/helplessness, which might be the final psychological subjective pathway of the interaction with stressful life events, seems of great relevance.

However, the hopelessness/helplessness concept for depression and suicide should not be over-generalised and the limitations of this concept should be taken into account. For example, evidence for this model in bipolar depression and suicide related to bipolar depression, and especially mixed states in bipolar depression, has not yet been demonstrated.

S02.2

The consequences of loss of control in animal models

F.A. Henn*. *University of Heidelberg, Central Institute of mental Health, Mannheim, Germany*

The presentation of adverse stimuli to animals under conditions in which they can not control the stimuli, i.e. end the stimuli, leads to symptoms of depression compared to animals that receive the same stimuli but have control over the end point. Eperiments with a yoked cage design have shown that the lack of control by itself is the crucial factor in the development of subsequent helpless behavior. This has been examined in rats and it was found that when exhibiting learned helplessness the animals had also altered HPA axis activity, changes in NE and 5HT systems and a variety of behavioral changes including decreased sleep, weight loss, impaired learning, decreased libido. This occurred preferentially in animals that could not control the termination of the adverse stimuli even though the animals in the yoked cages received exactly the same biological stimulus. Thus the psychological factor of control can be shown to influence the neuroplasticity of the rat brain,

https://doi.org/10.1016/S0924-9338(02)80018-9 Published online by Cambridge University Press