of major depression, social phobia and ADHD in childhood and adolescence.

Conclusion: Our results confirm 1) the familial aggregation of bipolar disorder; 2) the high risk of childhood psychopathology in the offspring of bipolars.

S41.4

Mixed affective and schizoaffective disorders: a challenge for research

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The pharmacological revolution and it's consequences caused also a renaissance of mixed affective disorders, which are now included in DSM-IV and ICD-10. Mixed affective disorders are characterized by relevant differences in comparison to other bipolar affective disorders: gender, family history, length of episodes, response to pharmacological treatment of the acute episode, response to mood stabilizer, course and longterm outcome. The above mentioned differences will be discussed from a data oriented and a theoretical point of view. We will present data from a prospective longitudinal study. The mixed bipolar schizoaffective disorders are only sparely investigated. But the existent research data suggested that mixed schizoaffective episodes: are longitudinally common, have many similarities with mixed affective episodes, and they are also a challenge regarding treatment and prophylaxis. They will also be discussed under data oriented and theoretical considerations.

S41.5

The treatment of bipolar disorder

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Bipolar disorder is a long-lasting condition with highly recurrent episodes which is associated to high levels of suffering, occupational dysfunction, and disruption of social life and relationships. The length of remission, when the individual is well, is reduced in many cases both with age and the number of previous episodes. More than acute episodes, the real challenge are long-term prophylactic strategies which aim to reduce the risks of relapse and improve interepisode function.

For many years lithium has been considered the first-line treatment of bipolar disorder. However, most of the pioneering studies with this drug used enriched designs and did not take in account of the withdrawal effects of lithium, thus overestimating its efficacy. The anticonvulsants valproate and carbamazepine are widely used in the prophylaxis of bipolar disorder as well, although prospective placebo-controlled studies to establish efficacy are scarce. Actually, there is only one good placebo-controlled prophylaxis trial assessing the long-term efficacy of valproate compared to lithium and placebo, which unfortunately could only show numerical (not statistical) superiority of both drugs against placebo in the prevention of mania, although valproate was better than lithium and placebo for the prevention of depression. For carbamazepine, there are only comparative trials which generally point to less efficacy than lithium in maintenance treatment. In recent years, atypical antipsychotics and novel anticonvulsants emerge as potentially effective alternatives, some of which, as long as controlled trials confirm the preliminary findings from open studies, may become first-line treatments for the treatment of acute episodes and the prevention of relapse in bipolar disorder. All these pharmacological tools should be used in combination with psychoeducational approaches directed to enhance treatment-compliance and early recognition of symptoms, which have been proved to improve the effectiveness of the treatment in two recent, randomized controlled studies.

S43. Recent research in suicidology

Chairs: L. Träskman-Bendz (S), C. Van Heeringen (B)

S43.1

Genetics and suicidal behaviour

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Although a familial aggregation of suicide has been observed by many psychiatrists, the reason for this has until recently been thought to reside in the shared socio-cultural and psychological environment, rather than in a shared genetic endowment. Even Franz Kallman, one of the major proponents of the idea of a genetic background of psychiatric disorder, considered a genetic background to suicide unlikely. Accummulating evidence for an association between low serotonin function and an increased risk of suicidal behaviour has, however, made a genetic background for suicide more plausible. Family and twin studies using modern techniqes and controlling for psychiatric illness support the idea that vulnerability to suicidal behaviour is to some extent under genetic control. Several genetic polymorphisms involved in serotonin transmission have been studied for a possible association with suicide. Among them, an modest excess of the tryptophan hydroxylase 17779C allele has repeatedly demonstrated in association with suicide, most recently in a study of surviving cotwins whose monozygotic twin had committed suicide. These, and some studies involving other genetic markers will be briefly reviewed in the presentation.

S43.2

Serotonergic disturbances in the prefrontal cortex of suicidal patients: implications for treatment and prevention

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Among the many potential approaches to the study of suicidal behaviour, research in biological and cognitive psychological domains has been particularly fruitful in identifying individual characteristics that may increase or decrease the probability of occurrence of suicidal behaviour. Biological research has mainly focused on two aspects, i.e. a hyper-reactivity of the stress-system and an impaired function of the serotonine neurotransmission system. These characteristics appear to be inter-related, as the stress hormone cortisol has been shown to have cytotoxic effects on the serotonergic system. Studies in the cognitive psychological area have identified three core characteristics, which distinguish depressed suicidal from depressed non-suicidal individuals. These psychological characteristics include tendencies to perceive oneself as a loser when confronted with psychosocial adversity, to perceive no escape from this situation (related to deficient problem solving), and to perceive no rescue (related to developing feelings of hopelessness). Recent psychobiological research suggests that the results from biological and psychological approaches converge to a considerable extent. For example, the extent of activation of the

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stress-system appears to correlate with the dimensional personality characteristic that modulates sensitivity in social communication. Moreover, we have recently demonstrated that levels of hopelessness correlate with serotonine receptor functioning in the prefrontal cortex, which is involved in the generation and choice of response alternatives when confronted with particular problems, and with trait-dependent regulation of anxiety. It thus appears that two interrelated clusters of psychobiological characteristics are involved in the development of suicidal behaviour, i.e. (1) a sensitivity to interpersonal events and activation of the stress system and (2) prefrontal serotonine function, hopelessness and the regulation of anxiety.

S43.3

The stress-system and suicidal behaviour

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The main objectives of our studies are to find adequate means of predicting recurrence of suicidal behaviour. In view of currently discussed theories on stress and kindling, we have lately concentrated on the role of stress in suicide attempts.

We study temperament, monoamines, steroids, and neuropeptides of patients who have deliberately harmed themselves, and we compare findings from them with findings from control populations.

Even though suicide attempters with major depression rate themselves significantly higher on trait anxiety than non-suicidal patients, suicide attempters form a heterogeneous group concerning temperament-ratings and biological findings. The most deviant patients (high trait anxiety, aggression, impulsiveness, suspiciousness combined with repeated suicide attempts) have low levels of steroids, monoamine-metabolites, and the neuropeptides CRH and NPY, while suicide attempters with normal temperament have high concentrations of e.g.cortisol, often corresponding with nonsuppression after dexamethasone administration.

We assume that "normal temperament" suicide attempters have not (yet?) reached the stage of sensitisation where the stress-system seems to be "burnt out". The genetic factors influencing body dissatisfaction and dieting-oriented behavior may constitute a part of the genetic vulnerability to eating disorders. These influences are likely to be age-specific and sex-specific.

S43.4

UK legislation on analgesic pack sizes: impact on suicidal behaviour

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Because of the growing problem of self-poisoning with analgesics, especially paracetamol, in September 1998 legislation was introduced in the United Kingdom to limit the size of analgesic packs (of paracetamol, aspirin and their compounds). In this presentation the background and rationale for this legislation will be discussed. The results of a prospective investigation in which the impact of the legislation on subsequent mortality and morbidity associated with analgesic self-poisoning will be presented. This investigation has focused on changes in sales figures, self-poisoning with analgesics, impact of paracetamol overdoses on liver toxicity, referrals to liver units and liver transplantation, and finally and most importantly, the impact of the legislation on deaths from analgesic poisoning. Overall, the initial results seem to have been very positive. Thus there was a decrease in paracetamol overdoses and in large overdoses of both paracetamol and aspirin. There are fewer liver transplants due to paracetamol liver damage. Finally, deaths from both paracetamol and aspirin self-poisoning decreased substantially. The implications of these findings for future trends and research will also be considered.

S43.5

Efficacy of St. John's wort extract WS® 5570 in major depression – a double-blind, placebo-controlled trial

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[4]*Biometrical Department, Dr. Willmar Schwabe Pharmaceuticals, Karlsruhe, Germany*

Objective: In a double-blind, randomized, placebo-controlled trial in 375 patients we investigated the antidepressant efficacy and safety of 3 x 300 mg/day hydroalcoholic Hypericum extract WS® 5570.

Method: The study participants were male and female, adult outpatients with mild to moderate major depression (single or recurrent episode; DSM-IV criteria). Following a single-blind placebo run-in phase, 186 patients were randomized to WS® 5570 and 189 to placebo and received double-blind treatment for 6 weeks. Follow-up visits were held after 1, 2, 4 and 6 weeks. The primary outcome measure was the change versus baseline of the 17-item Hamilton Rating Scale for Depression (HAM-D) total score. In addition, an analysis of responders (patients with =50% HAM-D total score reduction versus baseline) was carried out and subscale/subgroup analyses were conducted. The design included an adaptive interim analysis performed after randomization of a total of 169 patients with options for sample size adjustment or early stopping.

Results: WS® 5570 produced a sigificantly higher reduction in HAM-D total score and significantly more treatment responders than placebo. Hypericum extract was more effective in patients with higher baseline HAM-D scores and led to global reduction of depression-related core symptoms as investigated by the HAM-D melancholia subscale. Both groups were comparable regarding adverse events.

Conclusions: Hypericum extract WS® 5570 was found to be safe and more effective than placebo for the treatment of mild to moderate depression.

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S44. The dopamine D3 receptor and its ligands: psychiatric implications

Chairs: J.-C. Schwartz (F), G. Sedvall (S)

S44.1

Increased levels of D_3 dopamine receptor mRNA in blood lymphocytes of schizophrenic patients

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Dopamine is a major neurotransmitter in the central nervous system and its receptors are associated with a number of neuropathological disorders such as Parkinson's disease and schizophrenia.

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