A. Zobel, S. Schulze-Rauschebach, K. Barkow, O. v. Widdern, M. Metten, U. Pfeiffer, M. Wagner, F. Holsboer, W. Maier. *Dept. of Psychiatry, University of Bonn, Bonn, Germany*

Dysregulation of the HPA system is one of the most replicated neuroendocrine findings in depression. As shown in several studies, using the combined dexamethasone/Corticotropin Releasing Hormone (Dex/CRH) test, the HPA hyperactivity gradually normalizes during successful antidepressant treatment. Usually the normalization of the HPA system precedes the clinical remission. A persistent HPA dysregulation in spite of remission of clinical symptoms predicts a high risk for relapse. Thus, there is a close association between HPA regulation and depression, which also suggests a causal relationship. While the relationship between the global severity of the depression and the HPA activity is only weak, the normalisation of the HPA function during the treatment is strongly correlated with improvement of specific cerebral functions: there is a strong correlation between improvement of working memory function and reduction of the cortisol secretio. But HPA alterations also occur in healthy first degree relatives of depressed patients, which points to an increased vulnerability. Other vulnerability factors for depression are high scores in personality and temperament dimensions as neuroticism and depressive temperament. In a sample of healthy volunteers a correlation between neuroticism and depressive temperament on the one hand and HPA activity on the other could be shown. These findings point to a causal relationship of HPA dysregulation on the pathophysiology of depression and give reason to the development of treatment strategies, which aim directly to the restoration of the HPA integrity. One approach is the blockade of CRH1-receptors. In a first pilot study in 20 patients depressive symptomatology could markedly be reduced by application of a synthetic CRH1-receptor antagonist. Overall a large body of evidence supports the hypothesis that HPA dysregulation plays a crucial role in the development and maintenance of depression and opens new perspectives for treatment options.

## S-67-03

Influence of Borna disease virus infection on the course of depression

D. E. Dietrich, H. M. Emrich. *Dept. Clinical Psychiatry, Han, Hannover, Germany*

**Objective:** Borna disease virus (BDV), a spheric, enveloped, negative- and single-stranded RNA virus with a diameter of 90nm, is supposed to be spread worldwide and was detected in several naturally infected mammals. Meanwhile studies report that BDV has been found in human beings showing a high prevalence especially in patients suffering from neuropsychiatric diseases such as bipolar and recurrent depressive disorders (Bode et al. 2001). Therefore, BDV was hypothesized to represent an etiopathogenetic factor in these disorders. Experimental findings in animals showed a virus persistence especially in limbic structures and an alternation between active and latent viral infection. Moreover, it was demonstrated that BDV interacts with aspartate- and glutamate receptors in the hippocampal formation. The pathomechanism in infected humans is still unknown, but results of epidemiological studies suggest a possible impact of BDV on depressive disorders.

**Methods:** In our clinic we investigated the effect of the antiviral compound amantadine-sulphate on BDV parameters and symptoms in BDV-infected depressive patients in an open trial (n=25) as well as in a double-blind and placebo-controlled study (n=33). Furthermore, event-related brain potentials were used to investigate cognitive processing in BDV-infected and depressed patients with an obsessive-compulsive disorder (OCD).

**Results:** It appears that certain subtypes of affective disorders show a better response rate to the amantadine-treatment than others. In addition, the clinical improvement was paralleled by a reduction of BDV-infection parameters. Moreover, BDV also appeared to be correlated to certain changes of cognitive functions independent from depressive symptoms in OCD.

**Conclusion:** We will discuss these findings based on a model of the influence of BDV in neuropsychiatric diseases, suggesting that BDV-infection is a possible factor influencing the course of certain subtypes of depressive disorders.

## S-67-04

J. Joost. *Netherlands*

## S-67-05

Hippocampal changes and white matter lesions in early-onset depression

J. Janssen, H. Hulshoff Pol, I. Lamp, H. Schnack, F. E. de leeuw, R. Kahn, T. Heeren. *Utrecht University Medical Center, Utrecht, Netherlands*

**Objective:** Hippocampal volume reduction and increased prevalence of subcortical white matter lesions have been reported in late-life depression. We aimed to examine whether total number of subcortical white matter lesions were associated with reduced hippocampal volume in aged female subjects with early-onset depression (<45 years) and healthy comparison subjects.

**Methods:** The study included 28 middle aged and elderly subjects with major depression and 41 age-matched control subjects. Hippocampal, parahippocampal gyrus, and orbitofrontal cortex volumes were determined using manual tracing methods. White matter lesions were rated from T2-weighted MRI scans using a semi-quantitative classification scale.

**Results:** After controlling for total brain volume and age, patients had reduced hippocampal volume due to right hippocampal volume decrease (2.84 ml versus 3.12 ml, $F=16.6$, $p<.001$). Parahippocampal and orbitofrontal volumes did not differ significantly between groups. Multiple linear regression analysis indicated that reduced hippocampal volume did not significantly correlate with total number of subcortical white matter lesions ($t=.673$, $p=.518$).

**Conclusion:** Right hippocampal volume was reduced in aged female early-onset depressed subjects. Total number of subcortical white matter lesions was not associated with the decrease in right hippocampal volume. Our data suggests hippocampal involvement, independent of subcortical white matter lesions, in the neuropathology of early-onset depression.

**Monday, April 4, 2005**

# SS-10. Section symposium: Mood disorders and somatic syndromes

*Chairperson(s):* Martin Preisig (Prilly, Switzerland), Jules Angst (Zürich, Switzerland)
16.15 - 17.45, Gasteig - Lecture Hall Library

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## SS-10-01

Neurasthenia and atypical depression

J. Angst, F. Benazzi, V. Ajdacic-Gross, D. Eich-Höchli, W. Rössler, A. Gamma. *Psychiatrische Universitsätskl, Zürich, Switzerland*

**Introduction:** In the Zurich Cohort Study of a community sample we found a spectrum of fatigue syndromes with the following cumulative prevalence rates up to age 41: ICD-10. 3-months neurasthenia (6%), 2-weeks neurasthenia (9,7%) and recurrent brief neurasthenia (12.1%). Half of all ICD-10. neurasthenia cases were associated with major depressive or bipolar-II disorder. Comorbidity of ICD-10. neurasthenia with functional-somatic syndromes (stomach, intestines, circulation, back, headache) was increased. Atypical depression (AD) was specified by DSM-IV criteria (five symptoms) and by Zurich criteria as a triadic atypical depression (TAD), taking only three symptoms into account: overeating and oversleeping and excessive physical fatigue. The latter two symptoms form a considerable conceptual overlap between AD and neurasthenia, creating a significant association (Odds ratio=3.1) by definition. AD was associated with migraine, gastric, intestinal, cardiac and circulatory syndromes Triadic atypical major depression showed a prevalence rate of 6.8% and atypical subthreshold depression another 4%. This form of major AD is much more prevalent among women (15.1%) than men (3.2%) explaining the gender difference of depression.

## SS-10-02

Diabetes and comorbid depression

C. Kuehner, F. Lederbogen, M. Deuschle. *CIMH Genetic Epidemiology, Mannheim, Germany*

**Objective:** To review the literature on the association between diabetes and depression, and to determine depression prevalence rates in a sample of patients with diabetes. A second goal is to identify demographic and clinical characteristics associated with depression in these patients.

**Methods:** As a part of the "Augsburg Diabetes Family Study", 455 patients treated for type II diabetes were recruited from health care clinics and through physician referrals. These patients went through comprehensive laboratory tests at the study centre in Augsburg. The CES-D (Hautzinger & Bailer, 1993) was used to screen for depressive symptoms. Patients scoring >=16 participated in a SCID (Wittchen et al., 1997) interview by telephone for the assessment of depressive disorders according to DSM-IV.

**Results:** Identified prevalence rates of elevated depressive symptoms (CES-D >=16, 32.3%) and a current diagnosis of depression (SCID, 14.9%) match closely to those found in the literature. Compared with men, women were twice as likely to display elevated scores and to fulfil DSM-IV criteria for a depressive disorder (MDD, Dysthymia). Multiple logistic and linear regressions identified female gender, living without a partner, and multiple disease-related complications as independent factors associated with both depressed symptoms and diagnosis, while laboratory data (e.g., HbA1c levels, Cholesterol) were not connected with depression.

**Conclusion:** This study confirmed the high prevalence of depression in patients suffering from diabetes. Demographic and illness-related factors were similarly associated with depressive symptoms and with a DSM-IV diagnosis of depression. The literature suggests bi-directional influences in explaining this comorbidity.

## SS-10-03

Depression in neurological diseases: Emphasis on Parkinsons disease

F. Morkeberg Nilsson, M. Brandt-Christensen. *University Hospital of Copenha, Copenhagen, Denmark*

**Objective:** To investigate the temporal relationships between a range of neurological diseases and affective disorders.

**Methods:** Data derived from linkage of the Danish Psychiatric Central Register and the Danish National Hospital Register. Seven cohorts with neurological index diagnoses and two control group diagnoses were followed for up to 21 years. The rate of discharge diagnosis of depression on readmission was estimated with the use of competing risks in survival analysis. The rates were compared with the rates for readmission with a diagnosis of depression for patients with osteoarthritis, and patients with diabetes.

**Results:** We found an increased incidence of affective disorders in dementia, Parkinson's disease, epilepsy, stroke, and intra-cerebral haemorrhage compared with control groups. The association was found to be the strongest for dementia and Parkinson's disease when compared with the incidence in the control groups. In Parkinson's disease an increased probability of developing a diagnosis of depression was found for both women and men throughout their lifetime when this was compared with the control groups. No effect of age at onset of Parkinson's disease was found.

**Conclusion:** In neurological diseases there seems to be an increased incidence of affective disorders. The elevated incidence was found especially high for dementia and Parkinson's disease (neurodegenerative diseases). The findings support the hypothesis that depression in patients with Parkinson's disease may be a consequence of some kind of brain dysfunction.

## SS-10-04

Comorbidity of mood disorders and migraine

M. Preisig. *CHUV DUPA, Prilly, Switzerland*

**Objective:** Clinical and epidemiological studies have consistently revealed lifetime associations between mood disorders and migraine. However, the evidence regarding the nature of these associations remains unclear. Consequently, the goals of the present study were to 1) determine the association between migraine and unipolar as well as bipolar mood disorders; 2) assess the patterns of familial aggregation of migraine and mood disorders.

**Methods:** The present paper was based on data from a family study of 131 bipolar-I probands (18% with migraine), 156 unipolar depressive probands (24% with migraine), 95 normal controls (12% with migraine) as well as their adult first-degree relatives (n=1404). Diagnoses were made according to a best-estimate procedure based on a semi-structured interview (DIGS), a migraine interview, medical records and family history information.

**Results:** The major findings were that 1) migraine was more strongly associated with unipolar depression than bipolar disorder (OR = 2.0 vs. 1.6) in the relatives; 2) there was evidence of strong familial aggregation of bipolar-I disorder (OR = 5.8), whereas unipolar depression (OR= 1.5) and migraine (OR = 2.5) showed a

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lower degree of familial aggregation; 3) there was no evidence of cross-aggregation between mood disorders and migraine.

**Conclusion:** Our data confirm familial aggregation of bipolar-I disorder, unipolar depression and migraine. The finding of an increased risk of migraine with aura among relatives of probands with unipolar depression alone could indicate partially shared etiological factors underlying unipolar depression and subtypes of migraine.

## SS-10-05

Somatic health and illness and depressive symptomatology: Data from a population health survey

M. Kovacs, M. Kopp. *Semmelweis University, Budapest, Hungary*

**Objective:** To investigate the rate and associations of self-reported physical health and illnesses and depressive symptomatology, and also their impact on everyday psychosocial functioning and quality of life.

**Methods:** Data were obtained from the Hungarostudy 2002, a national representative health survey of the adult (18+) Hungarian population (Kopp et al., 2002, N=12668). Depressive symptomatology was measured by the shortened version of the Beck Depression Inventory (BDI). Participants signed their main illness caused the highest problems in the previous 12 months. General quality of life was measured by the WHO Well-being Index, and the Illness Intrusiveness Scale showed the extent of impairment in psychosocial functioning caused by the main illness.

**Results:** BDI scores were negatively correlated with the WHO Well-being, the self-assessed general health state, and positively with the Illness Intrusiveness scores. 69.6% of those with BDI above 19 reported decreased or missing well-being, this rate was 20.8% in those with BDI below 19 (OR: 8.7, 95%CI: 7.8-9.8). Depression was the main cause of daily limitations in 1.7% of the whole sample (2.3% in women and 0.8% in men). However this rate was much lower than the rate of those who signed musculosceletal (18.0%), or cardiovascular diseases (13.4%), regarding the extent of impairment, those with depression had the highest Illness Intrusiveness mean scores in both sexes, in all age groups.

**Conclusion:** Although depression was only the seventh most frequent cause of daily limitation, it caused the highest negative impact of everyday functioning, preceding all the other major illness groups, and significant decrease in the general well-being.

**Tuesday, April 5, 2005**

# SS-16. Section symposium: Biological rhythm in psychiatry

*Chairperson(s):* Manfred Ackenheil (München, Germany), J.P. Macher (France)
16.15 - 17.45, Gasteig - Room 0.131

## SS-16-01

Chronobiology and mood disorders

A. Wirz-Justice. *Universitätsklinik Psychiatrie Center für Chronobiologie, Basel, Switzerland*

Chronobiological abnormalities in mood disorders are well known to clinicians, however, the novel, non-pharmacological therapies that have arisen from biological rhythm research are not yet in general practice. The circadian clock in the suprachiasmatic nucleus drives the 24-hour pattern in psychological, physiological, neuroendocrine and biochemical functions, including the sleep-wake cycle. The main zeitgeber for the circadian clock is light, a treatment that has been most successfully applied in winter depression, but newly, also as an adjuvant to SSRIs in non-seasonal major depression. Bright light exposure rapidly increases serotonin turnover, thus acting on similar mechanisms as antidepressant drugs. The pineal hormone melatonin transduces the length of night into a "nighttime" signal. Exogenous administration of melatonin can resynchronise disturbed sleep-wake rhythms (such as in the blind); in depression, sleep quality is improved without any effect on mood. In spite of much research into circadian rhythms in affective disorders, there is no consensus as to which part of the clock mechanism has gone awry. When desynchrony occurs between rhythms, shifts and decrements of mood can be measured even in healthy subjects. Sleep deprivation or shifting sleep timing can improve depression. Chronotherapeutics - light, melatonin, (partial) sleep deprivation or sleep advance - have the disadvantage of not being patentable, not being in "easy-to-take" pill form, and not being promoted as simple everyday adjunct treatment strategies. They do have the advantage of appealing to the zeitgeist - patients would rather not take drugs - while being well-tested and neurobiologically active treatments.

## SS-16-02

Role of melatonin in the circadian system, melatonin and circadian organization of functions, melatonin and biological rhythms

P. Pevet. *Institut Federatif des Neurosciences de Strasbourg, Strasbourg, France*

The temporal organization of living organisms relies on clock(s) that generate rhythms and are capable for being entrained to environmental factors. Such clocks convey circadian information to the rest of the organism via nervous and/or endocrine pathways. Melatonin (Mel) secretion by the pineal during the night is under control of the circadian clock. The Mel rhythm is thus an efferent hormonal signal from the clock which can be used as a circadian mediator to any structure than can "read" it. Moreover, the duration of the nocturnal Mel secretion, which is proportional to the length of the night, allows the brain to integrate the photoperiod. Mel appears thus, to convey photic informations that are used for both circadian and seasonal organization.In Mammals, even if the presence of Mel receptors in the suprachiasmatic nucleus of many species indicates an hormonal feed-back on the clock, it was concluded that Mel has a very limited role in circadian organization. The Mel rhythm, however, is only one of the efferent signals of the clock and the little effect of pinealectomy on circadian organization could be explained by the integration of the circadian signal through other clock outputs. This does not preclude an important role for Mel in circadian organization. Indeed, i) subtle desynchrony of several physiological functions have been described after pinealectomy, ii) re-entrainment rate of the activity rhythm is modified in presence or absence of Mel after a phase-shift of the L/D cycle, iii) Mel administration in the SCN induces an increase in the amplitude of clock oscillations. Moreover, through involvement of Mel receptors within the clock, exogenous Mel can be used as a pharmacological tool to manipulate circadian processes (Chronobiotic effect). In rodents, Mel entrains

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