have suggested that a combination of susceptibility and possibly protective alleles at a number of loci determines the genetic risk of developing bipolar affective disorder in the individual. Some of the risk genes are possibly also involved in the etiology of schizophrenia.

Non-genetic risk factors have not been much studied. However, recently a few studies have suggested parental loss in childhood and possibly head trauma. Other non-genetic risk factors of importance in schizophrenia do not seem to influence risk in bipolar affective disorder.

Knowledge of specific risk factors will facilitate the identification of other risk factors.

The identification of risk factors involved in susceptibility to bipolar affective disorder will enable more specific knowledge on the etiology and development of the disorder. This may lead to improvement of treatment, treatment choice, diagnostic classification and perhaps even preventive measures.

S19. Severe OCD: recent advances in techniques for neurosurgical treatment

Chairs: P. Cosyns (B), S. Andréewitch (S)

S19.1

Neuroanatomy, neurophysiology and neuropathology of OCD

F. Hohagen*. *Universitätsklinikum Lübeck, Germany*

Research of the last decades has accumulated evidence that neurobiological factores play an essential role in the pathophysiology of obsessive–compulsive disorder (OCD). Clinical observations in neurological disorders with an underlying dysfunction of the basal ganglia system, e.g. Gilles de la Tourette-Syndrom or Sydenham's Chorea, have shown that patients exhibit significantly more often obsessive and compulsive symptoms in addition to the typical neurological symptoms. The most consistent finding from neuroimaging studies with Positron Emission Tomography (PET), Single Photon Emission Tomographie (SPECT) and functional Nuclear Magnetic Resonanz Tomography (fNMR) is that patients suffering from OCD show increased neuronal activities in the nucleus caudatus, orbitofrontal cortex and gyrus cinguli when compared to normal controls. Furthermore, confrontation with objects provoking obsessive–compulsive symptoms increase the activity of the fronto-striatal system, whereas successfull treatment with serotonin-reuptake-inhibitors or cognitive behavioural therapy decrease the activity of the frontostriatal loop. Thus, clinical observations and controlled studies using neuroimaging techniques provide evidence that dysfunction of the frontoorbitostriatal system may be crucial for the manifestation of the obsessive compulsive symptoms.

S19.2

Psychopharmacological treatment in severe and/or resistant OCD: augmentation strategies

E.-G. Hantouche*, J.F. Allilaire. *Mood Center, Pitié-Salpêtrière Hospital, Paris, France*

Despite significant progress in the pharmacotherapy of OCD, a large proportion of patients (30–40%) still resistant or respond poorly or partially to conventional treatments. The literature on the phenomenology and physiopathology of resistant OCD and on appropriate solutions still scare. Few strategies are successful and/or well documented by controlled or replicated studies. Moreover augmentation strategies proposed in refractory severe cases of depression are not always effective in severe resistant OCD. Promising data to augment the anti-OCD efficacy were obtained by using combinations of anti-OCD psychotropics (i.e. clomipramine plus SSRI), atypical neuroleptics plus SSRI (risperidone, olanzapine, pimozide), precursors of serotonine (i.e. tryptophan). Other probes acting on the 5HT transmission (such as buspirone, fenfluramine, lithium, clonazepam) or agents acting on impulsivity (such as antiandrogen drugs, valproate) were also tested. In the moment, the clinicians should be able to face complex and severe OCD without any rigid algorithm. A practical approach should include: 1) early screening of the illness in the primary care system (i.e. juvenile onset OCD); 2) maximizing the effectiveness of the first trials; 3) systematic searching for comorbidity (especially hidden soft bipolarity); 4) better understanding of OCD subtypes with regard to phenomenological clustering; 5) finally, better utilization of the available non-drug treatments (multimodal CBT, intensive individual and/or group therapy...).

S19.3

Capsulotomy, a valid treatment for extreme OCD?

S. Andréewitch*, C. Rück, K. Flyckt. *Karolinska Hospital, Department of Clinical Neurosciences, Stockholm, Sweden*

There is uncontrolled evidence to suggest that capsulotomy may benefit OCD-patients refractory to standard treatment. Since brain regions affected by surgery are assumed to be involved also in executive cognitive function, a crucial issue is whether there is a price, in terms of cognitive dysfunction, which the patient may have to pay for any symptom amelioration. Follow-up studies point to a highly significant symptom reduction in operated patients. Neuropsychological function seems to remain essentially intact over time. However, a subgroup of patients show more perseverative responses on the Wisconsin Card Sorting Test (WCST), indicating dysfunction in systems involving the frontal lobes. A recently completed follow-up study at our center, of patients with non-OCD anxiety, operated with thermo- capsulotomy between the years 1975–91, indicate a greater than expected incidence of cognitive side effects. Although a different diagnostic group, the neurosurgical intervention is identical to that performed on OCD-patients. A long term follow-up of OCD patients is currently under way. Issues of relevant follow-up evaluation and directions for further research will be discussed.

(1) Nyman H., Andréewitch S. Applied Neuropsychology, 8: 91–98, 2001
(2) Rück C, Andréewitch S. Poster, ANPA 2000

S19.4

Deep brain stimulation in severe treatment refractory OCD

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Stereotactic capsulotomy, making precisely aimed lesions in the anterior limbs of internal capsules, has been performed for years for severe, long-standing, treatment-refractory OCD. Both prospective and follow-up studies suggest that this last-resort therapeutic option may not be discarded. The complication rate is low. Symptoms improve substantially for +/- 40% to 60% of the carefully selected, refractory OCD patients.

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Ethical considerations concentrate around the irrevocable destruction of brain tissue against the physician's ethical obligation to at least present and discuss al appropriate options for treatment to patients who failed available pharmaco- and psychotherapy.

Deep Brain Stimulation (DBS) capitalises on the knowledge of specific dysfunctional brain circuits in OCD. DBS in the same target region as capsulotomy may improve OCD by altering activity within dysfunctional circuits. Advantages of DBS are its reversibility and dynamic character (parameter settings). The spatial extent can be modified postoperatively and parameters can be set and adjusted for optimal control of symptoms while minimalizing side effects. Moreover DBS can be turned on and off in a blinded fashion, allowing randomised controlled double-blind crossover studies to establish its efficiency.

S20. Is there a role for infectious agents in the etiology of psychiatric disorders

Chairs: H. Emrich (D), H. Karlsson (S)

S20.1
Epidemiology of schizophrenia

P.B. Mortensen. *Denmark*

No abstract was available at the time of printing.

S20.2
Toxoplasma infection in schizophrenia

R.H. Yolken. *USA*

No abstract was available at the time of printing.

S20.3
Persistent RNA viruses and nervous system dysfunctions

K. Kristensson*. *Department of Neuroscience, Karolinska institutet, Stockholm, Sweden*

A short review on how RNA viruses can be targeted to limbic structures and monaminergic groups of neurons in the brain will be given. Certain viruses may cause neuronal destruction and be cleared, but the host animal may be left with disturbances in their behaviour by a "hit-and-run" mechanism. Other viruses may remain at a low level of replication in the brain, in which production of certain immune-derived cytokines can persist. We will present data on how a neurotropic strain of influenza A virus can persist in the brain of immunodefective mice and after a foetal infection in wild type mice. Effects of this virus and cytokines on development of synaptic connectivities and the repertoire of neurotransmitters in neurons will then be described.

S20.4
Endogenous retroviruses and schizophrenia

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[2]*Department of Psychiatry, University of Heidelberg, Heidelberg, Germany*
[3]*Stanley Division of Developmental Neurovirology, Johns Hopkins University School of Medicine, Baltimore, MD, USA*

Despite many years of research, the cause of schizophrenia has not been identified. Even though evidence for genetic as well as environmental influences are accumulating, no gene or specific environmental agent has so far been shown to cause the disease. During screening for the presence of retroviral RNA in postmortem brain tissue from individuals with schizophrenia, we identified the differential presence of human endogenous retrovirus (HERV)-W sequences in cases as compared to controls. In postmortem tissue from chronic patients HERV-W sequences were differentially up-regulated as compared to the corresponding tissue from individuals with a diagnosis of bipolar disorder or healthy controls. These sequences were subsequently found to be present in particle fractions of both cerebrospinal fluids and plasma of individuals with recent onset schizophrenia or schizoaffective disorder. Such sequences were either absent or much less prevalent in healthy controls or individuals with non-inflammatory neurological disorders.

S20.5
Depression and Borna disease virus (BDV)

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Objectives: Risk-assessment of productive BDV infections in depressed patients using novel markers.

Methods: A tripel ELISA separately detecting BDV-specific circulating immune complexes (CICs), major proteins, and antibodies in plasma. Additionally, amplification of genetic material (BDV p40-gene) by RT-PCR.

Results: BDV, an unique enveloped RNA-virus (*Bornaviridae*), causes behavioural syndromes in animals, alike to mood disorders in man. Monitoring of blood from patients with Major Depression or Bipolar Disorder revealed the presence of BDV-CICs in up to 90–100%, indicating a high prevalence of active infections. Severity of depression correlated with high levels of BDV proteins (antigenemia) and RNA, paralleling CICs and antibodies. By contrast, healthy volunteers may carry (more or less) "latent" BDV infections in 20–30%.

Conclusions: Active BDV infection states appear to be a frequent risk in depression, which can now be assessed by high-quality blood tests and eventually treated.

S20.6
Amantadine treatment in neuropsychiatric disorders with BDV infection

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Borna disease virus (BDV) is a neurotropic, negative and single strained enveloped RNA virus that persistently infects various

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