

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

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### S19.1

Neuroanatomy, neurophysiology and neuropathology of OCD

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Research of the last decades has accumulated evidence that neurobiological factors 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 successful 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 fronto-orbito-striatal system may be crucial for the manifestation of the obsessive compulsive symptoms.

### S19.2

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

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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 scarce. 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 serotonin (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?

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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.