de la Tourette syndrome and self-injurious behaviour were each present in only one patient.

It is concluded that not only major depression but also atypical bipolar disorder, so called unstable mood disorder, can frequently be observed in DS. Moreover, a range of psychiatric and somatic disorders are important in the differential diagnosis of behavioural abnormalities in DS patients.

S31.4

Neuroanatomy and psychopathology of co-morbid learning disability and schizophrenia

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Reasons for the higher frequency of schizophrenia in learning disabled populations are uncertain. They were investigated by clinical, imaging and genetic studies of matched patients with learning disability and schizophrenia (co-morbid group), schizophrenia alone and learning disability alone. The co-morbid group had more negative symptoms, episodic memory deficits, and soft neurological signs than the other two groups. Co-morbid subjects had a tendency to belong to multiply affected families and showed high rates of chromosomal variants. Structural scans of the three groups were compared with those of matched normal controls. The scans of the co-morbid subjects were closely similar to those of the subjects with schizophrenia alone. The amygdala hippocampus on both sides was significantly smaller than that of the normal controls. The brain of the learning disabled patients were generally smaller than those of the other three groups, but the amygdalo-hippocampal complexes were not reduced in size. Thus, in terms of brain structure, patients with co-morbid learning disability and schizophrenia resemble patients with schizophrenia and not those with learning disability.

S32. Clinical aspects of cholecystokinin research

Chairs: J. Shlik (FIN), T. Gunnarsson (S)

S32.1

Mice lacking CCK2 receptors display reduced anxiety in the plus-maze

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Studies on rodents suggest that the neuropeptide cholecystokinin (CCK) increases anxiety via CCK2 receptors. In the present study the exploratory behaviour of female mice, lacking CCK2 receptors, was analysed in the elevated plus-maze. Furthermore, the action of diazepam, a benzodiazepine agonist, was studied in these animals. Homozygous (-/-) CCK2 receptor deficient mice made more visits to open arms and spent greater time in the open parts compared to wild-type (+/+) littermates. The administration of diazepam (0.5–3 mg/kg) significantly increased the exploratory behaviour of wild-type mice. However, the action of diazepam was even stronger in mutant animals. Diazepam (0.5–1 mg/kg) significantly affected the ethological parameters of plus-maze exploration in homozygous mice, but not in wild-type animals. The highest dose of diazepam (3 mg/kg) reduced the number of closed arm entries in mutant mice. Nevertheless, mice lacking CCK2 receptors spent a significantly longer time in the open arms compared to wild-type mice. Accordingly, the targeted disruption of the CCK2 receptor gene reduces anxiety of mice in the plus-maze. The anxiolytic and motor suppressant action of diazepam are also increased in mutant mice.

S32.2

Natriuretic peptides modulate the psychometric and endocrine effects of cholecystokinin tetrapeptide in man

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While Atrial Natriuretic Peptide (ANP) has a high affinity for natriuretic A-type receptors, C-type natriuretic peptide (CNP) binds primarily to natriuretic B-type receptors. In pre-clinical studies these two peptides show opposite effects on stress hormone secretion and anxiety behavior: ANP displays an anxiolytic action in rodents, whereas CNP is anxiogenic.

We investigated the effects of ANP and CNP upon experimentally provoked panic attacks in humans using cholecystokinin tetrapeptide (CCK-4).

In different studies, panic patients and healthy controls were pretreated with intravenous infusions of ANP, CNP and or placebo from 11:40 to 11:10 in double-blind, randomized and balanced designs. At 11:00 all subjects were given CCK-4 as an intravenous bolus injection. Provoked panic and anxiety symptoms were assessed before and after CCK-4. Adenocorticotropic Hormone (ACTH) was measured in plasma using a radioimmunoassay.

By ANP pre-treatment, Acute Panic Inventory ratings after CCK-4 were significantly lowered compared to placebo pre-treatment in panic patients ($p<0.05$), but not in controls. The release of ACTH after CCK- 4 was significantly reduced in both patients and controls by ANP vs. placebo pre-treatment. CNP pre-treatment significantly increased visual analogue scale ratings for "anxiety", while no effect upon panic symptoms was observed in normal controls. The stimulated release of ACTH was significantly increased by CNP.

Also in man ANP has anxiolytic-like effects on CCK-4-induced anxiety symptoms and concomittantly reduces ACTH activation. In contrast, CNP increases the anxiogenic action of CCK-4 and enhances the ACTH surge after CCK-4. The pharmacotherapeutic potential of both A-type natriuretic peptide receptor agonists and B-type antagonists as novel anxiolytics needs further research.

S32.3

Cholecystokinin-serotonin interactions

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Cholecystokinin (CCK) extensively interacts in the brain with other neurotransmitter systems. The relationship between CCK and serotonin (5-HT) is important for various brain functions including the regulation of anxiety, pain, food intake and neuroendocrine stress response. Furthermore, CCK neurotransmission may be involved in the mechanism of action of the 5-HT-acting medications that are increasingly used in the treatment of numerous psychiatric disorders. The studies so far suggest that treatment with drugs that enhance 5-HT transmission attenuates CCK-4-induced panic attacks in patients with panic disorder and indicate a possible role

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