

results have lead to the hypothesis that a dysfunction of prefrontal-striatal circuitry underlies this syndrome.

Recent studies have demonstrated a cognitive role for the cerebellum, including attention. Clinical data, such as subtle neurological signs or cerebellar-vestibular test impairment seen in children with ADHD, suggest that the cerebellum may also play a role in the pathophysiology of this syndrome.

Morphometric MRI studies have been conducted in 74 right-handed boys and girls with ADHD, and 87 healthy controls. Psychiatric interview and neuropsychological evaluation have been performed in every cases. Cerebellar and vermal volumes as well as vermal midsagittal area have been quantified using an image analysis software. Three groups were collected together with the separate age and sex and handedness matched healthy controls over a 5 years period at the NIMH: 1) a group of boys with ADHD 2) a separate group of ADHD medication naive subjects 3) a group of ADHD girls.

Total cerebellar volume did not differ between ADHD and control groups. Within the 3 studies results were similar. Vermis midsagittal area and volumes were significantly smaller for ADHD subjects than for controls. This reduction involved particularly the posterior-inferior lobe (lobules VIII-X) in the three groups. These results remain significant after adjustment for total brain volume, age, or IQ (analysis of covariance).

The studies suggest that dysfunction of cerebellar-thalamo-prefrontal circuitry may subserve the motor control and motor inhibition deficits encountered in ADHD. Cerebellum may also play a role in executive function deficits, acting probably as a co-processor interfering with prefronto-striatal loop enhancing speed and efficiency. Further clinical analyses and functional imaging studies have to be conducted in order to better understand neural networks involved in cognitive deficits in this syndrome.

#### S24-4

##### THE EFFECTIVENESS OF METHYLPHENIDATE ON ATTENTION PROCESSES IN ADHD CHILDREN

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It was investigated whether children with ADHD show abnormalities in early and/or late attentional processes, and in which way methylphenidate (MPH) influences such processes. Early attentional processes were studied in a selective attention paradigm, in both the auditory and the visual modality. The capacity of late attentional processing was studied in a visual dual task paradigm. During the tasks, event-related brain potentials (ERPs) were measured.

For each task, a group children with ADHD and a group normal control children, age 7-12, was measured. Thereafter, the ADHD children participated in a double-blind placebo controlled study, using the same tasks, in which the effects of 15 mg MPH were determined. With respect to early selection processes, it was found that ADHD children performed worse than controls in both modalities. Also, ADHD children showed smaller ERP-peaks which were related to early auditory selection processes. Effects of MPH, however, were most clearly seen in the visual condition.

With respect to later attentional processing, ADHD children showed worse performance. Evidence was found that ADHD children show a late attentional capacity allocation-defect. MPH had an enhancing effect on both performance and ERPs.

It was concluded that MPH has a non-specific ameliorating effect on performance and ERP-peaks, rather than alleviating specific defects.

#### S24-5

##### THE INFLUENCE OF METHYLPHENIDATE ON ATTENTION AND IMPULSIVITY OF ADHD-CHILDREN: A PHARMACOLOGICAL DISSECTION STUDY

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The effects of methylphenidate (MPH) on performance and ERP's in a selective attention task (Dichotic Listening), capacity-allocation task (irrelevant probe technique) and in a inhibition task (stop signal paradigm) were studied in 14, 14 and 16 schoolaged ADHD children. Besides the effect of methylphenidate, te effects of L-dopa and desipramaine on inhibitory-processes in 16 ADHD children were studied. Results showed that Methylphenidate enhanced performance on selective attention and cognitive evaluation but not oninhibition-task, while MPH enhanced PN and P<sub>3</sub> amplitudes. Desipramine (a noradrenergic agonist) was the only drug that influenced inhibition performance. Implications of these results will be discussed.

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## SEC25. Diagnosis and treatment of impulse regulation disorders in mentally retarded patients

Chairs: W Verhoeven (NL), S Tuinier (NL)

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#### SEC25-1

##### DIAGNOSIS AND NEUROBIOLOGY OF IMPULSE CONTROL DISORDERS

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Impulse control disorders encompass a broad variety of behavioral disorders grouped together on a descriptive level because they have as common denominator an exacerbation of some sort of behavior. In clinical psychiatry disordered impulse control in a restrictive sense is closely linked to the so-called personality disorders in spite of the fact that abnormalities on the behavioral level can occur in a variety of clinical conditions. The dimensional idea in biological psychiatry advocated the approach that biological dysfunctions may be linked to specific psychological dysfunctions irrespective the nosological context in which they occur. Meta analysis of these kind of studies revealed, however, that disturbed central serotonin metabolism is associated with impulsivity only within the context of other disorders e.g. personality disorders. In mental retardation treatment studies with serotonin modulating compounds (e.g. SSRI's and 5-HT<sub>1</sub> agonists), targeted at behavioral disorders, show beneficial effects that can at least partly be explained by the effect on non-targeted aspects such as arousal, stress reactivity and sensory hypersensitivity. In a variety of cases modification of disturbed behavior seems to be secondary to the successful treatment of underlying neuropsychiatric disorders that may present with atypical symptom profiles. Especially syndromes not regularly thought, are of importance such as: unstable mood disorder, cycloid psychosis, stress feed-back resistance and unspecified bipolar disorder. So, in spite of accumulating data from

the dimensional vantage point, careful neuropsychiatric diagnostic procedures remain mandatory.

- (1) Verhoeven WMA, Tuinier S. The effect of buspirone on challenging behaviour in mentally retarded patients: an open prospective multiple-case study. *Journal of Intellectual Disability Research*, 40: 502–508; 1996.

### SEC25-2

#### STRESS HORMONES AND IMPULSE REGULATION

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The precise nature of impulsive behavior and some of its consequences such as aggression, self-injurious behavior or challenging behavior and other types of behavioral disinhibition is not well understood. In the case of outward directed aggressive behavior several clinical studies suggest an involvement of central serotonergic activity in subgroups of patients (Tuinier et al. 1996). The nature of aggressive behavior in mentally retarded subjects has been far less studied with respect to its biological background. Frequent manifestations of disordered behavioral control include self-injurious behavior and stereotyped movement disorder, that has been linked to disturbances in the availability of endogenous opioids, dopamine hypersensitivity and central serotonergic dysfunction. Since these biological parameters are also closely linked to the functional status of the stress system, we studied basal levels of the stress hormonal parameters ACTH, beta-endorphin, prolactin, cortisol, free cortisol and transcorin in 64 mentally retarded subjects with either self-injurious behavior and/or stereotyped behavior or without these phenomena. We found major effects on stress parameters of concomitantly prescribed anticonvulsants and oral contraceptives, no indication that beta-endorphin is related to these behavioral disorders and some support for the hypothesis that stereotyped behavior and self-injurious behavior are related to disordered stress homeostasis. This finding is also supported by the observation that mentally retarded subjects as a group might be more vulnerable to develop pathological states of arousal and might also possess less capacity to counteract deviations from their emotional and behavioral set point with serotonergic mechanisms.

- (1) Tuinier S, Verhoeven WMA, Van Praag HM. Serotonin and disruptive behavior; A critical evaluation of the clinical data. *Human Psychopharmacology* 11; 469–482: 1996.

### SEC25-3

#### BEHAVIORAL PHENOTYPE AND DISTURBED IMPULSE CONTROL

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Behavioral phenotypes are recognizable characteristic patterns of behavior associated with genetically determined disorders. For some of the so called genetically determined syndromes associated with mental retardation the characteristic pattern includes oppositional, explosive and at times aggressive behavioral features.

One of our behavioral phenotype research projects was aimed at clarifying and documenting these manifestations of disturbed impulse control behavior. These distinctive behavior characteristics

for the demarcation of some of the genetically determined syndromes associated with mental retardation are reviewed for Prader-Willi syndrome, Velo-Cardio Facial syndrome, Smith-Magenis syndrome and a syndrome caused by a terminal deletion on chromosome 8p. Our experience indicates that patients with the association of mental subnormal development and disturbed impulse control should be examined by an experienced clinical geneticist.

### SEC25-4

#### DIFFERENT DIAGNOSTIC SYSTEMS IN DESCRIBING AGGRESSION IN MENTAL RETARDATION

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There is no diagnostic entity of aggression in either of the two major classificatory schedules in psychiatry, DSM-IV and ICD-10. Although aggressive behaviour is common in many mental illnesses and personality disorders it has not been considered that any one psychiatric illness or personality disorder is defined by abnormal control of aggression. These two schedules recognise the existence of disorders of control of impulsivity as discreet diagnostic entities, depicted by the terms emotionally labile personality disorder and intermittent explosive disorder in DSM-IV. Within a sample of people with mental retardation it is only the rare chronic aggressive subject that falls into either of these two categories.

Thirty chronically aggressive mentally retarded subjects in hospital were examined closely according to ICD-10 and DSM-IV schedules. An attempt was also made to classify each patient according to Sovner's four domain classification of behaviour disturbance.

The results showed that only a few patients could be adequately classified under the heading of impulsive or antisocial personality disorders. The majority of patients showed irritability and aggression related to environmental changes. Most of the patients were only satisfactorily classified under the heading of organic personality disorder or syndrome on the basis of pre-existing brain damage responsible for the degree of intellectual impairment.

In the classification of aggression it may be more heuristically valuable to describe aggression according to the nature of the aggressive act, e.g. verbal, physical, destructive, self-harming.

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## S26. The impact of schizophrenia on the patient's life

*Chairs:* H Häfner (D), D Naber (D)

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### S26-1

#### HISTORY OF TREATMENT SYSTEMS AND THEIR CONSEQUENCES FOR THE LIFE OF SCHIZOPHRENICS

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In the course of this century, treatment systems in psychiatry have undergone dramatic changes. From the asylum era of the first half of this century, there has been a sometimes gradual, sometimes irregular move in the direction of a community-based system of care delivered to geographically delimited catchment areas. People suffering from schizophrenia have been the main