

Studies to date suggest that offenders with these disorders present multiple difficulties and that in order to prevent further offending it is necessary to specifically address each of these difficulties. The present study was designed to: (1) identify the components of treatment, social services, and laws that effectively prevent crime among persons with major mental disorders; (2) to verify if different types of patients require different treatment programmes; (3) to measure the impact of varying legal powers of clinicians to enforce compliance with treatment; (4) to assess the predictive validity of the HCR-20 in determining the risk of violence; and (5) to assess the validity of hair analysis for measuring medication use and alcohol and drug consumption. In each of four sites, Canada, Finland, Germany and Sweden, two samples of patients with major mental disorders are recruited, one with and one without an official record of crime. As they enter the study, detailed historical information is collected from files and collaterals and they are intensively examined. During the next two years, they are repeatedly examined, collaterals are questioned, all the treatments and services that they receive are documented as well as criminal activities and aggressive behaviours.

S25.03

THE BEHAVIOURAL PSYCHOPATHOLOGY OF BLOOD DISORDERS. A CROSS-NATIONAL STUDY

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There are known higher levels of secondary psychological problems amongst children with Chronic Illness. Although there is some evidence of this in children with b-thalassaemia, the evidence is conflicting for children with haemophilia. This study addresses these themes in children from families with haemophilia or b-thalassaemia.

Children with haemophilia were half as likely to receive a diagnosis of psychiatric disorder and less likely to show a higher degree of impairment of general functioning and social dysfunction than thalassaemic boys. That was true too when children with thalassaemia were compared with their siblings. Clinical severity of haemophilia or thalassaemia was not associated with significant differences in prevalence of child psychiatric disorders or impairment or social dysfunction.

The relatively low prevalence of psychiatric impairment and social dysfunction in boys with haemophilia may be related to therapeutic advances that enable them to lead an almost normal life. The high prevalence of psychiatric impairment and social dysfunction, in children with beta-thalassaemia reported in this study suggests that different blood disorders are associated with a different impact.

S25.04

THE EURO-MDSBL PROJECT: DEVELOPING COMMON STANDARDS FOR THE ASSESSMENT OF DISABLEMENT IN MENTAL AND NEUROLOGICAL PATIENTS IN SIX EUROPEAN COUNTRIES

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The Euro-MDSBL project deals with the application of the ICIDH-2 in mental and neurological disorders and the development of dedicated assessment instruments for disablement, which can be

used, in both mental and physical disorders. It involves collaboration of six research centres from Greece, Italy, Luxembourg, the Netherlands, Spain and the UK. The network is functioning within the context of the WHO collaborative study of assessment instruments for disablements. The study involves the use of both qualitative and quantitative methods. The first phase, (Cross-cultural Applicability Study), involved the collection of data related to the effects cultures exert on the definition of the concept and domains, facets and severity of disablement. Through this procedure, the concepts of disablement were assessed at a very deep level and this study offered valuable insights and understanding, in order to reach to a classification and instruments applicable across cultures. After these studies, the findings were incorporated into the draft instrument (WHODAS-II). As a pre-test, 254 individuals from the six centers we assessed. Cases came from the following 5 populations: individuals with physical health problems, mental health problems, and alcohol problems, problems due to illicit drugs and general population. The study continued with the main study (reliability and validity) of the final instrument. A minimum of 100 individuals per site was assessed with the final WHODAS-II (34-item version) and other instruments assessing functioning and quality of life. This phase has also been completed. The results have shown the instrument to possess high test-retest reliability and validity across all six centres. The Euro-MDSBL is funded by the BIOMED-2 program (concerted action BMH 4-98-3388) and the WHO collaborative study for the assessment of disablement.

S26. Metabolism of amino-acids and synthesis of β -carbolines in relation to psychopathology

Chairs: L. Peppinkhuizen (NL), W.M.A. Verhoveven (NL)

S26.01

THE INTERRELATIONSHIP BETWEEN AMINO ACIDS AND β -CARBOLINES

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The amino acid tryptophan is not only the precursor of serotonin and nicotinamide, but also of the aromatic alkaloids called β -carbolines. The endogenous tetrahydro- β -carboline (THBC) may be formed by cyclisation of indoleamines or tryptophan with aldehydes or α -keto acids. The dehydrogenated form of THBC, the fully aromatic and lipophilic β -carboline norharman, is present in several mammals. The source of norharman in humans may also be from outside, because this substance is present in various foodstuffs as well as in some alcoholic beverages and tobacco smoke.

Specific binding sites of norharman have been demonstrated in rat brain, while this β -carboline has also low affinity for the benzodiazepine receptor. When injected in animals, norharman causes tremors, induces pro-conflict behaviour, convulsions, a decrease in motor and exploratory activity, sedation and muscle relaxation. The variation in the plasma concentrations of norharman in humans has been related to several psychopathological states, e.g. alcoholism, heroin addiction, psychoses and panic disorder.

The formation of β -carbolines, such as norharman, has been demonstrated tentatively in patients with acute polymorphic psychoses. In experiments with rats, the formation of norharman has

been demonstrated definitively, yielding consequently an experimental model for this type of psychosis.

In a study with morphine dependent rats it was found that norharman antagonizes the withdrawal symptoms, which were precipitated after injection of the opiate antagonist naloxone. Moreover, norharman inhibits cocaine selfadministration in rats made dependent on this drug. Furthermore, a physiological role for norharman is suggested because of the existence of a circadian rhythm in humans.

S26.02

ACUTE POLYMORPHOUS PSYCHOSIS DUE TO ENDOGENIC SYNTHESIS OF β -CARBOLINES

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In many patients the transient acute polymorphic disorders according to the ICD-10 is characterized by the presence of distortion of sensory perceptions, identical with those observed in hallucinogenic drug induced states.

In these patients deranged plasma concentrations of amino acids involved in one-carbon metabolism have been demonstrated. This has led to the hypothesis that a disturbed amino acid metabolism, that is accelerated breakdown of serine into glycine, will result in the excess formation of methylene-tetrahydrofolate. The latter will dissociate into TH₄ and formaldehyde which in turn will react with monoamines to form β -carbolines (like norharman) and tetrahydroisoquinolines.

After recovery from a psychotic episode, (double blind) performed oral challenge with low doses serine, glycine, methionine, and alanine did show the increased conversion of serine into glycine. Moreover, patients loaded with serine and some with glycine experienced depersonalization, psychedelic or even psychotic symptoms for many hours on the day of experimentation.

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S26.03

THE HALLUCINATIONS-INDUCING EFFECT OF β -CARBOLINES

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Hallucinations are a fundamental feature of mental illness. The symptoms of hallucinations of endogenous psychoses and during hallucinogenic drug inebriation overlaps (Hollister L, 1962). β -Carbolines (BC) might bridge over the gap between endogenously and exogenously induced hallucinations because they occur both in humans and plants (Honecker and Rommelspacher, 1978) and display hallucinogenic properties in humans (Naranjo C, 1979). In a first study, 30 chronic alcoholics with carcinoma of the upper digestive tract were studied. Despite prophylactic treatment 50% of the patients developed withdrawal hallucinations. They had increased norharman (BC) levels almost reaching 300% compared to patients with a vegetative withdrawal syndrome. Another group of patients treated with gammahydroxybutyric acid developed withdrawal hallucinations as well and had elevated harman (1-methyl-BC) levels preceding the psychosis (Spies et al., 1998). The relationship between increased norharman levels and withdrawal

hallucinations were confirmed in a second group of multiple-injured chronic alcoholics (Spies et al., 1996). One cause for the development of hallucinations could be the disposition to increased levels of BCs due to their increased biosynthesis under certain conditions like alcohol withdrawal and stress. A genetic polymorphism has been found recently which was associated with increased levels of norharman and harman. Studies are in progress to reveal relationships between the polymorphism and hallucinations.

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S26.04

AMINO ACIDS AND NORHARMAN IN DEPRESSION AND PANIC DISORDER

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Introduction: Brain serotonin (5-HT) is synthesized from the amino acid tryptophan (trp) via 5-hydroxytryptophan and is involved in many psychiatric disorders e.g. depression, panic disorder and behavior as hostility and aggression. The availability of trp in the brain is determined by the concentrations of this amino acid but also by the concentrations of other large neutral amino acids which compete for the same a carrier protein in the blood brain barrier.

The β carboline norharman is a aromatic alkaloid which can be detected in very low concentrations in human plasma. Norharman is probably synthesized from trp and has thought to have affinity for several brain receptors such as the benzodiazepine receptor.

Aim of the Study: To investigate the intercorrelations between biochemical (amino acids, norharman) and psychological (anxiety, aggression, depression) parameters in patients suffering from panic disorder and/or depression.

Methods: In 74 patients suffering from panic disorder and or depression and in 54 healthy controls trp, tyrosine (tyr), 5-HT, norharman and psychological functioning as rated on the SCL-90; Defense Mechanism Inventory (DMI) and Utrecht Coping List (UCL) are measured

Results: In the patient group as a whole we observed significant ($p < 0.05$) negative correlations between aggression, hostility and depression as measured on the DMI and SCL-90, and 5-HT in platelets and plasma. Low concentration of norharman discriminated the patientgroup with panic disorder from patients suffering of depression and controls.

Conclusions: The negative correlations between 5HT in platelets and plasma with aggression, depression and hostility support the suggested coupling between aggression and depression with a low functioning serotonergic system.

The negative correlation between norharman and panic disorder fits well in the possible activity of norharman as a benzodiazepine receptor agonist. A decrease in this agonist function could possibly lead to increased anxiety.