

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.