A17

DEPRESSIVE-PARANOID SYNDROME IN ALCOHOLISM AND SULPIRIDE THERAPY. C. Perez de Franciso and M. Farnos, National Institute of Neurology, Mexico City, Mexico.

The mixture of depressive and paranoid features in some syndromes occurring frequently among alcoholics can structure different clinical presentations (the jealous delirant snydrome, for instance). But the main characteristics are paranoid ideas and melancholic mood. Those are precisely two therapeutical dimensions of sulpiride, a polivalent benzamide. It is also useful for gastritis and some cenestopathies. Using the model that *Abe and Perez de Francisco* proposed recently about the pharmacological profile of sulpiride, the authors illustrate the indications and possibilities of the drug, in alcoholic psychopathological syndromes.

A18

GENETICS AND DEVELOPMENT OF ALDEHYDE DEHYDROGENASE IN THE MOUSE; EVIDENCE FOR THREE STRUCTURAL GENES. Roger S. Holmes and Glenn P. Timms, School of Science, Griffith University, Nathan. 4111. Australia.

The mouse is widely used as a model organism for studying genetic and biochemical aspects of alcohol metabolism in man. Aldehyde dehydrogenase (AHD) catalyses the second step in the oxidation of ethanol in mammals, converting acetaldehyde to acetate. Mouse liver AHD is differentially distributed in the cell, being found in the mitochondrial (AHDm), cytoplasmic (AHDs) and microsomal (AHDe) fractions. Electrophoretic variants for AHDm (R. S. Holmes. *Biochem. Genet. 16*: 1207 (1978)) and AHDs were used to provide evidence for 3 structural genes for AHD in this organism; *Ahd-1* (encoding AHDm); *Ahd-2* (encoding AHDs); and *Ahd-3* (encoding AHDe). *Ahd-1* and *Ahd-2* have been mapped on chromosomes 4 and 19 respectively. Developmental studies using fetal, neonatal and maturing animals provided evidence for extensive increases in activity of the 3 isozymes postnatally.

A19

REGULATION OF ALCOHOL PREFERENCE IN EXPERIMENTAL ANIMALS. C.J. Peter Eriksson, Ph.D., Research Laboratories of the State Alcohol Monopoly (Alko), Helsinki, Finland.

A number of studies have implicated ethanol and acetaldehyde metabolism and brain transmitter changes as central factors regulating voluntary alcohol intake in laboratory animals. The aim of the present study is to summarize the results of the investigations. The basis for this endeavor is to categorize the factors affecting drinking behavior into aversive and reinforcing mechanisms.

The only consistant aversive factor regulating alcohol preference seems to be acetaldehyde metabolism. Thus, animals with lower capacities for the elimination of acetaldehyde during ethanol oxidation exhibit lower alcohol preference than those with higher acetaldehyde elimination capacities. The proposed mechanism is an inhibition of brain aldehyde dehydrogenase activity, which results in higher brain aldehyde levels although a peripheral toxicity of acetaldehyde cannot be excluded.

Such a consistent pattern cannot be seen in the relationship between brain transmitters and preference. However, one factor, which may explain this inconsistency, is that the transmitter changes (mainly catecholamines and serotonin) not only affect directly the alcohol preference but also food intake and utilization. This in turn could be the main regulation and reinforcer of alcohol intake at least before any form of dependence is established. It is suggested that any factor which increases food utilization also increases alcohol preference of an experimental animal, providing that possible aversive factors are unchanged.

A20

Alcohol Feeding Alters ^{3}H Dopamine (DA) Uptake Into Rat Cortical and Brain Stem Synaptosomes. A.T. Tan, R. Dular and I.R. Innes. Dept. of Pharmacol. and Therap., Univ. of Manitoba, Fac. of Med., Winnipeg, Canada.

Reuptake into nerve endings is generally believed to be responsible for the termination of dopamine action in brain. Isolated nerve endings (synaptosomal fraction, P_2) from Long Evans male rats weighing approx. 450 g were incubated in Krebs Ringer phosphate buffer, pH 7.4, in the presence of 5×10^{-8}M ^{3}H DA. In 5 min, at room temperature, the ^{3}H DA uptake into cortical P2 from control, chronic alcoholic, and chronic alcoholic rats with 48 and 120 hr withdrawal from alcohol are: 6.54±0.01, 4.77±0.28, 9.32±0.22 and 9.24±0.01 n ole/g protein (n=3, ±S.E.M.), respectively. The corresponding values for brain stem P_2 are: 4.35±0.18, 3.08±0.28, 2.88±0.13 and 2.77±0.06. These alterations were also observed in rats given an acute dose of ethanol (2.5 g/kg) by i.p. injection. In vitro incubation of control P_2 with 50 and 100 mM ethanol did not significantly affect the ^{3}H DA uptake into cortical P_2 but slightly (about 15%) inhibited that into stem P_2. The highly significant ($P<.005$) changes of DA uptake into P_2 under various stages of alcohol intoxication suggest a possible effect of alcohol on central actions of dopamine.