POSTER SESSIONS

INTRAHIPPOCAMPAL INFUSION OF THE ß-CARBOLINE HARMAN IN LAD RATS INCREASES ALCOHOL DRINKING AND HIPPOCAMPAL LEVELS OF SEROTONIN AND NOREPINEPHRINE.

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Previous studies show that harman (1-methyl-ß-carboline) induces voluntary alcohol drinking in rats when it is administered systemically or ICV. The aim of the present study was to determine whether the long-term infusion of harman into the dorsal hippocampus evokes drinking of alcohol in the genetically bred low alcohol drinking (LAD) rat. Following a standard 3-30% alcohol preference test, a cerebral cannula was implanted in the dorsal hippocampus in each of 18 rats. The cannula was attached to an osmotic minipump which delivered vehicle or harman at a rate of 1.0 or 3.0 µg/h for a period of 14 days. Four days after surgery, all rats underwent a second 3-30% alcohol preference test. Both doses of harman increased the voluntary intake of ethanol to the same extent, particularly in 11 - 30% concentrations, and enhanced the daily intake of food. Hippocampal tissue levels of 5-HT and norepinephrine were elevated in a dose-dependent manner. These results demonstrate that the long-term exposure of hippocampal neurons to harman induces a preference for alcohol even in a line of rats without a genetic predisposition. This drinking response paralleled increased levels of serotonin and norepinephrine in the hippocampus. Supported by NIAAA Grant AA 04200-10.

NEW DRUG DEVELOPMENT --- ALZHEIMER'S DISEASE

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Tacrine (Cognex) is now FDA approved and is currently the only drug specific for Alzheimer's Disease. Because of the frequency of Alzheimer's disease and the disability it causes many new drugs are currently in development specifically for this condition. The mechanisms of action of these drugs will be discussed (10 different mechanisms) and 20 different drugs in development will be mentioned. Although none represent a cure, new drug development in Alzheimer's Disease is entering a new era.

Paroxetine in Major Depression: a double blind comparison with fluvoxamine.

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135 in and outpatients fulfilling the criteria for DSMIIIR major depression, who scored at least 18 points on the 21-item Hamilton Depression Rating Scale (HAMD) were entered into this 6 week double-blind study: 120 (56 paroxetine, 64 fluvoxamine were evaluable on an intention to treat basis. After a 1 week placebo run-in period patients were randomly allocated to receive paroxetine (20-40mg/d) or fluvoxamine (100-200mg/d) for a period of 6 weeks. Fluvoxamine patients received 50mg for the first week. Assessments performed at baseline and at the end of weeks 1,2,4 and 6 comprised the HAM-D, Hamilton Anxiety rating Scale (HAMA) the physicians Clinical Global Impression (CGI) and a comprehensive safety evaluation. The two treatment groups were demographically well matched and showed similar improvements in mean total HAM-D, HAM-A and CGI scores during the study. More reports of emergent events occurred in the fluvoxamine group (64 v 52%), where there were also significantly more severe events (28% v 13%), $p<0.05$. Adverse events led to the withdrawal of 3(5.4%) paroxetine and 11(17.2%) fluvoxamine treated patients ($p<0.05$). Taken together these results show similar efficacy for paroxetine and fluvoxamine and suggest and overall tolerability advantage for paroxetine.

SPATIAL MEMORY DEFICITS IN PARKINSONISM

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In rats, caudate lesions have been shown to impair performance on egocentric spatial memory tasks (Potegal, 1972; Cook and Kessner, 1988). Montegomery (1993) has demonstrated that Parkinson's Disease (PD) patients with a moderate condition showed deficits in a spatial memory task when moved in a wheelchair. In our study, 18 patients (Hoehn-Yahr 3) and 18 controls were tested on an active (walking and pointing) spatial memory task. Eight matched pairs were tested in Glasgow, Scotland and 10 pairs in New York City. Subjects (S) looked at a target (T), closed their eyes, walked forward and then pointed to T after variable distances. Although other PD Ss tested on a post rotation and memory test showed no difference between patients and controls, control Ss in the U.K. and the U.S. showed mean pointing errors of 7.6° and 12° respectively while the PD groups made errors of 22.6° and 30°. We propose that this deficit was not related to memory per se, but updating of memory during walking.