9

CENTRAL RECEPTOR MEDIATION OF NMDA-INDUCED DISPOGENESIS IN PIGEONS.

Scott P. Baron and James H. Woods, Departments of Pharmacology and Psychology, University of Michigan, Ann Arbor, MI 48109-0626, U.S.A.

A large dipsogenic response occurs in pigeons following intramuscular administration of NMDA and kainate (Baron and Woods, Pharmacol. Biochem. Behav. 32 [1989] 1080). The intramuscular administration of CGS 19755, the competitive NMDA-selective antagonist (Lehmann et al., J. Pharmacol. Exp. Ther. 245 [1988] 65), produced selective antagonism of NMDA-induced drinking. Herein we report the effects of centrally administered CGS 19755 (0.32 and 1.0 ug) produced antagonism of drinking following NMDA while having a markedly reduced effect on drinking following kainate administration. Doses of CGS 19755 higher than 1.0 ug produced profound ataxia and catalepsy (as defined as loss of righting reflex without head-drop). NMDA-induced drinking in pigeons appears to be mediated via receptors located within the central nervous system. (This research was supported by NIDA Grants DA 05325 and DA 05358.)

10

IN VIVO TEST OF TWO NEW NON-NMDA-RECEPTOR ANTAGONIST AGAINST KAINIC ACID NEUROTOXICITY.

M.Berg, T.Bruhn, F.F.Johansen, P.Krogsgaard-Larsen & N.H.Diemer.
PharmaBiotec Research Center and Cerebral Ischemia Group, Institute of Neuropathology, University of Copenhagen, Denmark.

The neuroprotective effects of two new non-NMDA receptor antagonists were determined by quantitative light microscopy after intracerebral injection of kainic acid (KA) into two rat brain regions. KA alone or KA in combination with either AMOA or AMNH, was stereotaxically injected into the striatum or into the CA3 region of hippocampus. Compounds were dissolved in Kreb's buffer and 1 µl of the solution containing KA (0.2 µg) with or without AMOA (3.6 µg) or AMNH (4.5 µg) were infused over a periode of 1 min. Histologically examination were performed 7 days after the injection and included cells counts in the respective regions. In striatum AMOA almost completely attenauted KA induced cell damage ($p < 0.05$), whereas AMNH showed no protective effect. In the CA3 region of hippocampus none of the test compounds possesed neuroprotective properties against KA induced pyramidal cell damage. These results indicate a difference in the mechanisms responsible for the neurotoxic action of KA in hippocampus compared to striatum.

NMDA: N-methyl-D-aspartate.
AMOA: α-amino-3-carboxymethoxy-5-methyl-4-isoaxazolepropionic acid.
AMNH: α-amino-2(3hydroxy-5-methyl-4-isoxazolyl)methyl-5-methyl-3-oxo-4-isoxazoline-4-propionic acid.

11

NONE OF THE KNOWN EXCITATORY AMINO ACID AGONISTS INDUCES CHEMICAL KINDLING

Michael L. Berger, Institute of Biochemical Pharmacology, University Vienna, Austria.

Recently, chemical kindling by repeated intra-amygdaloid (i.am.) injections of glutamate(glu) and/or aspartate(asp) has been described by 2 laboratories (Mori&Wada 1987, Brain Res.425,45; Croucher &Bradford 1989, Brain Res.501,58). In this poster, (up to now fruitless) efforts to induce a similar effect by repeated i.am. injections of several excitatory amino acid agonists are described. The studies were started with low doses of one of the most potent glu agonists, kainic acid (KA). 9 rats received more than 20 i.am. injections of 5 ng KA via chronically implanted fused silica cannulas. Occasionally, limbic motor seizures were induced, but in only one case the phenomenon was behaviourally reminiscent of electrical kindling (reproducible maximal seizure response after the 12^{th} injection). 7 rats received repeated injections of 100 ng $N\text{-}CH_3\text{-}D\text{-}asp$ (NMDA); again, we observed occasionally limbic motor seizures, but without any progression in severity. In the same way, 6 rats received repeatedly 100 ng quisqualic acid (quis), and 5 rats were injected each 2^{nd} day with 100 ng (RS)-α-NH_2-3-OH-5-CH_3-4-isoxazole propionic acid (AMPA). Occasionally, limbic seizures were induced, but no chemical kindling. Finally, we tried the following combinations: NMDA + KA, NMDA + quis, and NMDA + AMPA; without any success. One possible explanation for our negative results could be, that extremely high glu and/or asp doses induce chemical kindling by interaction with receptors different from known excitatory amino acid receptors, or that other brain regions close to the injected amygdala and reached by diffused glu and/or asp are involved.