Unusual Molecular Form of Cathepsin E Expressed at Early Stage of Excitotoxic Damage in Hippocampal Neurons of Rats

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Excitotoxic damage induced by excitatory amino acid has been implicated in the pathogenesis of a variety of neurodegenerative diseases. Recently, we have shown that cathepsin E (CE), a non-lysosomal aspartic proteinase, was markedly increased in the pathological process of ischemia and normal aging. Thus it is of special interest whether CE is involved in the process of excitotoxic neuronal death. By kainate treatment, the increased level of CE was found in the rat hippocampus by both immunohistochemistry and enzyme immunoassay (EIA). Increased CE immunoreactivity was observed especially in the neurons of the hippocampal CA3 subfield, and the content measured by EIA was 30-fold higher than the control level. Western blot analysis revealed that CE was expressed as an enzymatically inactive form with unusually high molecular weight. The results indicate that kainate induces the increased accumulation of the unusual form of CE in the neurons of CA3 hippocampal subfield, which is likely to lead to the neuronal death.

Metabotropic Glutamate Receptors Are Involved in Hypoxic/Hypoglycemic Injury of Hippocampal CA1 Neurons in vitro

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Ionotropic glutamate receptors are well known to play a major role in neuronal degeneration after cerebral ischemia. However, we are interested in the possible role of metabotropic glutamate receptors (mGluR) during ischemia. The aim of this study was to examine how agonists and antagonists with different affinity for the various mGluR subtypes may influence a hypoxic/hypoglycemic injury in rat hippocampal slices. For this purpose we monitored the electrophysiological recovery of CA1 neurons after a short hypoxic/hypoglycemic period, which was sufficient to abolish the electrophysiological response to test stimuli applied to Schaffer collateral/commissural pathway. Various agonists known to act at different mGluR subtypes were bath applied 20 min before the insult and washed out 10 min after it. In this model, the two mGluR antagonists L-aminophosphonopropionate (L-AP3) and (+)-α-methyl-4-carboxyphenylglycine (MCPG) were able to enhance this recovery significantly. Since the two substances exhibit different effects on forskolin induced cAMP formation, but are both able to antagonize ACPD induced phosphoinositide hydrolysis, we suppose that the blockade of the phospholipase C (PLC) coupled mGluRs could be the reason for the protective effects. The mGluR agonist ACPD, which is known to activate all 6 described mGluR subtypes, also exhibited a clear protective effect on the recovery of evoked field potentials. However, there was no effect of trans-azetidine-2,4-dicarboxylic acid (tADA), an agonist specific to the PLC coupled mGluR. Furthermore, 2S,3S,4S-α-(carboxycyclopropyl)glycine (L-CCG-I) , an mGluR agonist with a higher specificity to the PLC coupled class, was not able to enhance the posthypoxic/hypoglycemic recovery. These data suggest that various mGluR subtypes play different roles in hypoxic/hypoglycemic injury.

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Autohypnotraining -- method of psychological selfregulation.

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A modified method of selfregulation involving elements of hypnosis and autogenic training, and using tape recording. A scheme of training and psychopharmacological result of applying can be used in psychotherapy, psychohygiene by people under stressful conditions.

The results of using this method show effects of disturbered self imaging on state of stress and back influence.

THE RELATIONSHIP BETWEEN TRYPTOPHAN PYRROLASE ACTIVITY AND mRNA EXPRESSION IN RATS FOLLOWING CHRONIC ETHANOL ADMINISTRATION AND WITHDRAWAL. R. Oretti. A. Badawy. C. Morgan. P. Buckland P. McGuffin. Dept. of Psychological Medicine. UWCM. Cardiff. U.K.

Ethanol exerts a variety of effects on tryptophan and 5-hydroxytryptamine (5-HT) metabolism in man and in experimental animals. In rat models. whose tryptophan metabolism is nearest to that of man, chronic ethanol administration enhances brain 5-HT synthesis whereas inhibition of synthesis occurs during the subsequent withdrawal period. Both effects are caused by corresponding changes in tryptophan availability to the brain and are thought to be due to inhibition and enhancement of liver tryptophan pyrrolase activity respectively. It has been suggested that ethanol acts chronically by inhibiting apo-tryptophan pyrrolase synthesis. We have studied the relationship between tryptophan pyrrolase activity and the expression of hepatic tryptophan pyrrolase mRNA in rats chronically administered ethanol by means of an ethanol-containing liquid diet. Wistar rats were fed ethanol diet at concentrations of 5% and 8% (v/v) and for duration's of two and four weeks. Rats were withdrawn in a starved state for seven hours by which time there were demonstrable signs of withdrawal. Matched controls were fed equal amounts of isocaloric ethanol-free liquid diet. The livers were removed from each of the animals and both tryptophan pyrrolase activity and synthesis were measured. Tryptophan pyrrolase activity was decreased before withdrawal and greatly increased over baseline following withdrawal.