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ACUTE MYOCARDIAL INFARCTION AND CYTOKINE-MEDIATED SELECTIVE BLOOD BRAIN BARRIER LEAKAGE IN THE RAT.


Inflammation in the coronary vessels accompanies acute myocardial infarction (AMI). This inflammatory response may reach the brain when it becomes systemic. Mediators of inflammation like the pro-inflammatory cytokines can locally affect the integrity of the vascular wall which may lead to serum protein extravasations. In the brain this may have adverse effects on neuronal functioning to (rigid hitherto (AMÍ). This inflammatory response may react when it becomes systemic. Thromboses, Univ. & Acad. Hospital Groningen, Groningen. The Netherlands.

SELECTIVE BLOOD BRAIN BARRIER. LEAKAGE IN THE RAT. ACUTE MYOCARDIAL INFARCTION AND CYTOKINE-MEDIATED extravasation of serum proteins. This indicates leakage of the blood brain barrier. Detection of fCAM-positive small vessels in certain areas, including the prefrontal cortex, the somatosensory cortex, and the reticular formation. Staining for albumin and IgG revealed that specifically around the ICAM-positive vessels there had been leukocyte attachment to the walls of the cerebral vessels in certain well-defined areas. This non-specific immune reaction triggers extravasation of serum proteins and other blood constituents that may interfere with the functioning of the affected areas. Considering the locations and selectivity of the damage, it is tempting to speculate that immune activation underlies initiation of neurodegenerative diseases.

THE HUMAN BRAIN QUISQUALATE RECEPTOR AS AN ANTIGEN IN BLOOD SERUM TEST-KIT ALLOWING DIAGNOSIS OF EPILEPSY.

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The immunoreactive epitopes of human brain quisqualate receptor (QR) were used as an antigens for determination of autoantibodies (aAb) level to QR in the blood serum by ELISA technique. The blood serum analysis allowing carry out diagnostics of epilepsy by paroxysmal activity test (PA-test) was developed. The increased aAb level to QR (more than two-three times above the control values) was revealed in the blood samples of patients with epilepsy and paroxysmal activity. In the neurological patient's groups this effect was not seen. In majority (85 % ) of patients with epilepsy, revealed by PA-test, demonstrated positive correlation with long-time of the disease, frequencies of attack and the type of paroxysms. The level of autoantibodies to QR epitopes could be new clinical index substantially facilitating unbiased diagnosis of epilepsy, additional to clinical, neurophysiological and other method of examination. The role of quisqualate receptor in the molecular mechanism of epilepsy is discussed.

GABA DEPENDENT MODULATION OF [3H]TBOB BINDING.

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The molecular mechanisms of compounds interacting with the GABA<sub>a</sub> receptor complex are not yet fully unravelled. We investigated the regulation of gene expression of tyrosine hydroxylase, the rate limiting enzyme of dopamine synthesis. While tyrosine hydroxylase mRNA levels were not modified, protein levels were dramatically decreased (>95%) in the ventral midbrain of homozygote mice. This decrease is correlated with a decrease in dopamine levels (>95%) in the striatum. Immunohistochemistry with a tyrosine hydroxylase polyclonal antibody shows no difference in the number of dopamine neurons of the ventral midbrain in homozygote compared to wild type mice. Moreover, the decrease in tyrosine hydroxylase levels is less marked in the accumbens and olfactory tubercle than the striatum where dopamine transporter levels are normally higher. The dramatic extent of the down regulation documented here is only achieved in other animal models by destruction of dopamine neurons, which ultimately induce Parkinson-like syndromes. The mice lacking the dopamine transporter show a spontaneous increase in their locomotor activity despite the marked down regulation of tyrosine hydroxylase and dopamine levels strongly suggests that blockade of the dopamine transporter with highly selective antagonists could be beneficial in alleviating symptoms of Parkinson disease in humans.

Both compounds displaced [3H]-t-butylicyclohexanthozone ([3H]TBOB) binding to the GABA<sub>a</sub> receptor complex. The data were fitted to the Sigmoid Emax model. Both the EC<sub>50</sub> and the Hill parameter were dependent on the GABA concentration: The addition of 8 µM GABA decreased the EC<sub>50</sub> of thiopental from 100 µM to 15 µM and that of propofol from 40 µM to 5 µM. The Hill parameter of thiopental decreased from 2.2 to 1.4 and of propofol from 2.4 to 0.9. The sigmoid Emax model does not correspond to a molecular model. We present a molecular model which may explain the results and which describes the influence of the GABA binding site on the cooperation between two binding sites for thiopental or two sites for propofol.

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