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

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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 (rigger hitherto unknown) inflammatory response may react when it becomes systemic.

Extravasation of serum proteins. This indicates leakage of the blood brain barrier. Immunocytochemical detection of ICAM-positive small vessels in certain areas, including the prefrontal cortex, the somatosensory cortex, and the cingular formation. Staining for albumin and IgG revealed that specifically around the ICAM-positive vessels there had been extravasation of serum protein. This indicates leakage of the blood brain barrier (BBB), probably caused by cytokine producing leukocytes adhering to the vessel wall. In order to assess whether the inflammation rather than the surgery resulted in leakage of the BBB, we injected TNFα in the tail vein. Compared to the myocardial infarcted rats, after TNFα injections the ICAM-positive vessels and Albumin and IgG extravasation was observed in the same areas of the brain. Conclusion: Myocardial infarction results in a systemic inflammation which possibly causes 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 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 value) 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 effects of thiopental and propofol, either in the absence or in the presence of GABA, in receptor binding studies to rat brain membranes.

Both compounds displaced [3H]-t-butylbicyclooctanoozoate ([3H]TBOB) binding to the GABA<sub>B</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.

These in vitro studies show that the shape of the dose-response curve of a drug may depend on the co-presence of other compounds. This may explain inter- and intra-individual differences in responses to psychopharmacological agents including anti-epileptic drugs.

References: