Malignant Infarction In Cats Following Prolonged Middle Cerebral Artery Occlusion: Volumes Of Severe Blood Flow Reduction Predict Fatal Outcome

Graf R[1], Toyota S[1], Valentino M[1], Dohmen C[2], Heiss W-D[1,2]
[1]Max-Planck-Institut für neurologische Forschung and [2]Klinik für Neurologie der Universität Köln, Köln, Germany

Introduction: Severity and duration of cerebral blood flow (CBF) reduction are main determinants of injury in core and penumbra zones of focal brain ischemia. To study the putative role and predictive significance of the volume of these zones for induction of a malignant course due to edema formation in large hemispheric stroke, we examined reduction of CBF and oxygen metabolism (CMRO2) by sequential positron emission tomography (PET) in a transient ischemia model in cats that is susceptible to secondary deterioration after reperfusion.

Methods: In 11 halothane anesthetized cats, the left middle cerebral artery was occluded (MCAO) for 3 hours followed by 6 hours of reperfusion. Pressure sensors measured simultaneously mean arterial blood pressure and intracranial pressure (ICP), and cerebral perfusion pressure (CPP) was calculated. Sequential PET (during control, 1 hour after MCAO and repeatedly after reperfusion) determined regional changes of CBF and CMRO2 in relation to alterations of CPP by using 15O-water (bolus i.v. injection) and 15O-oxygen (bolus inhalation) on a CTI/Siemens ECAT EXACT HR PET scanner.

Results: MCAO reduced CBF and CMRO2 in all animals, but volumes of reduction varied, as did the relation between volumes of severe (< 50 % of contralateral side: ischemic core) and moderate (50-75 % of contralateral side: ischemic penumbra) CBF reduction (Fig. 1). ICP and CPP remained almost unchanged during the ischemic period.
Following reperfusion, 3 of 11 cats developed a malignant course. In these animals, volumes of severe ischemia covered 55-75% of the ipsilateral hemisphere, and volumes of moderate ischemia only 5-10%. Recirculation induced transient hyperperfusion in formerly ischemic regions followed by hypoperfusion that soon started to extend into neighbouring regions and finally covered not only the ipsi- but also the contralateral hemisphere. This rather fast progression into global ischemia was paralleled by a severe reduction of CMRO2, a dramatic elevation of ICP above 80 mmHg and a decrease of CPP below 50 mmHg. At a final stage, symptoms of transtentorial herniation were recognized. In the 8 remaining cats exhibiting a benign course after reperfusion, volumes of severe ischemia covered only 10-45% of the ipsilateral hemisphere, whereas volumes of moderate ischemia covered 15-30%. In these animals, recirculation also induced immediate hyperperfusion followed by hypoperfusion in regions that had been severely ischemic during MCAO. CBF reduction, however, did not spread into regions outside the ischemic focus. Remaining perfusional and metabolic deficits at the end of the observation period covered most parts of formerly ischemic regions. ICP did not increase above 20 mmHg, and CPP did not decrease below 80 mmHg.

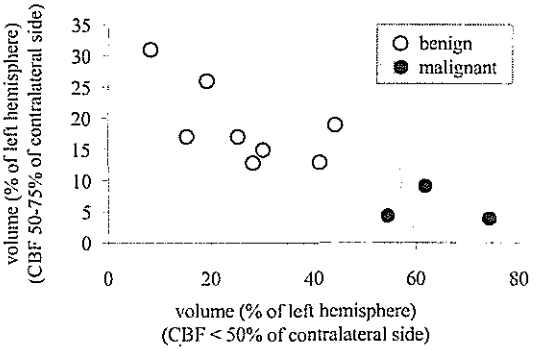

Fig.1: Volumes of core (CBF: <50% of contralateral side) related to volumes of penumbra (CB: 50-75%) determined early during MCAO by 15O-H2O-PET in individual cats. Note: In 3 cats with malignant course, core volume was largest and penumbra volume smallest.

Conclusion: We have demonstrated by sequential PET that in transient large hemispheric infarction in cats, large size ischemic core in conjunction with small size ischemic penumbra favour progression into a malignant course that is presumably caused by excessive edema formation. This progression is predicted by early determinations of CBF and CMRO2.

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