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Extracellular glutamate accumulates only in final, ischemic stage of progressive epidural mass lesion in cats

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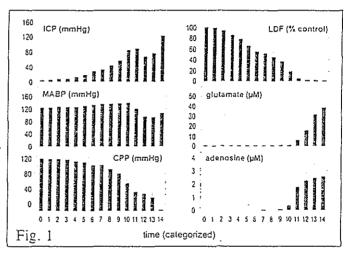
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Introduction

Epidural mass lesions may cause ischemia due to progressive intracranial hypertension. In order to 1) investigate the impact of intracranial pressure (ICP) on accumulation of neuroactive substances, and 2) test the significance of neurochemical monitoring for early prediction of fatal outcome, we gradually faised ICP in cats by inflation of an epidural balloon: We assessed extracellular substrate alterations in the contralateral cortex in relation to changes of ICP, cerebral perfusion pressure (CPP) and mean arterial blood pressure (MABP). In a complementary experiment, regional cerebral blood flow was assessed by sequential positron emission tomography (PET).

Methods

In halothane anesthetized cats (n=6), a miniature balloon was implanted epidurally above the right parietal cortex. In the cortex contralateral to the balloon, microdialysis probes (cut off 6000 Dalton; diameter: 250 µm; length of the active membrane: 1 mm, perfusion rate: 1µl/min) was inserted. Concentrations of amino acids and purine catabolites in dialysate were analyzed by HPLC. Adjacent to microdialysis probes, a laser Doppler probe measured regional CBF (LDF-. CBF), a strain-gauge MicroSensor measured ICP, and a thermocouple measured regional brain temperature. After completion of the preparation, the skull was sealed. In the PET experiment, CBF was repeatedly measured using ¹⁵O-H₂O (bolus i.v. injection) on a CTI/Siemens ECAT EXACT HR PET scanner.



Results

In all cats, balloon inflation gradually increased ICP and decreased CPP and LDF-CBF (see Fig. 1). Extracellular glutamate increased at a late, critical stage after tentorial herniation (see Fig. 1), when ICP had increased to more than 90 mmHg, CPP had decreased below 40-50 mmHg, and LDF-CBF had fallen to less than 10 % of control. Adenosine increased somewhat earlier than glutamate, but also after reaching the critical, terminal stage. Herniation was characterized by a sudden fall of MABP and a transient decrease of ICP. The effect of progressive mass lesion finally

leading to herniation and brain death was visualized in sequential PET CBF images (see Fig. 2). Regional PET assessments of CBF in the surrounding of the microdialysis probe revealed that the ischemic threshold for glutamate accumulation in the hernisphere contralateral to balloon inflation was in the range of 15 - 20 ml/100g/min.



Conclusion

In this model of progressive epidural compression it is evident that glutamate-mediated excitotoxic processes at sites remote from the initial focal lesion depend on processes such as delayed ischemia in combination with tentorial herniation and systemic hypotension. We conclude that neurochemical monitoring probably is of limited relevance as an indicator for early management of epidural mass lesions.