TITLE: THE CBF RESPONSE TO ISOFLURANE FOLLOWING BRAIN INJURY IN THE RABBIT

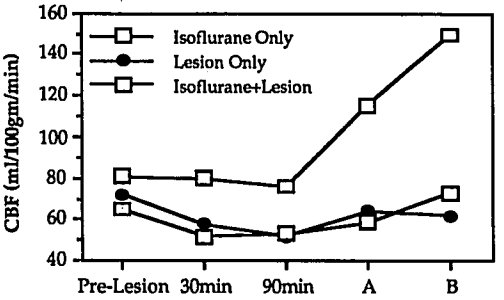
AUTHORS: R. Ramani, M. Todd, D. Warner
AFFILIATION: Department of Anesthesia, University of Iowa College of Medicine, Iowa City, Iowa.

The CBF effects of many anesthetic agents have been described, but there is little data concerning how such effects are influenced by a neurologic injury. We thus examined the response to isoflurane (ISOF) in rabbits with a cryogenic brain injury.

32 normocarbic, normothermic ventilated rabbits were anesthetized with morphine (10 mg/kg load, 2 mg/kg/hr infusion) and 70% N_2O and prepared for the measurement of CBF using radioactive microspheres. When the catheters were in place, the calvarium was exposed, and an epidural pressure monitor placed. Baseline data were then collected, including MAP, ICP, and CBF. Each animal then was randomly assigned to 1 of 3 groups. In Grps 1 and 2, a 30 sec cryogenic lesion was produced by pouring liquid N_2 into a 1 cm diameter funnel affixed to the skull over the left parietal area. Grp 3 animals did not receive a lesion. Data were collected 30 and 90 min after lesioning (or an equivalent time in Grp 3). 1% ISOF was then added in Grps 1 and 3, and CBF measured 30 min later (0.45 MAC ET). ISOF was then increased to 2.0% (≈0.8-0.9 MAC) and final data were obtained. MAP was maintained at 80-100 mmHg using angiotensin II. The brain was then fixed in formalin and cut into left and right hemispheres, weighed, and counted.

ICP changes were minimal, with mean ICP after isoflurane exposure in the Grp 1 = 6±3 mmHg. CBF changes for the lesioned hemispheres are shown in the Figure. In Grp 2 (Lesion only) there was a small and temporary reduction in CBF. When ISOF was given to lesioned animals (Grp 1), no significant change in CBF was seen, i.e. CBF rose from 53±24 ml/100mg/min at 90 min post-lesion to 73±36 ml/100gm/min with 2% ISOF (i.e. a 37% increase). A similar response was seen in the contralateral hemisphere. By contrast, in Grp 3 (ISOF alone), 2% ISOF resulted in CBF increasing from of 76± 21 to 150 ml/100gm/min respectively.

These results indicate that even a modest brain injury blunts the CBF response to ISOF as compared with the changes seen in normal animals. Of even greater interest is the fact that this attenuated response was seen in both hemispheres. These results suggest that vasodilation involves the mediation of some brain-wide chemical or neurogenic mechanism, as opposed to acting directly on vascular smooth muscle.



Points A and B represent 1 and 2% ISOF, or the equivalent point in time for the Lesion Only Group.

A681

Title:The effect of MK-801 on CBF during focal cerebral ischemia.
Authors: John C Drummond, Thomas S Ruta, Daniel J Cole
Affiliation:VAMC San Diego, University of California San Diego, University of Manitoba, Loma Linda University.

It has been suggested that MK-801's therapeutic efficacy in the setting of incomplete focal ischemia may be a non-specific effect of improvement of CBF. However, the available data provide contradictions as to MK-801's effect in this setting (1, 2).
METHODS. Animal Use Committee approval was obtained. The middle cerebral artery (MCA) was occluded by cautery in isoflurane anesthetized (1.2 MAC) Sprague-Dawley rats. Forty min later, MK-801, 0.5 mg/kg (n=10) or vehicle (n=10), was administered iv over 2 min. Fifteen min thereafter, CBF was determined using C14-IAP. Coronal autoradiographs were prepared. Two CBF analyses were performed. Ischemic hemisphere: 2 standard sections near the center of the MCA distribution were analyzed. The area of the hemisphere in which CBF fell within 3 ranges (0-9.9, 10-19.9, and 20-30 ml/100g/min) was measured. The data derived from the 2 sections were averaged. Non-ischemic hemisphere: average CBF for the entire "cortex" and "subcortex" were measured in the same 2 sections. CBF was also measured in individual structures.
RESULTS. Blood pressure, PaCO2 and temperature did not differ between groups at the time of CBF determination. There was a general trend for CBF to be less or unchanged in MK-801 treated animals (Table). Dorsal hippocampus, dentate gyrus and substantial nigra were exceptions. CBF range areas did not differ. Data are presented as mean±SE.
DISCUSSION: The results do not support suggestions that the decrease in infarct volume seen in MK-801 treated rats after MCAO (3) is the result of CBF augmentation. However, the hippocampus and dentate gyrus are not within the area of the significant ischemia produced by this model and CBF effects in these structures may be relevant when they are within the ischemic territory.

CBF Range Area*	Control	MK-801	
0-9.9	3.2±0.9	4.3±1.2	ns
10-19.9	5.0±1.2	5.7±1.0	ns
20-30	4.5±0.9	6.3±1.1	ns
Structure			
"Cortex"	312±33	227±23	p<.05
"Subcortex"	268±36	216±191	ns
Frontal cortex	321±31	262±25	ns
Caudate-putamen	373±45	272±12	p<.05
Corpus callosum	206±39	125±19	p<.05
Globus pallidus	280±36	191±25	p<.05
Cingulate cortex	308±46	252±37	ns
Internal capsule	153±31	107±21	ns
Hypothalamus	245±28	164±22	p<.05
Ventral thalamus	300±45	280±13	ns
Dorsal hippocampus	300±40	370±22	ns
Mamillary body	211±35	154±19	ns
Sensorimotor ctx	298±42	288±39	ns
Lateral geniculate	304±38	303±32	ns
Medial geniculate	333±36	364±19	ns
Entorhinal cortex	239±37	192±18	ns
Substantia nigra	206±32	245±14	ns
Reticular formation	333±37	375±24	ns
Dentate gyrus	335±40	407±14	p<.05
Auditory cortex	306±42	274±22	ns
Occipital cortex	339±37	315±41	ns

*expressed as a % of total area of the hemisphere ipsilat to MCAO.
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