BRAIN 31P-MAGNETIC RESONANCE SPECTROSCOPY (MRS) OF RABBITS ON EXTRACORPOREAL CIRCULATION WITH INTERMITTENT CIRCULATORY ARREST UP TO 2 HOURS UNDER DEEP HYPOTHERMIA

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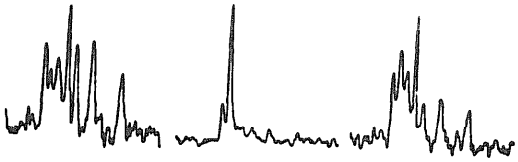
The risk of brain damage during circulatory arrest under deep hypothermia in infant cardiac surgery is still of concern. We studied 9 rabbits in vivo noninvasively by 31P-MRS. Phosphocreatine (PCr), adenosintriphosphate (ATP), inorganic phosphor (Pi), and intracellular pH were measured during extracorporeal circulation (ECC) with cooling, during circulatory arrest of 32, 56, and 120 min at 18 °C, and during reperfusion and rewarming. The normal initial brain spectra stayed constant throughout the cooling period (left spectrum). Circulatory arrest induced a significant fall of PCr, ATP, and pH (middle spectrum). After 2 hrs of arrest, reperfusion with rewarming brought a complete recovery of PCr but only an incomplete recovery of ATP and pH (right spectrum). After 56 min of arrest, ATP and pH recovery were nearly normal. This animal model allows the study of a "safe arrest time" concerning energy metabolism of rabbit brain which probably lies between 1 and 2 hrs. In addition, pharmacological intervention can be investigated.



MECHANISM OF ENDOTHELIN-INDUCED PULMONARY VASODILATION IN NEWBORN PIGLETS

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Endothelin significantly decreases pulmonary vascular resistance index (PVRI) in newborns. Although K+ channel activation is an important mediator of vasodilator responses in mature animals, its role in newborns is uncertain. To clarify endothelin's mechanism of action, we evaluated the capacity of K+ channel blockade with glybenclamide, 7.5 mg/kg iv, to inhibit endothelin response in 6 open-chested newborn piglets. Pulmonary and systemic vasodilator responses to the K+ channel agonist pinacidil, 300 mg/kg iv, were eliminated by glybenclamide but not by its vehicle. In contrast, endothelin-induced pulmonary vasodilation was unaffected by prior glybenclamide. Thus, bolus endothelin, 100 pmol/kg iv, decreased PVRI during hypoxia from 255±23 (SE) to 75±12 mmHg/L/min.kg ($p<.05$) after vehicle and from 202±35 to 56±22 mmHg/L/min.kg ($p<.05$) after glybenclamide. Mean systemic pressures and cardiac index were unaffected by endothelin and by glybenclamide. Similar results were observed during normoxia. Our findings indicate that K+ channel activation is unlikely to be involved in pulmonary vasodilator responses to endothelin in newborn piglets. These results suggest that mechanisms of pulmonary vasodilation may be distinctly different in newborns and mature animals.

MYOCARDIAL FUNCTION OF IMMATURE AND MATURE SHEEP WITH PRESSURE-OVERLOAD HYPERTROPHY

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To investigate whether myocardial function in hypertrophied ventricle depends on maturation, we studied 8 lambs (LVH-L) and 7 adult sheep (LVH-A) with similar left ventricular hypertrophy (LVH) induced by aortic banding, and age-matched controls (SHAM-L and SHAM-A, n=7 each). Myocardial function was evaluated by the shortening-preload-afterload relation based on the systolic myocardial stiffness concept with load alteration by methoxamine.

Midwall shortening at common preload and afterload (end-diastolic and end-systolic stress, σ_{ed} and σ_{aft}) was depressed in LVH-A (*$p<.05$ vs the others, ANOVA and Newman-Keuls test) and normal in LVH-L. The two factorial ANOVA showed significant interaction effect between maturation and hypertrophy on the midwall shortening-preload-afterload relationship.

	Midwall Shortening (mean±SD)			
σ_{ed}/σ_{aft}	: SHAM-L	LVH-L	SHAM-A	LVH-A
30/200(g/cm^2):	17±4%	18±3%	19±4%	10±5%*
50/200(g/cm^2):	20±4%	20±3%	22±4%	13±5%*
50/300(g/cm^2):	16±3%	15±5%	18±4%	9±4%*

We conclude that maturation reduces the capacity of hypertrophied myocardium to maintain normal contractility.

DEVELOPMENTAL EFFECTS OF ETHMOZINE ON ABNORMAL AUTOMATICITY OF CANINE PURKINJE FIBERS

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Ethmozine, a class I antiarrhythmic agent, has shown to be clinically effective in the treatment of atrial ectopic tachycardia, an automatic rhythm disturbance in children which is usually quite resistant to medical therapy. This study compares the in vitro effects of Ethmozine on abnormal automaticity of adult and neonatal canine Purkinje fibers (PF). Automaticity was induced by superfusion of PF with Krebs solution and .3 mM barium. Using standard microelectrode techniques, control automaticity was recorded. Ethmozine at concentrations of 10^{-6}M, 5 x 10^{-6}M, and 10^{-5}M was serially superfused and changes in automaticity rates were quantified. Developmental differences were analyzed.

Results: The control automaticity rate of the neonate was significantly higher than that of the adult (73 bpm vs 55 bpm, $p<.05$). At 10^{-6}M, the neonatal rate was reduced to 48 bpm ($p<.05$), while the adult automaticity was not significantly affected. Neonatal automaticity was significantly reduced at all concentrations of drug tested, while automaticity of adult PF was reduced only at the highest drug concentration, 10^{-5}M.

Conclusion: Automaticity of neonatal PF is more sensitive to the depressant effects of Ethmozine. This in vitro developmental evidence supports the potential utility of Ethmozine in pediatric dysrhythmias involving abnormal automaticity.