Hypoxia Increases Potassium Efflux from Mammalian Myocardium

A. Vleugels[1] and E. Carmeliet

Laboratorium voor Fysiologie, Universiteit Leuven, Dekenstraat 6, B–3000 Leuven (Belgium), 24 October 1975.

Summary. Hypoxia with or without simultaneous depletion of extracellular glucose increases ^{42}K-efflux in cat and guinea-pig papillary muscles and bovine Purkinje fibres. The change observed in K efflux may be the result of an increase in K conductance at rest.

Different hypotheses have been proposed to explain the shortening of the cardiac action potential by metabolic inhibition: 1. an increase of passive K outward current[2], 2. an inhibition of an electrogenic K pump[3] and 3. a decrease of Ca inward current[4]. Hypotheses 1 and 3 are not exclusive since they can both be produced by a mutual cause, i.e. a rise in intracellular Ca concentration[5]. McDonald and MacLeod[6] concluded from experiments with radioactive ^{42}K that K-efflux in guinea-pig ventricle was not increased by anoxia. In chick embryonic ventricle, on the other hand, we found that hypoxia induced an increase in K-efflux in preparations at rest and during electrical stimulation[7]. Because of these contradictory results it seemed necessary to study the effect of hypoxia on preparations of different species in order to see whether or not the increase of K-efflux is a general effect of hypoxia in heart muscle.

Materials and methods. The experiments were performed on bovine Purkinje fibres and papillary muscles of guinea-pig and cat. A Tyrode solution of the following composition was used (m*M*): NaCl 128; KCl 5.4; $CaCl_2$ 1.8; $MgCl_2$ 0.5; $NaHCO_3$ 22; glucose 5 or 0. The Tyrode was saturated with a mixture of 95% O_2–5% CO_2 (control) or 95% N_2–5%CO_2 (test). pH was 7.4 and temperature was maintained at 37 °C. The oxygen tension in the Tyrode gassed with N_2 was less than 30 mm Hg. ^{42}K was obtained from the SCK, Mol, Belgium. After 60 min incubation in a 5.4 m*M* ^{42}KCl Tyrode, the preparations were transferred through successive test tubes containing 4 ml inactive Tyrode. All solutions were pregassed (2 h) and prewarmed. The rate coefficient was calculated as the amount of ^{42}K ions collected during a certain period divided by the mean content of ^{42}K ions present in the preparation during that period.

Results. In the Figure the effect of hypoxia on the rate coefficient of ^{42}K-efflux is shown for bovine Purkinje fibres, cat and guinea-pig ventricular preparations. The experiments consisted of 3 successive periods of 60 min

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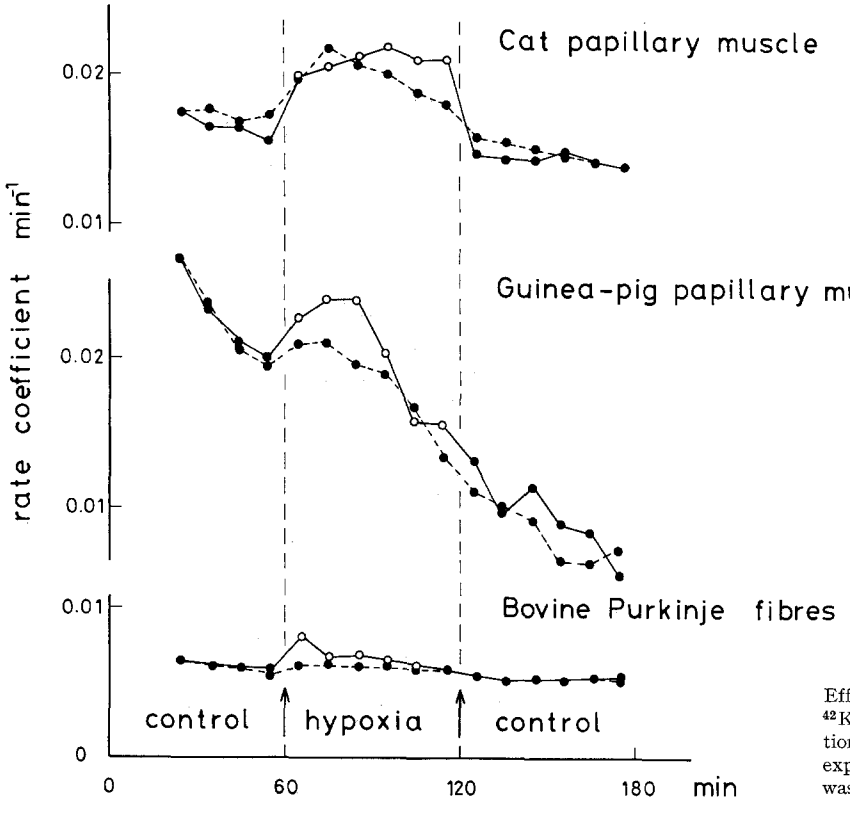

Effect of hypoxia on the rate coefficient of ^{42}K-efflux in different cardiac muscle preparations. Each curve represents the mean of 5 experiments. Extracellular glucose concentration was 0 (open circles) or 5 m*M* (filled circles).

of which the second was performed in the absence of oxygen with glucose present (filled circles) or without glucose (open circles).

1. *Control efflux.* During the first 60 min of efflux, in the presence of oxygen, the rate coefficient decreased fairly rapidly (10–20 min) to a steady state value in Purkinje fibres and cat papillary muscle. In guinea-pig, however, the rate coefficient continued to decrease during the whole efflux period. This deviation from single exponential kinetics may have different reasons (cells of different diameters or different permeability, complex extracellular or intracellular compartments) and complicates the quantitative estimation of changes occurring during hypoxia in this preparation.

2. *Hypoxia.* In all experiments hypoxia leads to an increase in the rate coefficient: the mean of the rate coefficients during the 60 min hypoxic period differs significantly ($p < 0.05$; paired t-test) from the control value (mean of the rate coefficients 30 min before and 30 min after hypoxia). The maximal effect is already reached 20 to 30 min after the onset of hypoxia, after which a gradual decline in the rate coefficient occurs. The sensitivity of the ^{42}K-efflux to hypoxia is larger for papillary muscles than for Purkinje fibres. It is known that the electrical effects of oxygen lack are also less pro nounced in Purkinje fibres[2]. In cat papillary muscle, the increase in ^{42}K-efflux was 22% and 37% respectively in the presence and absence of glucose; corresponding values were 18% and 24% in guinea-pig ventricle and 8% and 19% in bovine Purkinje fibres.

Discussion. The present results indicate that the increase of K-efflux is a general effect of hypoxia on cardiac cells. Although intracellular K or resting potential were not measured in the present experiments, data from the literature[8–11] indicate that a change in the driving force for K ions is absent or minimal during the first 30 min of hypoxia. The increase observed in K-efflux may therefore be the result of an increase in conductance of the passive K channel. Another possibility to explain the increase in K-efflux has been suggested by HAAS et al.[3]. According to these authors, metabolic inhibition would result in a reversal of an active electrogenic K pump. In order to decide between these two possibilities, measurements of K-efflux, K-influx and conductance under identical conditions would be necessary.

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Production of Temperature Signals in the Peripherally Denervated Spinal Cord of the Dog

C. JESSEN and CHRISTA SIMON-OPPERMANN

Max-Planck-Institut für Physiologische und Klinische Forschung, W. G. Kerckhoff-Institut, Parkstrasse 1, D–6350 Bad Nauheim (German Federal Republic, BRD); and Zentrum für Physiologie der Justus Liebig-Universität Giessen, D–6350 Bad Nauheim (German Federal Republic, BRD), 23 October 1975.

Summary. Selective warming of the spinal cord with ventral and dorsal roots cut can generate panting in the conscious dog.

The spinal cord of mammals contains thermosensitive structures which are linked to the temperature regulating system[1]. In some current models on nervous control of body temperature[2,3], these spinal thermosensitive structures have been thought to act as amplifiers in the afferent and efferent thermoregulatory pathways, the gain of which depends on spinal cord temperature. Thus generation of thermoregulatory responses by thermal stimulation of the spinal cord would require its afferent or efferent connections to be intact. This hypothesis can be tested by experiments answering the question whether the spinal cord ,after being deprived of all peripheral inputs, can generate temperature signals and, by conveying them to supraspinal components of the system, elicit panting whose efferent pathways are not directly influenced by spinal cord temperature.

The experiments were carried out on 3 young Beagle dogs whose body weight was between 6 and 8 kg. Under general anesthesia a laminectomy was performed exposing the lower part of vertebral canal, and ventral and dorsal roots of all spinal segments caudally of Th 10 were bilaterally cut. In dogs 1 and 3 this was done extradurally and in dog 2 intradurally. A U-shaped polyethylene thermode (i.d. 1.14 mm, o.d. 1.57 mm) was placed close to the spinal cord covering all segments caudally of Th 12. By perfusing this thermode with water of suitable temperature, the peripherally denervated lumbar and sacral spinal cord could be selectively heated or cooled. The power transferred to the animal via the thermode, which

Respiratory rate before and during warming of the peripherally denervated spinal cord

a	b	c (°C)	d (°C)	e (min)	f (min^{-1})	g (min^{-1})
1	4	30	46_{48}	23	64	96
2	3	30	48_{52}	15	22	27
3	7	27	45_{48}	35	35	52

a) Animal; b) number of periods; c) air temperature; d) temperature of the water entering the thermodes; e) total length of stimulation periods; f) mean respiratory rate during 5 min before start of stimulation; g) mean respiratory rate during all periods of spinal cord warming.

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