EFFECT OF LITHIUM SUBSTITUTION FOR SODIUM ON OXYGEN CONSUMPTION OF GUINEA PIG TAENIA COLI IN HIGH K MEDIUM

YUKIO SAITO, YUTAKA SAKAI

Medical Laboratory for Pharmacology, Central Research Laboratories, Sankyo Co. Ltd., Shinagawa-ku, Tokyo

MIYOSHI IKEDA AND NORIMOTO URAKAWA

Department of Veterinary Pharmacology, Faculty of Agriculture, University of Tokyo, Bunkyo-ku, Tokyo

Received for publication April 23, 1970

It was reported that high potassium solution (isotonic, 40 mm) induced a tension development in guinea pig taenia coli accompanied by an increase in oxygen consumption (1). Intracellular Ca space increased in high K medium as well as cellular Ca fraction which did not exchange within 4 minutes. The latter is referred to “tightly bound fraction (TBF)” (2). By addition of ouabain (2.5 × 10^{-4} m) to high K medium the increased oxygen consumption was maintained, although the developed tension was almost abolished, and both changes were dependent on external calcium (3). Moreover, the elevated intracellular Ca space was maintained by addition of ouabain, while the increased TBF returned to the control level in the high K medium (2).

When lithium was substituted for sodium at a level above 50 mm in high K (hypertonic, 40 mm) medium, the developed tension of the muscle gradually decreased to the original level (4, 5). In the present
communication, effect of lithium substitution on oxygen consumption of taenia coli suspended in the high K medium is described.

Strips of taenia coli from male white guinea pigs, weighing about 20-30 mg, was suspended immediately after isolation in the chamber of the apparatus for recording simultaneously changes in muscle tension and Po2 in medium. The apparatus and method were described in detail earlier (1).

The Tyrode solution used was as follows (mm); NaCl, 136.8; KCl, 5.4; CaCl2, 2.5; MgCl2, 1.0; NaH2PO4, 0.4; NaHCO3, 11.9 and glucose, 5.5. The medium was aerated continuously with a mixture of 95% O2 and 5% CO2 at 37°C and pH 7.2. The three solutions used in this experiment were 1) Tyrode solution containing hypertonic 40 mM KCl (high K solution), 2) Tyrode solution substituting 60 or 75 mM LiCl for equimolar NaCl in the high K solution (Li-high K solution), 3) Tyrode solution deprived of CaCl2 and added 0.1 mM EGTA in the Li-high K solution (Ca (0)-Li-high K solution).

The muscle was suspended first in normal medium flowing through the bath. Spontaneous changes in muscle tension and Po2 level in medium was shown (Fig. 1). When normal Tyrode solution was replaced by the high K one, the muscle showed a strong tension with a decreased Po2 level. Then, the high K solution was replaced by Li (60 mM)-high K solution. The developed tension was decreased gradually at attaining base line within 60 minutes without any change in the decreased the Po2 level. A depletion of Ca from the medium caused a decrease in the muscle tension and an increase in Po2 level, and most of these changes were reversible when Ca was replaced, although the reversibility was poor in some cases. Substitution with 75 mM Li in high K medium showed a similar result to the 60 mM Li substitution.

Thus, Li substitution for Na in the high K medium seems to have an ouabain-like effect on the increases in oxygen consumption and muscle tension. In the previous paper (2), the increased TBF of the muscle returned to control level by the Li substitution for Na in high K medium, but the increased intracellular Ca space was maintained.

It may be accepted that the Li substitution has an ouabain-like effect on tension development, oxygen

---

**FIG. 1. Effect of Li substitution for Na on muscle tension of taenia coli and Po2 level in high K medium.**

The upper and lower curves represent changes in Po2 level (mmHg) and muscle tension (g), respectively. Abscissa: minutes after the muscle, weighing 27.9 mg, was suspended in the chamber.

At A: Normal solution was replaced by high K solution.
At B: The high K solution was replaced by Li (60 mM)-high K solution.
At C: The Li-high K solution was replaced by Ca (0)-Li-high K solution.
At D: The Ca (0)-Li-high K solution was replaced by the Li-high K solution.

The muscle was suspended first in normal medium flowing through the bath. Spontaneous changes in muscle tension and Po2 level in medium was shown (Fig. 1). When normal Tyrode solution was replaced by the high K one, the muscle showed a strong tension with a decreased Po2 level. Then, the high K solution was replaced by Li (60 mM)-high K solution. The developed tension was decreased gradually attaining base line within 60 minutes without any change in the decreased the Po2 level. A depletion of Ca from the medium caused a decrease in the muscle tension and an increase in Po2 level, and most of these changes were reversible when Ca was replaced, although the reversibility was poor in some cases. Substitution with 75 mM Li in high K medium showed a similar result to the 60 mM Li substitution.

Thus, Li substitution for Na in the high K medium seems to have an ouabain-like effect on the increases in oxygen consumption and muscle tension. In the previous paper (2), the increased TBF of the muscle returned to control level by the Li substitution for Na in high K medium, but the increased intracellular Ca space was maintained.

It may be accepted that the Li substitution has an ouabain-like effect on tension development, oxygen
consumption and Ca distribution of the muscle in high K medium. These results seem to support the assumption (2) that Ca ions enter into the intracellular space through the membrane of the smooth muscle depolarized by high K solution, and participate in increase of oxygen consumption, while Ca ions entering into the “tightly bound fraction” play some roles in developing muscle tension.

REFERENCES

THE EFFECTS OF PARACHLOROPHENYLALANINE ON NON-TOLERANT RATS AND OF CHOLINERGIC BLOCKING DRUGS ON TOLERANT RATS TO MORPHINE

TETSUO OKA AND MASAKO NOZAKI

Department of Pharmacology, School of Medicine, Keio University, Shinjuku-ku, Tokyo

Received for publication June 6, 1970

The small amounts of morphine raise while the large amounts of morphine lower the body temperature of non-tolerant rat. On the other hand, morphine raise and its antagonist, nalmorphone, lower the body temperature of tolerant rat (1-3).

Feldberg and Meyers presented the new concepts that norepinephrine and 5-hydroxytryptamine (5-HT) in hypothalamus regulate the body temperature (4-6).

Collier (7) and Sharpless and Jaffe (8) are making efforts to explain the phenomena of tolerance, dependence and abstinence syndrome by pharmacological denerved supersensitivity (disuse supersensitivity). Their theories are based on the existence of interaction between morphine and humoral transmitters in the brain.

These evidences mentioned above stimulate us to study the relationship between morphine and humoral transmitters. In the present investigation, the changes of body temperature and spontaneous activity of rat were chosen as the indicators resulting from the interaction between morphine and humoral transmitters.

Thermistor probe was inserted 6 cm into rectum of the male rat of Donryu strain and taped on the tail. Rat can move relatively freely during measuring body temperature without touching and knowing what is being done. Under these conditions, the rectal temperature of the rat was measured outside of the chamber, the temperature of which is maintained at 20±0.5°C and the relative humidity at 70±10%.

The body temperature of non-tolerant rat was lowered significantly by the subcutaneous (s.c.) administration of 50 mg/kg of morphine-HCl, while this lowering action was completely prevented by the pretreatment with parachlorophenylalanine (300 mg/kg, i.p.) 72 hours before morphine injection. Parachlorophenylalanine is known to lower 5-HT level in brain to about 10% of normal without decreasing norepinephrine level in brain significantly (9) and has no effect on the body temperature of rats by its administration.