MECHANISM OF ACTION OF TWO Mg-ATPase BLOCKERS IN SKINNED SINGLE SKELETAL MUSCLE FIBRES.

Single fibres of skinned M. Gracillis (rabbit) skeletal muscle were activated by means of Ca²⁺ containing solutions. The free [Ca²⁺] was calculated according to Fabiato & Fabiato (J. Physiol. Paris 75-463 (1975)). Sarcomere length was set and controlled by means of laser-diffraction during the whole experiment. 2,3-Buaternone Monoxide (BDM) or Sodium Methasavandazide (NaV₃), Mg-ATPase blockers, were added to the solutions, yielding a concentration of resp. 3 mM and 25 mM. Isometric developed tension was measured with a strain gauge force transducer. The calcium sensitivity curve, the relation between pCa and the developed tension, measured as a function of sarcomere length, was characterized by the maximal developed tension, the pCa₅₀ (the pCa-value at which 50% of the maximal developed tension has been reached) and the slope of the sensitivity curve at the pCa₅₀ (n). From these measured data the Hill plot, the relation between the logarithm of (Tₐ₀(1-Tₐ₀)) and the pCa's, was constructed. Tₐ₀ is the relative developed tension. BDM and NaV₃ both reduce the maximal developed tension by 20-30% at used concentrations. Reduction using BDM was dependent upon sarcomere length, using NaV₃ not. pCa₅₀ is decreased by BDM, while NaV₃ does not affect it. NaV₃ increases the n by about 30%. From changes in the shape of the Hill-plot, it can be derived that NaV₃ interacts with the high affinity sites of TnC. BDM neither changes n nor the shape of the Hill-plot. In conclusion, both drugs decrease force development probably via a change in Mg-ATPase activity. In the case of BDM this is dependent on sarcomere length. Besides this, the drug reduces the sensitivity of TnC to Ca²⁺. NaV₃ increases the number of cooperatively working binding sites and at higher [Ca²⁺] it enhances the cooperativity between the high affinity binding sites, suggesting that the drug also has an affinity to Mg²⁺.


GASTRIN EMPTYING OF MEDIUM CHAIN TRIGLYCERIDES.

It is generally accepted that oral supplementation of carbohydrates (CHO) during exercise is beneficial for endurance performance. A drawback of CHO supplementation is the depression of the fat metabolism. If CHO supplementation is not optimal during an endurance event this might lead to overuse of endogenous CHO, early depletion of glycogen stores and a decrease in performance. Exogenous CHO availability is not limited by gastric emptying (GES) but by oxidation of the exogenous CHO. If one wants to supply more energy and overcome the depression of fat metabolism oral supplementation of fat can be considered. But, fat is a potent inhibitor of GES and is slowly absorbed in the small intestine so practical use is limited. Medium Chain Triglycerides (MCT) might not have the disadvantages of common fat due to the molecular composition, and could be a valuable addition to sport drinks. Nine male volunteers (age 24 yrs, weight 73 kg) participated in experiments in which the rate of GES of 4 liquid test meals (80 ml/kg bwld) consisting of equitoxic mixtures of CHO (Maltose-40%) and MCT was measured. (D1): 70% CHO - 30% MCT; (D2): 80% CHO - 20% MCT; (D3): 90% CHO - 10% MCT; (D4): 100% CHO - 0% MCT. GES was measured for 90 minutes after an overnight fast using the modified double sampling technique of George. GES rate (expressed as t½ of the 4 drinks was respectively 23.2, 34.0, 27.5 and 35.8 min. Statistical analysis showed that all drinks containing MCT emptied faster from the stomach as the 100% CHO drinks can be explained by the lower osmotic pressure and the lower CHO concentration of the MCT containing drinks. Furthermore MCT does not inhibit GES as common fat does. This can be explained by the shorter chain length of the carbonic acid part of the molecule which results in a better water solubility and an improved intestinal absorption. Conclusion is that mixtures of CHO and MCT empty faster from the stomach than equitoxic solutions of CHO alone.

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NORMINAL REGULATION OF ADULT PARTNER PREFERENCE BEHAVIOR IN NEUTERED ATD-TREATED AND CONTROL RATS.
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Male rats were neonatally treated with chlordiazep or ATD (1.4, 6-endrostet-1,7-dione), an aromatase inhibitor which blocks the conversion of testosterone (T) into Estradiol (E₂). When tested for partner preference behavior in a 3 compartment box, choice an estrous female or a sexually active male, ATD males show a much lower preference for estrous female than controls. Testicular hormones were found to be important in the expression of partner preference behavior. This was further studied through castration and subsequent hormone treatment (silastic capsules) which consisted of either dihydrotestosterone (DHT) for 3 wks with an additional 3 wks E₂ (group A), or 3 wks of E₂ treatment, followed by an additional 3 wks DHT (group B). Castration caused a gradually decreasing preference for females in all males, with no partner preference behavior in either group 14 wks postcastration. Pretreatment levels of partner preference behavior were reached after treatment with both T-metabolites, with ATD males of group B showing lower preference scores than controls. ATD males of group A showed an interesting phenomenon: with E₂ only a clearcut preference for the active male emerged. When DHT was added, these ATD males showed no preference: they spent as much time with the estrous female as with the male. In conclusion, partner preference behavior of male rats is neomatically "organized" and in adulthood "activated" by T or its metabolites DHT and E₂. There is a differential effect of order in which DHT and E₂ are administered. This needs further study.


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EFFECTS OF LONG-TERM D-FENFLURAMINE TREATMENT UPON ENERGY METABOLISM IN RATS.
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Chronic treatment with d-fenfluramine (d-FFL), a serotonin re-uptake blocker, leads to a reduction in appetite and body weight. Evidence is accumulating that d-FFL also has direct effects upon energy metabolism. In the present study, the efficacy of chronic intragastric treatment with d-FFL upon energy metabolism in rats were investigated at rest and during swimming. Rats were provided with two permanent cannulae. One for intragastric administration of d-FFL (1 mg/kg b.w., twice a day), and one for sampling of mixed venous blood for determination of nutrient and hormone concentrations. Energy metabolism was studied by means of indirect calorimetry.

Under baseline conditions, d-FFL induced an increased rate of carbohydrate oxidation ; 14.2 ± 7.0 mg/kg/min in control rats. The oxidation of fat, on the other hand, was decreased due to d-FFL treatment (2.8 ± 5.5 mg/kg/min). Plasma FFA was decreased (0.29 ± 0.55 mmol/l), ketone and insulin were increased after d-FFL treatment (0.64 ± 0.37 mmol/l and 61 ± 33 mmol/l respectively. During swimming, the shift in nutrient utilization remained present. The exercise-induced increase in blood glucose was reduced after d-FFL. In the d-FFL treated group blood glucose rose with 68 mmol/l in the control group with 2.0 mmol/l. Plasma FFA rose more in the d-FFL treated group of animals. At the end of swimming however, the FFA concentration was equal in the two groups. During swimming, no significant differences in lactate and insulin between the two groups were observed.

It is concluded that chronic d-FFL treatment leads to an increase in the oxidation of carbohydrates and a decrease in the oxidation of fat as a result of a decreased fatty acid availability at myocardial level. The significance of this shift for the weight reducing effect of d-FFL is unclear.

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