Analysis on mechanisms of glucose uptake on high K^+-induced contraction in smooth muscle

Abstract of Doctoral Thesis

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Summary

【Purpose】Smooth muscles are classified into phasic and tonic muscle by characters of electrophysiological and mechanical reaction. It has been suggested that differences between phasic and tonic muscle are also related to the dependence of the aerobic metabolism. Moreover, it may be suggested that the relationship between contractile response and mechanisms of glucose uptake in muscles differ from each tissues. However, there are few reports which show the relationship between glucose transporters and smooth muscle contraction. The present study examined that the relationship between muscle contraction and glucose uptake system in phasic and tonic muscle.【Materials and methods】Eyes from adult pigs of either sex were obtained from a local abattoir. Male Wister rats (250-300 g) were anesthetized using sodium pentobarbital (50 mg/kg, i.p.) and euthanized by exsanguination. The ileum, aorta and, kidney were quickly removed from each rat. Measurement of muscle contraction, assay of mRNA expression, assay of NADH/NAD ratio, measurement of creatine phosphate (PCr) and assay of glucose transporter 4 (GLUT4) were experimented.【Results】Inhibition of aerobic metabolism by aeration with N_2 or application of sodium cyanide

(NaCN) remarkably inhibited high K-induced muscle contraction in iris sphincter and ileum, but slightly inhibited that in aorta. Sodium glucose cotransporter 1 (SGLT1) mRNA was higher expressed in ileum, but was slightly expressed in aorta. Phloridzin reduced the activation of glycolysis and glucose uptake in ileum. On the other hand, GLUT4 mRNA was expressed in aorta. Insulin increased the glucose uptake and GLUT4 translocation on cell membrane via the PI3K/Akt signaling in aorta. Application of high K^+ or NaCN did not affect glucose uptake. Although, simultaneous application of high K^+ and NaCN, increased the glucose uptake and GLUT4 translocation on cell membrane via the AMPK signaling. 【Discussion】High K^+-induced contraction highly depended on aerobic metabolism in phasic iris sphincter and ileum as phasic muscle. Moreover, high K^+-induced contraction activated glucose uptake via the SGLT1, in ileum. On the other hand, aorta was expressed GLUT4, as well as skeletal muscle. In aorta, insulin dependent glucose uptake and signaling are similar to those of skeletal muscle, but high K^+-induced contraction did not stimulate the glucose uptake. However, simultaneous application of high K^+ and NaCN increased glucose uptake due to the activation of AMPK via GLUT4. Furthermore, it may be suggested that strength of stimulation of AMPK activated some other

glucose transporter like GLUT1. This study demonstrated that mechanisms of glucose uptake of smooth muscles differ between tissues and organs at the first time. These knowledges probably provide the data contribute to make the function of visceral organ in pathophysiological condition such as shock, starved state or diabetes.