Fibroblast growth factor-21 potentiates glucose transport in skeletal muscle fibers

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Abstract

Fibroblast growth factor 21 (FGF21) is a pleiotropic peptide hormone that is considered a myokine playing a role in a variety of endocrine functions, including regulation of glucose transport and lipid metabolism. Although FGF21 has been associated with glucose metabolism in skeletal muscle cells, its cellular mechanism in adult skeletal muscle fibers glucose uptake is poorly understood. In the present study, we found that FGF21 induced a dose-response effect, increasing glucose uptake in skeletal muscle fibers from the flexor digitorum brevis muscle of mice, evaluated using the fluorescent glucose analog 2-NBDG (300 mu M) in single living fibers. This effect was prevented by the use of either cytochalasin B (5 mu M) or indinavir (100 mu M), both antagonists of GLUT4 activity. The use of PI3K inhibitors such as LY294002 (50 mu M) completely prevented the FGF21-dependent glucose uptake. In fibers electroporated with the construct encoding GLUT4myc-eGFP chimera and stimulated with FGF21 (100 ng/mL), a strong sarcolemmal GLUT4 label was detected. This effect promoted by FGF21 was demonstrated to be dependent on atypical PKC-; by using selective PKC inhibitors. FGF21 at low concentrations potentiated the effect of insulin on glucose uptake but at high concentrations, completely inhibited the uptake in the presence of insulin. These results suggest that FGF21 regulates glucose uptake by a mechanism mediated by GLUT4 and dependent on atypical PKC-1 in skeletal muscle.

Palabras clave

Palabras clave de autor:2NBDG uptake; myokines; FGF receptors; adult fibers; insulin signaling
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