Exercise–Induced Transient Increase in IL-6 Stimulates GLUT4 Expression and Enhances Insulin Sensitivity in Mouse Skeletal Muscle

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A single bout of exercise induces transient increase in blood interleukin-6 (IL-6) level in human and rodents, however, the role of exercise–induced IL-6 is poorly understand. Prolonged, chronic increase in IL-6 reflects low-grade inflammation, which decrease insulin sensitivity in adipose tissue, liver and skeletal muscle. On the other hand, acute, short–period of IL-6 enhances insulin sensitivity. Because, the increase in IL-6 after exercise is transient, we hypothesized that transient increase in IL-6 after exercise enhances insulin sensitivity in skeletal muscle. C57BL6J mouse were i.v. injected normal IgG or IL-6 antibody before exercise. Twenty–four hours after a single bout of exercise (treadmill running: 20 m/min, 90 min with 10 degree incline), plantaris muscle was harvested and incubated in oxygenized KRB buffer to measure insulin-stimulated 2-deoxyglucose (2-DG) uptake. Compared with sedentary mouse, insulin-stimulated 2-DG uptake in plantaris muscle was increased 24 h after exercise in IgG-injected mouse, however, the increase induced by exercise was not observed in IL-6 antibody–injected mouse. Concomitant with this results, GLUT4 expression was increased 24 h after exercise in IgG-injected mouse, the increase was canceled in IL-6 antibody–injected mouse. Recombinant mouse IL-6 injection increased GLUT4 expression both fast–twitch plantaris muscle and slow–twitch soleus muscle in C57BL6J mouse. Furthermore, short period incubation of IL-6 (3–12 hours) increased GLUT4 expression in differentiated C2C12 myotubes, however long period (24 h) did not. These results suggests that exercise–induced transient increase in IL-6 affects skeletal muscle in autocrine/paracrine manner, which enhances GLUT4 expression leading to increase insulin sensitivity in skeletal muscle.