

Deuterium-reinforced polyunsaturated fatty acids protect against muscle atrophy by STZ-induced diabetic mice

Hiroaki Eshima, Tomoaki Ishihara, Ayaka Tabuchi, Yutaka Kano, Kenji Kurokawa,
Mikhail S Shchepinov

Abstract

Oxidative stress and reactive oxygen species (ROS) have been linked to muscle atrophy and weakness. Diabetes increases the oxidative status in all tissues, including muscle tissues, but the role of lipid ROS on diabetes-induced muscle atrophy is not fully understood. Deuterium reinforced polyunsaturated fatty acids (D-PUFA) are more resistant to ROS-initiated chain reaction of lipid peroxidation than regular hydrogenated PUFA (H-PUFA). In this study, we tested the hypothesis that D-PUFA would protect muscle atrophy induced by diabetes driven by an accumulation of lipid hydroperoxides (LOOH). C57BL/6J mice were dosed with H-PUFA or D-PUFA for four weeks through dietary supplementation (10 mg/day) and then injected with streptozotocin (STZ) to induce insulin-deficient diabetes. After two weeks, muscles tissues were analyzed for individual muscle mass, force generating capacity and cross-sectional area. Skeletal muscle fibers from diabetic mice exhibited increased total ROS and LOOH. This was abolished by the D-PUFA supplementation regardless of accumulated iron. D-PUFA were found to be protective against muscle atrophy and weakness from STZ-induced diabetes. Prevention of muscle atrophy and weakness by D-PUFA might be independent of ACSL4/LPCAT3/15-LOX pathway. These findings provide novel insights into the role of LOOH in the mechanistic link between oxidative stress and diabetic myopathy and suggest a novel therapeutic approach to diabetes-associated muscle weakness.

Keywords: D-PUFA; Diabetes; Lipid hydroperoxides; Oxidative stress; Polyunsaturated fatty acids; Reactive oxygen species; Skeletal muscle.