Impaired fatigue resistance, sarcoplasmic reticulum function, and mitochondrial activity in soleus muscle of db/db mice.

Abstract

Type 2 diabetes mellitus (T2DM) is characterized by reduced exercise tolerance due to increased fatigability in skeletal muscle. In this study, we investigated muscle fatigue resistance of soleus (SOL) muscle in obese type 2 diabetic model mice (db/db). No differences in muscle volume, absolute force, or specific force in SOL muscle were observed between db/db mice and control mice (db/+), while fatigue resistance evaluated by repeated tetanic contractions was significantly lower in db/db mice (30th tetani, db/+: 63.7 ± 4.7%, db/db: 51.3 ± 4.8%). The protein abundance related to Ca2+ release from the sarcoplasmic reticulum (SR) in SOL muscle was not different between db/db mice and db/+ mice, while SR Ca^{2+} -ATPase (Ca^{2+} reuptake to SR) protein was decreased in db/db mice compared to db/+ mice (db/+: 1.00 ± 0.17, db/db: 0.60 ± 0.04, relative units). In addition, mitochondrial oxidative enzyme activity (succinate dehydrogenase) was decreased in the SOL muscle of db/db mice ($p < 0.05$). These data suggest that fatigue resistance in slow-twitch dominant muscle is impaired in mice with T2DM. Decreased mitochondrial oxidative enzyme activity and impairment of Ca^{2+} uptake to SR, or both might be involved in the mechanisms.