Type I diabetes suppresses intracellular calcium ion increase normally evoked by heat stress in rat skeletal muscle

Abstract

Heat stress, via its effects on muscle intracellular Ca^{2+} concentrations ($[Ca^{2+}]_i$), has been invoked as a putative therapeutic countermeasure to type 1 diabetes-induced muscle atrophy. Using a circulation- and neurally intact in vivo muscle preparation, we tested the hypothesis that impaired muscle Ca^{2+} homeostasis in type 1 diabetic rats is due to attenuated heat stress tolerance mediated via transient receptor potential vanilloid 1 (TRPV1). Male Wistar rats were randomly assigned to one of the following four groups: 1) healthy control 30°C (CONT 30°C); 2) CONT 40°C; 3) diabetes 30°C (DIA 30°C); and 4) DIA 40°C. The temperature of 40°C was selected because it exceeds the TRPV1 activation threshold. Spinotrapezius muscles of Wistar rats were exteriorized in vivo and loaded with the fluorescent Ca^{2+} probe Fura-2 AM. $[Ca^{2+}]_i$ was estimated over 20 min using fluorescence microscopy (340/380 nm ratio) in quiescent muscle held at the required temperature, using a calibrated heat source applied to the ventral muscle surface. Western blotting was performed to determine the protein expression levels of TRPV1 in spinotrapezius muscle. After 20 min of heat stress, the CONT 40°C condition induced a 12.3 ± 5% $[Ca^{2+}]_i$ ($P < 0.05$) elevation that was markedly absent in the DIA 40° C or other conditions. Thus, no significant differences were found among DIA 40°C, DIA 30°C, and CONT 30°C. TRPV1 protein expression was decreased by 42.0 ± 9% in DIA compared with CONT ($P < 0.05$) and, unlike CONT, heat stress did not increase TRPV1 phosphorylation. In conclusion, diabetes suppresses TRPV1 protein expression and function and inhibits the elevated myocyte $[Ca^{2+}]_i$ evoked normally by heat stress. These results suggest that capsaicin or other therapeutic strategies to increase Ca^{2+} accumulation via TRPV1 might be more effective than hyperthermic therapy for type 1 diabetic patients.