

Augmented Mechanoreflex in Type 2 Diabetic Rats: Piezo Channels, an Important Part of the Puzzle?

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ABSTRACT

Type 2 diabetics (T2DM) have an abnormal cardiovascular response to exercise. The exercise pressor reflex, which is evoked by metabolic and mechanical stimuli arising from the contracting muscle, is a critical cardiovascular regulatory mechanism during exercise and is exaggerated in hypertension, heart failure, and peripheral artery disease. A recent study found that T2DM patients have an augmented metaboreflex. However, whether the mechanoreflex is also augmented in T2DM is not known. **PURPOSE:** The purpose of the study was to test whether the mechanoreflex is exaggerated in T2DM. Furthermore, we tested the contribution of mechano-gated Piezo 1 and 2 channels to the mechanoreflex in T2DM. **METHODS:** In unanaesthetized, decerebrated rats we stretched the Achilles tendon for 30 s and measured changes in mean arterial pressure (MAP) and heart rate (HR) in 12 mo old male T2DM rats (BW=546±26 g, glucose=549±28 mg/dl, HbA1c=12.82±0.18%) and healthy male controls (CTL: BW=453±22 g, glucose=229±31 mg/dl, HbA1c=4.6±0.1%). To test the contribution of Piezo channels, we injected GsMTx-4 (10 µg), a known antagonist of Piezo 1 and 2 channels, into the arterial supply of the hindlimb and repeated the stretch maneuver. **RESULTS:** We found that the pressor (T2DM: Δ MAP=69±6 mmHg, n=5; CTL: Δ MAP=13±2 mmHg, n=5) and cardioaccelerator (T2DM: Δ HR=28±4 bpm, n=5; CTL: Δ HR=5±3 bpm, n=5) responses to tendon stretch were significantly greater in T2DM rats compared to CTL; p<0.05. Injection of GsMTx-4 into the arterial supply of the hindlimb reduced the pressor response (before GsMTx-4; MAP: 80±7 mmHg; after GsMTx-4; MAP: 55±9 mmHg, n=2) to tendon stretch by approximately 30%. Likewise, GsMTx-4 lowered the cardioaccelerator response (before GsMTx-4; HR: 31±9 bpm; after GsMTx-4; HR: 12±2 bpm, n=2) by approximately 61%; p<0.05. **CONCLUSION:** We conclude that T2DM significantly exaggerates the pressor and cardioaccelerator response to mechanoreflex activation and that Piezo channels play a significant role in evoking the mechanoreflex in T2DM rats.