TACSM Abstract

Sex Differences in the Augmented Metaboreflex in Type 1 Diabetic Rats

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ABSTRACT

Studies have shown that blood pressure and heart rate responses to metabolites produced during muscle contraction (i.e., metaboreflex) are exaggerated in type 1 diabetes (T1DM). It is not known, however, if these responses differ between females and males. **PURPOSE**: The purpose of this study was to determine if the metaboreflex, stimulated by either lactic acid or ATP, differs between sexes and if these differences change with the progression of the disease. **METHODS**: We compared adult female (F) and male (M) Sprague Dawley rats one week, three weeks, and six weeks after the induction of T1DM (Streptozotocin, 50mg/kg; F: n = 37; M: n = 46) to their corresponding vehicle-injection controls (CTL; citrate buffer; F: n = 31; M: n = 40). On the day of the experiment, the metaboreflex was evoked in decerebrate, unanesthetized rats by injecting α,β meth-ATP (10µg/0.2mLµl) or lactic acid (0.2 mL, 24mM) into the arterial supply of the left hindlimb. Peak pressor and cardioaccelerator responses were recorded within 30 s of injecting either stimuli. Non-fasted blood glucose and body weight were measured before and after induction of T1DM. All data are reported as mean ± SD. **RESULTS**: All T1DM rats were considered diabetic if blood glucose > 300 mg/dl. Pressor and cardioaccelerator responses to injecting lactic acid into the arterial supply of the hindlimb evoked a significant pressor response in all rats ($p<0.05$). The pressor response in T1DM rats was not significantly greater in either sex compared to their corresponding CTL group matched for disease duration. The pressor response to lactic acid in male rats 6 weeks after T1DM was trending toward being significantly different compared to its CTL (M: T1DM = 26 ± 5 mmHg, n= 7; CTL = 16 ± 10 mmHg, n= 8; $p=0.12$). The cardioaccelerator response in T1DM rats was significantly greater ($p < 0.001$) in female rats compared to their corresponding CTL group one week after induction of T1DM (F: T1DM = 28 ± 17 bpm, n= 9; CTL= 1 ± 4 bpm n= 9; $p<0.001$), but no significant differences were seen in cardioaccelerator responses to lactic acid three or six weeks after induction of T1DM. Likewise pressor and cardioaccelerator responses to injecting α,β meth-ATP into the arterial supply of the hindlimb evoked a significant pressor response in all rats ($p<0.05$). There was a significant main effect of sex, regardless of disease state, on the pressor response to α,β meth-ATP in rats one week after induction of T1DM (F: 27 ± 12 mmHg, n = 9; M: 19 ± 13 mmHg, n = 8; $p = 0.02$). There were also significant main effects of sex (F: 30 ± 6 mmHg, n = 6; M: 25 ± 10 mmHg, n = 10; $p = 0.03$) and disease state (T1DM F: 26 ± 25 mmHg, n = 5; CTL F: 30 ± 6 mmHg, n = 6; $p = 0.04$) on the pressor response to α,β meth-ATP in rats six weeks after induction of T1DM. Moreover, no significant differences were seen in cardioaccelerator responses to α,β meth-ATP one, three, or six weeks after induction of T1DM ($p>0.05$). **CONCLUSION**: Overall, we conclude that changes in cardioaccelerator and pressor responses to lactic acid and α,β meth-ATP may exist in T1DM and should be investigated further in future studies.