Streptozotocin-induced type I diabetes mediates structural and electrophysiological changes in the rat atria: A substrate for atrial fibrillation

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Background and Aims: Diabetes is an independent risk factor for atrial fibrillation (AF). Although research on type II diabetes-related cardiovascular disease is well established, the electrophysiological impact of type I diabetes (T1DM) is less well understood.

Methodology: Zucker lean rats (3 months) were subjected to an i.p injection of saline (control, n=10) or 30mg/kg Streptozotocin (T1DM, n=10). Following a 3 month period the animals were sacrificed for experiments. The atria were excised and placed with the epicardial surface in contact with a 9 × 10 multi-electrode array (0.5mm inter-electrode spacing). A 100MΩ aluminosilicate microelectrode was inserted into the endocardial surface during a standard S1-S2 pacing protocol to simultaneously record intracellular action potentials. Action potential duration (APD) at 90%, 50% and 20% of repolarisation, effective refractory period (ERP), body weight, blood glucose levels and blood pressure measurements were obtained. Post-experiments, tissues were weighed and stored for hematoxylin and eosin staining to determine cardiomyocyte size.

Results: No significant differences were found in body weight (control 353.8 ± 4.5, T1DM 373.4 ± 8.5, $P = 0.07$) and chamber weights (control *vs* T1DM all chambers $P > 0.05$) between groups. In T1DM animals, fasting blood glucose (control 13.7 ± 1.3mmol/L, T1DM 18.5 ± 1.2mmol/L, $P = 0.04$) and blood pressure levels were elevated (control 129.4mmHg ± 5.7, T1DM 137.5 ± 3.7mmHg, $P = 0.04$). While AP repolarisation parameters were significantly prolonged across all pacing cycle lengths in both atria for T1DM animals (see table), the reverse occurred for the ERP; there was a shortening of the ERP in both atria in T1DM animals compared to control animals (LA: control 62.4 ± 1.3ms, T1DM 53.2 ± 1.0ms, P P <0.0001). Cardiomyocytes were also found to be larger for both atria in the T1DM animals (LA: control 8.8 ± 0.1µm, T1DM 12.0 µm, $p < 0.0001$; RA: control 8.3 ± 0.1µm, T1DM 11.2 ± 0.3µm, $P < 0.0001$).

Conclusion: Our results suggest that T1DM may have an important role in mediating atrial structural and electrophysiological changes to provide a potentially vulnerable substrate in favour of increased predisposition to AF.