## Sympathetic modulation of cardiac function in diabetes - *in vivo* and *ex vivo* study

*H.P.A. Thaung,[1] J.C. Baldi,[2] D.O. Schwenke[1] and R.R. Lamberts,[1] [1]Department of Physiology, Otago School of Medical Science, University of Otago, Dunedin, New Zealand and [2]School of Medicine, University of Otago, Dunedin, New Zealand.*

The burden of type 2 diabetes mellitus (T2DM) is increasing globally. The majority of T2DM patients suffer from diabetes-related cardiovascular disease, such as heart failure. Literature hints at augmented sympathetic nerve activity (SNA) as being accountable for this increased risk of cardiovascular disease. Prior findings on cardiac SNA in T2DM were interpreted based on data obtained from recording of muscle or renal SNA, or plasma norepinephrine spillover. Since central control of SNA is highly differentially regulated to different organs, this highlights the importance of assessing SNA to the heart in diabetes. We directly recorded cardiac SNA, hence measuring the direct nerve input to the heart, and hypothesized that resting cardiac SNA is elevated in diabetic rats. Additionally, we also assessed β-adrenergic receptor (β-AR) responsiveness in the heart to β-adrenergic stimulation in isolated hearts. Cardiac SNA was directly recorded in Zucker Diabetic Fatty rats (T2DM model) and their non-diabetic littermates anesthetized with urethane *in vivo* (1.5 g/kg, intraperitoneal). Cardiac responsiveness to dobutamine (β-AR agonist, $1.0\times10^{-5}$ M) was assessed using the Langendorff-perfused isolated heart retrieved from the same animal *ex vivo*. Preliminary data suggest that the sympathetic drive to the heart in diabetic rats is elevated (SNA = 0.90 ± 0.53 *vs* 0.66 ± 0.14 μV·s; diabetic (n = 5) *vs* non-diabetic (n = 5), respectively). Cardiac responsiveness to β-adrenergic stimulation indicated a reduced response in diabetic rats (left ventricular pulse pressure = 124 ± 12 *vs* 186 ± 16 mmHg in diabetic *vs* non-diabetic, respectively). This study is the first to directly record SNA to the heart in diabetes, providing a unique opportunity to further explore and understand the central regulation of sympathetic nervous system in diabetes.