Autonomic dysregulation in the diabetic heart

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Resting heart rate is the strongest predictor of mortality in patients with cardiac disease, and incompetence in heart rate regulation is an undervalued feature of the diabetic heart. The sympathetic and parasympathetic branches of the autonomic nervous system are well known to influence heart rate regulation, although also intrinsic regulation of heart rate is emerging.

The data to be presented aimed to determine whether changes in heart rate in type 2 diabetes are intrinsic to the heart or relate to changes in autonomic nervous control. To this end, we collated and compared heart rate data (resting, after autonomic inhibition and intrinsic heart rate) from our studies in humans with uncomplicated type 2 diabetes and from our studies in type 2 diabetic Zucker Diabetic Fatty rats.

We found that in humans resting heart rate was faster in type 2 diabetic compared to non-diabetic individuals. Conversely, resting heart rate in conscious type 2 diabetic rats with telemetric recordings was slower compared to non-diabetic littermates, and intrinsic heart rate was also slower in isolated diabetic rat hearts. Inhibition of the sympathetic system with specific β-adrenoceptor blockers (nadolol, atenolol, CGP20712A) slowed resting heart rate in rats. However, none of these inhibitions affected the diabetes-induced difference. The chronotropic responsiveness to β-adrenoceptor stimulation was increased under conscious conditions in diabetic animals, but not different to non-diabetics in the isolated hearts. The chronotropic responsiveness was attributable to the β1-adrenoceptor subtype, and not the β2-adrenoceptor subtype. Determination of expression levels of membrane-clock and calcium-clock proteins in the sinoatrial node revealed interesting differences.

In conclusion, the type 2 diabetes-induced changes in heart rate in humans and rats seem mostly related to intrinsic changes of the heart, rather than caused by alterations of autonomic nervous control.