Continuous Glucose Monitoring via Telemetry in Rats

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Introduction

The current standard for routine glucose measurements in preclinical research is often glucometers and test strips. These pose significant limitations in terms of accuracy, animal stress, and frequency of sampling. Until now, continuous monitoring options for preclinical research have been very limited. The present study evaluates the use of a novel prototype telemetry device (Data Sciences International) incorporating an implantable glucose sensor (Nova Biomedical, Waltham, MA) for acute and chronic glucose measurements in the arterial blood of rats.

Materials and Methods

The 1.4cc telemetry device provides direct continuous blood glucose readings along with temperature and activity for 4 weeks or longer. The devices were evaluated in 4 lean and 4 diabetic Zucker fa/fa (ZDF) rats (Harlan Laboratories, Indianapolis, IN) and in 10 Zucker diabetic/Sprague Dawley (ZDSD) rats (PreClinOmics). Each animal was surgically instrumented with glucose sensors in the abdominal aorta and the telemetry device placed in the intraperitoneal (ip) cavity. Continuous glucose readings were recorded with the Datquest A.R.T. data acquisition system (DSI) for at least 28 days with periodic fasting glucose tolerance tests (GTTs) (glucose, 2-3 g/kg, po or ip). Daily and GTT reference values were recorded with a non-clinical version of the StatStrip Xpres glucometer and strips (Nova Biomedical) capable of measuring blood glucose levels up to 900mg/dL. Reference meter values were used for calibration in Microsoft Excel based on the initial OGTT with baseline corrections thereafter based on the daily meter values.

Results

Results from OGTT and IPGTT tests demonstrate excellent correlation between the strip measurements and the continuous telemetry signal with StatStrip samples at 0, 30, 60, 120 and 180 minutes. Figures 2 and 3 demonstrate the ability to differentiate glucose and temperature levels between a group of 3 diabetic fa/fa rats and 3 lean rats. Each animal had an OGTT around day 7, an IPGTT around day 14, and an IPGTT around day 23. Figure 5 shows individual rats with GLP1 analog treatment (30nmol/kg) started on day 28 and the glucose levels in each rat drop as expected following the start of treatment.

Conclusions/Perspectives

The glucose sensors provided high resolution data during acute challenges and demonstrated the ability to accurately assess chronic diurnal patterns matching with the feeding pattern of rats from three days up to seven weeks after surgery. These devices hold great potential for comparing physiologic processes associated with glucose regulation in normal and disease condition rats; monitoring diabetes progression and developing preventive treatments for type II diabetes.

The potential for decreasing sensitivity over time in hyperglycemic animals may lead to a short-term recommendation to overpopulate study groups to maintain the required statistical power.

Results - Chronic Sensor Performance

All rats that maintained average glucose levels below 300mg/dL provided very stable and consistent signals throughout the 28 day test period. Several of the diabetic hyperglycemic rats with average glucose levels in excess of 300mg/dL showed decreasing sensitivity in the sensor output over time with about 25% of the animals producing unusable data by day 28. Figure 10 below shows the impact of loss of sensor sensitivity and the corresponding noise induced by the baseline correction based on reference meter values. This remains under investigation by the authors.

Figure 1: DSI HD-SG Implant and Nova StatStrip Xpres glucometer

Figure 2: OGTT in rats

Figure 3: IPGTT in rats

Figure 4: Continuous glucose and temperature in normal vs diabetic rat groups

Figure 5: GLP1 analog treatment in normal vs diabetic rats

Figure 6: OGTT response in randomized groups (pre)

Figure 7: OGTT response in randomized groups (post)

Figure 8: OGTT in randomized groups (pre)

Figure 9: OGTT in randomized groups (post)

Figure 10: Loss of sensor sensitivity in diabetic rat