Advantages of Glucose Monitoring with an Implantable Telemetry Device in Freely Moving, Conscious Non-Human Primates

Poster 911-P

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INTRODUCTION

Insulin-resistant diabetes (Type 2 diabetes mellitus, T2DM) is the most common form of diabetes in man. Non-human primates (NHPs) that spontaneously develop diabetes are an excellent model for studying the mechanisms of human insulin resistance and diabetes due to presenting similar disease onset and progression. Blood glucose is conventionally tested using a handheld glucometer, clinical chemistry analyzer, or analox analyzer. These methods all require periodic blood sampling, and continuous long-term glucose monitoring is therefore challenging. In this study, we demonstrate the use of an HD-XG transmitter device (Data Sciences International, Inc., USA) implanted in conscious cynomolgus monkeys (*Macaca fascicularis)* to continuously measure blood glucose fluctuations following the circadian rhythm, a meal, ivGTT, or glucose clamp.

METHODS

The glucose sensor was implanted into the femoral artery and its reference electrode plus the device body was implanted subcutaneously nearby. A small repeater was carried in the monkey jacket for remote signal collection from outside the cage (**Fig. 1**). Blood glucose, body temperature, and physical activity were simultaneously monitored wirelessly and recorded continuously for more than 6 weeks. The blood glucose levels were found to be in the range of 50-80mg/dl in normoglycemic monkeys (n=4) and 100-200mg/dl in prediabetic or diabetic monkeys (n=2).

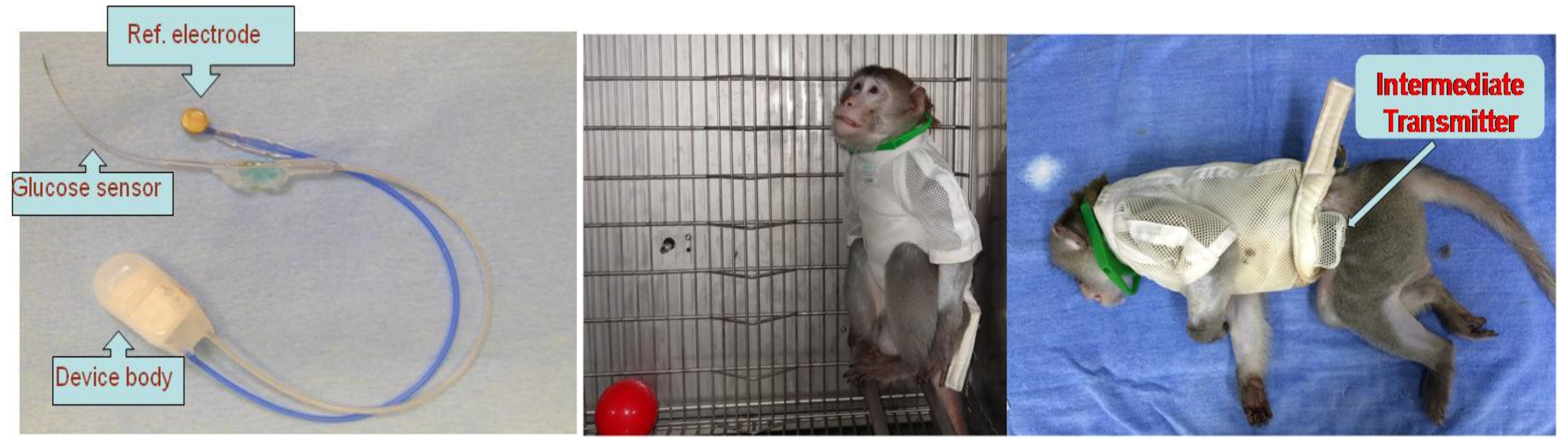

Figure 1: The device was implanted into the monkey and the transmitter was placed into the jacket pocket.

RESULTS

Blood glucose levels showed circadian oscillations (**Fig. 2** and **Fig. 3**). In most of the studied monkeys, no obvious postprandial hyperglycemia was observed after morning feeding; however, blood glucose levels increased by 20 to 30% after afternoon feeding (**Fig. 4**). Correlation analysis showed that glucose readings were well matched between glucometer reading and telemetry device readings (**Fig. 5A**). To monitor the device performance during rapid changes of blood glucose levels, dual ivGTTs and glucose clamp were applied and the results are shown in **Fig. 5B** (ivGTT) and **Fig. 5C** (glucose clamp). To test if the telemetric device measurements were also practically applicable to oGTT and ITT, the animals were gavaged orally with 1.75g/kg glucose for oGTT (**Fig. 6A**), and intravenously administrated with insulin (**Fig. 6B**).

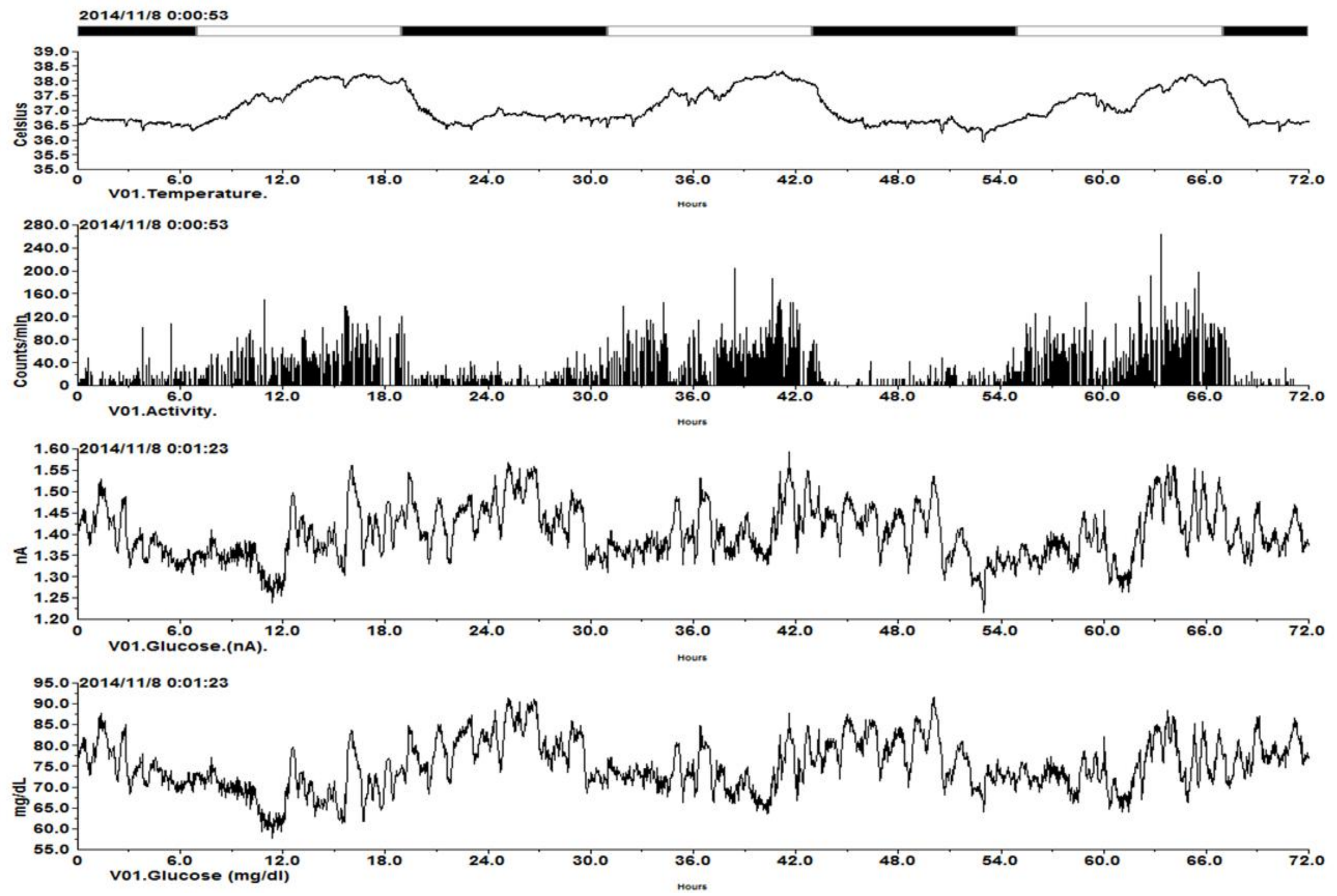

Figure 2. Continuous monitoring of blood glucose levels in one conscious NHP.

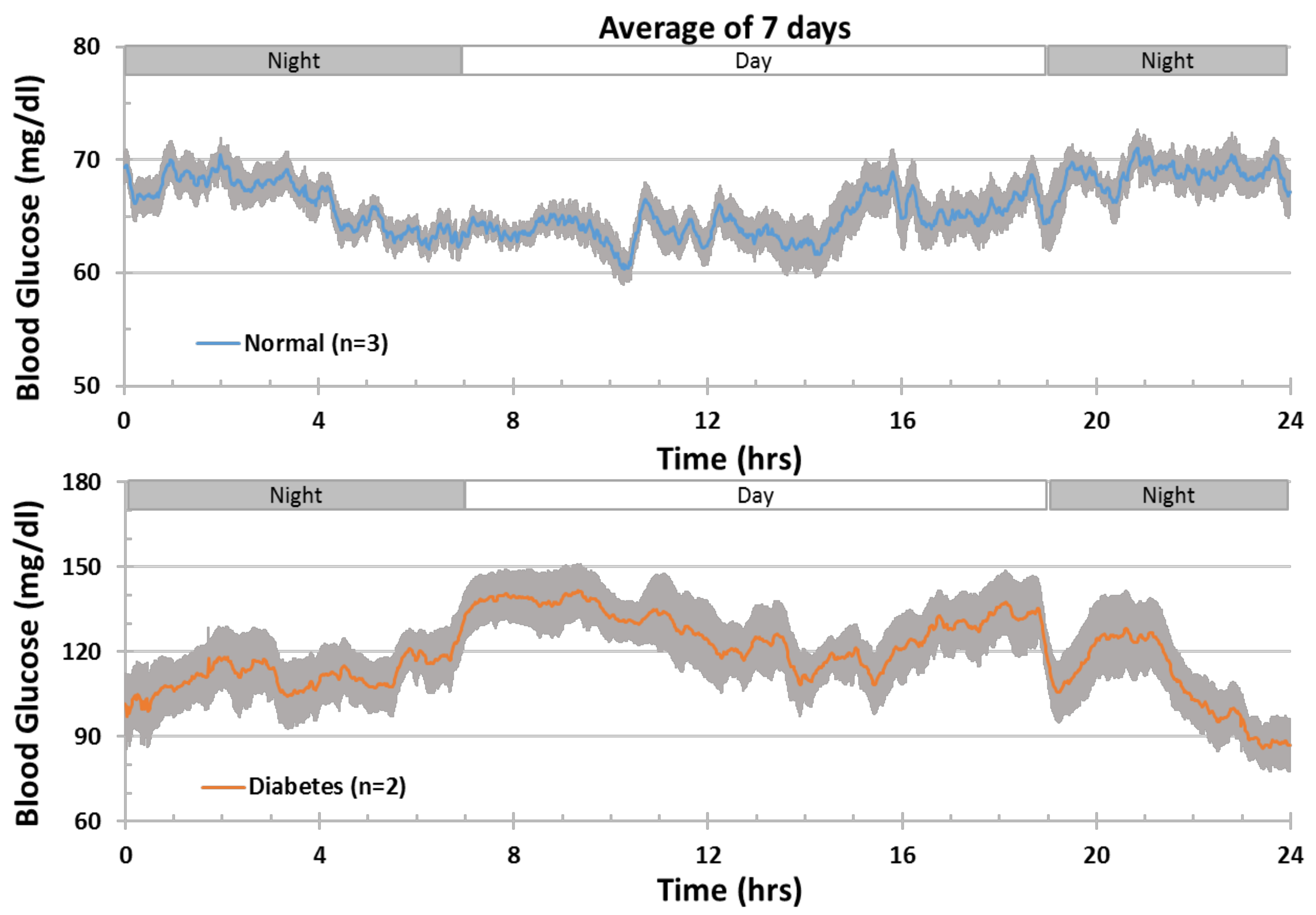

Figure 3. Averaged daily fluctuations of blood glucose levels from 7 day monitoring of normal and diabetic NHPs.

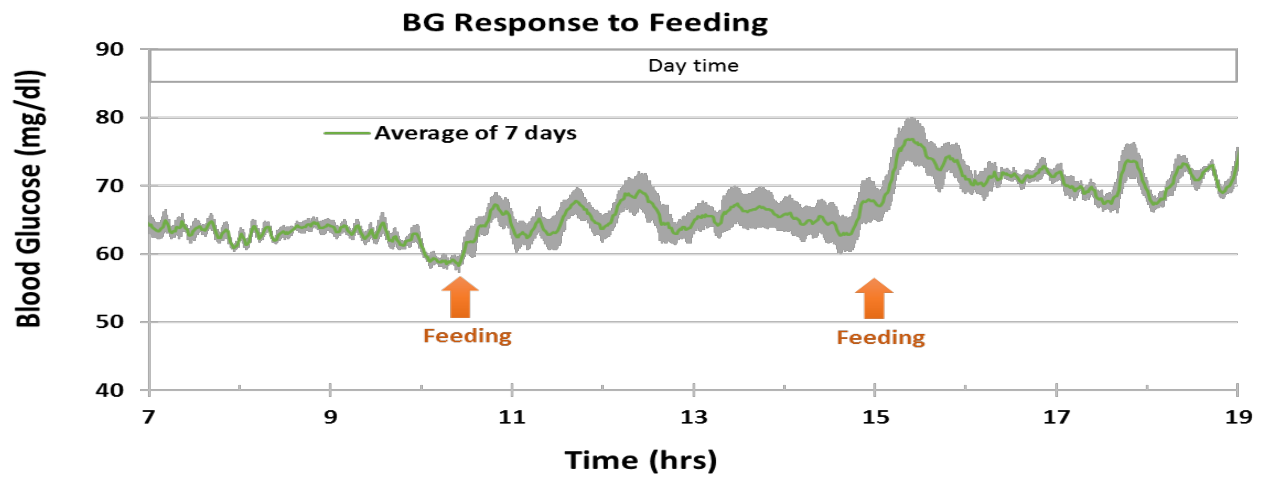

Figure 4. Typical effects of feeding on 7 day-averaged blood glucose levels from one conscious NHP.

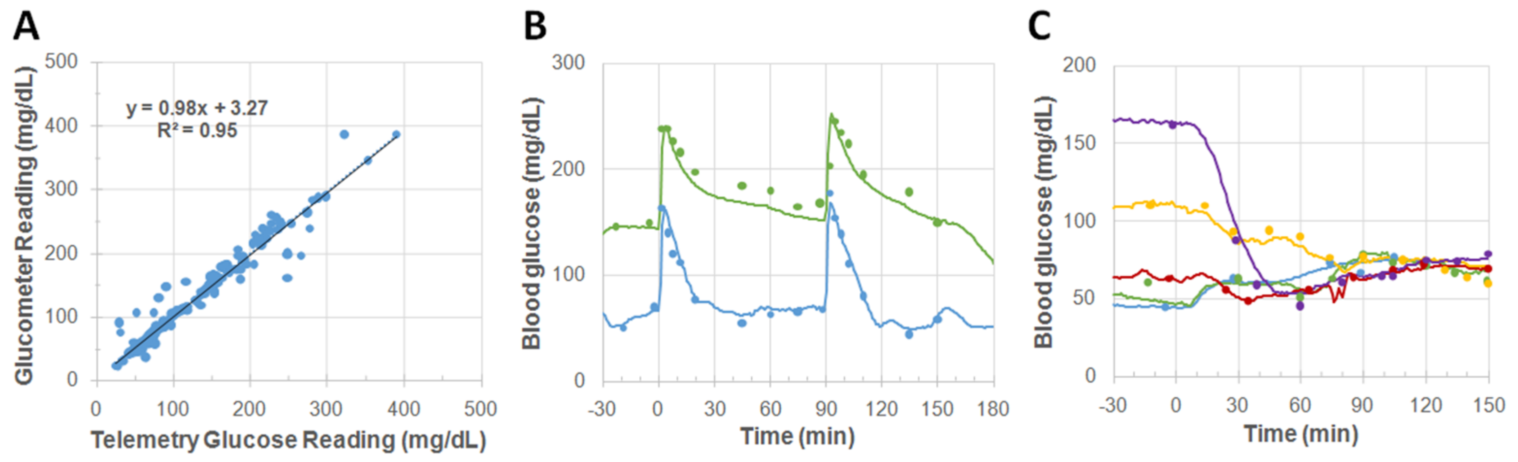

Figure 5. Blood glucose correlation (*A*), dual ivGTTs (*B*), and hyperinsulinic-euroglycemic clamps (*C*) tested with telemetry (solid line) or glucometer (dotted circles) in normo- and hyperglycemic NHPs.

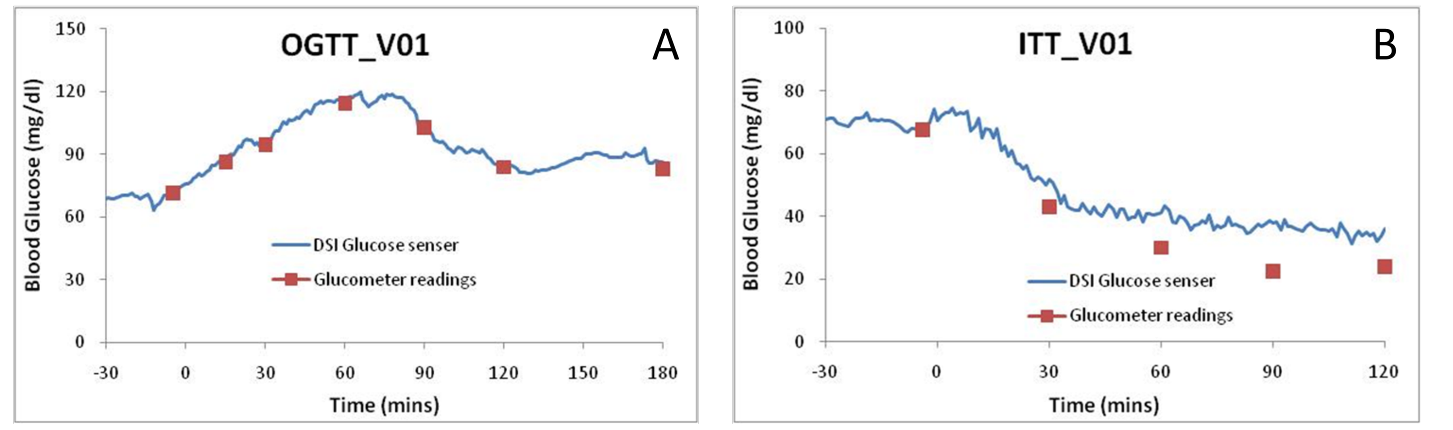

Figure 6. Blood glucose changes measured with telemetry (solid line) or glucometer (dotted squares) during oGTT (*A*) and ITT (*B*).

SUMMARY

- Blood glucose levels measured with a telemetric device correlated well with the readings obtained with a standard glucometer.
- Blood glucose levels were found to be higher during daytime than nighttime in diabetic monkeys, but not in normoglycemic controls. Postprandial increase in blood glucose levels was more obvious after afternoon than morning feeding.
- Advantages of monitoring blood glucose levels by telemetry include: 1) consecutive data collection reflecting circadian and postprandial changes; 2) no bleeding; 3) no restriction; 4) no anesthesia; 5) no stress; 6) lower labor intensity during ivGTT, oGTT, and clamp; 7) instant results, without post measurement lab work.
- Remotely and continuously monitoring blood glucose via telemetric device in conscious, stress-free, freely moving monkeys is feasible and provides a sophisticated approach to investigate glucose level changes due to daily activities, neuronal and hormonal changes, and other challenges.