Long-term Continuous Glucose Monitoring in Conscious Stress-free Non-human Primates with Implanted Telemetry Device

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Abstract

Diabetes becomes a global epidemic issue. Aging non-human primates (NHPs) develop insulin resistance and high blood glucose in a way similar to the progression and onset of type 2 diabetes in humans, which makes them an excellent model for diabetes research. The conventional tests of blood glucose are by handheld glucometer, clinical chemistry analyzer or analox analyzer. These methods require periodical blood sampling with potential subject stress and ethical volume limitation, especially during research. This study investigated HD-XG transmitter, a Data Sciences International implantable device, for continuous monitoring of blood glucose in conscious NHPs. The glucose sensor was implanted into the femoral artery and its reference electrode plus the device body was implanted subcutaneously nearby. A small receiver/amplifier was carried in the monkey jacket for remote signal collection from outside cage. Blood glucose, body temperature and physical activity were monitored wirelessly and recorded continuously for over a month. Many classical diabetes assays, such as ivGTT, oGTT, ITT, clamp, were tested with this remote method and compared with the conventional glucometer method. Our data demonstrate the 1st success of remote, continuous monitoring of blood glucose in conscious, stress-free NHPs and its potential advantages bringing to diabetes research and drug discovery.

Introduction

Aging nonhuman primates (NHPs) develop insulin resistance and high blood glucose in a way similar to the progression and onset of type 2 diabetes in humans, which makes them an excellent model for diabetes research. The conventional tests of blood glucose are by handheld glucometer, clinical chemistry analyzer or analox analyzer. These methods require periodical blood sampling with potential subject stress and ethical volume limitation, especially during research. This study investigated HD-XG transmitter, a Data Sciences International implantable device, for continuous monitoring of blood glucose in conscious NHPs.

Methods

An animal was anesthetized and a surgical operation was conducted under a sterilized condition. One glucose sensor was implanted into a femoral artery and the reference electrode plus its device body was implanted subcutaneously nearby. The animal recovered for a week before doing any data collection.

During data collection a small receiver/amplifier was carried in the monkey jacket for remote signal collection from the outside of the cage. Blood glucose, body temperature and physical activity were monitored wirelessly and recorded continuously for over a month.

Several classical diabetes assays, such as ivGTT, oGTT, ITT and glucose clamp were tested with this telemetry method and compared with the conventional glucometer assay.

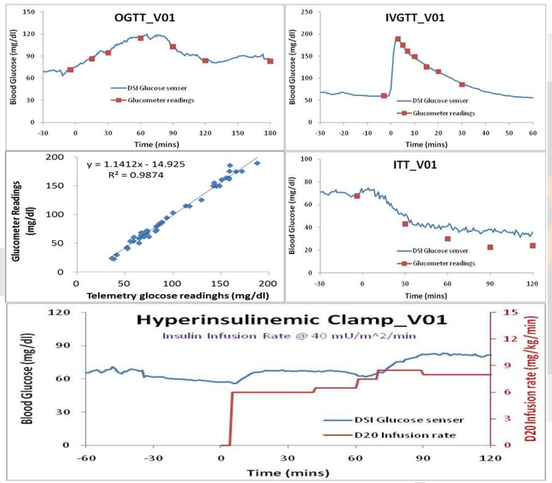

Figure 4. Evaluation of several classic assays with the implantable glucose monitoring system for diabetes research. Data were collected during oGTT (Top left panel), ivGTT (Top right panel), ITT (Middle right panel) and Glucose clamp (Bottom panel; D20, 20% glucose solution) in one monkey with an implanted telemetry device. The correlation between blood glucose levels measured by the glucometry or telemetry is shown (Middle left panel).

Results

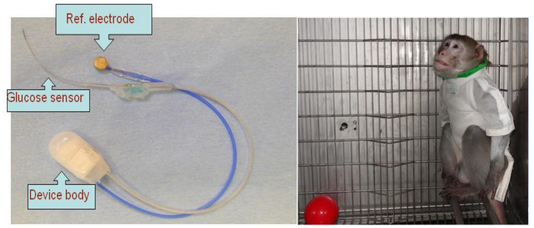

Figure 1. Implantable glucose telemetry device (left panel) and experimental animal (right panel). The device-implanted monkey wearing a monkey jacket in which a small receiver/amplifier was placed for signal collection from outside cage.

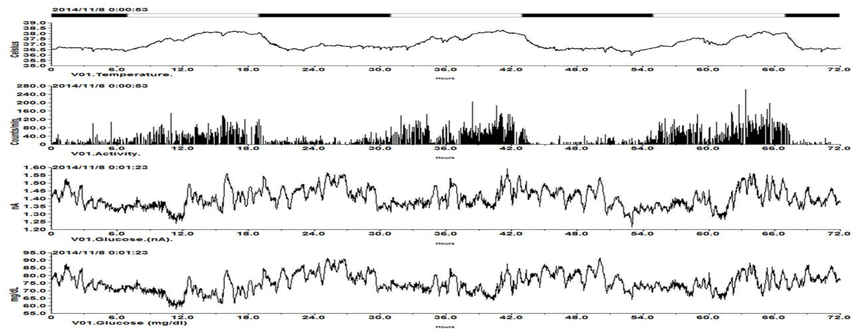

Figure 2. Representative data collected continuously from a conscious monkey with an implanted device. From top to bottom: body temperature (1st trace) with the maker of day and night cycle, physical activity (2nd trace), blood glucose signal (3rd trace), blood glucose (4th trace).

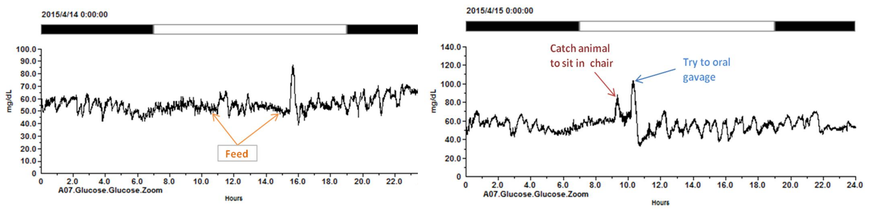

Figure 3. Blood glucose fluctuations by feeding or by conventional operation procedures. Left panel, feeding-induced blood glucose changes; **Right panel,** placed the monkey to a monkey chair and gave an oral gavage.

Conclusions

1. **Blood glucose levels can be reliably and continuously monitored by the technology in conscious and freely-moving NHPs without notable stress**
2. **The system can continuously monitor blood glucose levels for over 4 weeks**
3. **This technology can be used for monitoring glucose changes during oGTT, ivGTT, ITT, MMTT and glucose clamp**
4. **This monitoring system does not require animal restriction, anesthesia and blood collection to obtain blood glucose information**