SUN 720: Blood Glucose Fluctuations during Daily Activities and Stress Procedures in Cynomolgus Monkeys Monitored By Implanted Telemetry Device

Bingdi Wang[1], Wei Qiao[1], Guofeng Sun[1], Yongqiang Liu[1], Jiqiu Qiao[1], Weiwei Ye[1], Hui Wang[1], Xiaoli Wang[1], Ryan Lindquist[2], Yixin (Jim) Wang[1,3], Yong-Fu Xiao[1]

Crown Bioscience, Inc., Taicang, Jiangsu Province, China; [2]DSI, St. Paul, MN, USA; [3]Crown Bioscience Inc., Kannapolis, NC, USA

INTRODUCTION

Insulin-resistant diabetes (Type 2 diabetes mellitus, T2DM) is the most common form of diabetes in clinics. Nonhuman primates (NHPs) can naturally develop to insulin resistance and high blood glucose in a way similar to the progression and onset of T2DM in humans, which makes them as 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 sampling blood periodically. This study investigated the changes of blood glucose during circadian, meal, stress and drug exposure monitored continuously by implanted HD-XG transmitter device (Data Sciences International, Inc) in conscious NHPs (*Macaca fascicularis*).

METHODS

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 (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 in the range of 50-80 mg/dL in the selected normogalycemic monkeys (n=4) and 100-200 mg/dL in the selected pre-diabetic or diabetic monkeys (n=2).

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

RESULTS

Blood glucose levels showed circadian oscillations (Fig. 2 and 3). In most of the studied monkeys, there was no obvious postprandial hyperglycemia after morning feeding, but blood glucose increased by 20 to 30% after afternoon feeding (Fig. 4). Gripping out a monkey from its cage for sitting in monkey chair caused a transient increase in blood glucose by ~50% in both normoglycemic and diabetic monkeys, which took 30 min back to its baseline level in normoglycemic monkeys and almost 2 hrs in diabetic ones (Fig. 5). The stress-induced hyperglycemia by oral gavage operation was similar to gripping monkey from hosing cage (Fig. 5). To mimic stree-induced hyperglycemia, AngiotensinII (2 μg/kg, iv bolus injection, conscious) and norepinephrine (0.4 μg/kg/min, iv infusion for 40 mins, anesthetized with 10 mg/kg ketamine, im) induced an increase in blood glucose by ~30% in normal monkeys and ~15% in diabetic monkeys (Fig. 6). However, intravenous injection of acetylcholine (1 μg/kg) had no obvious effect on blood glucose.

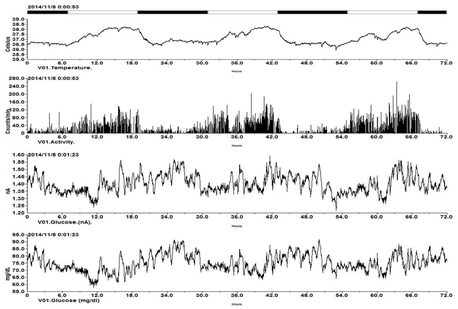
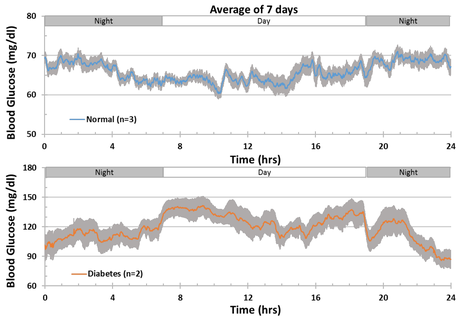


Figure 2. Continuously monitoring blood glucose in one conscious NHP



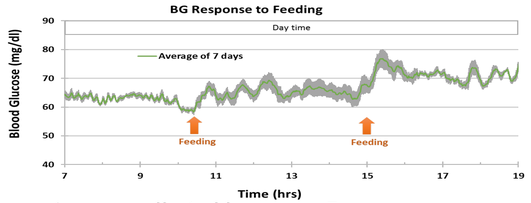


Figure 4. Typical effect of feeding on 7 day-averaged blood glucose levels from one conscious NHP.

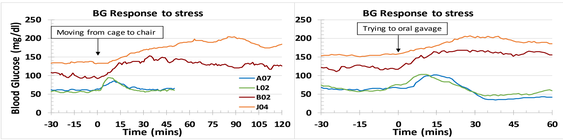


Figure 5. Typical stress response to operation procedure in conscious NHPs.

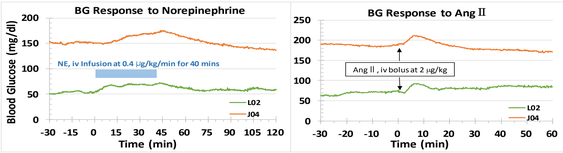


Figure 6. Effect of norepinephrine (0.4 μg/kg/min, iv infusion for 40 min, anesthetized with 10 mg/kg ketamine, im) and AngiotensinII (2 μg/kg, iv bolus injection, conscious) on blood glucose.

SUMMARY

- The results show that blood glucose had circadian variation and compared with the nighttime, blood glucose was higher during daytime in the diabetic monkeys, but not in the normoglycemic ones. Postprandial increase in blood glucose was more obvious after afternoon feeding than morning one.
- Procedure-induced increase in blood glucose lasted much longer in diabetes than in normoglycemia monkeys. Stress-related hormones, such as norepinephrine and angiotensinII, also increased blood glucose.
- In conclusion, remote and continuous monitor of blood glucose via telemetry device in conscious NHPs provides a sophisticated approach to investigate daily activity and neurological regulation of blood glucose due to behavior and hormonal changes.