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Continuous glucose monitoring in a mouse model of islet transplantation

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Introduction: Blood glucose concentrations are an important end-point in diabetes research and are usually measured at a single point during the day. Using continuous blood glucose monitoring in unrestrained mice we measured blood glucose fluctuations in mice in normoglycaemic conditions, after streptozotocin injection to induce hyperglycaemia and after islet transplantation. The aim of this study was to measure fluctuations in blood glucose in mice in different states of hyperglycaemia to determine the extent and timings of blood glucose fluctuations which may impact accuracy of the measurements.

Methods: C57Bl/6 mice were implanted with continuous glucose telemetry devices with blood glucose measured in the carotid artery. Continuous blood glucose monitoring started seven days after probe implantation (HD-XG, DSI), with averages reported every 10 seconds. After five days of baseline measurements the mice were injected with 180mg/kg streptozotocin (STZ) to induce diabetes. Five days later, 200 C57Bl/6 islets were implanted under the kidney capsule and animals were maintained 14 days. Blood glucose was also regularly measured using a single point 9am glucometer reading for comparison. Excursions were measured from lowest to highest point within 24 hours.

Results: In normoglycaemic mice, average day blood glucose was lower than average night blood glucose (8.2±0.2mM vs 8.6±0.1mM; $p<0.05$, paired t-test, n=5). Persistent hyperglycaemia was reached at an average of 40.2±9.0 hours after STZ injection. Islet transplantation reduced blood glucose in all mice. Average day blood glucose was lower than night (12.6±0.6mM vs 15.5±0.6mM, P=0.0003, two-way RM ANOVA, n=5). Considerable glucose excursions were present throughout the day and night with larger fluctuations at night (median: 9.2mM vs 10.1mM respectively, $p<0.05$, Wilcoxon Rank Sum Test, n=5). Daily excursions were also larger in hyperglycaemic versus normoglycaemic mice (13.4±1.2mM vs 6.7±1.2mM; p=0.017, t-test, n=5). Although the glucometer readings were consistent with points on the dynamic probe traces, considerable blood glucose fluctuations were seen. At some points, morning blood glucose peaked in the hyperglycaemic range when the single point 9am blood glucose showed a normoglycaemic blood glucose concentration.

Conclusion: Using continuous glucose monitoring it is clear that blood glucose excursions are considerable in mice. While average day time blood glucose concentrations are lower than night time, fluctuations throughout the day could mean that a single blood glucose measurement may misrepresent the overall glycaemic control of the mouse.