

P058 Exposure to low glucose increases mitochondrial superoxide production and mitochondrial damage in pancreatic beta-cells

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Excessive formation of oxygen radicals is a well established mediator of hyperglycaemic damage to tissues in diabetes. Glucose stimulation is believed by many to increase mitochondrial superoxide production in pancreatic β -cells. Recent reports suggest that lowering glucose actually increases the level of β -cell reactive oxygen species (ROS) production. In this study we aim to test the hypothesis that low glucose increases β -cell ROS production and that this causes subsequent mitochondrial damage. Two commonly used rodent Insulinoma lines INS-1 and MIN6 were used to assess the impact of glucose exposure on ROS production, oxygen consumption and mitochondrial function. We demonstrate that the insulinoma β -cell line, INS-1 acutely increases mitochondrial respiration as glucose levels are reduced, and this increases mitochondrial superoxide. Incubation with 1mM glucose (for 24hrs) impaired mitochondrial function, significantly reducing the mitochondrial respiratory control ratio (a measure of mitochondrial efficiency) without decreasing cell viability. This decline in mitochondrial function is probably due to increases in mitochondrial superoxide because it can be prevented by superoxide scavengers. Our results support a correlation between increased oxidative phosphorylation and mitochondrial superoxide production under reduced glucose conditions and subsequent mitochondrial dysfunction. The risks of poor blood glucose control could be as significant as sustained hyperglycemia in the progression of diabetes.