

P021 Early, reversible loss of islets in the high-fat fed female ZDF rat model of Type 2 diabetes.

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This study investigated the ability of the high-fat fed female ZDF rat model of type 2 diabetes to recover glycaemic control following return to chow diet. ZDF rats were housed in reverse light conditions and blood glucose and plasma insulin measured at 08.00h (“non-fed”) and 12.00h (“prandial”). High-fat (48% of calories, HF) feeding for 8 weeks increased non-fed glucose from $9.4 \pm 0.3 \text{mM}$ to $18.6 \pm 3.5 \text{mM}$ and prandial blood glucose from $10.9 \pm 1.1 \text{mM}$ to $22.5 \pm 3.3 \text{mM}$. Non-fed plasma insulin was reduced from $32 \pm 2 \text{ng/ml}$ to $18 \pm 5 \text{ng/ml}$ on HF diet. The insulin response to feeding was abolished. Islet numbers were reduced following HF feeding (524 ± 93 islets/section vs 318 ± 29 islets/section). Independent groups were reversed to chow diet after early (day 10) or late (day 19) HF feeding. In the early group, plasma insulin remained elevated at $28 \pm 4 \text{ng/ml}$ and blood glucose recovered from $18.0 \pm 1.5 \text{mM}$ to $10.4 \pm 1.1 \text{mM}$ (non-fed). In contrast, following late diet reversal, plasma insulin continued to decline to $10 \pm 2 \text{ng/ml}$ (non-fed) and $10 \pm 2 \text{ng/ml}$ (prandial) whilst glucose control was not regained. Islet numbers were restored in the early but not the late reversal group.

These data suggest an early, reversible effect of high-fat feeding, with a limited window for improvement of pancreatic function.