Delayed post-prandial insulin secretion in individuals with low diabetes risk and its reversibility with exercise training

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Introduction: Delayed post-prandial plasma insulin responses could be used as an early risk factor for the development of diabetes in contrast to traditional clinical markers such as elevated fasting and 2 hour post-prandial glucose concentrations (Hayashi *et al*., 2013). It is currently unclear whether lifestyle interventions can normalize these abnormal insulin secretion responses. We aimed to determine whether delayed insulin secretory responses are present in a young, healthy adult population that would usually be considered low risk for diabetes. Secondly, we aimed to determine whether these delayed insulin secretory responses can be improved by a 10 week exercise training intervention.

Methods: To determine the presence of delayed insulin responses in young adults, 49 participants with no known history of diabetes or cardiovascular disease were recruited (23 male, 26 females, age 24±1 years, BMI 25.3±0.5 $kg.m^{-2}$). Plasma glucose and C-peptide were measured during an oral glucose tolerance test prior to and at 10, 20, 30, 60, 90, 120, 150 and 180 minutes. The time of peak C-peptide concentrations were used to allocate subjects to the following groups: C-peptide peak at ≤30 minutes (CP30), 60 minutes (CP60), 90 minutes (CP90) and ≥120 minutes (CP120). To determine the effect of exercise on the postprandial insulin response, secondary analysis was performed on data collected from a 10-week endurance and high intensity interval training exercise intervention (Shepherd *et al*., 2015). A 2 hour OGTT was performed on 71 previously sedentary adults (23 male, 48 female, age 43±1 years, BMI 27.6±0.6 $kg.m^{-2}$) before and after the exercise training intervention. The time to peak insulin concentrations were used to allocate subjects to the following groups: insulin peak at 30 minutes (IP30), 60 minutes (IP60), 90 minutes (IP90) and at 120 minutes (IP120).

Results: Delayed insulin secretory responses occurred in 63% of the young, healthy population based on the peak C-peptide concentration occurring ≥60 minutes. The delayed insulin response coincided with heightened glycaemic excursions, despite glucose levels largely remaining within the 'normal tolerance' diagnostic range. Age, BMI, blood pressure, fasting glucose and C-peptide concentrations, and indices of insulin sensitivity were similar in all groups based on time of peak C-peptide concentrations. In response to the exercise training intervention, there was a decrease (P<0.05) in the peak insulin concentrations in all groups, and a decrease (P<0.05) in the insulin area under the curve for IP30 and IP60. The time to peak insulin concentrations also occurred earlier in IP90 and IP120 groups following exercise training.

Conclusion: These results indicate that delayed post-prandial insulin secretion is an early metabolic manifestation that is present in young individuals who are considered at low risk of diabetes, which precedes clinical markers used in the diagnosis of prediabetes. Importantly, these defects in the time course of insulin secretion can be reversed with exercise training.

Hayashi T, Boyko EJ, Sato KK, McNeely MJ, Leonetti DL, Kahn SE, Fujimoto WY (2013. Patterns of insulin concentration during the OGTT predict the risk of type 2 diabetes in Japanese Americans. *Diabetes Care* **36**, 1229-35.

Shepherd SO, Wilson OJ, Taylor AS, Thogersen-Ntoumani C, Adlan AM, Wagenmakers AJM, Shaw CS (2015). Low-volume high-intensity interval training in a gym setting improves cardio-metabolic and psychological health. *PloS one* **10**, e0139056.