The Effect of Type 1 Diabetes on the Metabolic Response to Exercise

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Introduction

- Type 1 Diabetes Mellitus (T1DM) is an autoimmune disorder that results in insufficient endogenous insulin production[1].
- Regular exercise has numerous health benefits for individuals with T1DM, however, most insulin-dependent diabetics avoid physical activity due to the fear of exercise-induced hypoglycemia (low blood glucose/BG)[2].
- The risk of hypoglycemia in this population may be partly due to lower liver glycogen stores which is a major source of blood glucose during exercise.
  - However, the mechanism that leads to lower glycogen stores in T1DM is unknown.
- The purpose of this study was to determine the effect of an acute bout of moderate-intensity aerobic exercise on:
  - Glycogen storage in the liver and skeletal muscle of T1DM rats.
  - Content of gluconeogenic enzymes including Glucose 6-Phosphatase (G6Pase) and Phosphoenolpyruvate Carboxykinase (PEPCK) in T1DM rats.

Methods

Animals:

- 3 groups of rats were used in this study; 6 T1DM sedentary males (DS), 8 T1DM exercise males (DE), and 7 Control (non-T1DM) males (C).

Experimental Procedures:

- TIDM Induction - Streptozotocin (STZ) injections of 20 mg/kg were administered daily for five days until BG was ≥18 mmol/L.
  - One insulin pellet was implanted subcutaneously to maintain BG levels between 9-15 mmol/L (2 units of insulin/day).
- Exercise Training Protocol - Animals in the DE experimental group underwent a moderate-intensity acute bout of aerobic exercise which involved running on a motorized treadmill for 1 hour (27 m/min on a 6% incline gradient, ~ 70-80% of VO_2Max)[3].

Experimental Measures:

- BG measurements were taken at 0-, 30-, and 60-mins during exercise (DE group).
- Animals were either immediately sacrificed following the acute bout of exercise (DE group) or before exercise (DS & C) and liver and lower limb muscle tissues were removed.
- Western blot analysis was conducted for G6Pase, PEPCK, and AKT protein content. Glycogen content in liver and skeletal muscle was determined calorimetrically as described by Lo and Russell[4].

Results

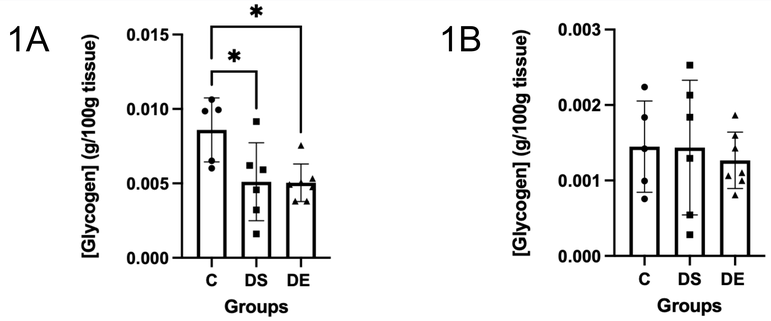
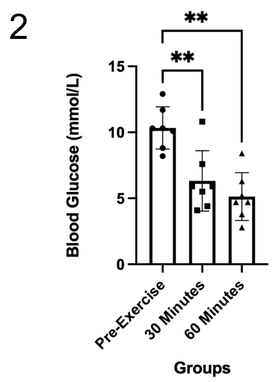


*Figure 1: (A) Liver glycogen and (B) muscle glycogen levels (g/100g tissue) following an acute bout of moderate-intensity aerobic exercise. * Denotes significance (P < 0.05).*



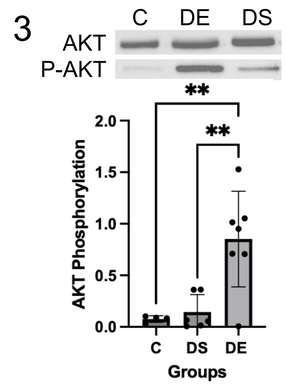


*Figure 2: Blood glucose (mmol/L) at 0-, 30-, and 60-mins during exercise (DE group). ** Denotes significance (P < 0.005).*
*Figure 3: Phosphorylation ratio of AKT following an acute bout of moderate-intensity aerobic exercise. ** Denotes significance (P < 0.005).*

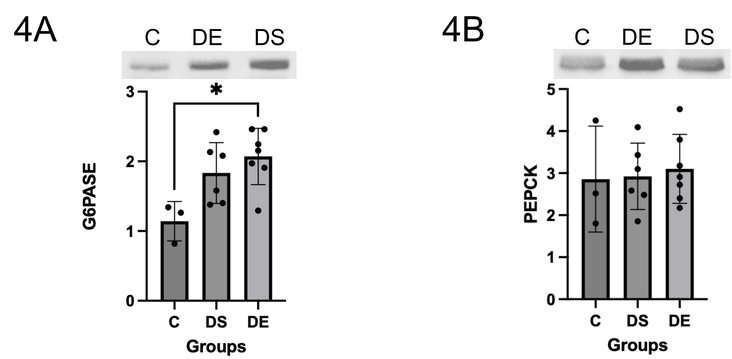


*Figure 4: (A) Liver G6PASE and (B) PEPCK protein content in arbitrary units following an acute bout of moderate-intensity aerobic exercise. * Denotes significance (P < 0.05).*

Summary

- While a decrease in liver glycogen was evident, there were no changes in muscle glycogen in male T1DM rodents during exercise, suggesting that they were unable to utilize muscle glycogen.
- Instead, they seem to rely heavily on glucose from the bloodstream causing a significant decrease in BG levels during exercise.
- This may be due to an insulin mediated increase in the phosphorylation of AKT in muscle during exercise.
- G6Pase appears to be elevated in male T1DM rodents that engaged in exercise compared to the control rodents, suggesting an increase in gluconeogenesis, however, there were no significant differences in PEPCK content between groups.

Conclusion

- AKT phosphorylation leads to the activation of glycogen synthase which prevents the conversion of glycogen to glucose in muscle, thereby, limiting the usage of muscle glycogen and promoting the use of BG.
- Future research should examine enzymes downstream of AKT in the insulin signalling pathway such as Glycogen Synthase Kinase 3 (GSK-3) and Glycogen Synthase to confirm that AKT phosphorylation is activating these substrates.

References

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