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Peer Review

Review of: "High-Resolution Imaging Atlas Reveals Context-Dependent Role of Pancreatic Sympathetic Innervation in Diabetic Mice"

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In this study, the authors provide a detailed examination of how pancreatic nerve projections change with age and in diabetic models (db/db and DIO mice). They also investigate the effects of local sympathetic denervation using 6-OHDA on blood glucose levels. Similar studies have been reported previously, making it difficult to find novelty in this work. If the authors aim to emphasize the differences between db/db and DIO mice, it would be necessary to analyze more deeply the factors responsible for these differences.

Major Points:

1) The data on blood glucose levels for the DIO and db/db models is missing. It is essential to quantitatively demonstrate the progression of diabetes at 10 and 26 weeks.

2) In Figures 5 and 6, the analyses of TH-positive nerves in the pancreas of DIO and db/db mice following 6-OHDA-induced cPSD are missing. To consider the causes of the conflicting results between DIO and db/db mice, such data should be provided to confirm whether TH-positive nerves were effectively ablated.

For example, in 26-week-old DIO mice, the proportion of cells in contact with TH-positive nerves was already significantly reduced even without 6-OHDA treatment, raising questions about the extent of the effect of 6-OHDA.

3) In the discussion, descriptions of the effects of age (10 weeks vs. 26 weeks) are mixed with descriptions of diabetes-induced changes, making it difficult to follow.

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Minor Points:

The quality of pancreatic slice images in Figures S1B and S2C is insufficient. Islets were not clearly distinguished using insulin and glucagon staining, and insulin and glucagon signals overlap in some areas.

Declarations

Potential competing interests: No potential competing interests to declare.