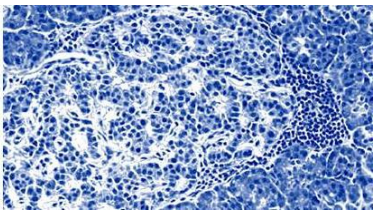
nPOD
Network for Pancreatic Organ Donors with Diabetes



Pancreatic Islet and Exocrine Tissue Innervation is Not Altered in Type 1 Diabetes

AUTHORS

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PURPOSE

Impaired counterregulatory response of glucagon to hypoglycemia is a common complication of type 1 diabetes (T1D). One proposed contributor to abnormal glucagon secretion is decreased sympathetic innervation in T1D islets.

METHODS

To systematically assess the innervation of human pancreatic tissues, we examined samples from donors with recent-onset T1D (<10 yrs, age 13-45 yrs, n = 11), longstanding T1D (>10 yrs, age 24-63 yrs, n = 11), and non-diabetic controls (age 10-55 yrs, n = 12). Islet and exocrine tissue innervation was visualized by pan-neuronal marker tubulin β-3 and analyzed by a 2-D morphometry and 3-D rendering.

SUMMARY OF RESULTS

By quantifying the nerve fiber length (0.41±0.07 nm/μm^2) and density (202±25 fibers/mm^2), we found that innervation in control human islets was nearly 20-fold less than previously reported in mouse islets. In contrast to mouse, human exocrine tissue was far more innervated than islets with fiber length of 5.3±0.99 nm/μm^2 ($p<0.05$), and density of 912±111 fibers/mm^2 ($p<0.05$). The 3-D analysis showed that nerve fibers follow extracellular matrix (ECM) formed around acini and from there, they extend further into islets along the ECM made by islet vasculature. Although T1D islets were primarily composed of α cells, the analyzed islet area was similar to controls (control: 15.5±1.5 mm^2, recent-onset T1D: 16.5±1.4 mm^2, long-standing T1D: 16.7±1.5 mm^2; $p>0.05$), and so was the 3-D arrangement of nerve fibers in exocrine tissue and islets. Regardless of T1D duration, the islet fiber length (recent-onset: 0.84±0.29 nm/μm^2; long-standing: 0.91±0.16 nm/μm^2) and density (recent-onset: 338±78 fibers/mm^2; longstanding: 430±57 fibers/mm^2), as well as exocrine fiber length (recent-onset: 5.94±0.75 nm/μm^2; longstanding: 7.13±1.11 nm/μm^2) and density (recent-onset: 1193±68 fibers/mm^2; longstanding: 1559±175 fibers/mm^2) did not differ from controls ($p>0.05$).

CONCLUSIONS

These data indicate that neuronal patterning of human pancreas is significantly different from that of mouse and islet innervation does not appear to be altered in T1D.