The sympathetic nervous system is crucial for the regulation of visceral organ function. For instance, the activation of the sympathetic nervous system promotes glycogenolysis in the liver and modulates glucagon and insulin release from the pancreas, thereby raising blood glucose levels. A decrease in sympathetic nerve activity has the opposite effect. Although such acute effects of sympathetic activity changes have been studied, their long-term outcomes have not been previously examined. In this study, we removed the celiac/superior mesenteric ganglia, where sympathetic postganglionic neurons innervating pancreas and liver locate, and examined its effects on glucose homeostasis and islet size several weeks after surgery. Consistent with the reduction in gluconeogenesis, glucose tolerance improved in gangliectomized mice. However, contrary to our expectation that the inhibition of pancreatic function by sympathetic nerves would be relieved with gangliectomy, insulin or C-peptide release did not increase. Examining the size distribution of pancreatic islets, we identified that the gangliectomy led to a size reduction in large islets and a decrease in the proportion of α and β cells within each islet, as analyzed by immunostaining for insulin and glucagon, respectively. These results indicate that the absence of sympathetic nerve activity reduces the size of the pancreatic islets within a few weeks to reinstate the homeostatic mechanism of blood glucose levels.