Pancreatic innervation is not essential for exercise-induced changes in glucagon and insulin or glucose kinetics

ROBERT H. COKER,1 YOSHIHARU KOYAMA,1 D. BROOKS LACY,2 PHILLIP E. WILLIAMS,3 NATHALIE RHEAUME,1 AND DAVID H. WASSERMAN1
1Department of Molecular Physiology and Biophysics, 2The Diabetes Research and Training Center, and 3Department of Surgery, Vanderbilt University School of Medicine, Nashville, Tennessee 37232-0615

Coker, Robert H., Yoshiharu Koyama, D. Brooks Lacy, Phillip E. Williams, Nathalie Rheaume, and David H. Wasserman. Pancreatic innervation is not essential for exercise-induced changes in glucagon and insulin or glucose kinetics. Am. J. Physiol. 277 (Endocrinol. Metab. 40): E1122–E1129, 1999.—The purpose of this study was to determine the role of pancreatic innervation in mediating exercise-induced changes in pancreatic hormone secretion and glucose kinetics. Dogs underwent surgery >16 days before an experiment, at which time flow probes were implanted on the portal vein and the hepatic artery, and Silastic catheters were inserted in the carotid artery, portal vein, and hepatic vein for sampling. In one group of dogs (DP) all nerves and plexuses to the pancreas were sectioned during surgery. A second group of dogs underwent sham denervation (SHAM). Pancreatic tissue norepinephrine was reduced by >98% in DP dogs. Each study consisted of basal (~30 to 0 min) and moderate exercise (0 to 150 min, 100 m/min, 12% grade) periods. Isotope ([3-3H]glucose) dilution and arteriovenous differences were used to assess hepatic function. Arterial and portal vein glucagon and insulin concentrations and the rate of net extrahepatic splanchnic glucagon release (NESGR) were similar in DP and SHAM during the basal period. Arterial and portal vein glucagon and NESGR increased similarly in DP and SHAM during exercise. Arterial and portal vein insulin were similar during exercise. Arterial glucose, tracer-determined endogenous glucose production, and net hepatic glucose output were similar in DP and SHAM during the basal and exercise periods. These results demonstrate that pancreatic nerves are not essential to pancreatic hormone secretion or glucose homeostasis during rest or moderate exercise.

pancreas; nerves and hormones

CHANGES IN THE PANCREATIC SECRETION of glucagon and insulin play an important role in glucoregulation during exercise (38). The factors that control glucagon and insulin release from the pancreas have not, however, been well defined. It is known that the pancreas is innervated by the vagus and splanchnic nerves and that the stimulation of these nerves can alter glucagon and insulin secretion (42). Although vagally induced insulin secretion is mediated predominantly by muscarinic mechanisms, nonmuscarinic (possibly peptidergic) mechanisms mediate vagally induced changes in glucagon secretion (2). α- and β-Adrenergic stimulation increases the pancreatic secretion of glucagon (7, 23, 35). α-Adrenergic stimulation inhibits insulin secretion, whereas β-adrenergic stimulation increases insulin release (7, 14, 23). Even though insulin and glucagon secretion can be regulated by nerve stimulation, the role of pancreatic innervation in the mediation of exercise-induced changes in these hormones has not been established.

Partial denervation of the canine pancreas has been shown to attenuate the rise in glucagon but not the fall in insulin in response to exercise (16). Despite the blunted glucagon response, arterial glucose levels did not fall. Specific assessment of glucose kinetics was not made in these studies (16). Furthermore, only the nerves that follow the pancreatic branches of the cranial pancreatocoduodenal artery were sectioned in these studies, and nerves that follow the caudal pancreatocoduodenal artery were not sectioned (26). It is possible that complete denervation of the pancreas might have resulted in more profound differences in the glucoregulatory response to exercise.

The present study was designed to determine the role of pancreatic innervation in mediating the exercise-induced changes in pancreatic hormone secretion and glucose kinetics. For these purposes, nonhepatic splanchnic and hepatic arteriovenous differences were measured and isotopic techniques were utilized in pancreatic-denervated or sham-denervated dogs.

METHODS

Animals and surgical procedures. Experiments were performed on a total of 14 overnight-fasted mongrel dogs (mean wt 22.0 ± 0.6 kg) of either sex that had been fed a standard diet (Pedigree beef dinner and Wayne Lab Blox: 51% carbohydrate, 31% protein, 11% fat, and 7% fiber based on dry wt). The dogs were housed in a facility that met American Association for the Accreditation of Laboratory Animal Care guidelines, and the protocols were approved by the Vanderbilt University Animal Care Subcommittee. At least 16 days before each experiment, a laparotomy was performed while the dogs were under general anesthesia (0.04 mg/kg of atropine and 15 mg/kg pentobarbital sodium presurgery and 1.0% isoflurane inhalation anesthetic during surgery). An incision in the neck region allowed the isolation of the carotid artery into which a Silastic catheter (0.04 in ID) was inserted and advanced to the aortic arch for sampling and hemodynamic measurements during experiments. Silastic catheters (0.04 in. ID) were inserted into the portal vein and left common hepatic vein for sampling. Silastic catheters (0.03 in. ID) were inserted into the vena cava for infusion of [3-3H]glucose. Catheters were filled with heparinized saline, and the free ends were knotted. Ultrasonic transit time flow probes were fitted and secured to the portal vein and hepatic artery.
The leukocyte count was below 18,000/mm$^3$.

6 days before the experiment to determine the leukocyte count and the hematocrit of the animal. Only animals with 1) a leukocyte count below 18,000/mm$^3$, 2) a hematocrit above 36%, 3) a good appetite (consumption of daily food ration), and 4) normal stools were used.

All studies were conducted in dogs after an 18-h fast. The free catheter ends and flow probe leads were accessed through small skin incisions made under local anesthesia (2% lidocaine; Astra Pharmaceutical Products, Worcester, MA) in the abdominal and neck regions on the morning of the experiment. The contents of the catheters were then aspirated and flushed with saline. The exposed catheters were connected to Silastic tubing, which was secured to the back of the dog with quick-drying glue.

Experimental procedures. Experiments consisted of a tracer equilibration period (−130 to −30 min), a basal period (−30 to 0 min), and an exercise period (0 to 150 min, 100 m/min, 12% grade). This exercise protocol is advantageous in that sympathetic stimulation is undetectable [as indicated by the pancreatic polypeptide (PP) response to exercise], thereby allowing the study of sympathetic stimulation to the pancreas. A primed (50 μCi) infusion of [3-3H]glucose (New England Nuclear, Boston, MA) was initiated at t = −130 min. The [3-3H]glucose infusion was increased during exercise in proportion to the increased glucose flux normally present during exercise of this intensity in both protocols (Fig. 1) (29). Portal vein and hepatic artery blood flows were monitored on-line throughout the experiments.

Blood sample collection and processing. Arterial blood samples were drawn at t = −30, −15, 0, 2.5, 5, 7.5, 10, 15, 20, 40, 60, 80, 100, 130, and 150 min. Portal vein and hepatic vein blood samples were drawn at the same times with the exception of t = −2.5, 7.5, and 15 min. Dogs were euthanized by an overdose of pentobarbital sodium at the conclusion of the study, and tissue samples were taken from the head, middle, and tail of the pancreas and frozen immediately in liquid N$_2$.

Plasma glucose concentrations were determined by the glucose oxidase method using a glucose analyzer (Beckman Instruments, Fullerton, CA). For the determination of plasma glucose radioactivity, samples were deproteinized with barium hydroxide and zinc sulfate and were centrifuged. The supernatant was then evaporated to remove H$_2$O and reconstituted in 1 ml of water and 10 ml of scintillation fluid [Ecolume (+); ICN Biomedicals, Irvine, CA]. Radioactivity was determined on a Beckman liquid scintillation counter. Immunoreactive insulin was measured using a double-antibody procedure [interassay coefficient of variation (CV) of 16% (28)]. Immunoreactive glucagon (3,500 mol wt) was measured in plasma samples containing 500 kallikrein-inhibitor units/ml aprotenin (Trasyld, FBA Pharmaceuticals, NY) by use of a double-antibody system (CV of 8%) modified from the method developed by Morgan and Lazarow for insulin (28). Materials for these assays have been published previously (9). PP was measured using a double-antibody system developed by Ginerich et al. (15). Pancreas tissue was powdered over liquid N$_2$ immediately after the study and homogenized in a 5 mM solution of 4% perchloric acid. Samples were then centrifuged at 4°C, and the supernatant was extracted for pancreas norepinephrine analysis by HPLC. Blood samples for norepinephrine and epinephrine were collected in tubes containing EGTA and glutathione and were centrifuged at 4°C; plasma was stored at −70°C for subsequent HPLC analysis. Catecholamine concentrations were calculated on the basis of linear regression using dihydroxybenzylamine as an internal standard. The CV values with this method were 5 and 7% for norepinephrine and epinephrine, respectively. Plasma cortisol was measured with the Clinical Assays Gamma Coat radioimmunoassay kit (Clinical Assays, Travenol-Genetech Diagnostics, Cambridge, MA) with an interassay CV of 6%.

Calculations. Net hepatic glucose output (NHGO) was determined according to the formula HAF × ([H] − [A]) + PVF × ([H] − [P]), where [A], [P], and [H] are the arterial, portal vein, and hepatic vein glucose concentrations, and HAF and PVF are the hepatic artery and portal vein blood flows.

Net nonhepatic splanchic glucagon release (NESGR) was calculated according to the formula ([P] − [A]) × PVF, where [P] and [A] are the portal vein and arterial plasma glucagon concentrations. Endogenous glucose production (R$_g$) and glucose utilization (R$_d$) were calculated using the two-compartment approach described by Mari (24). Changes in specific activity were minimized during the exercise period by increasing the infusion rate of [3-3H]glucose in proportion to exercise-induced changes in glucose flux to increase the accuracy of the R$_g$ calculation (29).

Statistical analysis. Superanova (Abacus Concepts, Berkeley, CA) software installed on a Macintosh Power PC was used to perform statistical analyses. Statistical comparisons between groups and over time were made using ANOVA designed to account for repeated measures. Specific time
points were examined for significance using contrasts solved by univariate repeated measures. Statistics are reported in the corresponding table or figure legend for each variable. Data are presented as means ± SE. Statistical significance was defined as P < 0.05.

RESULTS

Arterial and portal vein plasma glucagon, insulin, glucagon-to-insulin ratio, and arterial plasma PP. Arterial glucagon was similar during the basal period in DP (44 ± 6 pg/ml) and SHAM (47 ± 3 pg/ml). Arterial glucagon increased (P < 0.05) similarly in DP (61 ± 6 pg/ml, t = 150 min) and SHAM (59 ± 3 pg/ml, t = 150 min) during exercise (Fig. 2). In addition, basal portal vein glucagon was not different between DP (51 ± 6 pg/ml) and SHAM (56 ± 6 pg/ml) and increased (P < 0.05) to the same extent in DP (108 ± 12 pg/ml, t = 150 min) and SHAM (96 ± 8 pg/ml, t = 150 min) during exercise (Fig. 2). Basal arterial insulin was not different in DP (9 ± 1 µU/ml) or SHAM (9 ± 1 µU/ml). Arterial insulin fell (P < 0.05) similarly in DP (5 ± 1 µU/ml, t = 150 min) and SHAM (6 ± 1 µU/ml, t = 150 min) during exercise (Fig. 3). Portal vein insulin was similar in DP (17 ± 1 µU/ml) and SHAM (19 ± 1 µU/ml) during the basal period and was unchanged by exercise in both groups (Fig. 3). The basal arterial glucagon-to-insulin ratio was not different (P > 0.05) in DP (6 ± 1 pg/µU) and SHAM (5 ± 1 pg/µU). In addition, the arterial glucagon-to-insulin ratio increased (P < 0.05) similarly during exercise in DP (12 ± 2 pg/µU, t = 150 min) and SHAM (10 ± 1 pg/µU, t = 150 min) (Fig. 4). The basal portal vein glucagon-to-insulin ratio was not
different (P > 0.05) between DP (4 ± 1 pg/µU) and SHAM (3 ± 1 pg/µU). The portal vein glucagon-to-insulin ratio increased (P < 0.05) similarly in DP (9 ± 2 pg/µU, t = 150 min) and SHAM (7 ± 2 pg/µU, t = 150 min) during exercise (Fig. 4).

Basal PP was similar in DP (142 ± 25 pg/ml) and SHAM (114 ± 25 pg/ml). PP was not significantly increased by exercise in either group (Fig. 5).

NESGR. Basal NESGR was not significantly different between DP (88 ± 25 pg·kg⁻¹·min⁻¹) and SHAM (120 ± 25 pg·kg⁻¹·min⁻¹). NESGR was also similar in DP (482 ± 108 pg·kg⁻¹·min⁻¹, t = 150 min) and SHAM (487 ± 130 pg·kg⁻¹·min⁻¹, t = 150 min) during exercise (Fig. 6).

Arterial plasma epinephrine and norepinephrine concentrations. Basal arterial plasma epinephrine was similar in DP (104 ± 12 pg/ml) and SHAM (125 ± 14 pg/ml). Plasma epinephrine increased (P < 0.05) in both groups and was not different in DP (531 ± 105 pg/ml, t = 150 min) compared with SHAM (574 ± 101 pg/ml, t = 150 min) during exercise (Fig. 7). Basal plasma norepinephrine was similar in DP (189 ± 9 pg/ml) and SHAM (205 ± 12 pg/ml). Plasma norepinephrine increased (P < 0.05) in both groups and was not different between DP (750 ± 92 pg/ml, t = 150 min) and SHAM (636 ± 69 pg/ml, t = 150 min) during exercise (Fig. 7).

Arterial plasma cortisol. Basal arterial cortisol was similar in DP (2 ± 0 µg/ml) and SHAM (2 ± 1 µg/ml). Arterial cortisol increased (P < 0.05) in both groups and was not different in DP (8 ± 2 µg/ml, t = 150 min) compared with SHAM (11 ± 3 µg/ml, t = 150 min) during exercise (Fig. 8).

Arterial glucose concentration and kinetics. Basal arterial plasma glucose was similar in DP and SHAM. In addition, arterial glucose remained unchanged with exercise in both groups (Fig. 9). Basal NHGO was similar in DP (1.8 ± 0.2 mg·kg⁻¹·min⁻¹) and SHAM.
At 150 min of exercise, NHGO had risen \( \left( P, 0.05 \right) \) to \( 7.8 \pm 1.2 \) mg·kg\(^{-1}\)·min\(^{-1}\) in DP and \( 7.0 \pm 0.9 \) mg·kg\(^{-1}\)·min\(^{-1}\) in SHAM (Fig. 9). In agreement with arteriovenous difference measurements, basal \( R_a \) was similar in DP \( (2.5 \pm 0.1 \) mg·kg\(^{-1}\)·min\(^{-1}\)) and SHAM \( (2.7 \pm 0.1 \) mg·kg\(^{-1}\)·min\(^{-1}\)). \( R_a \) increased \( (P < 0.05) \) similarly in DP \( (7.8 \pm 0.8 \) mg·kg\(^{-1}\)·min\(^{-1}\), \( t = 150 \) min) and SHAM \( (7.2 \pm 0.8 \) mg·kg\(^{-1}\)·min\(^{-1}\), \( t = 150 \) min) during exercise (Fig. 10). Basal \( R_d \) was similar in DP \( (2.5 \pm 0.2 \) mg·kg\(^{-1}\)·min\(^{-1}\)) and SHAM \( (2.6 \pm 0.1 \) mg·kg\(^{-1}\)·min\(^{-1}\)) and SHAM \( (2.6 \pm 0.1 \) mg·kg\(^{-1}\)·min\(^{-1}\), \( t = 150 \) min) during exercise and was not different between DP \( (7.7 \pm 0.7 \) mg·kg\(^{-1}\)·min\(^{-1}\), \( t = 150 \) min) and SHAM \( (7.0 \pm 0.9 \) mg·kg\(^{-1}\)·min\(^{-1}\), \( t = 150 \) min) (Fig. 10).

Hepatic blood flows. Portal vein and hepatic artery blood flows were not significantly different between groups during the basal and exercise periods (Table 1).

**DISCUSSION**

Sympathetic nerves have been proposed to mediate the increase in glucagon and decrease in insulin during exercise (17, 25, 35). As a result of these divergent changes in insulin and glucagon, glucose production is increased to match the increased rate of glucose utilization, and glucose homeostasis is maintained (39, 40). The results of this study show that pancreatic innervation is not essential in the regulation of exercise-induced changes in insulin, glucagon, NESGR, \( R_a \), and NHGO or glucose homeostasis.

Pancreas norepinephrine levels were reduced by >98% in dogs ~17 days after denervation, substantiating the effectiveness of the surgical technique in this study. This is consistent with previous studies in rats that also showed that pancreas norepinephrine levels were reduced by ~98% 1 wk after surgical pancreatic denervation (43). The virtual elimination of pancreas norepinephrine supports the premise that denervation removed all of the sympathetic innervation of the pancreas. It is important to note that parasympathetic nerve fibers lie in close proximity with sympathetic nerve fibers as they innervate the pancreas via the cranial and caudal pancreaticoduodenal arteries (27). Because parasympathetic and sympathetic nerves are parallel in their anatomic arrangement, it was presumed that parasympathetic fibers would also be removed by surgical denervation. Reinnervation of pancreas tissue by parasympathetic and sympathetic nerves requires ~13 wk (22) and should not, therefore, be a factor in these studies in which experiments were conducted ~2.5 wk after surgery.

Stimulation of PP secretion is thought to be under vagal control so that changes in PP levels directly correspond to changes in vagal activity (1, 36). Despite the use of surgical procedures designed to remove sympathetic and parasympathetic innervation to the pancreas, preliminary studies have demonstrated increases in PP in response to overt hypoglycemia in dogs that have undergone the same surgical pancreatic denervation procedure utilized in this study (37). This suggests that parasympathetic fibers may remain intact, even when sympathetic fibers have been eliminated. Although stimulation of PP release has been shown during exercise in some experiments (6, 19), the exercise protocol used in the present study does not...
release, however, the action of norepinephrine on release has an inhibitory effect on insulin release, whereas b-cell (27). Stimulation of norepinephrine and inhibits insulin secretion from the secretion (2, 35). Splanchnic nerve stimulation releases nerve stimulation can modulate pancreatic hormone SHAM) are surprising, because vagal and splanchnic induced glucagon and insulin responses in DP and the interpretation of the results from the present study. The findings of the present study (similar exercise-induced glucagon and insulin responses in DP and SHAM) are surprising, because vagal and splanchnic nerve stimulation can modulate pancreatic hormone secretion (2, 35). Splanchnic nerve stimulation releases norepinephrine and inhibits insulin secretion from the b-cell (27). Stimulation of a2-receptors by norepinephrine has an inhibitory effect on insulin release, whereas stimulation of b-adrenergic receptors increases insulin release. However, the action of norepinephrine on a2-receptors predominates, and insulin secretion is normally reduced during exercise (42). Electrical stimulation of the splanchnic nerve can simultaneously activate a- and b-adrenergic receptors on the a-cell and increase glucagon secretion (3, 42). However, specific surgical denervation of the pancreas in the present study did not affect exercise-induced changes in the arterial and portal vein concentrations of glucagon or arterial insulin. These findings suggest that although nerves are capable of controlling changes in pancreatic hormones, they are not essential to the exercise response. The present study contrasts with experiments performed in dogs with a partial pancreatic nerve section (3 wk before study). These animals had a blunted arterial glucagon response to exercise after pancreatic denervation (16). The interpretation of these earlier studies is complicated by an increase in plasma glucose concentrations compared with the response in the same dogs before denervation. The elevation in plasma glucose might have attenuated the increment in glucagon that would normally have resulted. In addition, the denervation procedure used in the previous study was only partial, as it did not remove nerves that followed the caudal pancreaticoduodenal artery. Portis et al. (32) reported an elevation instead of a gradual fall in arterial insulin during exercise in long-term islet cell-autografted dogs compared with sham dogs. The paradoxical increase in insulin during exercise in these studies lends support to the premise that the normal insulin response to exercise is under autonomic control. Nevertheless, the arterial plasma glucagon and glucose responses to exercise were similar. It is important to note that the catecholamine levels were higher in the islet cell-autografted dogs and could have compensated for the lack of pancreatic innervation. A recent study in pancreas transplant patients (presumably free of pancreatic innervation) reported alterations in glucagon, C-peptide, and insulin during exercise (33). No significant difference was reported in arterial plasma glucose between the two groups. The use of a patient population (33) complicates the interpretation of these studies. The absolute work intensity (33 W) in these pancreas transplant patients may have been too low to elicit significant pancreatic hormone responses.

Although the nerves that innervated the pancreas were sectioned during surgery, pancreatic adrenergic receptors and adrenal glands remained intact. There is only limited evidence for supersensitivity of the denervated pancreas to catecholamines (30). Nevertheless, such an adaptation could make the role of circulating catecholamines more prominent. Therefore, exercise-induced increases in epinephrine could have influenced glucagon and insulin secretion. However, adrenomedullated rats infused with saline or epinephrine replacement to achieve normal physiological levels have similar pancreatic hormone levels during exercise (4). Although pancreatic denervation in the present study, adrenomedullation in rodents (4), and adrenalectomy in humans (18, 20) alone do not seem to affect pancreatic hormone secretion during exercise, a combination of these procedures may impair the pancreatic hormone response. For example, changes in glucagon and insulin are diminished in adrenomedullated rats that were also chemically sympathectomized with 6-hydroxydopamine (34). The physiological importance of adrenergic drive is also supported by pharmacological evidence. For example, inhibition of insulin release can be reversed by a-adrenergic receptor blockade during exercise, and the blockade of a- and b-adrenergic receptors can diminish the exercise-induced increase in glucagon (20, 23). The catecholamine and glucagon responses to exercise are closely correlated in DP and SHAM, which is consistent with a possible role of circulating catecholamines in control of exercise-induced changes in glucagon secretion (see Figs. 2 and

<table>
<thead>
<tr>
<th>Table 1. Portal vein and hepatic artery blood flows during basal and exercise periods in denervated pancreas and sham dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td><strong>Portion vein blood flow, ml·kg(^{-1})·min(^{-1})</strong></td>
</tr>
<tr>
<td>Sham</td>
</tr>
<tr>
<td>Denervated pancreas</td>
</tr>
<tr>
<td><strong>Hepatic artery blood flow, ml·kg(^{-1})·min(^{-1})</strong></td>
</tr>
<tr>
<td>Sham</td>
</tr>
<tr>
<td>Denervated pancreas</td>
</tr>
</tbody>
</table>

Data are means ± SE of sham (n = 6) and denervated (n = 8) dogs.
7). On the basis of these observations, circulating catecholamines may stimulate changes in pancreatic hormones during exercise in combination with neural input, when pancreatic nerves are left intact, or as a compensatory mechanism when the pancreas is denervated.

Although arterial insulin fell gradually in DP and SHAM during exercise, portal vein insulin did not fall in either group. This would appear to suggest that increased hepatic insulin clearance may be a cause of the reduced arterial insulin levels during exercise. In fact, a rise in insulin clearance during exercise has been demonstrated through the simultaneous measurement of insulin and C-peptide in humans (41). Previous studies in our laboratory have shown both a decrease in portal vein insulin (5, 39) and unchanged portal vein insulin (8) in response to exercise. The reason for the variation in portal vein insulin response may be due to potential errors with portal vein insulin sampling, coupled with difficulties in detecting small differences in insulin. Streaming of newly secreted insulin can confound the precise measurement of portal vein insulin and possibly glucagon, particularly when portal vein blood flow is laminar (21). Therefore, the full interpretation of portal vein insulin requires consideration of portal vein blood flow dynamics.

In addition to catecholamine-mediated changes in islet cell function, galanin is a neurotransmitter that may affect hormone secretion (10, 11, 13). Galanin is released from extrapancreatic and pancreatic sympathetic nerves and inhibits insulin and stimulates glucagon secretion in the dog (13). Because nonhepatic splanchnic norepinephrine spillover (an index of sympathetic drive) increases during exercise in the normal dog (8), and galanin is co-released with norepinephrine (13), one would expect portal vein galanin levels to be higher. It is interesting to note that immunoneutralization of galanin eliminated the swimming-induced inhibition of insulin in rats (12). Only the pancreatic nerves were sectioned in the present study, and the increased release of galanin from nonpancreatic sources during exercise may have contributed to changes in pancreatic hormonal secretion.

In conclusion, exercise-induced changes in insulin and glucagon were maintained despite the elimination of pancreatic sympathetic nerves (>98% reduction in pancreas norepinephrine). As a result, exercise-induced increases in NHGO and R4 were not affected, and glucose homeostasis was preserved. It seems plausible that exercise-induced changes in circulating catecholamines or some other factor may serve as the mediator of pancreatic hormone secretion or as part of a compensatory glucoregulatory mechanism that can compensate for the absence of sympathetic nerves. The preservation of normal exercise-induced changes in glucagon and insulin despite pancreatic denervation has important implications for pancreas transplant and islet cell transplant patients who wish to take advantage of the health benefits of regular exercise.

We are grateful to Deanna Bracy, Eric Allen, Pamela Venson, and Wanda Sneed for excellent technical assistance.

This research was supported by National Institute of Diabetes and Digestive and Kidney Diseases Grant R01-DK-50277. Part of this work was presented at the 58th Annual Meeting of the American Diabetes Association, Chicago, IL in June, 1998. Robert H. Coker was the recipient of a Postdoctoral Fellowship Award from the Juvenile Diabetes Foundation International.

Address for correspondence and reprint requests: R. H. Coker, 220 Turner Center, Dept. of Exercise Science, University of Mississippi, University, MS 38677 (E-mail: rhcoker@olemiss.edu).

Received 11 February 1999; accepted in final form 17 August 1999.

REFERENCES


