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MECHANISMS OF HYPERSOMATOSTATINEMIA IN SPONTANEOUSLY DIABETIC BB RATS. Mary Doris Ruggere* and Yogesh C. Patel, Fraser Laboratories, McGill University, Royal Victoria Hospital, Montreal, Quebec.

We have previously reported elevated somatostatin (SLI) plasma levels in insulinopenic BB rats. The present studies examine dynamic pancreatic and gastric SLI secretion and hepatic metabolism of SLI in the BB rat. Isolated pancreases of 3 groups of 5 untreated diabetic (UD), insulin treated diabetic (TD), and non-diabetic (ND) rats were perfused under basal and stimulatory (19.5 mM glucose + 10 mM theophylline + 20 mM arginine) conditions. Isolated stomach of 3 similar groups of 4 rats were perfused under basal and stimulatory (5.5 nM glucagon) conditions. SLI release was quantitated. In recirculating circuits, isolated livers of 3 groups of 6 rats were perfused for 60 min with 2 ng/ml of somatostatin-14 (S-14) or somatostatin-28 (S-28);hepatic extraction of SLI was measured. In insulinopenic BB rats,

	SLI Secretion, ng/perfusion period				SLI Degradation	
	Pancreas (20 min)		Stomach (15 min)		Hepatic Extraction, %	
	Basal	Stimulated	Basal	Stimulated	S-14	S-28
UD	7.2 ± 1.8	9.1 ± 1.0**	7.3 ± 1.0*	15.4 ± 0.6*	27.1 ± 4.6**	9.8 ± 0.6*
TD	0.6 ± 0.1**	3.7 ± 0.1**	4.0 ± 0.3*	8.7 ± 0.6*	42.0 ± 2.3	13.1 ± 1.8
ND	7.7 ± 1.6	15.8 ± 1.2	4.8 ± 0.2	12.4 ± 0.7	42.8 ± 2.5	13.7 ± 1.6

* P <0.05, ** P <0.01 compared with ND

pancreatic SLI secretion is decreased, gastric SLI secretion is increased and liver SLI degradation is impaired. Insulin treatment normalizes the hepatic defect, impairs gastric SLI secretion, and further diminishes pancreatic SLI secretion. We conclude that hypersomatostatinemia in this diabetic model is not of pancreatic origin, but is due to augmented gastric secretion and decreased hepatic degradation of SLI.

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DEGRADATION OF THE N-TERMINUS AND CENTRAL CORE OF SOMATOSTATIN (SRIF) BY INTACT RAT LIVER. H. Sacks* and L. Cass Terry, Dept. of Medicine, University of Tennessee Center for the Health Sciences, Memphis, TN, and Dept. of Neurology, University of Michigan Medical School, Ann Arbor, MI, USA.

The liver is an important site for SRIF metabolism. To examine the process(es) involved, we monitored clearance of SRIF-like immunoreactivity (SLI) from a recirculating liver (3-4g) perfusate (85 ml) using N-terminus (Sheep B) and core-directed (R101) immunoassays. The t 1/2 of SLI measured with Sheep B was 20.9 ± 2.0 min (S.E., n=4) versus 51.0 ± 6.3 min for R101. The t 1/2 of R101 SLI during perfusion with somatostatin-28 was not statistically different (39.4 ± 5.5 min, n=4) but was significantly shorter (25.9 ± 3.4 min, n=3) with des-(ala^1,gly^2)-N-Ac-SRIF, indicating that extension or deletion at the N-terminus does not impede SRIF clearance. HPLC showed a small (14%) conversion of SRIF-28 to SRIF by liver in 1 hr. The t 1/2 of immunoprecipitable ^{125}I-Tyr-SRIF was 9.0 min. The t 1/2 of immunoprecipitable ^{125}I-Tyr^{11}-SRIF was 55.7 min, which was similar to that of SRIF measured by antiserum R101. For both tracers, there was a prompt appearance of non-immunoprecipitable degradation products as intact peptide was cleared. By contrast, appearance of non-immunoprecipitable degradation products of ^{125}I-insulin was preceded by a 5-10 min delay while intact hormone was removed. Conclusions: 1) SRIF is metabolized in the intact liver by endopeptidase and aminopeptidase activities. 2) The two processes have different degradation rates. 3) The kinetics of ^{125}I-labelled SRIF and insulin metabolism differ. 4) The absence of a delay in product formation suggests that SRIF metabolism by liver does not involve an internalization step.