University of Louisville

ThinkIR: The University of Louisville's Institutional Repository

Electronic Theses and Dissertations

1940

The effect of hypophysectomy on gastric motility in the dog.

Edmund A. Smolik
University of Louisville

Follow this and additional works at: <https://ir.library.louisville.edu/etd>

Part of the [Gastroenterology Commons](#)

Recommended Citation

Smolik, Edmund A., "The effect of hypophysectomy on gastric motility in the dog." (1940). *Electronic Theses and Dissertations*. Paper 1956.
<https://doi.org/10.18297/etd/1956>

This Master's Thesis is brought to you for free and open access by ThinkIR: The University of Louisville's Institutional Repository. It has been accepted for inclusion in Electronic Theses and Dissertations by an authorized administrator of ThinkIR: The University of Louisville's Institutional Repository. This title appears here courtesy of the author, who has retained all other copyrights. For more information, please contact thinkir@louisville.edu.

UNIVERSITY OF LOUISVILLE

THE EFFECT OF HYPOPHYSECTOMY ON GASTRIC
MOTILITY IN THE DOG

A Dissertation

Submitted to the Faculty

Of the Graduate School of the University of Louisville

In Partial Fulfillment of the

Requirements for the Degree

Of Master of Science

Department of Physiology

By

Edmund A. Smolik

1940

LIBRARY
UNIVERSITY OF LOUISVILLE
1940

Date _____

Approved by

Committee:

English Department:

ACKNOWLEDGMENT

**The writer wishes to acknowledge
his indebtedness to Doctor Hampden C.
Lawson under whose direction this work
was carried out.**

3 Dec '40 Pk.

TABLE OF CONTENTS

	Page
INTRODUCTION	1
METHODS AND RESULTS	4
DISCUSSION	8
SUMMARY AND CONCLUSIONS	9
FIGURES AND TABLES	10
REFERENCES	20

**THE EFFECT OF HYPOPHYSECTOMY ON GASTRIC HUNGER
MOTILITY IN THE DOG**

INTRODUCTION

Many theories have been stated concerning the cause of hunger contractions of the stomach. In particular the relationship of the level of blood sugar and carbohydrate metabolism to gastric motility has been investigated by several workers. Boldyreff (1) first demonstrated an augmentation of the motility of the stomach during hunger. Carlson and his coworkers (2) have shown that other conditions influence gastric hunger contractions such as fasting, moderate exercise, hemorrhage, and exposure to cold.

Carlson and Bulatao (3) showed that injections of insulin increase the gastric activity of normal fasting dogs while Quigley, Johnson and Solomon (4) demonstrated a similar phenomenon in man. Bulatao and Carlson (3) reported that stomach hunger motility was depressed by the intravenous injection of glucose solutions.

Quigley and Hallaran (5) and Malinos (6) found no agreement with the theory that the spontaneous motility of the empty stomach is inversely related to the blood sugar level. Quigley, however, did demonstrate (7) an inhibition of gastric motility by injected carbohydrates and suggested that there is a humoral factor involved in the control of stomach motility.

Carlson in 1919 (8) demonstrated gastric hypermotility in human diabetes as well as experimental pancreatic diabetes

2

in the dog. It has been recognized since the work of Houssay (9) that the hypophysis is concerned with carbohydrate metabolism. Houssay animals — pancreatectomized and hypophysectomized — have blood sugars which are normal or only moderately high, no ketosis, normal R.Q., and very nearly normal glucose tolerance curves (10).

Houssay and Magenta (11), Smith (12) and many others have found an increased sensitivity to insulin in the hypophysectomized animal. Heinbecker (13) showed in hypophysectomized dogs a low, fasting blood sugar. Jones (14) advanced ample proof of a difference in insulin response in completely hypophysectomized animals and partially hypophysectomized animals. The former manifested a hypoglycemia and the latter a hyperglycemia after insulin. He suggests this response as a test for the degree of hypophysectomy.

Further observations on the possible influence of the hypophysis on gastric motility were advanced by Cushing (15) in a classical paper. He noted the occurrence of ulcerative lesions in the alimentary tract in cases of intracranial tumor and injury especially in the interbrain. Others (16, 17, 18) have likewise noted this relationship. Cushing injected pituitrin directly into the ventricles in man and by means of barium meals under fluoroscope found increased motility and tone in the stomach which were not produced on subcutaneous injection of pituitrin.

A comprehensive search of the literature reveals only

one reference to the influence of hypophysectomy on gastric tone. Houssay and collaborators (19) found in hypophysectomized toads (*Bufo Arenarum*) which were in the stage of advanced cachexia a dilated stomach and feeble peristalsis of the intestine together with a great diminution of sensitivity to adrenalin and acetylcholine. These observations were made on isolated segments in Ringer's solution.

In view of the evidence that the anterior lobe of the pituitary is almost certainly a portion of the complex mechanism regulating carbohydrate metabolism, and since posterior lobe extracts not only effect blood sugar but have effects on the motor activity of the alimentary tract, it seems likely that hypophysectomy would produce striking changes in gastric motility.

Since, further, the mechanisms of digestive motility and hunger motility may not be the same, it is possible that hypophysectomy would have different effects on the two types of gastric activity.

In addition, the effect of hypophysectomy on the carbohydrate and insulin response mechanism suggested that observations on the gastric response to insulin might throw light on the relationship between insulin hypermotility and spontaneous hunger motility.

METHODS
AND
RESULTS

METHODS:

Complete data were obtained on 4 dogs. Normal controls were obtained in 10 dogs but only 4 survived hypophysectomy long enough for extended observations.

The dogs weighed from 14.1 to 20 Kg. They were trained to lie fully relaxed on comfortable pads during each experiment which lasted for not less than $2\frac{1}{2}$ hours to not longer than $6\frac{1}{2}$ hours.

The activity of the stomach was studied by the balloon method. The dogs were trained to swallow a stomach tube with a standard length 7 cm. condom balloon attached and records on the empty stomach taken according to the method suggested by Boldyreff and perfected by Carlson. A bromoform manometer was used. Twenty cc. of air was injected into the deflated balloon system at each period of observation, and 15 minutes usually allowed for adjustment of the balloon in the stomach before kymographic tracings were begun.

The dogs were kept on a constant diet of standard laboratory food preparations (Thorobread Crackels 500 Gms. and Our Buddy Canned Dog Food 250 Gms.), being adequate in vitamins and minerals.

Digestion motility was studied immediately after consumption of a meal — usually for a period of $2\frac{1}{2}$ hours. Hunger motility was studied on dogs starved exactly 18 hours and records run for 3 to 6 hours, usually 5 hours. In each case before injection of insulin the records were continued so that a satis-

factory normal motility was obtained.

All injections were made into the posterior crural vein. One cc. of normal saline or Ringer's solution was given intravenously routinely for control. Insulin was Eli Lilly & Company preparation "Iletin." All injections were given in a uniform volume of 1 cc. The Folin-Wu method of determining blood sugar was used.

The method of extirpating the pituitary was the temporal intracranial route as devised by Dandy and Reichert (20). Prior to operation instead of injecting hypertonic saline as suggested by Weed and McKibbin (21), we found that injecting 50 cc. of 50% sucrose $\frac{1}{2}$ hour before operation caused the brain to shrink remarkably, rendering the exposure of the pituitary much easier. This was based on the work of Bullock and associates (22) who demonstrated a fall in cerebrospinal fluid pressure for 12 hours without any evidence of a secondary rise.

This is a satisfactory method of hypophysectomy in the dog. It is quick and easy. The success of the method depends on the avoidance of cerebral trauma and adequate exposure of the pituitary gland, which conditions are achieved by the use of hypertonic sucrose, suction, the inverted position of the head and puncture of the cisterna interpeduncularis.

RESULTS:

Digestion Motility: Neither tone, contraction height (amplitude), nor rhythm during digestion appeared to be signifi-

cantly changed in any of the animals following hypophysectomy (fig. I and table I). Table I gives the readings of gastric tone during digestion before and after hypophysectomy.

Hunger Motility: Gross inspection of the records revealed no striking difference in the activity of the empty stomach after hypophysectomy. The records were therefore studied in detail in the hope that differences might be revealed. As shown in tables II, III, and IV, no significant effect of hypophysectomy was demonstrated on average tonus (interval pressure), contraction height or the total duration of inactivity in a 30 minute sample tracing. Measurements of tone, contraction amplitude and rhythm were made during a 7 minute sequence of greatest activity. The total duration of inactivity was derived by adding all quiet intervals, however brief, during the sample period.

Response to Insulin: In the absence of data on the threshold of dosage of insulin required for augmentation of gastric hunger motility and on the relationship between the magnitude of the response and the size of the dose, preliminary studies were made on 2 dogs, with arbitrarily selected constant dose of 0.5 units per Kg. This dose consistently augmented 18 hour fasting motility before hypophysectomy in both dogs. Following hypophysectomy, it was not possible to detect any quantitative difference in the magnitude of the response in either animal.

It was found in these animals, however, that a dose of 0.05 units after hypophysectomy produced a gastric response quantitatively indistinguishable from that following 0.5 units. Since the gastric response appeared not to be proportional to the dose, it was decided to attempt to determine the threshold dosage before and after hypophysectomy.

Data of this sort were obtained on 2 animals (table VI). In both the threshold was lowered from about 0.075 units per Kg. in the normal to 0.012 units per Kg. after hypophysectomy. Typical responses to these minimal doses are shown in fig. 2 and fig. 3.

An attempt was made to correlate the increased gastric sensitivity to insulin with the increased hypoglycemic response which is known to occur, by recording blood sugars at intervals of 15 minutes for an hour following the injection. The hypoglycemic response of the normal dogs to these very small doses was inconstant, and did not differ markedly in degree or duration from the response after hypophysectomy. Fig. 4 presents the data obtained on the dog whose responses were the more striking.

DISCUSSION

DISCUSSION:

The only positive finding in this work is the demonstration of an increased gastric sensitivity to insulin following hypophysectomy. This does not appear to be related to the increased hypoglycemia since the minimal doses of insulin used were not demonstrably different in their effect in the normal and in the hypophysectomized animal.

Since there was no demonstrable augmentation of fasting motility in the dog following hypophysectomy it is doubtful that the increased gastric sensitivity to insulin is of any physiological significance. Furthermore these data constitute additional evidence that starvation and insulin hypermotility are of different mechanisms since hypophysectomy has different effects on the two.

The relatively high blood sugars in our hypophysectomized animals at the end of the 18 hour starvation period suggests that this period may not be long enough to produce full effects. The work should be repeated using starvation periods of 24 to 30 hours if necessary to produce hypoglycemia, and starvation motility at these starvation periods compared with the normal.

In view of the fact that hypothalamic centers are known to control gastric motility, it might be expected that some disturbance of motility might occur because of hypothalamic damage produced by operative trauma. Digestion motility may be taken as incomplete evidence that damage was slight.

SUMMARY AND CONCLUSIONS

SUMMARY:

1. Gastric hunger motility was studied in unanesthetized dogs by the balloon method at periods of 18 hour starvation.

2. The gastric threshold for motor effects of insulin is significantly lowered by hypophysectomy.

3. Digestion motility is not appreciably affected by hypophysectomy.

4. Spontaneous gastric hunger motility as determined by tone, contraction height and rhythm is not appreciably affected by hypophysectomy.

**FIGURES
AND
TABLES**

TABLE I

AVERAGE TONE DURING DIGESTION

(mm. Bromoform)

Dog 2		Dog 3		Dog 4		Dog 21	
N	HPT	N	HPT	N	HPT	N	HPT
18	22	21	16	17	18	25	23
20	18.6	18	18	14.5	20	18	18
26	24.3	15	18	23	16	26	16
22	20	16	20	16	18	23	12
14	15	18	22	18	25	21	26
16	17.3	22	23	16	20	26	
18	22.3		20	21	23		
	24.3		22	18			
	20.6			22			
	20.3			18			
	24						
	18						
AVERAGES							
19.42	20.58	18.3	19.8	17.35	20.0	23.16	18.4

TABLE II

AVERAGE TONE DURING 18 HOURS HUNGER

(mm. Bromoform)

Dog 2		Dog 3		Dog 4		Dog 21	
N	HPT	N	HPT	N	HPT	N	HPT
9	2	10	17	17	8	7	8
11	11	6	11.5	0	17	8.3	2
20	5	4.6	6	2	10	7	3
5.3	15	1	11.5	0	4	9	5
14.3	3.1	4.3	12	10	11	4	0
10.6	0	6	24	1	3	3.5	5.3
3	6.3	1			6		4.6
5.6	7.3	12			16		0
9.6	0	20			6		0
3.6	5.3	20					
AVERAGES							
9.22	5.5	8.49	13.66	5.25	9	5.97	3.1

TABLE III

AVERAGE CONTRACTION HEIGHT DURING 18 HOURS HUNGER

(mm. Bromoform)

Dog 2		Dog 3		Dog 4		Dog 21	
N	HPT	N	HPT	N	HPT	N	HPT
36	63	32	61.5	11	44	68	27
31	62	53	34	26.5	15.3	68	44
33	19	63	38	14	13	28	23.3
56	42	31	23	23	10	73.3	33.3
33.3	48.3	20	36	15	20	70	15
15	36	31.6	20	20	45.6	63.3	51.6
53.3	15.3	22		26			48.3
36	26	36.3		35			78.3
51.6	32.6	48		30			48.3
40	45	50					
AVERAGES							
38.62	38.92	38.60	35.4	16.2	26.53	65.3	41.56

TABLE IV

AVERAGE RHYTHM IN 7 MIN. OF 18 HOURS HUNGER MOTILITY
(mm. Bromoform)

Dog 2		Dog 3		Dog 4		Dog 21	
N	HPT	N	HPT	N	HPT	N	HPT
6	2	8	8	32	9	4	14
6	6	8	9	7	22	5	5
6	6	6	5	9	7	7	7
5	7	7	8	7	7	7	5
9	3	8	9	20	8	6	7
8	3	5	7	6	4	6	5
4	6	7			7		5
8	6	6			7		6
7	6	8			3		4
6	5						
AVERAGES							
6.5	5	6.9	7.8	13.25	8.22	6.07	7.22

TABLE V

TOTAL QUIET INTERVAL IN MINUTES DURING 30 MINUTES TRACING
(mm. Bromoform)

Dog 2		Dog 3		Dog 4		Dog 21	
N	HPT	N	HPT	N	HPT	N	HPT
17.7	28	11.6	23.3	6	11.6	19.3	14
17.5	25.6	14	18.6	12	8.4	14	16.3
14	16.3	18.6	7.0	16.3	25	14	18.6
12	11.6	21	16.3	18.8	13.06	8.4	21
16.3	21	21	14.2	6	14	25	14
17.5	26	23.4	20	14.8	9.8	14.5	19.6
15.4	20	20.3			9.5		16.3
16.2	18	18.2			21		8
17	4.6	16.5			25.6		16.3
18.6	21	20					
AVERAGES							
16.2	19.2	18.4	16.9	11.3	15.3	15.8	16.01

TABLE VI

GASTRIC RESPONSE TO MINIMAL DOSES OF INSULIN

Dog #	Condition	Doses in Units per Kg.				
		0.012	0.025	0.050	0.075	0.150
4	Normal	0	0	0	+	+
			0	0	+	
21	Normal	0	0	0	0	+
		0	0		?	+
4	HPT	+	+	+	+	
		+	+	+		
		+	+			
		+				
21	HPT	0	+	+	+	
		+	+	+		
		+	+			
		0	+			

FIGURE I
DIGESTION MOTILITY

Dog no. 4. Normal

Dog no. 4. Hypophysectomized

FIGURE II

GASTRIC RESPONSE TO MINIMAL DOSES OF INSULIN

A. Dog no. 4. Normal
Insulin 0.05 u./Kg. Time 4 sec.

B. Dog no. 4. Hypophysectomized
Insulin 0.012 u./Kg. Time 4 sec.

FIGURE III

GASTRIC RESPONSE TO MINIMAL DOSES OF INSULIN

A. Dog no. 4. Normal
Insulin 0.025 u./Kg. Time 4 sec.

B. Dog no. 4. Hypophysectomized
Insulin 0.025 u./Kg. Time 4 sec.

Fig. 4

Dog 21

Blood sugar responses
to minimal doses of
insulin

REFERENCES

1. Boldyreff, W. Le travail periodique de l'appareil digestif en dehors de la digestion. Arch. d. Sc. Biol., 1905, 11:1.
2. Carlson, A. J. The Control of Hunger in Health and Disease, Chicago, 1916.
3. Bulatao, E. and Carlson, A. J. The Influence of Experimental Changes in Blood Sugar Level in Gastric Hunger Contraction, Am. J. Physiol., 1924, 69: 107.
4. Quigley, J. P. et al. Action of Insulin on Motility of the Gastro-intestinal Tract, Am. J. Physiol., 1929, 90: 89.
5. Quigley, J. P. and Hallaran, W. R. The Independence of Spontaneous Gastro-intestinal Motility and Blood Sugar Levels, Am. J. Physiol., 1932, 100: 102.
6. Mulinos, M. G. The Influence of Experimental Alterations of Blood Sugar Content on Gastric Hunger Contractions. Am. J. Physiol., 1933, 104: 379.
7. Quigley, J. P. and Phelps, K. R. Mechanisms of Gastric Motor Inhibitions from Ingested Carbohydrates. Am. J. Physiol., 1934, 109: 133.
8. Carlson, A. J. The Control of Hunger in Health and Disease, Chicago, 1919.
9. Houssay, B. A. Quoted in H. B. Van Dyke, The Physiology and Pharmacology of the Pituitary Body, Chicago, 1936.
10. Russell, J. A. The Relation of the Anterior Pituitary to Carbohydrate Metabolism, Physiol. Rev., 1938, 18: 1.

11. Houssay, B. A. and Magenta. Sensibilite des chiens hypophysectemies a l'egard de l'insuline, Comp. rend. Soc. d. biol., 1925, 92: 822.
12. Smith, P. E. et al. Response of Normal and Hypophysectomized Rhesus Monkeys to Insulin, Proc. Soc. Exper. Biol. & Med., 1936, 34: 250.
13. Heinbecker, P. M. Effect of Diet on Insulin Response in Normal and Hypophysectomized Dogs, Proc. Soc. Exper. Biol. & Med., 1937, 36: 804.
14. Jones, Herman. Effect of Insulin on Partially Hypophysectomized Rats, Proc. Soc. Exper. Biol. & Med., 1938, 40: 68.
15. Cushing, Harvey. Peptic Ulcers and the Interbrain, Surg., Gynecol. & Obst., 1924, 55: 1
16. Oppper, L. and Zimmerman, H. M. Ulcers of the Digestive Tract in Association with Cerebral Lesions, Yale J. Biol. & Med., 1938, 11: 39.
17. Masten, M. G. and Bunts, R. C. Neurogenic Erosions and Perforations of Stomach and Esophagus in Cerebral Lesions, Arch. Int. Med., 1934, 54: 916.
18. Gause, H. Gastro-intestinal Symptoms in Diseases of the Brain, J.A.M.A., 1939, 112: 701.
19. Houssay, B. A. et al. Motricite et absorption gastro-intestinale pendant l'asthenie hypophysaire ou surrenale du crapaud, Comp. rend. Soc. d. biol., 1937, 126: 627.

20. Dandy, W. E. and Reichert, F. L. Studies in Experimental Hypophysectomy, Effect on Maintenance of Life, Bull. Johns Hopkins Hosp., 1925, 37: 1.
21. Weed, L. H. and McKibbin, P. S. Pressure Changes in Cerebrospinal Fluid Following Intravenous Injection of Solutions of Various Concentrations, Am. J. Physiol., 1919, 48: 512.
21. Weed, L. H. and McKibbin, P. S. Experimental Alterations of Brain Bulk, Am. J. Physiol., 1919, 48: 531.
22. Bullock, Gregersen and Kenney. The Use of Hypertonic Sucrose Intravenously to Reduce Cerebrospinal Fluid Pressure without a Secondary Rise, Am. J. Physiol., 1935, 112: 82.