Effects of Intracisternal Glucose or Insulin Injections on Glucose Homeostasis in Cat

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SUMMARY

The injection of glucose (100 mg) into the cisterna magna of intact anesthetized cats elicited immediate glycosuria and natriuresis without significant changes in blood glucose concentration. Immunoreactive insulin (IRI) increased 140% in plasma, and Na^+ concentration decreased in cerebrospinal fluid (CSF). After kidney denervation there was a significant decrease in glucose and Na^+ concentrations in urine. Control injections with manitol did not elicit changes in the studied parameters. Abdominal vagotomy abolished the rise in IRI levels and the decrease in Na^+ concentration in CSF. Vagotomy or adrenalectomy also attenuated the glycosuria and the rise in urine Na^+ concentration. The intracisternal injection of insulin (0.5 U/kg) caused first, a decrease in glucose concentration in CSF and afterwards a longer latency in plasma. Again, these responses were significantly attenuated when insulin was administered in vagotomized cats.

These experiments indicate that the nervous system, through the vagi, adrenal glands, and kidneys, plays an important role in glucose homeostasis after increasing glucose or insulin levels in the CSF above physiologic concentrations. The results obtained with a denervated kidney confirm the participation of nervous system in the effector mechanism that brings the sugar and Na^+ into the urine. Evidence is presented for an interrelationship between glucose and Na^+ concentrations in blood, urine, and CSF. DIABETES 1986; 35:826–31.

The central nervous system (CNS) involvement in blood glucose regulation was confirmed by producing conditioned hypoglycemic reflexes in dogs and rats.[1–4] In further studies, vagus nerve influence in these reflexes was established. Central stimulation of abdominal vagus elicited a short-latency rise in glucose uptake by the brain without changing immunoreactive insulin (IRI) levels in plasma, suggesting an afferent function of the vagi in glucose homeostasis.[5,6] Enhanced insulin secretion after peripheral vagal stimulation,[7,8] and the fact that hypoglycemic conditioned reflex could not be obtained in atropinized animals,[2] pointed to an effector function of this nerve in the control of blood sugar level.

The hypothesis that the CNS is involved in the regulation of blood glucose was strengthened by the presence of specific insulin receptors in the CNS.[9,10] Electrophysiologic studies also suggested the presence of a glucose-sensing mechanism in the hypothalamus. Electrical activity in this area is selectively altered by varying the glucose or insulin concentrations either in the blood or in the extracellular space close to the hypothalamic neurons.[11,12] However, the effector mechanism by which the brain controls glucose homeostasis is largely unknown. Several studies have tried to establish a correlation between changes of insulin or glucose levels in the CNS and those in the blood. An infusion of insulin into the cerebrospinal fluid (CSF) provokes a decrease in blood glucose concentration,[13–15] which is, at least in part, mediated by an enhanced pancreatic insulin secretion with vagal nerve participation.[14,16] However, a clear relationship between CNS glucose load and the pattern of pancreatic insulin response is still lacking. Some researchers propose a pancreatic insulin secretion after a central glucose infusion,[17] whereas others do not observe changes in peripheral insulin, although plasma glucose levels do change.[18]

In this study we examine the short-term effects of a single intracisternal glucose or insulin injection on glucose levels in the blood and urine. A comparison is made between the results obtained in intact, vagotomized, and adrenalectomized cats. To explore the physiologic mechanisms involved in renal glucose and Na^+ handling, intact and denervated kidneys were compared.

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METHODS

Animals and surgical procedures. Male and female cats weighing between 2 and 2.5 kg were housed for at least 15 days before the experiments and were fasted 12 h before surgery. Anesthesia was induced by an intraperitoneal (i.p.) injection of 30 mg/kg sodium pentobarbital and maintained light (active palpebral reflex) by an intravenous (i.v.) infusion of sodium pentobarbital (18 mg/100 ml saline with 1.50 U/100 ml heparin at 6 drops/min). A heating pad was used to maintain rectal temperature at 38.5 ± 5°C. Artificial respiration was applied throughout the experiments monitoring pO_2 and pH to be constant. Polyethylene catheters (PE-90 and -100 Clay Adams, Parsippany, NJ) filled with a solution of heparin (200 U/100 ml saline) were inserted into the femoral vein and artery to obtain blood samples by previously described techniques.[6] A thin polyethylene catheter (PE-20 Clay Adams) through which injections could be made was inserted into the cisterna magna, and clear blood-free samples of CSF could be obtained throughout the experiment. To obtain urine samples, the bladder was permanently catheterized (from the beginning of the experiment) through the urethra with a blunt-made polyethylene catheter (PE-120 Clay Adams); in some experiments, each renal pelvis was cannulated separately through its ureter with a thin polyethylene catheter (PE-20 Clay Adams).

In animals selected for vagotomy, the periesophageal abdominal plexus of the vagi was isolated by blunt dissection and lateral displacement of the esophagus. The two major trunks of the vagi and their interconnecting rami were severed below the diaphragm. (Adrenalectomies were performed by dorsally ligating the vessels to the gland.) In some experiments the left kidney was denervated by decapsulating and sectioning the nerves that run along renal vessels and ureter. After closing all the incisions, a 30-min recovery period was allowed.

Experimental design. Glucose or manitol (as a control) 100 mg (0.34 mM) in 1 ml saline was injected for 1 min. In other experiments, porcine insulin (Ely Lilly, 0.5 U/kg) or the same volume of phenol-water (the vehicle for insulin) was injected. Three arterial blood samples were obtained during an 8-min basal period, and four samples (at 5, 15, 30, 60 min) were taken after the injections. At each interval, 0.3 ml of venous blood and 0.3 ml of CSF were also obtained; IRI was only measured in arterial blood. Immediately before collecting a sample, 0.5 ml of circulating blood or CSF was drawn out and reinjected three times to flush each catheter; 1-ml urine samples were obtained at the same intervals, emptying the bladder each time.

Biochemical methods. A fraction of the blood, urine, or CSF samples was used for glucose assay by the glucose oxidase method with a Beckman Glucose Analyzer (Beckman, Fullerton, CA); a second aliquot was used to measure the Na^+ concentration by flame photometry (Pye Unicam, Cambridge, UK). IRI levels were determined in arterial blood with the radioimmunoassay kit (Sorin Biomedica, Saluggia, Italy).

Experimental protocol. Each animal was subjected to one of the following experimental interventions: *1*) glucose injection into the cisterna magna, *2*) manitol injection into the cisterna, 3) glucose injection into the cisterna in vagotomized cats, *4*) glucose injection into the cisterna in adrenalectomized cats, *5*) injection of insulin into the cisterna magna, *6*) injection of phenol-water into the cisterna magna, *7*) injection of insulin into the cisterna magna in vagotomized cats, *8*) injection of insulin into the femoral vein.

Data were analyzed by the Student's *t* test and the Friedman test; when the variances were not homogeneous, the

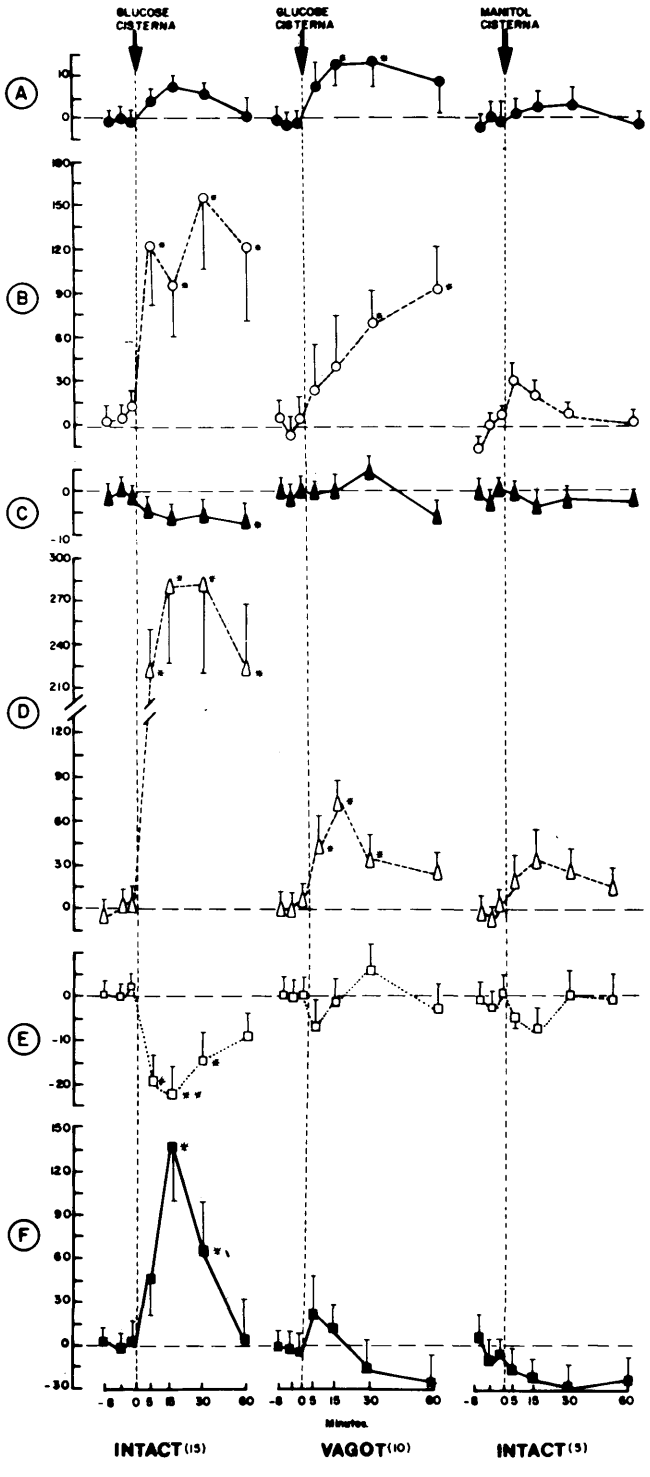

FIGURE 1. Effects of intracisternal glucose or manitol injections (100 mg/dl) on glucose concentration in plasma (*A*) and urine (*B*); Na^+ concentration in plasma (*C*), urine (*D*), and CSF (*E*); and IRI levels in plasma (*F*). Data are presented as percent of basal. Each *point* is mean ± SEM. Number of animals is in parentheses. *$P < .05$, **$P < .001$.

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TABLE 1
The effects of intracisternal glucose (100 mg/dl) on blood and urine glucose levels and on plasma IRI concentration in intact, vagotomized, and adrenalectomized cats

	Intact + glucose (N = 15)			Intact + manitol (N = 5)			Vagotomy + glucose (N = 10)			Adrenalectomy + glucose (N = 9)	
Time (min)	P.Glu. (mg/dl)	U.Glu. (mg/dl)	IRI (μU/ml)	P.Glu. (mg/dl)	U.Glu. (mg/dl)	IRI (μU/ml)	P.Glu. (mg/dl)	U.Glu. (mg/dl)	IRI (μU/ml)	P.Glu. (mg/dl)	U.Glu. (mg/dl)
−8	139 ± 7	27 ± 12	16 ± 3	127 ± 7	20 ± 5	21 ± 5	147 ± 8	38 ± 9	17 ± 4	136 ± 14	63 ± 7
−4	139 ± 6	29 ± 10	14 ± 1	131 ± 9	24 ± 6	18 ± 7	146 ± 7	32 ± 12	17 ± 3	137 ± 13	54 ± 6
0	138 ± 6	30 ± 11	16 ± 2	129 ± 11	26 ± 8	19 ± 7	146 ± 7	36 ± 12	16 ± 3	137 ± 14	64 ± 6
+5	147 ± 9	65 ± 12*	23 ± 5	133 ± 9	31 ± 6	17 ± 6	160 ± 9	45 ± 12	21 ± 4	147 ± 13	72 ± 7
+15	150 ± 9	60 ± 12*	37 ± 6*	136 ± 8	29 ± 6	16 ± 5	165 ± 12*	50 ± 12	19 ± 4	141 ± 14	78 ± 8
+30	148 ± 8	75 ± 14*	26 ± 3*	134 ± 10	25 ± 7	14 ± 5	165 ± 10*	60 ± 11*	14 ± 3	143 ± 15	98 ± 10*
+60	140 ± 9	64 ± 15*	16 ± 3	127 ± 7	24 ± 5	16 ± 4	160 ± 9	69 ± 14*	13 ± 2	144 ± 15	107 ± 12*

Values are means ± SEM. P.Glu., plasma glucose; U.Glu., urine glucose; IRI, plasma immunoreactive insulin.
*$P < .05$.

Student's *t* test modified by Cochran and Cox[19] was used, with a significance of $P < .05$. The values in figures are shown as percentages before the stimuli were applied. Tables show the absolute values.

RESULTS

Effects of intracisternal glucose injections in intact, vagotomized, and adrenalectomized cats. Fifteen intact cats received a 1-ml injection of 10% glucose into the cisterna magna. The results are shown in Figure 1 and Tables 1 and 2. Glucose concentration in plasma increased <10% (Figure 1*A, left panel*), whereas in urine (Figure 1*B, left panel*), 5 min postinjection, it increased 116% and remained high even after 60 min when blood glucose already had recovered to its basal level. Simultaneous determinations of Na^+ concentration showed no significant change in blood during the first 30 min after the injection (Figure 1*C, left panel*), a rapid and sustained increase in urine (Figure 1*D, left panel*), and a significant decrease in CSF (Figure 1*E, left panel*). Fifteen minutes after the injection, plasma IRI increased from 16 ± 2 to 37 ± 6 μU/ml. In control experiments, manitol injections had no significant effect on glucose, Na^+ or IRI (Figure 1, *right panels*).

The short latency of the excretion response to high glucose in the CSF suggests a direct neural mechanism to this phenomenon. To further test this hypothesis, the left kidney was denervated in five cats. On injection of glucose into the cisterna magna, glycosuria and natriuria were statistically augmented during the first 15 min only in the intact right kidneys (Table 3), in spite of a greater basal value. The values obtained in the denervated kidney showed no significant change in blood and only a delayed rise in urine Na^+ (30 and 60 min postinjection).

The results show that the CNS, independent of blood glucose concentration, causes an increase in urine glucose concentration. To test the participation of the vagus nerve in this neuroregulation, glucose injection into the cisterna magna was repeated in 10 vagotomized animals. Under these conditions, plasma glucose concentration increased above the values observed in intact cats (Figure 1*A, center panel*). This increase was significant ($P < .05$) at 5 and 30 min postinjection. The effects on glucose and Na^+ levels in urine, however, were attenuated and appeared with a longer latency (Figure 1, *B* and *D, center panels*). Vagotomy also eliminated the concentration decrease in CSF Na^+ and the increase in blood IRI (Figure 1, *E* and *F, center panels*; see also Tables 1 and 2).

In nine adrenalectomized cats an important depression on the effects elicited by intracisternal glucose was observed. In these animals, basal levels of glucose concentration in urine were high (60 compared with 30 mg/dl), but the post-glucose increase was only significant at 30 min postinjection

TABLE 2
The effects of intracisternal glucose (100 mg/dl) on CSF, blood, and urine Na^+ concentration in intact, vagotomized, and adrenalectomized cats

	Intact + glucose (N = 15)			Intact + manitol (N = 5)			Vagotomy + glucose (N = 10)			Adrenalectomy + glucose (N = 9)		
Time (min)	P.Na^+	U.Na^+	CSF Na^+	P.Na^+	U.Na^+	CSF Na^+	P.Na^+	U.Na^+	CSF Na^+	P.Na^+	U.Na^+	CSF Na^+
−8	147 ± 4	43 ± 7	163 ± 8	142 ± 5	50 ± 9	150 ± 8	138 ± 2	71 ± 10	142 ± 8	134 ± 6	77 ± 7	142 ± 4
−4	148 ± 5	45 ± 6	162 ± 7	139 ± 6	47 ± 7	148 ± 6	139 ± 4	72 ± 8	142 ± 7	135 ± 6	78 ± 8	141 ± 3
0	146 ± 5	45 ± 7	166 ± 6	141 ± 8	53 ± 7	153 ± 8	138 ± 2	74 ± 9	143 ± 7	134 ± 5	76 ± 9	142 ± 4
+5	143 ± 4	144 ± 19*	135 ± 3†	141 ± 5	62 ± 8	145 ± 5	138 ± 5	107 ± 10*	134 ± 5	134 ± 3	84 ± 9	130 ± 3*
+15	141 ± 6	169 ± 20*	130 ± 5†	138 ± 6	67 ± 9	141 ± 6	140 ± 4	125 ± 12*	142 ± 6	139 ± 3	91 ± 8	135 ± 3
+30	142 ± 5	170 ± 18†	134 ± 4*	139 ± 6	65 ± 7	153 ± 7	145 ± 3	100 ± 12*	152 ± 9	139 ± 3	94 ± 9	135 ± 4
+60	139 ± 6*	144 ± 19	151 ± 4	138 ± 5	59 ± 6	151 ± 5	132 ± 6	94 ± 13	138 ± 12	135 ± 4	71 ± 8	140 ± 4

Values are in meq/L, means ± SEM. CSF Na^+, cerebrospinal fluid sodium; P.Na^+, plasma sodium; U.Na^+, urine sodium.
*$P < .05$, †$P < .001$.

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TABLE 3
The effects of intracisternal glucose (100 mg/dl) on urine glucose and sodium levels in intact and denervated kidneys

	Intact + glucose		Denervated + glucose	
Time (min)	U.Glu. (mg/dl)	U.Na^+ (meq/L)	U.Glu. (mg/dl)	U.Na^+ (meq/L)
−8	83 ± 18	44 ± 5	67 ± 15	67 ± 12
−4	76 ± 17	47 ± 7	74 ± 17	68 ± 11
0	88 ± 18	49 ± 8	78 ± 18	70 ± 9
+5	96 ± 17	89 ± 14*	83 ± 17	83 ± 11
+15	124 ± 21*	117 ± 20†	91 ± 19	91 ± 10
+30	148 ± 27*	133 ± 24†	88 ± 19	130 ± 27*
+60	152 ± 28†	133 ± 22†	96 ± 20	133 ± 29*

Values are means ± SEM. $N = 5$. U.Glu., urine glucose; U.Na^+, urine sodium.
*$P < .05$, †$P < .001$.

(Table 1). The effects on Na^+ parameters were suppressed (Table 2). Therefore, neither vagotomy nor adrenalectomy abolished the rise of urine glucose, but in both cases these effects appeared with a longer latency.

Effects of intracisternal insulin injection in intact and vagotomized cats. Ten intact cats received 0.5 U/kg injection of insulin into the cisterna magna. Figure 2 and Table 4 show the resulting changes in glucose and Na^+ concentrations in CSF and in blood. Venous glucose increased during the first 5 min after insulin injection and dropped only at 15 min, reaching its lowest value 30 min postinjection (117 mg/dl; Figure 2*A, left panel*). In contrast, CSF glucose dropped immediately, reaching its lowest value 5 min after insulin injection (72 mg/dl) and recovering to the basal level by 30 min (Figure 2*B, left panel*). Glucose concentration in urine did not change significantly. Five minutes after the same injection, the Na^+ concentration increased in blood (Figure 2*C, left panel*) and decreased in CSF (Figure 2*D, left panel*; $P < .05$). After abdominal vagotomy in five cats, the injection of the same dose of insulin (0.5 U/kg) into the cisterna magna elicited the effects depicted in Figure 2 and Table 4. Changes in plasma and CSF glucose were lower, whereas the effect on Na^+ concentration was abolished. Glucose concentration in urine did not vary (result not shown). In 10 control experiments in intact cats an equivalent volume of phenol-water solution injected into the cisterna magna did not cause significant changes of glucose concentration either in plasma or in CSF (Figure 2).

Effects of i.v. insulin injections in intact cats. Intravenous injection of insulin (0.5 U/kg, 10 cats) elicited a similar decrease in blood to that produced by intracisternal administration (Figure 2, cf. *A, left panel*, with *E, right panel*). However, the temporal pattern of CSF glucose change was quite different. Glucose concentration in CSF after i.v. insulin injection decreased with a latency of 15 min and remained low even after 60 min. The observed glucose decrease in CSF was always preceded by a lowering in blood glucose. Insulin in CSF did not change significantly in spite of an immediate increase in plasma IRI level (Figure 2, *E–H*, Table 5).

DISCUSSION

Our experiments demonstrated that augmented CSF glucose was followed by a slight increase of blood glucose, whereas urine glucose and IRI levels in blood rose significantly. Increased central glucose levels resulted in a decrease of CSF Na^+ concentration and a simultaneous rise in the urine Na^+ concentration. The effects reported were not caused by the osmolality of the glucose solution, because manitol did not provoke consistent changes in the studied parameters. The light basal glycosuria was always present in our experiments and could be due to anesthesia and surgical procedures; it was more apparent in cats with a denervated kidney where the stress was bigger (Table 3). The glycosuria that appeared during the first 5 min after the central glucose increase could explain the lack of peripheral hyperglycemia, and this renal excretion probably represents the physiologic mechanism to produce a progressive decrease of augmented CSF glucose levels.

The results obtained with a denervated kidney strongly

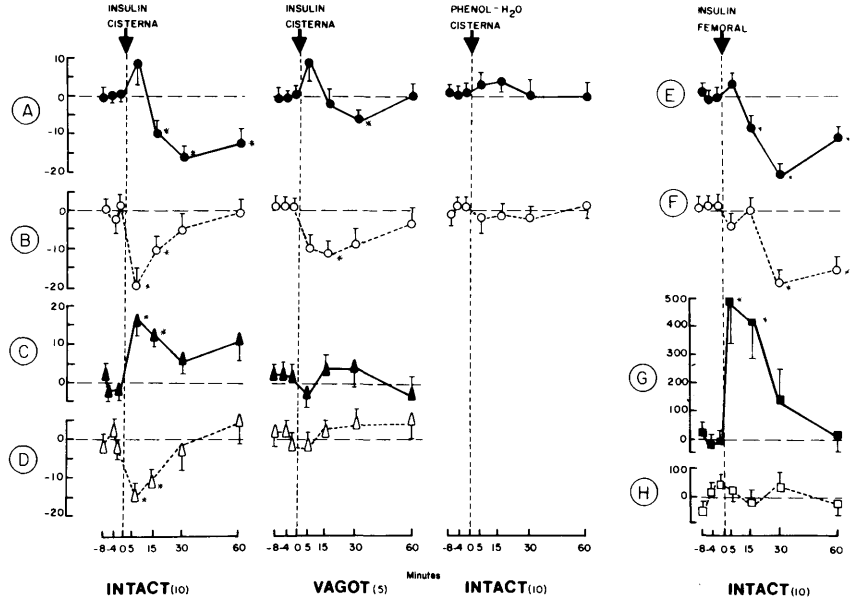

FIGURE 2. Effects of intracisternal insulin (0.5 U/kg) or control solution (solvent for insulin) injections on glucose concentrations in plasma (*A*) and CSF (*B*) and Na^+ concentrations in plasma (*C*) and CSF (*D*). Effects of insulin (0.5 U/kg i.v.) injection on mean glucose concentrations in plasma (*E*) and CSF (*F*) and mean IRI levels in plasma (*G*) and CSF (*H*). Data are presented as percent of basal. Each *point* is mean ± SEM. Number of animals is in parentheses. *$P < .05$.

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TABLE 4
The effects of intracisternal insulin (0.5 U/kg) on CSF and blood glucose levels and Na^+ concentrations in intact and vagotomized cats

	Intact cats (N = 10)				Vagotomized cats (N = 5)			
Time (min)	P.Glu. (mg/dl)	CSF Glu. (mg/dl)	P.Na^+ (meq/L)	CSF Na^+ (meq/L)	P.Glu. (mg/dl)	CSF Glu. (mg/dl)	P.Na^+ (meq/L)	CSF Na^+ (meq/L)
−8	140 ± 9	97 ± 6	144 ± 10	161 ± 10	122 ± 5	89 ± 5	140 ± 5	149 ± 5
−4	140 ± 8	87 ± 7	139 ± 12	167 ± 12	123 ± 6	90 ± 5	142 ± 8	149 ± 7
0	141 ± 8	91 ± 5	140 ± 18	165 ± 11	124 ± 7	89 ± 5	140 ± 7	145 ± 7
+5	150 ± 9	72 ± 5*	163 ± 10*	140 ± 5*	131 ± 6	80 ± 4	138 ± 10	144 ± 8
+15	125 ± 5*	78 ± 5*	158 ± 10*	147 ± 6*	118 ± 6	77 ± 4*	145 ± 7	149 ± 11
+30	117 ± 6*	85 ± 6	149 ± 6	161 ± 9	113 ± 5*	81 ± 4	145 ± 10	155 ± 8
+60	121 ± 5*	89 ± 6	156 ± 6	173 ± 7	124 ± 6	84 ± 5	135 ± 8	154 ± 10

Values are means ± SEM. Abbreviations as in Tables 1 and 2.
*$P < .05$.

confirm the participation of the nervous system in this effector mechanism that causes the release of sugar into the urine. In an earlier study, kidney denervation resulted in the disappearance of conditioned glycosuria.[20] Another, but related, pathway seems to be responsible for the increase in peripheral insulin. A humoral factor that stimulates pancreatic insulin has been reported after a central glucose infusion.[21,22] However, the results depicted in Figure 1 show that vagotomy abolished plasma IRI rise and attenuated the increase in urine glucose concentration, despite a high blood glucose level. The peripheral hyperglycemia observed in vagotomized cats is probably due to the lack of insulin secretion[16] and to the attenuated glycosuria during the 1st min after the injection. These results suggest that the CNS responds to an increase of glucose by causing pancreatic insulin secretion through the vagi nerves. The full response of the kidney is probably partially dependent on the surge of insulin. The presence of glucosensitive neurons in the hypothalamus has been reported,[23] as well as CNS control over reabsorption of glucose by the renal tubules.[20] Our data have confirmed earlier reports by Chieri et al.[17] that the infusion of glucose to the brain led to insulin secretion in control dogs but not in vagotomized animals. In the same way, these results also confirmed the nervous system influence on pancreatic activity.[15] In another study, however, CSF glucose in rats decreased peripheral glucose levels without changing peripheral IRI.[18] These contradictory results might be due to differences in glucose administration and/or to the sampling period after glucose injections. In this work we analyzed short-term events.

Intracisternal glucose administration increased natriuresis 280% in 15 min and decreased CSF Na^+ level. These changes almost disappeared after vagotomy. Although the physiologic mechanisms underlying the glucose-induced natriuresis reported here are unknown, several explanations seem plausible. From clearance experiments with micropunctured kidneys in dogs, glucose clearly has significant effects on renal tubular electrolyte transport, and tubular Na^+ reabsorption is inhibited after glucose administration.[24] Moreover, studies by Rostand et al.[25] revealed that the baseline renal Na^+ excretion rate is greater in kidneys from diabetic rats than in kidneys from control rats. Neural elements in the hypothalamus through the vagi and the renal nerves may act to decrease tubular Na^+ reabsorption, increasing Na^+ excretion.[26]

Adrenalectomized animals showed an increase in urine basal glucose and Na^+ concentrations and a decrease in blood and CSF values compared with intact cats. The changes observed after glucose injection into the cisterna were lower. There is support for these results in the literature, because increased CSF glucose levels have been reported to cause a decrease in sympathetic activity with diminished catecholamine output from the adrenal medulla.[18,27]

Insulin injection into the cisterna magna was followed by a short-latency decrease in CSF glucose concentration, reaching its lowest value 5 min postinjection. This effect is probably due to the direct action of insulin on nervous tissue rather than secondarily due to blood changes, because during this time, an increase in blood glucose levels was observed. No changes were observed in urine. Woods and Porte[15] also reported a decrease in CSF glucose in dogs after insulin injections into the cisterna; in this species, CSF glucose recovers with three times longer latency than in our experiments; level of anesthesia or the species difference could explain this discrepancy. Experiments have also confirmed earlier reports that cerebral intraventricular or cisternal insulin injection lead to a decrease of plasma glucose and that abdominal vagotomy greatly diminishes the effects obtained in cats with intact vagi.[15,28] These results demonstrate that the cat, like the rat,[29] has low amounts of IRI within the CSF; our data are also consistent in the assumption that CSF insulin does not follow rises of peripheral insulin,[15,18] at least during the first 60 min. When the same dose of insulin was administered in the femoral vein, although a tremendous elevation of plasma IRI was observed (500%), CSF insulin did not change (Figure 2, *E–H*, Table 5). However, other authors

TABLE 5
The effects of insulin (0.5 U/kg i.v.) on CSF and blood glucose levels and on IRI in plasma in intact cats

Time (min)	P.Glu. (mg/dl)	CSF Glu. (mg/dl)	P. IRI (μU/ml)	CSF IRI (μU/ml)
−8	102 ± 7	66 ± 4	23 ± 4	1.3 ± 0.3
−4	101 ± 6	67 ± 5	18 ± 3	3.1 ± 0.4
0	101 ± 4	68 ± 6	19 ± 3	4.2 ± 0.8
+5	103 ± 5	65 ± 5	118 ± 25*	3.4 ± 0.7
+15	92 ± 6*	67 ± 6	103 ± 22*	7.4 ± 1.7
+30	80 ± 5*	54 ± 5*	49 ± 18	3.5 ± 0.6
+60	90 ± 4*	56 ± 6*	21 ± 15	2.6 ± 0.8

Values are means ± SEM. N = 15. Abbreviations as in Table 1.
*$P < .05$.

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suggest that CSF insulin can be derived from plasma insulin in the dog.[30]

The need for Na^+ in the active transport of glucose in the choroid plexus[31] led us to compare the changes in glucose and Na^+ concentrations after augmenting central insulin levels. Increased insulin concentration would stimulate a rapid central glucose uptake, causing a decrease in glucose and Na^+ levels in the CSF with an apposite effect in plasma. Note that intracisternal administration of 0.5 U/kg insulin raises the concentration of this hormone above physiologic levels.

Although the CSF injections of glucose create nonphysiologic local concentrations of this substance in the CNS, it seems plausible that the CNS exerts an important influence in the excretory mechanism of glucose in response to a high CSF hyperglycemia. This effect is multifactorial: direct neural through kidney innervation and probably indirect through the vagi nerves and adrenal glands. Further investigation is needed to analyze the precise role of adrenal glands in this regulation and the interplay with the vagal function.

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