**Effect of the Injury of the Lobulus Posterior Medianus (Ingvar)
of the Cerebellum upon the Blood Pressure, the Blood Sugar
Content and the Epinephrine Secretion in Non-
Anaesthetized, Non-Fastened Dogs.[§]**

By

Masao Wada, Mitizane Seo and Kimio Abe.

(和田正男) (瀬尾道真) (安部公男)

*(From the Physiological Laboratory of Prof. Y. Satake,
Tohoku Imperial University, Sendai.)*

In a recent publication, one of us (W) in collaboration with Yen and Kaiwa¹⁾ described the increased rate of epinephrine secretion from the suprarenal gland associated with hyperglycaemia as a result of the piqûre of Cl. Bernard of the fourth-ventricle floor, which was tried in non-anaesthetized, non-fastened and non-laparotomized dogs.

However, in most of the experiments the posterior part of the cerebellum was injured in addition to the proper region of the medulla oblongata, which fact might have some bearing on the explanation of the outcome. In the next experiments,²⁾ the piqûre was conducted therefore without disturbing the cerebellum in any way, yet the blood sugar content fluctuated as before, and the magnitude was as in the former experiments. From the comparison of both series of experiments, it is sure, the injury of the cerebellum had no significant share in the hyperglycaemia caused by the piqûre diabétique in the first set. A similar view may possibly apply also to the epinephrine discharge event, but at that time no determinations were run for the liberation rate of epinephrine.

But we should not be in hurry to assume the complete identi-

§ Presented before the XII. Annual Meeting of the Japanese Physiological Congress, held at Kanazawa, July 1933 (Jap. J. of Med. Sci., Biophysics, 1934, 3, 46*).

1) Yen, Kaiwa and Wada, Tohoku J. of Exp. Med., 1931, 17, 345.

2) Kaiwa and Wada, Ibid., 1934, 23, 536.

fication of the hyperglycaemia, in both the magnitude and the timely course, as evidence of non-influence of injury of the cerebellum upon the carbohydrate metabolism, as in reality we have some previous references of causal relation between the two.

In following them up, we attempted to ascertain the injury to what regions of the cerebellum results in disturbances in the carbohydrate metabolism and in the epinephrine discharge as well.

It will be in order to give here a more detailed review of the literature concerning the effect of the cerebellar injury on the carbohydrate metabolism, though they were briefly cited in the foregoing paper.¹⁾ As early as 1872, C. Eckhard,³⁾ working with rabbits, demonstrated that the mechanical, chemical, or electrical stimulation of the posterior part of the vermis gives rise to glycosuria associated with diuresis, and further suggested that the chief source of the nervous elements closely related to these outcomes locates in the second lobe of the vermis (lobulus hydruricus et diabeticus Eckhards), which is identical with the uvula in the classical terminology. In the subsequent experiments⁴⁾ carried out on dogs, he failed to find any definite glycosuria after similar stimulation of the same region of the vermis, against his expectation. The glycosuric effect of the cerebellar injury was ascertained, about eight years later, by his son,⁵⁾ experimenting on rabbits. About half a century later Dresel and Lewy⁶⁾ obtained a considerable hyperglycaemia and glycosuria in dogs and rabbits, the maximum of which was reached one and a half to two hours after puncture of the vermis and thereupon disappeared either rapidly or gradually. They inferred that this effect is connected with the injury of a certain region of the vermis. At almost the same time, Shimidzu⁷⁾ noted in his publication concerning the epinephrine secretion that the injury of the cerebellum, tried in a single urethanized rabbits according to the technique of Eckhard, caused an increase in the blood sugar level such as from 0.10% to 0.28% in thirty minutes. As a consequence of the profound lesion of the cerebellum of dogs, Papilian and Cruceanu⁸⁾ noted a conspicuous hyperglycaemia i.e. 0.36%, which was reached within some days following the operation. If the animals survived this

3) C. Eckhard, Beitr. z. Anat. u. Physiol., 1872, 6, 51.

4) C. Eckhard, Ibid., 92 f.

5) F. Eckhard, Arch. f. exp. Path. u. Pharm., 1880, 12, 276.

6) Dresel and Lewy, Deut. Z. f. Nervenheilk., 1924, 81, 82.

7) Shimidzu, Arch. f. exp. Path. u. Pharm., 1924, 103, 60 f.

8) Papilian and Cruceanu, C. R. Soc. Biol., 1925, 92, 722.

operation the hyperglycaemic effect disappeared within 15 to 20 days. A systematic study with reference to the change in the glycaemic level resulting from the lesions of the different portions of the cerebellum was made by Shinosaki⁹⁾ on dogs in Lewy's laboratory. Shinosaki divided the data obtained into four groups according to the magnitude of the resulting hyperglycaemia: very strong positive, strong positive, slight positive, and negative. The first group consisted of three dogs in which the uvula was punctured; the blood sugar level showed a considerable increase lasting for 1 to 4 days, its maximum being determined as 0.275%–0.192%. The second group comprised four animals in which the uvula was injured only superficially; the hyperglycaemia caused thereby continued for 3 to 5 hours and its highest level was 0.200%–0.226%. In the third, consisting of six animals in which the pyramis, mainly in its posterior part, was destroyed, the blood sugar change lasted for 1 to 2½ hours and its maximum was noted as 0.173%–0.198%. In seven animals of the last group the destruction of either the portion of the vermis before the second fissure or the hemisphere caused, according to his statement, no noteworthy hyperglycaemia. However, it may be pointed out, on examining his data, that two animals involved in the last group showed a hyperglycaemia of considerable magnitude lasting for ½ to 1 hour, as a result of the injury of the left hemisphere and the tuber, the maximum being determined respectively as 0.192% and 0.203%. In order to determine the effect of ether anaesthesia on the glycaemic level which was employed in all his experiments during the course of the preparatory procedures, he carried out only a single control experiment, with an increase to 0.148%. Shinosaki thus joined to the view of Dresel and Lewy that the afferent impulses for the blood sugar regulation pass through the posterior portion of the vermis. Recently Hiller,¹⁰⁾ in collaboration with Tannenbaum, tried to determine the effect of the expansive destruction of the cerebellum on the blood sugar level of the urethanized rabbits and came to see an appreciable hyperglycaemia, averaging 0.093% above the initial value. Opposed to the assertions of the previous workers, he noted a more marked rise of the glycaemic level in the animal in which the uvula was freed from injury than in the one with the uvula completely destroyed, stating that it is not the lesion of the uvula

9) Shinosaki, *Ztschr. f. ges. Neur. u. Psych.*, 1926, **106**, 483; Lewy and Shinosaki, *Klin. Wschr.*, 1926, 2312; *Skand. Arch. f. Physiol.*, 1926, **49**, 169.

10) Hiller, *Ztschr. f. ges. Neur. u. Psych.*, 1931, **132**, 95.

that causes a conspicuous hyperglycaemia on the cerebellar injury. On the other hand, the rôle of the lobus posterior of the cerebellum on the blood sugar regulation was left unaccepted by some authors,¹¹⁾¹²⁾ for the reason that the medulla oblongata might be secondarily disturbed by the injury of the posterior part of the vermis.

As regards the behaviour of the epinephrine secretion from the suprarenal glands, we have the single information of Shimidzu,⁷⁾ so far as we are aware. The author noted that a pupil of a rabbit which was sensitized to circulating epinephrine by removal of the superior cervical ganglion and instillation of atropine was dilated in the course of 20 minutes after the cerebellar puncture attempted according to the technique of Eckhard. This widening of the pupil, according to his experiments, corresponded to that caused by adrenaline injected intravenously at a rate of 0.3 thousandth milligram per kilo and per minute.

In this connection we recall the observations of Cannon and Rapport¹³⁾ in which acceleration of the denervated heart of the "reduced" animal under ether anaesthesia caused by the sciatic or brachial stimulation was not affected by the removal of the cerebellum. They stated that the cerebellum is clearly not essential to reflex discharge of the epinephrine.

On the question as to whether the vermis contributes to the blood pressure regulation, less plausible evidences were known. C. Eckhard, using dogs, failed to observe any noteworthy change in the blood pressure after puncturing the vermis, supporting the view of Owsjannikow,¹⁴⁾ working with rabbits and cats, that the partial or entire removal of the cerebellum has no influence upon the blood pressure. Dresel and Lewy⁶⁾ indicated a definite rise in the pressure following electrical stimulation of the posterior part of the vermis. This is similar to the outcome of C. Eckhard, which was discarded by himself because of little pertinence of the mode of the stimulation. Recently Fuse¹⁵⁾ reported that an electrical stimulation of the lobulus posterior medianus of the cerebellum resulted in a fall of the blood pressure in twenty cases, in the urethanized, fastened rabbits, while in three cases a rise of the pressure was observed.

In reviewing the references here quoted, the present writers at-

11) Brun, *Das Kleinhirn*, Berlin 1927, 54 f.

12) Rijnberk, *Ergb. d. Physiol.*, 1931, **31**, 673 f.

13) Cannon and Rapport, *Am. J. Physiol.*, 1922, **58**, 340 f.

14) Owsjannikow, *Ber. üb. Verhandl. d. Ges. d. W. Leipzig, Math.-phys. Cl.*, 1871, **23**, 145 f.

15) Fuse, *Sinkeigaku Zassi*, 1930(-31), **32**, 120.

tempted to follow the same alternatives as before in non-anaesthetized, non-fastened dogs after puncturing the lobulus posterior medialis of the cerebellum: the epinephrine output rate, the blood sugar concentration, the arterial blood pressure and the pulse rate.

METHODS.

The observations were made on 8 dogs, weighing from 11.3 to 21.0 kilos. The D₁₀-L₃ dorsal spinal roots were cut previously under morphine-ether anaesthesia. About three weeks to eight months after this operation, when the animals were in healthy condition, the nuchal part of the occipital bone covering the posterior part of the vermis was laid bare and cut away under the same anaesthesia, using the same technique, as was described by Kaiwa and Wada.²⁾ Three to six days later the suprarenal vein was prepared through the lumbar approach for collecting the blood outpouring from the suprarenal gland, according to the method of Satake, Sugawara and Watanabe,¹⁶⁾ during which the animals were also, as usual, kept unanaesthetized and non-fastened. Both femoral arteries were uncovered under local anaesthesia with 0.5% novocaine solution and arranged respectively for the blood sampling for sugar determination and the blood pressure recording. Then, the dura was cut and torn away by the aid of scissors and fine forceps, and during this manipulation the head of the animal was firmly held by the hand of an assistant. A period of from 2½ to 3 hours was left between the completion of the arrangements and the puncture. On holding the head of the animal in an unstrained natural posture, mostly lying down on the table, and without bending it forward, the puncture was made in the median line of the vermis by means of a sharp-pointed, curved lancet, the point of which was directed horizontally from behind. By its means, the puncture produced at most about 4 mms. breadth of destruction.

The blood pressure curves were taken, using a mercury manometer, keeping the animal in approximately the same posture, namely lying down on the table, and the heart rate and the respiratory movements were counted from the kymograph record. The quantity of the epinephrine in the suprarenal vein blood, which was sampled without fastening the animal or causing any excitement or emotional

16) Satake, Sugawara and M. Watanabe, *Tohoku J. Exp. Med.*, 1927, 8, 501.

display, was determined alternately by the method of the rabbit intestine segment¹⁷⁾ and by means of the paradoxical eye reaction of cat,¹⁸⁾ excepting three cases in which either the former method (Dog 4) or the latter alone was resorted to (Dogs 2 & 6). The horizontal diameter of the sensitized pupil was measured with the aid of a reading microscope (cathetometer-type), which was adjusted to be able to read, with accuracy, to 1/9th of one millimeter; the distance between the object and the microscope objective was 8.5 cm. The blood sugar was estimated by Hagedorn and Jensen's method.

After termination of each experiment the animal was killed by bleeding, and the cerebellum together with the medulla oblongata was removed with atmost care and preserved in formaline solution in order to ascertain the seat of the lesion.

We wish to take this opportunity of expressing our thanks to Assistant Professor T. Ogawa in the Anatomical Laboratory, for helpful advice on examining the seat of injury.

RESULTS.

All the results involving the autopsy findings are given in Table.

The puncture was performed adequately without injuring the fourth ventricle as shown by Fig. 1—illustrating the seat of lesion in the arbor vitae.

Symptoms other than those under special discussion may be given first.

In two instances (Dogs 1 & 8) the symptoms were rather slight: slight, transitory excitement, and mydriasis with nictitation occurred also for a short period. In the remaining cases, the animals stretched the four limbs rigidly on puncturing, mydriasis and rotatory nystagmus also simultaneously occurred, but the symptoms diminished in intensity with the lapse of time. For the most part they were visible for about ten minutes to one and a half hours, although they were observable in Dog 2 through the whole experimental course, viz. for two hours. The mydriasis lasted in the main for a short period. In Dog 7 a slight excitement was seen soon after performing the puncture, but twenty minutes later, the animal stretched out

17) Sugawara, M. Watanabe and Saito, *Tohoku J. Exp. Med.*, 1927, 7, 3.

18) Sugawara, *Ibid.*, 1927, 8, 357.

its four limbs suddenly, with development of mydriasis, nystagmus, and also exhibited an abrupt and marked rise of blood pressure. The

Fig. 1. Showing the seat of the puncture lesion in the arbor vitae. Shadow represents the bleeding.

There is no definite evidence to indicate that the artificial stimulation of the sharply defined regions of the cerebellum causes a spontaneous nystagmus, except the flocculus,¹⁹⁾ although the existent vestibular nystagmus is influenced

the autopsy findings showed that the pyramis alone was injured, but bleeding was found in the uvula, nodulus, and other neighbouring places. Some time would no doubt have to elapse for bleeding to reach an appreciable extent.

In Dog 4, in which severe symptoms became manifest, the pyramis and the uvula were destroyed, but the nodulus remained uninjured.

It is interesting to note that extensive puncture of the portion of the lobulus posterior medianus posterior to the fissura secunda brought about nystagmus without exception.

Judging from the experiments of this small number, destruction of the posterior portion of the lobulus posterior medianus has seemingly some causal relation to the development of nystagmus. But here we will however quote the prevailing view of the relation of the vermis to the nystagmus.

19) Ferrier, *Les fonctions du cerveau* (Traduit de l'anglais) 1878, 159f.; Barany, *Jahrb. f. Psych. u. Neurol.*, 1914, 36, 631; *Klin. Beitr. z. Ohrenheilk., Festschr. f. Urbantschitsch*, 1919, 47.

qualitatively or quantitatively by the stimulation of the vermis.²⁰⁾ Presumably the development of the nystagmus following the puncture may be due to the disturbance of the vestibulo-cerebellar tract (van Gehuchten), the fibres of which distribute, as is well known since Ingvar, almost exclusively, in the lobus posterior, to the cortex of the uvula and nodulus, that is the portion of lobulus posterior medianus posterior to the fissura secunda, and to the flocculus.

The blood pressure.

The blood pressure of the animals prepared as above described, showed before the puncture a normal value, but in some cases low range of normal values. The puncture invariably brought about a rise of the arterial blood pressure; its magnitude seeming dependent to the lesion produced. In the cases where the puncture was done in the portion of the vermis before the fissura secunda, the pressure was only transitorily raised, and that more or less remarkably, as about 20 to 40 mms. Hg. above the initial. It returned to the initial height 10 to 15 seconds later. In the cases where the portion of the lobulus posterior medianus posterior to the second fissure was injured, as Fig. 2 shows, the rise was more eminent and continued somewhat longer. The greatest increase was about 30 to 65 mms. Hg. above the initial, and in most cases the initial level was regained within half an hour.

Fig. 2 (Reduced to $\frac{1}{3}$). Record of blood pressure of Dog 5, non-anaesthetized and non-fasted. At arrow the lobulus posterior medianus was punctured. Time in seconds.

20) Bauer and Leidler, Arb. Neurol. Inst. Wien, 1912, 19, 155; Leidler, Klin. Beitr. z. Ohrenheilk., Festschr. f. Urbantschitsch, 1919, 403; Gatscher, Ibid., 289; Hoshino, Acta oto-laryng., 1921, Suppl. 2, 1; Démétriades and Spiegel, Ztschr. f. Hals- und Ohrenheilk., 1928, 19, 250.

This result is clearly opposite to the previous investigators who failed to obtain any significant rise in the blood pressure on puncturing the vermis. Fuse¹⁵⁾ reported a fall of the pressure as an outstanding feature of the electrical stimulation of the lobulus posterior medianus. Such fall of the pressure was observed in none of our puncture experiments.

On puncturing the vermis, the rate of the heart beat remained unaltered in two cases (Dogs 1 & 3), while in other cases (Dogs 2, 5, 6, 7, 8 & 9) it underwent some acceleration, which is independent of the magnitude of the blood pressure rise, and it was only transitory. In Dog 2, the heart was soon accelerated by about seventy beats per minute by the puncture, but the initial rate was regained in five minutes; in the remaining cases the acceleration was of small scale, as under 20 beats per minute.

In all cases the rate of respiration showed a considerable increase soon after the puncture, without regard to whether the lesion was found in the anterior portion of the lobulus posterior medianus or in its posterior portion. Fuse also observed an accelerated breathing on puncturing the vermis in the urethanized rabbits. In our animals the acceleration in the respiratory movements appeared mostly for a short period.

The rate of epinephrine secretion.

The epinephrine concentration in the suprarenal vein blood was determined, as above described, alternately by the rabbit intestine segment and by the cat paradoxical eye, or by either one of them. In the samples obtained successively at a very short interval, the amount of the epinephrine content, which was determined by both methods, showed satisfactorily approximate values. The course and the form of the change in the epinephrine output rate did not differ materially according to the method employed, as noted already in the previous publication from this laboratory.²¹⁾

Before the puncture the amount of the epinephrine liberated from a single suprarenal gland was determined within normal limits; it ranged between 0.000005 and 0.00004 mgrm. per kilo per minute. The increase in the epinephrine output rate is one of the outstanding features in the present cerebellum experiments. In the majority of cases the blood flow through the gland was increased on puncturing

21) Sato and Aomura, Tohoku J. Exp. Med., 1930, 15, 17.

TABLE.

Effect of puncture of the lobulus posterior medianus of cerebellum upon the epinephrine secretion, the blood sugar and the blood pressure.

* Estimated by the cat paradoxical pupilreaction.

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)		Epinephrine (mgrm.)		Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)	
		Quantity Duration of collection (sec.)	Quantity per minute	Quantity contained in 1 c.c.	Epinephrine output per minute							
					per ani- mal							per kilo

Experiment I.

Dog 1. 12.5 kilos. ♂ 19. VII. 1932.

15. VI. 1932.	13.0 kilos.	D ₁₀ -L ₅ dorsal spinal roots severed under morphine-ether anaesthesia.
14. VII. 1932.	13.5 kilos.	The occipital bone exposed and its nuchal part removed under morphine-ether anaesthesia.

9:40-11:03 a.m. The right lumbar route preparation completed. The right (for blood pressure) and the left femoral artery (for blood sugar) laid bare and cannulae inserted. The dura perforated and the vermis exposed.

12:55 p.m. Dog behaved quite normal.

1:04	Lying down quietly.					(I+III)			0.109					
1:05	I	1.9	30	3.8	0.30	0.000075	0.00031	0.000025						
	II	4.2	60	4.2	0.34	0.00005	0.00021	0.000017*						
	III	2.2	30	4.4	0.35									
1:17	Lying down quietly.									93	90	12	39.0	23
1:19						(IV+VI)			0.109					
1:20	IV	1.8	30	3.6	0.29	0.000075	0.00030	0.000024						
	V	4.0	60	4.0	0.32	0.00005	0.00020	0.000016*						
	VI	2.2	30	4.4	0.35									
1:35	Punctured the lobul. post. medianus: Dog excited slightly, but soon became quiet. Remarkable widening of pupils associated with nictitation developed, but disappeared in about three minutes. Urination and defecation occurred (1:37 p.m.). Dog somewhat irritable. Nystagmus not occurred. The blood pressure rose very slightly from 82 to 100 mms. Hg., but soon recovered the initial level. The heart rate remained unchanged (84 per minute). The rate of respiration increased from 12 to 24 per minute.													
1:40	Lying down quietly.					Salivation not appeared.				97	92	15	39.0	23
1:42									0.104					
1:43	VII	1.7	30	3.4	0.27	0.0004	0.00136	0.000109						
	VIII	2.8	60	2.8	0.22	0.0004	0.00112	0.000090*						
	IX	1.4	30	2.8	0.22	0.0004-	0.00112-	0.000090-						
1:55	Lying down quietly.									86	72	12		23
2:05	Lying down quietly.									88	72	12	39.0	23
2:09						(X+XII)			0.115					
2:10	X	1.8	30	3.6	0.29	0.00015	0.00054	0.000043						
	XI	3.8	60	3.8	0.30	0.00025	0.00095	0.000076*						
	XII	1.8	30	3.6	0.29									
2:30	Lying down quietly.									92	84	12		23
2:40	Lying down quietly.									91	75	12	39.0	23
2:42									0.107					
2:43	XIII	1.4	30	2.8	0.22	0.00025	0.00070	0.000056*						
	XIV	1.4	30	2.8	0.22			0.000040						
	XV	1.0	30	2.0	0.16	0.00025	0.00050							
3:05	Lying down quietly.									93	81	12	39.0	23
3:06									0.108					

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)				Epinephrine (mgrm.)			Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)
		Quantity	Duration of collection (sec.)	Quantity per minute		Quantity contained in 1 c.c.	Epinephrine output per minute							
				per ani- mal	per kilo		per animal	per kilo						
3:35	Lying down quietly.					(XVI+ XVIII)			0.107	94	75	12	39.0	23
3:40														
3:45	XVI	1.7	60	1.7	0.14	0.0002+	0.00038+	0.000030+						
	XVII	2.3	60	2.3	0.18	0.0002	0.00046	0.000037*						
	XVIII	2.1	60	2.1	0.17									

Autopsy: The puncture was between the sulcus praepyramidalis and the fissura secunda in the median line. The lobul. med. medianus was partly destroyed. The portion of the lobul. post. medianus posterior to the fissura secunda was entirely freed from injury. The fourth ventricle floor was not injured, no bleeding in the ventricle.

Experiment II.

Dog 2. 11.3 kilos. ♂ 26. VII. 1932.

[27. V. 1932. 12.0 kilos. D ₁₀ -L ₃ dorsal spinal roots severed under morphine-ether anaesthesia.]														
[21. VII. 1932. 11.2 kilos. The occipital bone exposed and its nuchal part removed under morphine-ether anaesthesia.]														
9:40 a.m.-11:03 a.m. The right lumbar route preparation completed. The right (for blood pressure) and the left femoral artery (for blood sugar) laid bare and cannulae inserted. The dura perforated and the vermis exposed.														
2:00 p.m.	Dog behaved quite normal. Lying down quietly.										113	144	22	38.8 30
2:04										0.118				
2:05	I	2.2	30	4.4	0.39									
	II	3.8	60	3.8	0.34	0.000175	0.00067	0.000059*						
	III	2.0	30	4.0	0.35									
2:10														
2:14										0.115	107	132	18	39.0 30
2:20	IV	1.5	30	3.0	0.27									
	V	2.6	60	2.6	0.23	0.00015	0.00039	0.000035*						
	VI	1.5	30	3.0	0.27									
2:33	Punctured the lobul. post. medianus: Dog extended rigidly the fore and hind legs. Mydriasis and nystagmus occurred. A few minutes later widening of pupils disappeared. Very slight salivation appeared. The blood pressure fell slightly, but soon rose from 105 to 135 mms. Hg. The heart rate increased from 156 to 228 per minute. The rate of respiration increased from 17 to 28 per minute.													
2:37	Lying down quietly. Nystagmus and rigidity of the legs still appearing.										123	138	22	39.0 30
2:38										0.113				
2:42	VII	1.4	30	2.8	0.25									
	VIII	1.7	30	3.4	0.30	0.0007	0.00238	0.000211*						
	IX	1.4	30	2.8	0.25									
2:50	Lying down. The symptoms still appearing.										123	216	20	39.3 30
2:51										0.109				
3:00	Lying down. The symptoms still appearing.										111	192	14	39.3 30
3:03										0.115				
3:07	X	1.7	30	3.4	0.30									
	XI	2.0	30	4.0	0.35	0.0003	0.00120	0.000106*						
	XII	1.7	30	3.4	0.30									
3:30	Lying down. The symptoms still appearing.										111	150	22	40.0 30
3:34										0.113				
3:35	XIII	1.5	30	3.0	0.27									
	XIV	1.6	30	3.2	0.28	0.00025	0.00080	0.000071*						

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)				Epinephrine (mgrm.)			Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)
		Quantity	Duration of collection (sec.)	Quantity per minute	Quantity contained in 1 c.c.	Epinephrine output per minute								
						per ani- mal	per kilo	per animal						
4:00	XV	1.5	30	3.0	0.27									
4:01	Lying down.			The symptoms still appearing.					0.109	114	204	13	40.0	30
4:25	Lying down.			The symptoms still appearing.						117	234	18	40.0	30
4:28									0.117					
4:30	XVI	1.5	30	3.0	0.27	0.0002	0.00060	0.000053*						
	XVII	1.4	30	2.8	0.25									
	XVIII	1.4	30	2.8	0.25									

Autopsy: The puncture was at the fissura secunda in the median line. The portion of the pyramid close to this fissura, the uvula and the nodulus were destroyed. The fourth ventricle floor was not injured, nor was bleeding found in the ventricle.

Experiment III.

Dog 3. 21.0 kilos. ♂ 7. IX. 1932.

[		8. I. 1932.	24.3 kilos.	D ₁₀ -L ₃ dorsal spinal roots severed under morphine-ether anaesthesia.										
		3. IX. 1932.	22.0 kilos.	The occipital bone exposed and its nuchal part removed under morphine-ether anaesthesia.										
9:55 a.m.-12:22 p.m.		The left lumbar route preparation completed. The left (for blood pressure) and the right femoral artery (for blood sugar) laid bare and cannulae inserted. The dura perforated and the vermis exposed.												
2:30 p.m.		Dog behaved quite normal. Lying down quietly.												
2:35						(I+III)			0.109	130	156	14	39.8	25
2:45	I	3.0	30	6.0	0.29	0.000075-	0.00046-	0.000022-						
	II	2.9	30	5.8	0.28	0.00005	0.00029	0.000014*						
	III	3.1	30	6.2	0.30									
3:00	Lying down quietly.													
3:02						(IV+VI)			0.100	102	156	15	39.8	25
3:03	IV	3.0	30	6.0	0.29	0.000075	0.00044	0.000021						
	V	3.4	30	6.8	0.32	0.00005	0.00034	0.000016*						
	VI	2.8	30	5.6	0.27									
3:25	Punctured the lobul. post. medianus: Dog extended rigidly the hind legs. Mydriasis and nystagmus appeared, but less pronounced, as time passed. The blood pressure rose abruptly from 124 to 181 mms. Hg. The heart rate unaltered (138 per minute). The rate of respiration increased slightly from 19 to 22 per minute.													
3:27 p.m.		Lying down quietly. Pupils slightly dilated. Very slight salivation occurred.												
3:28									0.096					
3:30	VII	2.8	30	5.6	0.27	0.0006	0.00336	0.000160						
	VIII	2.5	30	5.0	0.24	0.0006	0.00300	0.000143*						
	IX	2.5	30	5.0	0.24	0.0006	0.00300	0.000143						
3:50	Lying down quietly. Rigidity of the legs and nystagmus still appearing.													
3:52									0.094	122	144	20	40.3	25
3:57	X	2.5	30	5.0	0.24	0.0002	0.00100	0.000048						
	XI	2.7	30	5.4	0.26	0.0002	0.00108	0.000051*						
	XII	2.4	30	4.8	0.23	0.0002	0.00096	0.000046						
4:10	Lying down. The symptoms still appearing.													
4:11									0.097	126	126	16	40.3	25

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)				Epinephrine (mgrm.)			Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)
		Quantity	Duration of collection (sec.)	Quantity per minute		Quantity contained in 1 c.c.	Epinephrine output per minute							
				per ani- mal	per kilo		per animal	per kilo						
4:30	Lying down quietly.					The rigidity of the legs	diminished.							
4:31						(XIII+XV)			0.103	137	108	18	40.3	25
4:32	XIII	1.8	30	3.6	0.17	0.0001	0.00039	0.000019						
	XIV	1.8	30	3.6	0.17	0.0001	0.00036	0.000017*						
	XV	2.1	30	4.2	0.20									
4:50	Nystagmus still appearing.									135	96	18	40.2	25
4:51									0.102					
5:25	Lying down quietly.					Nystagmus indistinct.				129	120	14	40.0	25
5:27						(XVI+XVIII)			0.107					
5:28	XVI	2.2	30	4.4	0.21	0.00005	0.00022	0.000010						
	XVII	2.3	30	4.6	0.22	0.00005	0.00023	0.000011*						
	XVIII	2.0	30	4.0	0.19									

Autopsy: The puncture was between the sulcus praepyrimaldis and the fissura secunda in the median line. The pyramis, the uvula and the nodulus were destroyed. The remaining portion of the cerebellum was entirely freed from injury. The fourth ventricle floor was not injured, nor was bleeding found in the ventricle.

Experiment IV.

Dog 4. 15.4 kilos. ♂ 14. IX. 1932.

28. VI. 1932.		16.7 kilos.		D ₁₀ -L ₃ dorsal spinal roots severed under morphine-ether anaesthesia.											
9. IX. 1932.		16.1 kilos.		The occipital bone exposed and its nuchal part removed under morphine-ether anaesthesia.											
9:35-11:45 a.m. The left lumbar route preparation completed. The right (for blood pressure) and the left femoral artery (for blood sugar) laid bare and cannulae inserted. The dura perforated and the vermis exposed.															
2:15 p.m. Dog behaved quite normal. Lying down quietly,															
2:17										0.102	97	132	19	41.0	25
2:19	I	4.2	30	8.4	0.55	0.000025	0.00021	0.000014							
	II	4.2	30	8.4	0.55										
2:30	Lying down quietly.										90	126	20	41.1	25
2:35						(III+IV)				0.107					
2:37	III	2.2	30	4.4	0.29	0.00005	0.00023	0.000014							
	IV	2.3	30	4.6	0.30										
	V	2.5	30	5.0	0.32										
2:48 Punctured the lobul. post. medianus: Dog extended rigidly the hind legs. Pupils dilated ad maximum. Nystagmus occurred. Abundant salivation appeared. The blood pressure rose from 89 to 202 mms. Hg. The heart rate reduced markedly from 102 to 66 per minute. The respiration accelerated.															
2:53	Lying down. Nystagmus still appearing. Abundant salivation. Pupils regained almost the initial size.										140	69	15	41.3	25
2:55										0.149					
2:58	VI	3.5	30	7.0	0.45	0.0004+	0.00280+	0.00018+							
	VII	4.0	30	8.0	0.52										
	VIII	3.5	30	7.0	0.45	0.0004	0.00280	0.00018							
3:05	Lying down quietly. Abundant salivation still appearing.										91	66	30		25
3:07										0.171					
3:15	Lying down quietly. Pupils not dilated. Nystagmus diminished in frequency.										92	72	26	41.1	25

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)				Epinephrine (mgrm.)			Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)
		Quantity	Duration of collection (sec.)	Quantity per minute		Quantity contained in 1 c.c.	Epinephrine output per minute							
				per ani- mal	per kilo		per animal	per kilo						
3:19									0.149					
3:20	IX	3.0	30	6.0	0.39	0.00015	0.00090	0.000058						
	X	3.4	30	6.8	0.44									
	XI	6.1	60	6.1	0.40	0.00015-	0.00092-	0.000059-						
3:30	The symptoms still appearing.													
3:35									0.136	88	84	16		25
3:45	Lying down quietly.													
4:10	XII	3.5	30	7.0	0.45	0.000075	0.00052	0.000034		89	102	18	41.1	25
	XIII	3.0	30	6.0	0.39									
4:20	The rigidity of the legs still appearing.													
4:21									0.122	91	120	34	40.9	25
4:45	Nystagmus and salivation still appearing.													
4:50									0.115	88	120	36		25
4:55	XIV	2.4	30	4.8	0.31	(XIV+XVI) 0.00005	0.00025	0.000016						
	XV	2.9	30	5.8	0.38									
	XVI	2.7	30	5.4	0.35									

Autopsy: The puncture was between the sulcus praepyramidalis and the fissura secunda in the median line. The pyramid and the uvula were destroyed. The nodulus remained intact. The left ala cinerea was injured at the level about 5 mms. above the calamus. Slight bleeding was found in the fourth ventricle.

Experiment V.

Dog 5. 19.2 kilos. ♂ 28. IX. 1932.

[14. VII. 1932. 21.5 kilos. D ₁₀ -L ₃ dorsal spinal roots severed under morphine-ether anaesthesia.]														
[22. IX. 1932. 20.2 kilos. The occipital bone exposed and its nuchal part removed under morphine-ether anaesthesia.]														
9:30 a.m.-12:05 p.m.	The left lumbar route preparation completed. The right (for blood pressure) and the left femoral artery (for blood sugar) laid bare and cannulae inserted. The dura perforated and the vermis exposed.													
2:25 p.m.	Dog behaved quite normal. Lying down quietly.													
2:34						(I+II)			0.119	126	144	21	40.2	20
2:35	I	2.3	30	4.6	0.24	0.00005+	0.00023+	0.000012+						
	II	2.3	30	4.6	0.24									
	III	2.9	30	5.8	0.30	0.00005	0.00029	0.000015*						
2:50	Lying down quietly.													
2:54						(IV+V)			0.107	121	132	18	40.5	20
2:55	IV	2.3	30	4.6	0.24	0.000025+	0.00012+	0.000006+						
	V	2.6	30	5.2	0.27									
	VI	2.6	30	5.2	0.27	0.000025	0.00013	0.000007*						
3:16	Punctured the lobul. post. medianus: Dog extended rigidly the four legs. Conspicuous widening of pupils and nystagmus occurred. The blood pressure rose abruptly from 121 to 185 mms. Hg. The heart rate accelerated from 102 to 120 per minute. The rate of respiration augmented from 18 to 30 per minute. 3:20 p.m. mydriasis less pronounced.													
3:21	Lying down.													
3:22									0.115	144	102	23	40.3	20.5
3:25	VII	4.2	30	8.4	0.44	0.0003	0.00252	0.000131						
	VIII	3.7	30	7.4	0.38	0.00035	0.00259	0.000135*						
	IX	3.0	30	6.0	0.32	0.00045	0.00270	0.000141						

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)				Epinephrine (mgrm.)			Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)	
		Quantity	Duration of collection (sec.)	Quantity per minute		Quantity contained in 1 c.c.	Epinephrine output per minute								
				per ani- mal	per kilo		per animal	per kilo							
3:40		The rigidity of the limbs diminished.								0.119	130	114	19	40.2	20.5
3:41															
3:50		Lying down quietly. Nystagmus still appearing, otherwise appearance quite normal.									125	96	18	40.1	20.5
3:53										0.124					
3:55		X	3.8	30	7.6	0.39	0.0001+	0.00076+	0.000039+						
		XI	3.0	30	6.0	0.32	0.000125	0.00075	0.000039*						
4:18		Lying down quietly. Nystagmus still appearing, pupils not dilated.									117	90	15	39.6	20.5
4:20										0.123					
4:25		XII	2.8	30	5.6	0.30	(XII + XIV) 0.0001	0.90056	0.000029						
		XIII	3.0	30	6.0	0.31	0.0001	0.00060	0.000031*						
		XIV	2.7	30	5.4	0.28									
4:48		Lying down quietly.									118	108	13	39.3	20.5
4:50										0.115					
5:12		Lying down quietly. Nystagmus less pronounced.									116	114	16	39.1	20.5
5:14										0.112					
5:15		XV	1.8	20	5.4	0.28	(XV + XVIII) 0.00005-	0.00027-	0.000014-						
		XVI	2.1	30	4.2	0.22	0.00005	0.00021	0.000011*						
		XVII	1.4	20	4.2	0.22									

Autopsy: The puncture was at the fissura secunda in the median line. The portion of the pyramis close to this fissura, the uvula and the nodulus were destroyed. The fourth ventricle floor was not injured. No trace of bleeding was found in the fourth ventricle.

Experiment VI.

Dog 6. 14.7 kilos. ♂ 12. X. 1932.

- [17. IX. 1932. 15.8 kilos. D₁₀-L₃ dorsal spinal roots severed under morphine-ether anaesthesia.
8. X. 1932. 14.9 kilos. The occipital bone exposed and its nuchal part removed under morphine-ether anaesthesia.]

9:30 a.m.-1:30 p.m. The left lumbar route preparation completed. The left (for blood pressure) and the right femoral artery (for blood sugar) laid bare and cannulae inserted. The dura perforated and the vermis exposed.

3:10 p.m. Dog behaved quite normal. Lying down quietly. Slight shivering appearing. 100 156 14 39.9 20

3:14 I 2.8 60 2.8 0.19 0.000025- 0.00007- 0.000005-* 0.098

3:20 II 2.6 60 2.5 0.17 0.000025- 0.00006- 0.000004-*

III 2.8 60 2.8 0.19 0.000025+ 0.00007+ 0.000005+*

3:30 Lying down quietly. Slight shivering appearing. 98 168 14 40.1 21

4:10 IV 2.8 60 2.8 0.19 0.000025- 0.00007- 0.000005-* 0.098

V 1.2 30 2.4 0.16 0.000025 0.00006 0.000004*

4:20 Punctured the lobul. post. medianus: Dog extended rigidly the fore and hind limbs, but soon became quiet. Mydriasis and nystagmus appeared. Urination occurred. The blood pressure rose abruptly from 96 to 142 mms. Hg. The rate of heart beat increased slightly from 126 to 132 per minute. The rate of respiration augmented from 12 to 24 per minute.

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)				Epinephrine (mgrm.)			Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)	
		Quantity	Duration of collection (sec.)	Quantity per minute		Quantity contained in 1 c.c.	Epinephrine output per minute								
				per ani- mal	per kilo		per animal	per kilo							
4:23	Lying down quietly.								0.103	119	114	18	40.2	20	
4:24															
4:30	VI	2.8	30	5.6	0.38	0.0003	0.00168	0.000117*							
4:40	VII	2.6	30	5.2	0.35	0.0003	0.00156	0.000106*		109	114	20	40.4	20	
4:41	Mydriasis disappeared.								0.108	105	120	20	40.3	20	
4:55	Lying down quietly.					Nystagmus indistinct.			0.110						
5:19						(VIII+IX)									
5:20	VIII	0.8	30	1.6	0.11	0.00015	0.00030	0.000020*							
	IX	1.2	30	2.4	0.16										
	X	1.2	30	2.4	0.16	0.0001	0.00024	0.000016*		98	120	18		20	
5:25	Lying down quietly.								0.110	102	126	20	40.0	20	
5:27															
5:40	Lying down quietly.								0.112	103	126	20		20	
5:42									0.105	101	138	18	39.9	20	
5:55	Lying down quietly.														
5:56									0.108						
6:15	Lying down quietly.					No salivation occurred.									
6:17															

Autopsy: The puncture was between the sulcus praepyrimaldis and the fissura secunda in the median line. The portion of the pyramis close to this fissura, the uvula and the nodulus were destroyed. Bleeding was found in the tissue of the lobus medius. The medulla oblongata was freed from injury and no trace of bleeding was found in the fourth ventricle.

Experiment VII.

Dog 7. 14.0 kilos. ♂ 19. X. 1932.

[illegible]

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)				Epinephrine (mgrm.)			Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)
		Quantity	Duration of collection (sec.)	Quantity per minute		Quantity contained in 1 c.c.	Epinephrine output per minute							
				per ani- mal	per kilo		per animal	per kilo						
3:22	Lying down quietly.								0.096	89	132	16	39.1	19
3:27	VII	3.7	30	7.4	0.53	0.000175	0.00130	0.000093*						
	VIII	3.4	30	6.8	0.49	0.0002	0.00136	0.000097						
	IX	3.4	30	6.8	0.49	0.0002	0.00136	0.000097						
3:40	Dog extended suddenly the fore and hind legs. Mydriasis and nystagmus developed. Abrupt and marked rise of blood pressure resulted.													
3:45	Lying down quietly. Mydriasis and nystagmus still appearing.													
3:47									0.108					
3:50	X	3.3	30	6.6	0.47	0.00035	0.00231	0.000165*						
	XI	3.4	30	6.8	0.49	0.00035	0.00238	0.000170						
	XII	3.2	30	6.4	0.46	0.00035	0.00224	0.000160						
4:05	Lying down quietly. Rigidity of the legs still appearing.													
4:06									0.105	81	114	18		19
4:25	Lying down quietly. Nystagmus less pronounced.													
4:27									0.103	80	114	18	38.7	19
4:30	XIII	2.5	30	5.0	0.36	0.000175	0.00088	0.000063*						
	XIV	2.6	30	5.2	0.37	0.000175	0.00089	0.000064						
	XV	2.5	30	5.0	0.36	(XIV + XV)								
4:45	Lying down quietly. Rigidity of the legs almost disappeared.													
4:46									0.099	80	132	20	38.6	19
5:00	Lying down quietly. Pupils not dilated. Nystagmus indistinct. No salivation occurred.													
5:05									0.094	82	138	18	38.3	19
5:14	XVI	2.0	30	4.0	0.29	0.00015	0.00060	0.000043*						
	XVII	1.9	30	3.8	0.27	0.00015	0.00057	0.000041						
	XVIII	1.9	30	3.8	0.27	(XVII + XVIII)								
5:20	Lying down quietly.													
5:22-5:25 p.m.	Asphyxiated the animal until the respiration completely stopped. Artificial respiration resorted to during about 30 seconds. The respiratory movements recommenced. 5:27, heart rate 96, respiration 36, blood sugar 0.191%. 5:34, heart rate 102, respiration 27, blood sugar 0.174%. 5:47, heart rate 120, respiration 28, body temperature 38.0°C., room temperature 19°C., blood sugar 0.168%.													

Autopsy: The puncture was between the sulcus praepyramidalis and the fissura secunda in the median line. The pyramid alone was injured. Bleeding was found in the tissue of the uvula, the nodulus, the tuber and the declive. The fourth ventricle floor was not injured, no bleeding in the ventricle.

Experiment VIII.

Dog 8. 20.0 kilos. ♂ 2. XI. 1932.

13. IX. 1932.	22.0 kilos.	D ₁₀ -L ₃ dorsal spinal roots severed under morphine-ether anaesthesia.
27. X. 1932.	21.0 kilos.	The occipital bone exposed and its nuchal part removed under morphine-ether anaesthesia.

9:35 a.m.-12:20 p.m. The left lumbar route preparation completed. The left (for blood pressure) and the right femoral artery (for blood sugar) laid bare and cannulae inserted. The dura perforated and the vermis exposed.

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)				Epinephrine (mgrm.)			Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)
		Quantity	Duration of collection (sec.)	Quantity per minute		Quantity contained in 1 c.c.	Epinephrine output per minute							
				per ani- mal	per kilo		per animal	per kilo						
2:20 p.m.	Dog behaved quite normal.					Lying down quietly.								
2:25									0.096	97	174	22	40.1	18
2:28	I	3.6	30	7.2	0.36									
	II	3.5	30	7.0	0.35	0.0001	0.00070	0.000035						
	III	3.4	30	6.8	0.34	0.0001	0.00068	0.000034*						
2:40	Lying down quietly.													
2:43									0.105	86	168	20	40.1	18.5
2:48	IV	3.8	30	7.6	0.38									
	V	3.8	30	7.6	0.38	0.00005	0.00038	0.000019*						
	VI	3.5	30	7.0	0.35	0.00005+	0.00035+	0.000017+						
3:00										94	162	18	40.1	18.5
3:05	Punctured the lobul. post. medianus: Very slight excitement displayed. Widening of the pupils associated with nictitation occurred. Nystagmus not occurred, no extending of the legs. The blood pressure rose slightly, i.e. from 92 to 109 mms. Hg., but returned to the initial in about 15 seconds. The heart rate increased from 168 to 180 per minute. The respiration increased from 18 to 26 per minute.													
3:11	Lying down quietly.													
3:13	VII	4.3	30	8.6	0.43				0.109					
	VIII	4.2	30	8.4	0.42	0.0002	0.00168	0.000084*						
	IX	4.3	30	8.6	0.43	0.0002	0.00172	0.000085						
3:20	Lying down quietly.									87	174	22	40.3	19
3:22									0.114					
3:35	Lying down quietly. Dilatation of the pupils indistinct.									91	168	22	40.5	19
3:36									0.112					
3:42	X	3.8	30	7.6	0.38									
	XI	3.7	30	7.4	0.37	0.00015	0.00111	0.000056*						
	XII	3.4	30	6.8	0.34	0.00015	0.00102	0.000051						
4:05	Lying down quietly.									87	198	26	40.7	18
4:06									0.105					
4:10	XIII	2.6	30	5.2	0.26									
	XIV	2.1	30	4.2	0.21	0.0001	0.00042	0.000021*						
	XV	2.3	30	4.6	0.23	0.0001	0.00046	0.000023						
4:30	Lying down quietly.									80	210	28	40.6	18
4:32									0.094					
5:05	Lying down quietly.									79	192	26	40.5	17
5:09									0.091					
5:20	XVI	2.4	30	4.8	0.24									
	XXII	2.4	30	4.8	0.24	0.00005	0.00024	0.000012						
	XVIII	2.5	30	5.0	0.25	0.00005	0.00025	0.000013*						
5:30-5:34 p.m.	Asphyxiated the animal until the respiration completely ceased. Artificial respiration resorted to during about 1 minute. The respiratory movements recommenced. 5:36, heart rate 126, respiration 38, blood sugar 0.206%. 5:37, body temperature 40.1°C. 5:40, heart rate 136, respiration 20, blood sugar 0.204%. 5:45, heart rate 148, respiration 20. 5:50, heart rate 180, respiration 22, body temperature 40.1°C., room temperature 17°C., blood sugar 0.170%.													

Autopsy: The puncture was between the sulcus praepyramidalis and the fissura secunda in the median line. The pyramis alone was destroyed. The portion of the lobul. post. medianus posterior to the fissura secunda was entirely freed from injury. No trace of lesion was found in the fourth ventricle floor.

Time of procedure (hour : min.)	No. of specimen	Blood flow (c.c.)			Epinephrine (mgrm.)			Blood sugar (%)	Blood pressure (mms. Hg.)	Rate of heart beat per minute	Rate of respira- tion per minute	Body temperature (°C.)	Room temperature (°C.)
		Quantity	Duration of collection (sec.)	Quantity per minute	Quantity contained in 1 c.c.	Epinephrine output per minute							
						per ani- mal	per kilo						

Experiment IX.

Dog 9. 17.0 kilos. ♂ 22. XII. 1932.

3. IX. 1932. 17.8 kilos. D₁₀-L₃ dorsal spinal roots severed under morphine-ether anaesthesia.
 19. XII. 1932. 17.5 kilos. The occipital bone exposed and its nuchal part removed under morphine-ether anaesthesia.

10:09 a.m.-12:32 p.m. The left lumbar route preparation completed. The right (for blood pressure) and the right femoral artery (for blood sugar) laid bare and cannulae inserted. The dura perforated and the vermis exposed.

2:30 p.m. Dog somewhat depressed.

2:35									0.105	110	114	18	40.6	20
2:38	Lying down quietly.									103	162	24	40.6	20
2:40	I	2.7	60	2.7	0.16	0.0001	0.00027	0.000016*						
	II	1.8	30	3.6	0.21	0.000075	0.00024	0.000014*						
	III	1.4	30	2.8	0.16	(II + III)								
2:55	Lying down quietly.					(IV + V)			0.104	100	162	18	40.6	20
3:05						0.0001-	0.00020-	0.000012-						
3:10	IV	1.8	60	1.8	0.11									
	V	1.5	40	2.25	0.13									
	VI	1.6	40	2.4	0.14	0.0001	0.00024	0.000014*						

3:33 Punctured the lobul. post. medianus: Dog extended rigidly the fore and hind legs. Mydriasis and nystagmus developed. Urination occurred. The blood pressure rose abruptly from 103 to 150 mms. Hg. The heart beat accelerated from 144 to 156 per minute. The respiration increased from 24 to 36 per minute.

3:36	Lying down quietly. Mydriasis and nystagmus still appearing								0.108	125	174	28	40.8	20
3:38														
3:35	VII	1.8	30	3.6	0.21	0.0004-	0.00144-	0.000085-						
	VIII	2.1	30	4.2	0.21	0.00035	0.00147	0.000086						
	IX	3.5	40	5.25	0.31	0.0003	0.00157	0.000093*						
	3:49, slight struggling displayed.													
3:53	Lying down quietly. Dilatation of the pupils less pronounced								0.113	102	168	24	41.1	20
3:54														
4:03	Lying down quietly. Rigidity of the legs disappeared.								0.111	100	168	24	40.8	20
4:04														
4:33	Lying down quietly. Nystagmus indistinct.								0.109	104	192	30	40.8	20
4:34														
4:35	X	1.2	30	2.4	0.14	0.0002	0.00048	0.000028*						
5:03	Lying down quietly.								0.102	95	204	22	40.5	20
5:04														
5:33									0.099	84	192	24	39.8	19
5:34														

5:37-5:40 p.m. Asphyxiated the animal until the respiration completely stopped. Artificial respiration resorted to during about 1 minute. The respiratory movements recommenced. 5:40, heart rate 120, respiration 9, blood sugar 0.145%. 5:43, heart rate 138, respiration 9. 5:45, body temperature 39.0°C., blood sugar 0.163%. 5:48, heart rate 216, respiration 18. 5:50, body temperature 39.0°C., room temperature 17.5°C., blood sugar 0.156%.

Autopsy: The puncture was between the sulcus praepyramidalis and the fissura secunda in the median line. The pyramis, the uvula and the nodulus were destroyed. The fourth ventricle floor was completely freed from injury. No trace of bleeding was found in the ventricle.

Fig. 3. Intestine tracings of Dog 7 (Reduced to $\frac{1}{2}$).

In all the intestine tracings, at the mark "x" atropine-Tyrod's solution, in which the rabbit intestine segment was beating rhythmically, was replaced by indifferent blood solution, and at the "numeral" by the indifferent blood solution to which a certain quantity of adrenalin-chloride of Sankyo Co. was added, or by the specimen solution. All the blood solutions were prepared by diluting with 4 volumes of Tyrod's solution, and the quantity of the blood employed for one assay was 0.5 c.c.

The numeral of specimen and the quantity of adrenaline solution, which is showed in c.c. and in concentration, were added to each observation. For example, "0.1 1/2000" shows "0.1 c.c. of adrenaline solution with the concentration of 1/2000 mgrm. in 1 c.c." i.e. 0.00005 mgrm. adrenaline. To show the I specimen, we used the numeral "I".

In all tracings, time intervals are 30 seconds.

Specimen II+III: Weaker than 0.1 1/2000 and almost as strong as 0.05 1/2000 (Fig. 3 a). Estimated as 0.00005 mgrm. in 1 c.c.

Specimen IV+V: Almost as strong as II+III and 0.05 1/2000 (Fig. 3 a & b). Estimated as 0.00005 mgrm. in 1 c.c.

Specimen VIII: Stronger than 0.15 1/2000 and as strong as 0.2 1/2000 (Fig. 3 b). Estimated as 0.0002 mgrm. in 1 c.c.

Specimen IX: Stronger than 0.15 1/2000 and almost as strong as 0.2 1/2000 (Fig. 3 b & c). Estimated as 0.0002 mgrm. in 1 c.c.

Specimen XI: Stronger than 0.3 1/2000 and almost as strong as Spec. XII (Fig. 3 c & d). Estimated as 0.00035 mgrm. in 1 c.c.

Specimen XII: Stronger than 0.3 1/2000 and almost as strong as 0.35 1/2000 (Fig. 3 c & d). Estimated as 0.00035 mgrm. in 1 c.c.

Specimen XIV+XV: Weaker than 0.2 1/2000 almost as strong as 0.175 1/2000 (Fig. 3 d & e). Estimated as 0.000175 mgrm. in 1 c.c.

Specimen XVII+XVIII: Weaker than 0.175 1/2000 and almost as strong as 0.15 1/2000 (Fig. 3 e). Estimated as 0.00015 mgrm. in 1 c.c.

EXAMPLE.

*Determination of epinephrine content of the samples from Dog 6,
by means of the paradoxical cat pupil reaction.*

Cat 1.50 kilos. ♂ 13. X. 1932.

5.X. 1932. 2.01 kilos. Both splanchnic nerves sectioned by lumbar route and left superior cervical ganglion removed.

2:47 p.m. 2.5 grms. urethane given by stomach tube.

3:20 Cannula inserted and tied into trachea.

3:24 Cannula inserted and tied into right external jugular vein.

Time (hour: min.)	No. and quan- tity (c.c.) of specimen or concentration and quantity (c.c.) of adrena- line solution		Double Tyrode's solution (c.c.)	Tyrode's solution (c.c.)	Indifferent blood (c.c.)	Duration of injec- tion (c.c.)	Time at which pupil began to dilate after starting injection(sec.)	Time at which pupil reached to maximum width after starting injection (sec.)	Transverse diameter of pupil (mms.)		
									before in- jection	after injec- tion	increase
3:43 p.m.				1.0	1.5	7			30/9	30/9	no re- action
3:50	1/1000,000	0.1	0.1	0.8	1.5	7	10	19	35/9	50/9	15/9
3:53	1/1000,000	0.05	0.05	0.9	1.5	6	13	20	37/9	45/9	8/9
3:59	1/1000,000	0.1	0.1	0.8	1.5	6	10	19	33/9	52/9	19/9
4:03	1/1000,000	0.2	0.2	0.6	1.5	7	11	22	30/9	60/9	30/9
4:08	I	1.5		1.0		6	12	21	32/9	37/9	5/9
4:12	1/1000,000	0.025	0.025	0.95	1.5	7	11	20	30/9	36/9	6/9
4:16	II	1.5		1.0		6	12	19	29/9	36/9	7/9
4:24	1/1000,000	0.025	0.025	0.95	1.5	5	10	21	26/9	32/9	6/9
4:28	III	1.5		1.0		5	10	21	27/9	35/9	8/9
4:35	1/1000,000	0.025	0.025	0.95	1.5	6	11	21	31/9	39/9	8/9
4:39	1/1000,000	0.05	0.05	0.9	1.5	6	10	18	35/9	44/9	9/9
4:43	IV	1.5		1.0		6	10	19	35/9	39/9	4/9
4:50	1/1000,000	0.025	0.025	0.95	1.5	6	10	18	30/9	34/9	4/9
4:55	V	1.0		1.0		6	11	18	31/9	35/9	4/9
5:00	1/1000,000	0.025	0.025	1.45	1.0	6	10	20	36/9	40/9	4/9
5:05	VI	0.5		2.0		6	11	24	36/9	60/9	24/9
5:48	1/1000,000	0.1	0.1	1.8	0.5	6	10	22	36/9	56/9	20/9
5:15	1/1000,000	0.15	0.15	1.7	0.5	6	10	24	36/9	60/9	24/9
5:18	VI	0.5		2.0		6	10	20	39/9	62/9	23/9
5:22	VII	0.5		2.0		6	11	21	37/9	61/9	24/9
5:27	1/1000,000	0.2	0.2	1.6	0.5	6	9	20	33/9	67/9	34/9
5:33	1/1000,000	0.15	0.15	1.7	0.5	6	12	23	23/9	49/9	26/9
5:37	VIII+IX	0.5		2.0		6	12	20	18/9	33/9	15/9
5:43	1/1000,000	0.1	0.1	1.8	0.5	7	13	21	12/9	32/9	20/9
5:46	1/1000,000	0.075	0.075	1.85	0.5	7	12	24	20/9	35/9	15/9
5:51	X	0.5		2.0		7	13	22	21/9	30/9	9/9
5:56	1/1000,000	0.1	0.1	1.8	0.5	7	12	24	21/9	36/9	15/9
6:00	1/1000,000	0.05	0.05	1.9	0.5	7	13	21	21/9	31/9	10/9
6:03				2.0	0.5	6			20/9	20/9	no re- action
6:07	X	0.5		2.0		6	22	22	20/9	30/9	10/9
6:10	1/1000,000	0.05	0.05	1.9	0.5	6	24	24	22/9	32/9	10/9

To sum up:

Specimen I: 1.5 c.c. of specimen is almost as strong as 0.025 c.c. of 1/1000,000 adrenaline. It is assayed as less than 0.000025 mgrm. in 1 c.c.

Specimen II: 1.5 c.c. of specimen is almost as strong as 0.025 c.c. of 1/1000,000 adrenaline. It is estimated as less than 0.000025 mgrm. in 1 c.c.

Specimen III: 1.5 c.c. of specimen is as strong as 0.05 c.c. of 1/1000,000 adrenaline. It is estimated as a little larger than 0.000025 mgrm. in 1 c.c.

Specimen IV: 1.5 c.c. of specimen is as strong as 0.025 c.c. of 1/1000,000 adrenaline. It is estimated as less than 0.000025 mgrm. in 1 c.c.

Specimen V: 1.0 c.c. of specimen is as strong as 0.025 c.c. of 1/1000,000 adrenaline. It is estimated as about 0.000025 mgrm. in 1 c.c.

Specimen VI: 0.5 c.c. of specimen is almost as strong as 0.15 c.c. of 1/1000,000 adrenaline. It is estimated as about 0.0003 mgrm. in 1 c.c.

Specimen VII: 0.5 c.c. of specimen is almost as strong as 0.15 c.c. of 1/1000,000 adrenaline. It is estimated as about 0.0003 mgrm. in 1 c.c.

Specimen VIII+IX: 0.5 c.c. of specimen is almost as strong as 0.075 c.c. of 1/1000,000 adrenaline. It is estimated as about 0.00015 mgrm. in 1 c.c.

Specimen X: 0.5 c.c. of specimen is almost as strong as 0.05 c.c. of 1/1000,000 adrenaline. It is estimated as about 0.0001 mgrm. in 1 c.c.

the vermis, but in some cases no change or a slight reduction was exhibited. The epinephrine content in 1 c.c. of blood also invariably increased from 0.000025–0.00015 mgrm. to 0.000175–0.0007 mgrm. As a consequence of the increase in the outflow and the epinephrine content of the suprarenal vein blood, the rate of the epinephrine secretion was found augmented to from 0.0002 to 0.0004 mgrm. per kilo per minute. The greatest values were reached in the samples collected at about 5 to 15 minutes after the puncture.

No clear difference was seen in the magnitude of acceleration of the epinephrine discharge between the cases where the pyramis, uvula and nodulus were wholly destroyed and those where the pyramis alone was destroyed. In Dogs 7 (before development of severe symptoms) and 8 the acceleration was small, but in Dog 9 about the same degree of acceleration was noted; in Dogs 7 & 8 destruction was limited before the fissura secunda, while the lobulus posterior medianus was expansively destroyed in Dog 9. When the symptoms became excessive about 20 minutes after the puncture, the acceleration was measured as enlarged in Dog 7; this apparently indicates an expansion of lesion by bleeding into the uvula and nodulus.

Comparison of the output rates before and after the puncture showed that it was increased by about four to thirty times as a result of the cerebellar puncture. This hyperepinephrinaemia lasted for a period extending about one and half to two hours or longer.

The increased rate of the epinephrine discharge on the puncture of the lobulus posterior medianus is generally not so considerable as to be causable by the *piqûre diabétique* of Cl. Bernard, namely by the puncture of the fourth ventricle floor with simultaneous injury of the vermis. For clearness, the changes in the output rate of the

epinephrine resulting from these two kinds of the puncture are illustrated in Fig. 4. The solid line represents the average rate of the epinephrine secretion obtained from seven dogs, in which the lobulus

Fig. 4. Comparison of the effect of the puncture of the lobulus posterior medianus upon the epinephrine output rate from both the suprarenal glands with that of the piqûre diabétique. Solid circles connected with solid lines represent the average output rate for 7 dogs on the puncture of the lobulus posterior medianus, light circles with dotted lines the average output rate for 6 dogs on the piqûre diabétique. The figures in parentheses indicate the output rate of epinephrine in mgrm. per kilo and per minute.

posterior medianus was injured (Dogs. 1, 2, 3, 5, 6, 8 & 9), and the broken line that obtained from six dogs on the sugar puncture of Cl. Bernard, which was indicated in the previous publication¹⁾; the output rate from both glands being determined by doubling the amount secreted from one gland. The figure shows that the average rate of the epinephrine secretion increased from the quiet value of 0.00003 mgrm. per kilo per minute to 0.00025 mgrm. at the end of 10 minutes after the cerebellar puncture and then decreased gradually until it

reached to the vicinity of the initial rate at the end of two hours.

The peak of such an increased rate is satisfactorily approximate to the value shown by Shimidzu (0.0003 mgrm. per kilo per minute), working with the aid of the paradoxical pupil reaction of a rabbit under conditions different from the present experiments.

On puncturing the vermis, the average amount of epinephrine secreted in the first thirty minutes was 0.005 mgrm. per kilo, in the

second thirty minutes 0.003 mgrm. per kilo and in the second hour 0.004 mgrm. per kilo, the total amount secreted during two hours being calculated as 0.012 mgrm. per kilo. On the other hand, the amount of the epinephrine outpoured on the piqûre of Cl. Bernard was, as previously indicated, 0.013 mgrm. per kilo in the first thirty minutes, 0.012 mgrm. per kilo in the second thirty minutes and 0.015 mgrm. per kilo in the second hour; the total amount during two hours being determined as 0.04 mgrm. per kilo. This shows that the total amount liberated in two hours after the puncture of the lobulus posterior medianus of the cerebellum may be said to be about one third of that secreted by the piqûre of Cl. Bernard and about three times that to be normally secreted for the same duration.

The blood sugar content.

It will be seen from the table that the glycaemic level was not influenced to any noteworthy degree by injuring the lobulus posterior medianus.

The blood sugar concentration just before the puncture was either already normal (Dogs 6 & 7) or little greater; that is in some cases the carbohydrate disturbances due to the preparatory procedures already disappeared, while in the remaining they were still existing though slightly. On puncturing the vermis, the blood sugar concentration showed a tendency to increase, though small, the maximum being noted about twenty to thirty minutes to one hour after the puncture. The blood sugar content in Dog 2 showed no increase after the puncture, but the prepuncture value was still exaggerated, that is, the disturbances due to the preparatory procedures had not yet wholly subsided, and the highest value after the puncture harmonized with the other experiments. The value determined soon after the puncture was in Dogs 1, 2 & 3 smaller than the prepuncture value but this should not be taken as caused by the puncture itself, but must be assumed as a sign of subsidence of the carbohydrate disturbances due to the preparatory routine. The hyperglycaemia due to the vermis puncture is only small, as ad maximum 0.12%, and its occurrence does not depend upon the width of lesions and their localization. Between the cases where the lobulus posterior medianus was wholly destroyed or largely destroyed (Dogs 2, 3, 5, 6 & 9) and those where the uvula and nodulus remained entirely unaffected (Dogs 1 & 8), no visible difference was witnessed in the magnitude and the timely course of hyperglycaemia.

Our results are thus in disharmony with the previous investigators who noted a remarkable hyperglycaemia on puncturing the cerebellum.

To test the cause of this discrepancy we have taken into consideration on our sides a possible poor storage of the liver glycogen, though it was improbable from the first, since quite the same preparatory procedures as the present were conducted in our previous experiments in which the piqure diabétique of Cl. Bernard was capable of causing a copious hyperglycaemia in accordance with the former investigators. By way of precaution, we tried asphyxiation in three cases (Dogs 7, 8 & 9) towards the end of each proper experiment. The technique was that given in a previous publication from this laboratory.²²⁾

The animals were asphyxiated until the respiratory movements ceased completely and thereupon artificial respiration was employed about $\frac{1}{2}$ to 1 minute, thereby spontaneous respiration being resumed. The blood samples for sugar determination were taken at intervals of some minutes. The glycaemic level which had been almost uninfluenced by the cerebellar injury, rose to a striking degree after the asphyxiation and remained at a high level for a long period. In Dogs 7 and 8 the samples taken two minutes after discontinuance of the asphyxiation showed a highest percentage of sugar as 0.191% and 0.206% respectively. In Dog 9 the sugar content in the blood sample obtained five minutes after the asphyxiation was 0.163%.

Another kind of the control was accidentally done in a single case. As above quoted, in the previous experiments of Yen, Kaiwa and Wada, which were done in quite the same experimental conditions, the piqure of Cl. Bernard occasioned a hyperglycaemia of 0.12-0.2%, and serve as the check of non-insufficiency of the glycogen store in the dogs in the present investigation. But they were done about four years ago. However, non-occurrence of any significant change in the carbohydrate metabolism in the feeding and treatment of animals, and in the experimental procedures, which might intervene in some obscure way in the lapse of some years, was proved by the following.

The fourth ventricle floor was accidentally injured in Dog 4, prepared in exactly the same manner, together with the lobulus posterior medianus, and a striking increase in the sugar percentage, such as from 0.107% to 0.171%, was measured at 20 minutes after the puncture. The amount of the epinephrine secreted from both glands was determined as increased from 0.000028 to 0.00036 mgrm. per kilo per minute at ten minutes after the puncture. The blood pressure underwent a considerable rise accompanied by retardation of the heart beat. The result involving the symptoms produced are in satisfactory agreement with those described in previous publications.

Our present data, that is a slight hyperglycaemia or rather negative outcome, compared with a conspicuous hyperglycaemia obtained by the previous investigators,^{3, 5-10)} can not be accounted for by an in-

22) Sato, T. Inaba and Takahashi, Tohoku J. Exp. Med., 1932, 19, 421.

sufficiency of glycogen storage, but must be looked upon as being due to the fact that the puncture was done in the cerebellum alone, especially in the lobulus posterior medianus and all the other experimental conditions, which necessarily interfere with the blood sugar concentration, were avoided as far as possible. The old experience of C. Eckhard⁴⁾ on dogs seems to check with ours.

Briefly stated, an injury of the cerebellum, such as destroying the whole lobulus posterior medianus, can evoke only slight hyperglycaemia; any significant bearing on the carbohydrate metabolism cannot be attributed to that part of the brain.

That being so, one must now question why nearly all the previous workers came to observe a considerable rise of the blood sugar on injuring or stimulating the cerebellum. Fastening, anaesthetizing with ether, etc., and sensory stimulation are known as potent hyperglycaemic agents. When we performed the preparatory procedures as in the present investigations in dogs, fastened and narcotized with ether, a considerable hyperglycaemia occurred as 0.15% to 0.29% in 7 out of 9 cases, while in the remaining 2 cases 0.12% and 0.13% were measured.¹⁾ In the dogs of Shinosaki all the procedures were done under ether anaesthesia. C. Eckhard,⁴⁾ Dresel and Lewy⁶⁾ and Papilian and Cruceanu⁸⁾ did not give any description of anaesthetic, which may be assumed to be necessarily applied to their dogs, judging from the other experimental conditions.

SUMMARY.

The lobulus posterior medianus of the cerebellum was punctured in the dogs, non-anaesthetized, non-fastened and the epinephrine secretion rate was determined by collecting the suprarenal vein blood through the lumbar approach and the rabbit intestine segment method as well as the paradoxical cat pupil method.

(1) On puncturing, the epinephrine output rate increased, the acme being reached about five to fifteen minutes later, and the increased secretion lasted for one to two hours. The acceleration was generally small, the excess being 0.00015–0.00035 mgrm. epinephrine per kilo per minute from both glands, about one third of that achievable by the piqûre diabétique of Cl. Bernard.

The total amount secreted from both glands during two hours after the puncture of the posterior portion of the lobulus posterior medianus was on an average 0.012 mgrm. per kilo of body weight, also one third of the piqûre diabétique.

(2) The blood sugar concentration was only slightly influenced by the puncture of the lobulus posterior medianus, contrary to the

piqûre diabétique of Cl. Bernard, and in fact contrary to the previous experimentalists. In most cases it increased, but only insignificantly, having a maximal increase of 0.02%. That previous experimentalists obtained an excessive hyperglycaemia by destroying the cerebellum might be due to some complicated experimental conditions, which vitiate the outcome. The present writers are therefore of the view that the vermis has no special significance in the carbohydrate metabolism, contrary to some previous authors.

(3) The arterial blood pressure ascended invariably on puncturing, while some previous experimentalists failed to see any ascent. Its amount seemingly depends upon the region which was punctured; when the portion posterior to the fissura second was extensively attacked it was large and continued somewhat long. Destruction of the vermis before the fissure causes only a transitory and a somewhat smaller rise. The heart rate increased in most cases, but usually in a small degree; never was diminution noted, contrary to the piqûre diabétique. The increase continued usually for some minutes. The respiration rate increased too.

(4) In conclusion it may be added here that the puncture of the portion of the lobulus posterior medianus posterior to the fissura secunda brought about nystagmus without exception.