"The Comparative Physiology of the Suprarenal Capsules." By SWALE VINCENT, M.B. (Lond.), British Medical Association Research Scholar. Communicated by E. A. SCHÄFER, F.R.S. Received February 18,—Read March 11, 1897.

(From the Physiological Laboratory, University College, London.)

Notwithstanding the belief of Cuvier, "qu'il était probablement réservé à l'anatomie comparée d'expliquer le véritable usage des capsules surrénales," this method of comparative investigation has been but little employed in the attempt to discover the functions of these organs.

It has, in fact, been doubtful as to what are to be regarded as suprarenals and what are not, in certain of the lower vertebrates, especially in fishes. Thus it has been suggested that the lymphatic "head-kidney" of Teleosts may represent these bodies (Weldon, 19, 20); even the presence or absence of suprarenals in any given order has often been a matter of considerable doubt. I have, in previous papers (15, 16, 17, 18) endeavoured to clear up some of these points, and have described the anatomy and histology of the suprarenal capsules in fishes, amphibians, and reptiles, and I hope in the present communication to give some experimental confirmation of the correctness of the opinions I had previously maintained from histological considerations.

It will be advisable to prefix a few words about the comparative anatomy of the suprarenal capsules. Suprarenals of some sort are probably present in most, if not all, vertebrate animals. In the Cyclostomata this is at present doubtful,* so that it is not until we come to the Elasmobranch fishes that we find with certainty anything in the way of suprarenals. Here we meet with two kinds of structure concerning which there has been much discussion. In the first place, we find a series of paired bodies arranged segmentally on the intercostal arteries, and extending the whole length of the abdominal cavity. They are situated in close proximity to the sympathetic nervous system. Secondly, we have a single or paired, yellow, rod-shaped organ lying between the two halves of the kidney and near the dorsal aspect of this organ. This is the "interrenal" of Balfour (1).

The histology of these two organs I have described elsewhere (*loc. cit.*), and also I have expressed my belief that the paired segmental bodies correspond to the medulla of the suprarenals of higher vertebrates, while the interrenal body corresponds to the cortex. That this was the case was surmised long ago by Leydig (6, 7), and it is

* See, however, Collinge and Vincent, 'Anat. Anz.,' vol. 12, Nos. 9 and 10, 1896.

experimental evidence in favour of this view which I now wish to put forward. Before doing so, however, it will be well to state here that, so far as I have been able to make out, one only (viz., that which corresponds to the cortex) of the two suprarenal constituents is present in Teleostean fishes. The same probably applies to Ganoids.

With regard to the development of the suprarenals it is only necessary to note that many observers believe that the medullary portion is derived from, or at any rate, developed in connection with, the sympathetic nervous system (Balfour, 1), and it seems clear from the researches of Mihálkovics (8) that the cortex is developed from the germinal epithelium.

The researches of Oliver and Schäfer (9, 10, 11), followed by those of Cybulski and Szymonowicz (2, 3, 4, 13, 14), have shown that the medulla of the suprarenal capsules of mammals and the suprarenal capsules of birds and amphibians (Szymonowicz, 14) (presumably the medulla only also in these), produce a remarkable and characteristic rise of blood-pressure, when an extract is injected into the circulation of a living animal. But, so far as I know, no one has previously tested the effects of extracts of the suprarenal bodies of fishes.

The following experiments were accordingly undertaken at the suggestion of Professor Schäfer, to whom I am indebted for advice and assistance on many points connected with the research. I have already published a preliminary notice (17), giving the results of initial perfusion experiments. I have now repeated and confirmed these perfusion experiments, and, in addition, have tested the effect of the materials in question upon the arterial system of mammals.

Effects of Extract of Fishes' Suprarenals upon the Arterial System.—The methods employed have been:—

1. The perfusion of normal saline solution or Ringer's circulating fluid containing the extract to be tested, through the blood vessels of large toads after the brain and spinal cord had been destroyed by pithing.

2. The injection of the extracts into the blood-vessels of a living mammal and recording in the usual way the blood-pressure tracing with the mercurial kymograph. Dogs and cats have been used in these experiments.

The suprarenals employed in this research have been obtained mainly from *Scyllium canicula* among the Elasmobranchs and from *Anguilla anguilla* as a representative of the Teleosts, but I have also used *Scyllium catulus*, *Acanthias vulgaris*, *Galeus canis*, and others in the first-named order, and *Gadus morrhua* and several other species of Teleosts. The effects produced upon blood-pressure were practically identical in the corresponding organs of different species.

The extracts employed were obtained in various ways. Some were prepared by pounding the glands with sand and normal saline in a pestle and mortar, and subsequently filtering. Others were alcoholic, while still others were got by boiling for a short time a certain quantity of the material in a known amount of normal saline and filtering. In all cases care has been taken to obtain the solution free from particles before injection or perfusion.

For intravenous injection an extract of 1 in 25 of the fresh, moist gland has been usually employed. I have not ascertained the minimal effective dose, but 1 c.c. of such an extract (= 0·04 gram of the fresh gland) from the active glands produced a powerful effect.

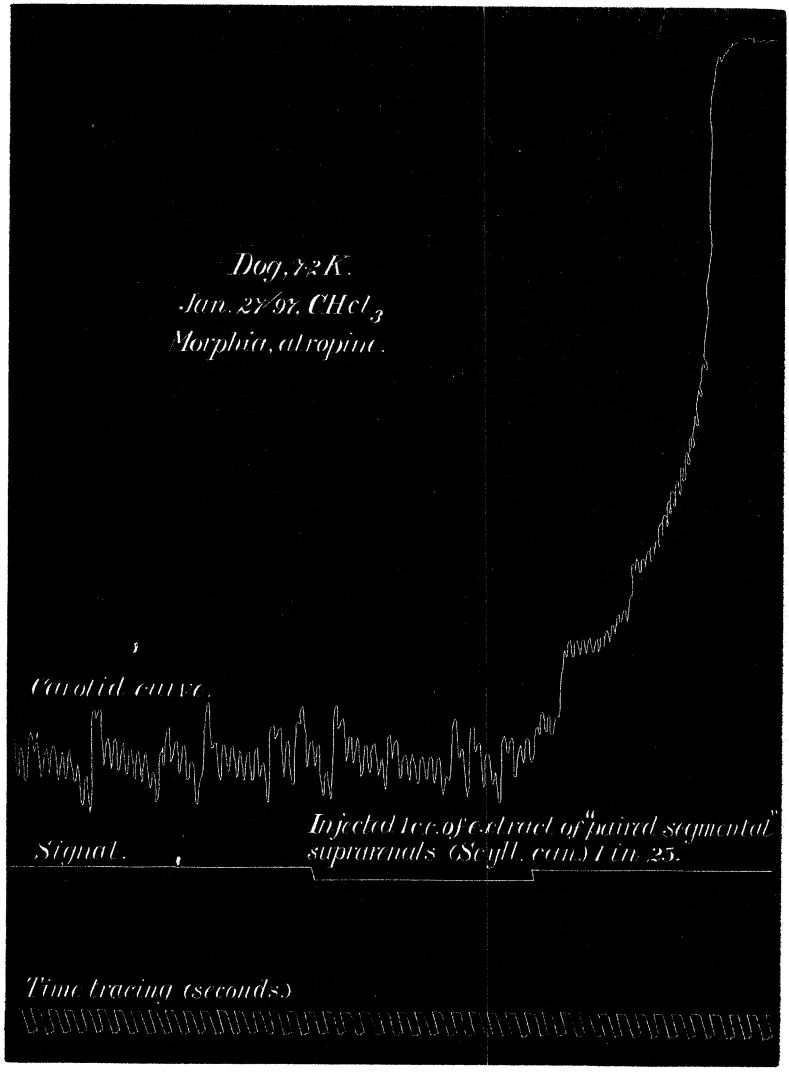
The results obtained by these two methods are quite harmonious. I had anticipated the possibility that the extract from a fish might be inactive upon a mammal, but it will be seen that this anticipation was unfounded. There is in all cases, where "medullary" substance has been injected, very striking evidence of contraction of the arterioles throughout the body. This was made manifest when using dogs or cats with the mercurial kymograph by an enormous rise of blood pressure (see fig. 1). In the perfusion experiments upon toads the result was seen in an almost complete cessation of flow of fluid through the blood-vessels (see Experiment 1). When "cortical" substance was employed little or no effect in these directions was obtained (figs. 2 and 3, and Experiments 1 and 2). It is true there was always a slight rise of blood-pressure or a small diminution of flow of fluid when extract of interrenal was used (Experiment 1 and fig. 2), but an explanation of this is, I believe, readily to be found. The extracts from the suprarenals of Teleosts have always given negative results when tested by both methods (see Experiment 2 and fig. 3).

The effect of the active principle upon the arterioles is due to a direct action upon the muscular tissue of the blood-vessels, and is not in any way connected with the action of the central nervous system. This is perfectly clear from the fact that the effects are well marked in the toad when brain and spinal cord have been destroyed by pithing. Oliver and Schäfer found this to be the case with mammalian suprarenal extract, though Szymonowicz and Cybulski maintain the contrary. The results of Oliver and Schäfer have since been completely confirmed by Velich.*

Fig. 1 shows the most typical effect; the lever rises gradually at first, then afterwards almost vertically. In some cases the pressure was too high to be recorded, as the mercury escaped from the end of the manometer. The effect passes off after a variable period, and the blood-pressure returns to normal. There is no need to give further details, but it will be sufficient to say that the experiments

* 'Wien. Med. Blätter,' Nr. 15, bis 21, 1896.

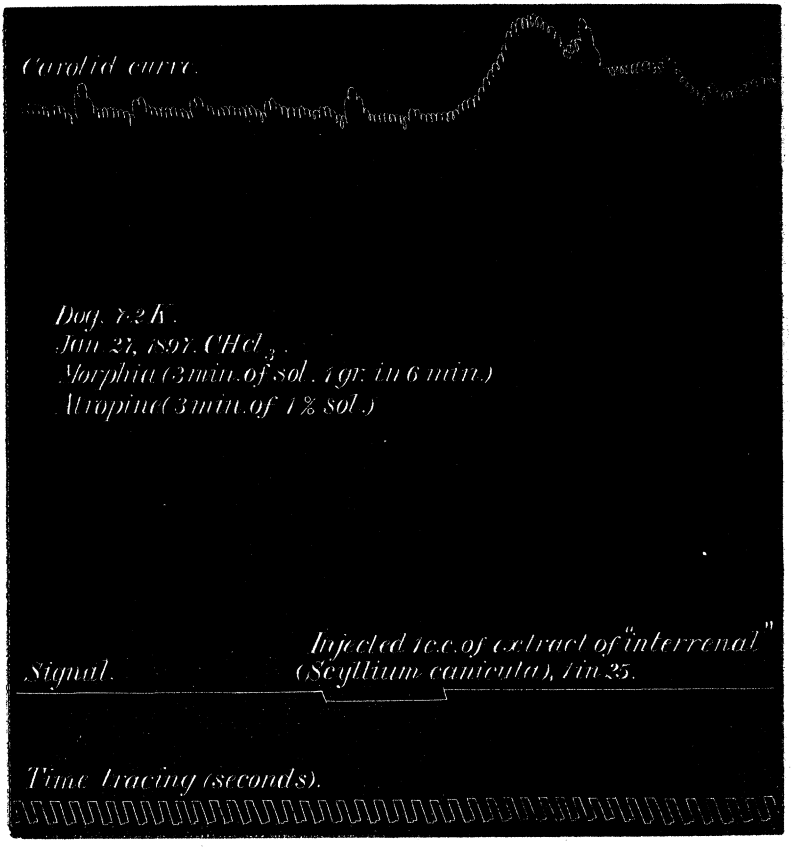
FIG. 1.



all point to the fact that the "paired segmental" suprarenal bodies of Elasmobranchs correspond precisely in physiological action to the medulla of mammalian suprarenal.

With extracts of the interrenal body of Elasmobranchs, partial effects only in the same direction are obtained. Fig. 2 shows a tracing obtained by injecting the same amount of "interrenal" as

Fig. 2.

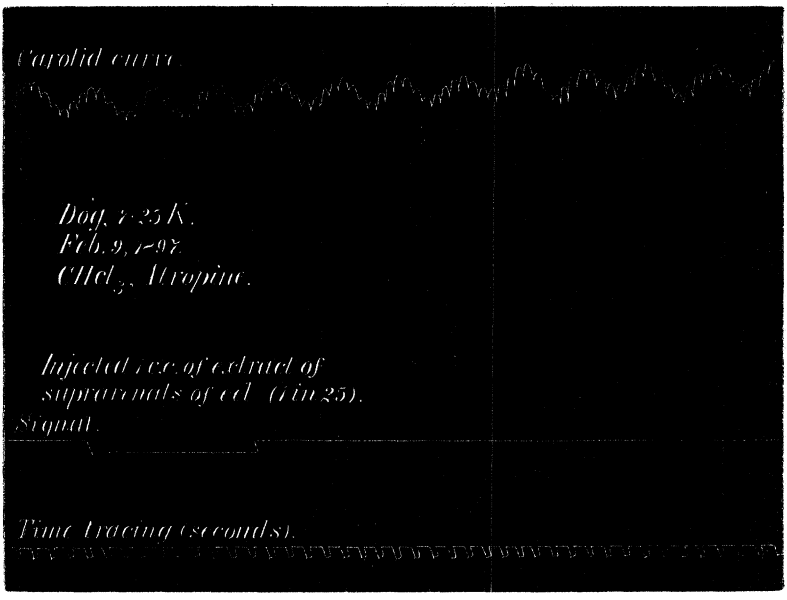


was used of "segmental suprarenal" in fig. 1. There is a striking difference between the two results.

With extracts of the suprarenals of Teleosts no effects whatever are produced. Fig. 3 shows a blood-pressure curve unaffected by the injection of extract of suprarenals of eels to the same amount as was previously employed in other experiments. Subsequent employment of mammalian suprarenal extract in the same experiment produced its proper effect.

Thus we have negative evidence of a physiological character that the interrenal body of Elasmobranchs corresponds to the "corpuscles of Stannius," the known suprarenal bodies in Teleosts, a conclusion both Diamare (5) and I myself (5, 17) had arrived at from anatomical and histological considerations.

FIG. 3.



Control experiments with extracts of "head-kidney" and muscle of fishes always gave negative results.

Perfusion Experiments.—These have been performed upon large toads. A cannula was tied into one aorta, the ligature also including the other. A snip was made in the sinus venosus, and then normal saline (0·6—0·9 per cent.) or Ringer's circulating fluid was perfused through the blood-vessels from a funnel placed about 9 to 12 inches above the animal. The toad was held in a suitable holder, and the fluid which ran through was collected in graduated cylinders and measured at the end of every five minutes. I have performed eleven of these experiment with practically uniform results. It will only be necessary to give the details of two typical ones.

In other experiments an extract made from the lymphatic "head-kidney" of different Teleosts was perfused, and also one made from muscle of various fishes. Both these always gave negative results when properly filtered.

In Experiment 1 it will be noticed that the interrenal gives a very definite result, though not so marked as that of the medullary glands. This point will be referred to again immediately. It is clear from Experiment 2 that extracts of the suprarenal bodies of Teleosts are inactive as regards the flow of fluid through the blood-vessels of a toad.

Exp. 1.—Material taken from a fair-sized Specimen of *Galeus canis*.

Large *Bufo vulgaris*. Fluid had been running about 30 minutes, pressure 25 cm.

Time.	Outflow in c.c.		Time.	Outflow in c.c.	
4·40	55	Normal saline.	5·35	32·0	"Paired segmental" suprarenal.
4·45	50		5·40	50·0	
4·50	50		5·45	20·0	
4·55	50	"Interrenal."	5·50	2·5	
5·0	33		5·55	1·5	
5·5	11		6·0	2·5	Normal saline.
5·10	5		6·5	1·5	
5·15	6		6·10	4·5	
5·20	6		6·15	0·5	
5·25	7		6·20	0·5	
5·30	24	Normal saline.	6·25	0·5	

Flow does not return to normal, although a much longer time is allowed to elapse.

Exp. 2.—Material from *Gadus œglefinus*, *Molva vulgaris*, and *Pleuronectes platessa*.

Large *Bufo vulgaris*. Fluid had been running about 45 minutes, pressure 30 cm.

Time.	Outflow in c.c.		Time.	Outflow in c.c.	
1·45	58	Normal saline.	2·0	90	
1·50	95		2·5	85	Fresh saline.
1·55	90	Suprarenal extract from *Gadus œglefinus*, then immediately from other two.	2·10	85	
			2·15	93	
			2·20	95	
			2·25	94	
			2·30	95	

There seems no reason to doubt that the active material in the "medullary glands" of Elasmobranch fishes is the same as that in the medulla of mammalian suprarenal, but so little of the material is procurable for chemical analysis that I have found it impossible to compare its reactions with that obtained from the higher animals. It is worth noting, however, that the extract in water or alcohol is of a pale brown tint, exactly resembling that of the medulla of mammals.* But that this brown pigment is not the active substance

* These glands become dark brown when treated with a solution of bichromate

is clear from the fact that when the material (in spirit) is kept for some time, this brown colour increases in intensity, although the extract may become quite inactive. I have found extracts in 80 per cent. alcohol become quite inactive after a lapse of two months.* The brown coloration appears to be the result of the oxidation of a chromogen previously existing in the extract.

It will have been observed that in the foregoing experiments the extract of the interrenal body produced a certain effect upon blood-pressure; this I believe can be entirely explained as the result of more or less admixture with "medullary glands." The latter are to be found close by the side of the former, so that it is practically impossible to remove it without some of them adhering. In my later experiments I tried to avoid this contamination by very careful removal of the interrenal, and, although I have not succeeded by this means in getting an extract of the interrenal quite inactive, yet I find that the more carefully it is removed, the less effect is produced by an injection of its extract. Thus I found the rise of blood-pressure due to interrenal to be much less when I had changed knife and forceps after removal of the medullary bodies, so as to avoid conveyance of the active principle in this manner.

Another explanation might be urged. The Polish physiologists find that a slight rise of blood-pressure is produced by an extract obtained from cortex only, and if this were the case it is conceivable that my results, in the case of the interrenal, are due to this slight specific action. But, when the greatest care is taken to avoid contamination, Oliver and Schäfer find the cortex quite inactive. Besides, the "cortical" glands of Teleosts give no effect and there can be little doubt that these are strictly homologous to the interrenal of Elasmobranchs.

The morphological conclusion that the two kinds of gland in Elasmobranch fishes really correspond to the cortex and medulla of mammalian suprarenal is not without its physiological significance. The cortex is always much more abundant than the medulla in mammals, resembles a secreting gland in many points of structure, and has possibly a function distinct from the medulla. The anatomical union of the two constituent portions may be in some sense accidental.

Conclusions.

1. The suprarenal capsule of the mammalia corresponds to two distinct glands in Elasmobranch fishes, the medulla corresponding *in structure and function* to the "paired segmental" suprarenal

of potassium, and this constitutes a ready means of displaying them in a dissection (Semper). This test probably applies to "medulla" throughout the vertebrata.

* When there is free access of air.

bodies ("medullary glands" they may be called), while the cortex corresponds to the interrenal body.

2. In Teleosts the medulla appears to be unrepresented, the known suprarenal bodies ("corpuscles of Stannius") consisting entirely of cortical substance, and corresponding in structure, and most probably in function, to the interrenal body of Elasmobranchs.

3. The same is most probably true of Ganoids, although I am guided here solely by histological evidence; I have not been able to obtain sufficient and suitable material for physiological investigation.

Thus it appears from these researches that two primary groups of the class *Pisces* (Teleosts and Ganoids) have no "medulla" but only "cortex."* So far as I know, the only piece of work published on the physiology of the suprarenal capsules in fishes is that of Pettit (12). This observer has made out a true physiological compensatory hypertrophy of one suprarenal in the eel after the other one has been removed. This renders it probable (what indeed was suggested by histological appearances) that this "cortical gland" has a secreting function. Pettit looks upon this organ in the eel as the fundamental type of the suprarenal capsule, but it appears to me much more probable that it represents cortex alone.

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* This fact would seem to suggest that the cortex may be more important than the medulla, for, whereas in certain vertebrates the medulla can be dispensed with, the cortex is universally present.

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"The Origin and Destination of certain Afferent and Efferent Tracts in the Medulla Oblongata." By J. S. RISIEN RUSSELL, M.D., M.R.C.P., Research Scholar to the British Medical Association, Senior Assistant Physician to the Metropolitan Hospital, and Pathologist to the National Hospital for the Paralysed and Epileptic, Queen Square, London. Communicated by Professor VICTOR HORSLEY, F.R.S. Received February 18,—Read March 11, 1897.

(Abstract.)

In attempting to arrive at definite conclusions with regard to the origin and destination of some of the afferent and efferent tracts which exist in the medulla oblongata, the following experimental procedures were adopted.

1. Section or destruction of the lateral region of the medulla between the ascending root of the fifth nerve and the inferior olive.

2. Division of the restiform body.

3. Division of the direct sensory cerebellar tract of Edinger.

4. Severance of Deiters' nucleus from its connections with the medulla.

5. Section of the posterior columns and their nuclei in the medulla.

The first of these procedures was followed by degeneration of two efferent tracts which could be traced throughout the whole length of the spinal cord, the one occupying the antero-lateral region, and the other being closely related to the crossed pyramidal tract, as regards position. In addition to this, afferent fibres degenerate from the seat of lesion, some of which pass to the cerebellum by way of the restiform body, others course through the medulla and pons external to the superior olive and on the ventral side of the emergent roots of the seventh and fifth cranial nerves to eventually reach the middle lobe of the cerebellum by way of its anterior peduncle. Situated internally to the tract just described is another bundle of more scattered fibres, close to the outer end of the fillet, with the fibres of which system they remain intimately associated in their further course towards the mesencephalon, and can be traced to the region of the anterior corpora quadrigemina. Owing to destruction

FIG. 1.

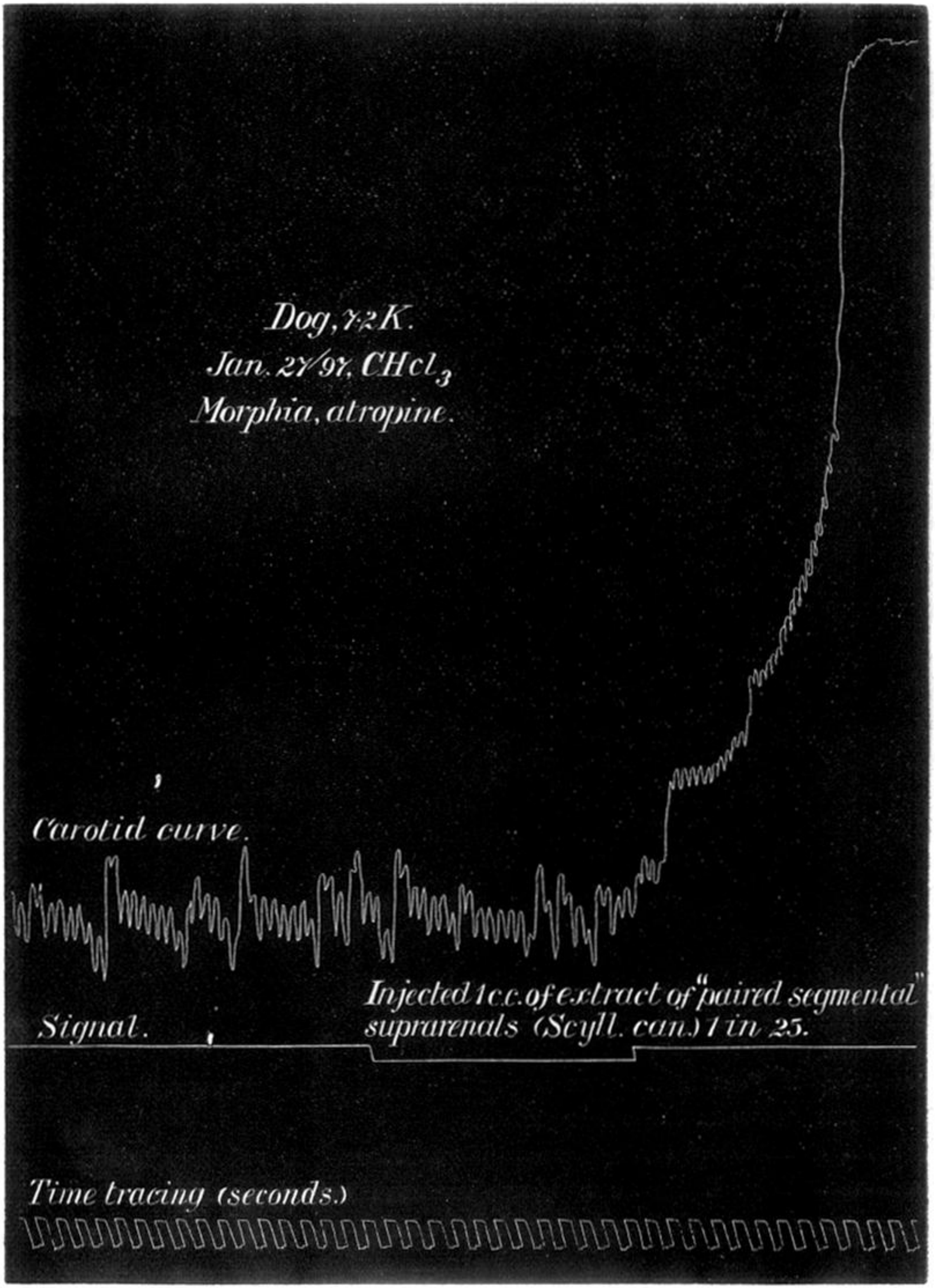

Dog, 7·2 K.
Jan. 27/97. $CHCl_3$
Morphia, atropine.
Carotid curve.
Signal.
Injected 1 c.c. of extract of "paired segmental" suprarenals (Scyll. can.) 1 in 25.
Time tracing (seconds.)

FIG. 2.

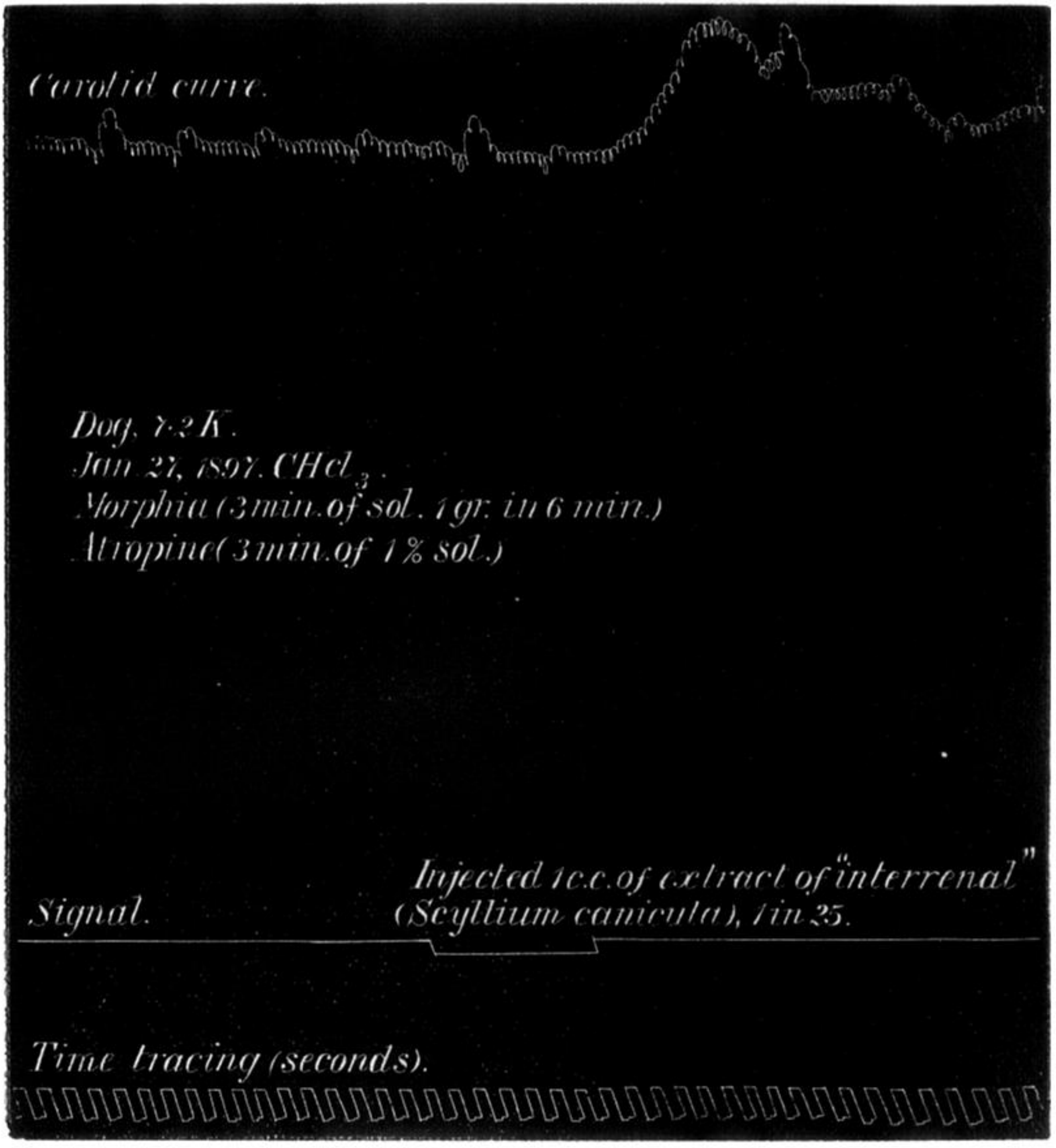
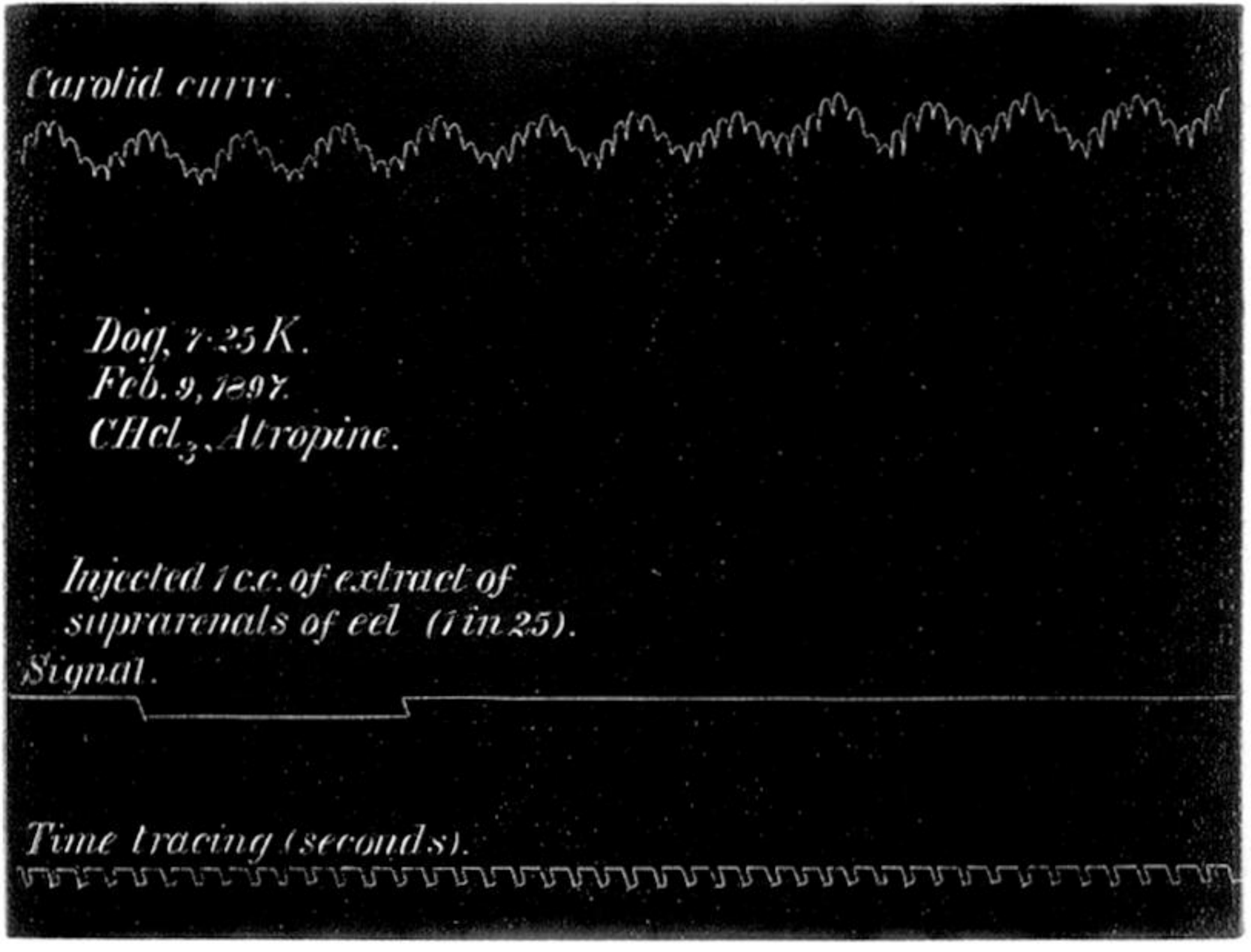

Carotid curve.
Dog. 7·2 K.
Jan 27, 1897. $CHCl_3$.
Morphia (3 min. of sol. 1 gr. in 6 min.)
Atropine (3 min. of 1% sol.)
Injected 1 c.c. of extract of "interrenal" (Scyllium canicula), 1 in 25.
Signal.
Time tracing (seconds).

FIG. 3.


Carotid curve.
Dog, 7·25 K.
Feb. 9, 1897.
$CHCl_3$, Atropine.
Injected 1 c.c. of extract of suprarenals of eel (1 in 25).
Signal.
Time tracing (seconds).