A TECHNIQUE FOR OPERATIONS ON THE HYPO-THALAMO-HYPOPHYSIAL REGION OF THE RABBIT

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Numerous operations have been described for reaching the hypophysial region, the routes suggested varying with the type of animal used. We shall not attempt to give here an account of the buccal, nasal, temporal, para-pharyngeal, orbital or sphenoidal routes which have been elaborated, for good reviews of these may be found in various textbooks of endocrinology and surgery (Aschner, 1912; Biedl, 1913; Blair Bell, 1919 and Hirsch, 1929). The thesis of Popescu (1934) and Frasin (1935) contain lists of references to many relevant papers under the headings, "Hypophysectomie", "Chirurgie de l'hypophyse", and "Extirpation de l'hypophyse".

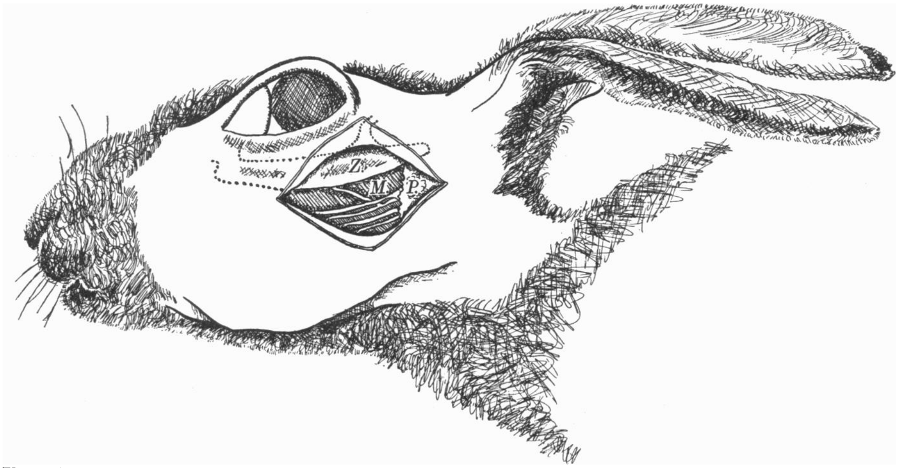
It was of importance, for the purpose of some of our experiments, to find a method of operating on the hypophysial region of the rabbit. For hypophysectomy in this rodent, White (1934), and Firor (1933), have described buccal and orbital routes, respectively. After attempting to section the pituitary stalk by both these operations, the conclusion was drawn that a method giving a better exposure of the hypothalamo-hypophysial region was required, leading to the investigation of the temporal route, which is described below.

OPERATIVE TECHNIQUE

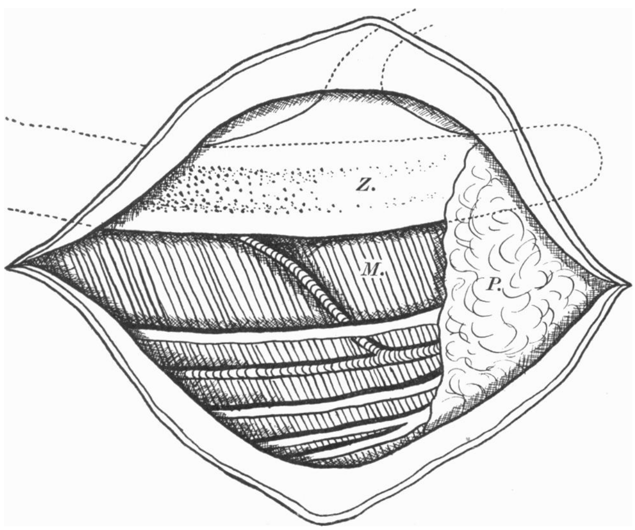
The skin over the lateral aspect of the head and face is first shaved and the animal is then anaesthetized. The most satisfactory anaesthetic was found to be ether administered through a tracheal cannula. At the completion of the operation, the trachea and pharynx must be carefully cleaned from mucus before suturing the trachea with one or two stitches.

The first stage of the operation (Text-figs. 1 and 2) deals with the removal of part of the zygomatic arch.

The skin incision should be made over the posterior two-thirds of the zygomatic arch, to the root of the ear. The cut should be made firmly and deeply through the superficial fascia as well as the skin, for if these two structures are not reflected together, and they are easily separable, gangrenous changes in the skin are likely to supervene later. The periosteum over this region of the zygomatic arch is then reflected, particular care being taken not to damage large vessels at the anterior and posterior margins of the masseter muscle, which are branches of the external carotid artery (a. occipitalis,



Text-fig. 1. Exposure of zygomatic arch. *M.* upper and posterior part of masseter muscle; *P.* parotid gland; *Z.* zygomatic arch. Note also, the transverse facial vessels, parotid duct, and branches of the facial nerve.

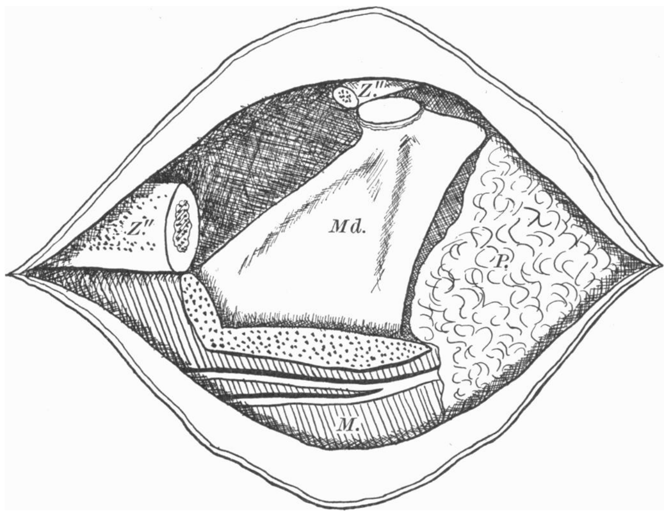


Text-fig. 2. Operative field, as shown in Text-fig. 1 enlarged.

a. temporalis superficialis and a. maxillaris interna) and of the external jugular vein (v. facialis anterior and v. facialis posterior).

The zygomatic arch must next be cut through with bone forceps, first at the junction of the anterior one-third with the posterior two-thirds and then at its posterior extremity, the masseter muscle still being attached. (If the masseter muscle is separated before the arch is cut, the masseteric vessels will bleed, and cannot be ligatured or compressed until the arch is removed.) The masseter muscle is then cut at its origin and the piece of zygoma removed. The remains of the posterior end of the zygomatic arch is then entirely removed with bone nibblers, thus exposing the temporo-mandibular joint. Haemorrhage is likely to occur at this stage from the masseteric vessels and from the vessels around the jaw joint. This is unavoidable but can be controlled by pressure.

The second stage (Text-fig. 3) is the removal of the upper one-third of the ramus of the mandible.



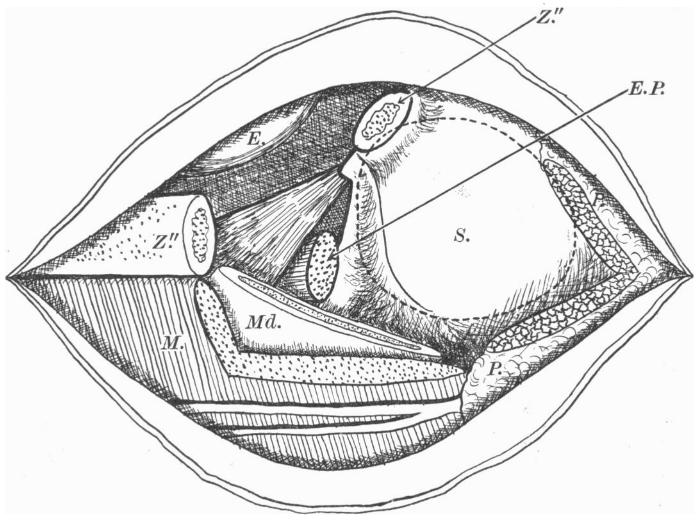
Text-fig. 3. Removal of zygomatic arch and part of masseter muscle. *M.* masseter muscle; *Md.* superior half of the ramus of the mandible; *P.* parotid gland; *Z.,″ Z.″* two cut ends of zygomatic arch.

The masseter muscle overlying this area of bone is cut through cleanly and laid aside on a piece of aseptic towelling for use as a muscle compress. The periosteum is removed from the exposed bone surface. The ramus is lifted gently, and the mandibular articular surface of the temporo-mandibular joint is separated from the mandible by gentle pressure; it is then possible to reflect the periosteum further down the medial aspect of the ramus. Gauze swabs may then be pushed underneath the ramus, tending to compress the underlying structures and raise the bone so that it may be cut across more easily with the bone forceps.

The third stage (Text-fig. 4) consists of exposing and removing part of the squamous temporal bone.

The pterygoideus externus muscle is clipped away piece by piece and the pterygo-maxillary fossa is gradually cleared. The haemorrhage met with in this region may be quite considerable, but with practice and care can be checked by compression with gauze pads, or better, pieces of muscle. The area of the skull to be exposed is that part lying superior to the pterygoid process and posterior-inferior to the structures in the orbit. It is advisable not to dissect too deeply into the pterygomaxillary fossa for here lies the internal maxillary artery with its branches, and the main divisions of the trigeminal nerve.

Before attempting to open the skull it is important that all bleeding and oozing should be stopped. While awaiting the cessation of the haemorrhage, the opportunity should be taken of injecting about 10 c.c. of 15 % saline into the marginal vein of the ear; this will cause a decrease in the volume of the brain, which will be of great advantage in the later stages of the operation.

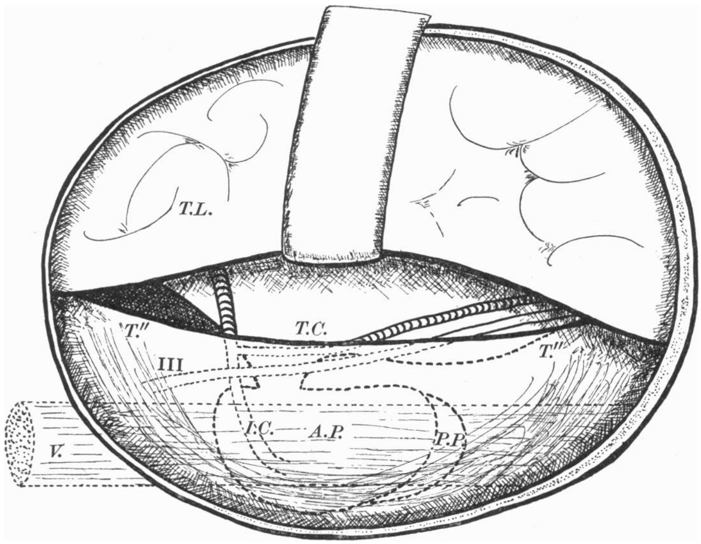


Text-fig. 4. Exposure of the skull. *E.* structures in the orbit; *E.P.* external pterygoid muscle; *M.* masseter muscle; *Md.* cut end of ramus of mandible; *P.* parotid gland cut; *S.* surface of skull; *Z.*″, *Z.*″ two cut ends of zygomatic arch. The area of skull removed is shown by the dotted line.

The skull is attacked in the temporo-sphenoidal region, just anterior to the tympanic bulla and superior to the pterygoid process, where the bone is very thin. A small piece of this delicate plate of bone may be removed by gently tapping a scalpel held with its point at a very oblique angle to the surface of the skull, until a spicule of bone is displaced. This opening is then enlarged with a small pair of bone nibblers, exposing the dura mater covering the temporal lobe of the brain. The dura mater is then incised with a fine iridectomy knife and reflected.

The fourth and final stage of the operation now begins (Text-fig. 5), consisting of the exposure of the hypothalamus and hypophysial region.

The temporal lobe of the brain is very carefully and slowly retracted and at the same time the cerebrospinal fluid is absorbed with fine swabs. At this stage it is advantageous to use a head-lamp, for the field of operation is now deep and small. On full retraction of the brain the edge of the tentorium cerebelli comes into view, above which may be seen the hypothalamus. The essential landmark in this region is the small internal carotid artery which may be easily seen if the retraction has been properly performed, on account of the colour contrast of the red artery against the white background of the brain substance. Its position may also be gauged by palpation of the anterior clinoid process, the posterior end of which marks the point of appearance of the artery above the tentorium. Postero-medial to the artery lies the tuber cinereum and the hypophysial stalk. Further posterior may sometimes be seen the oculomotor nerve, disappearing from view. Thus the whole region is laid bare before the operator.



Text-fig. 5. Retraction of temporal lobe of brain. *A.P.* anterior lobe of pituitary; *I.C.* interna carotid artery; *P.P.* posterior lobe of pituitary; *T.*" tentorium cerebelli; *T.C.* tuber cinereum; *T.L.* temporal lobe of brain; III. oculomotor nerve; V. trigeminal nerve.

The instrument that was used in our experiment for making lesions in the pituitary stalk consisted of a small piece of razor blade, ground to the required shape and mounted at the end of a curved probe.

On completion of the operation, the brain is allowed to fall gently back into place, the dura mater replaced as far as possible over its surface, and then the skin sutured with Michel's clips and painted with iodine and colloidon-ether solution.

CRITICISM OF THE METHOD

The drawbacks of this technique may be divided into two groups, operative and post-operative complications.

There are two main operative difficulties, haemorrhage and damage to the brain. All the haemorrhage met with may be controlled by pressure from gauze pads or pieces of muscle, except the intracranial bleeding which results when the internal carotid artery or its branches are damaged. If this latter occurs, the animal had best be killed before recovering consciousness, as it is impossible to control this haemorrhage. Damage to the brain can be avoided by previous intravenous injection of hypertonic saline; by use of a retractor well adapted to the surface of the brain; and by exercising patience and care when retracting and when swabbing the cerebrospinal fluid.

The post-operative complications consist of (i) inflammation and oedema of the conjunctiva of the eye on the operated side, (ii) gangrenous changes in the skin of the wound, (iii) infection of the wound, and (iv) interference with the masticatory mechanism. The conjunctivitis and oedema can be avoided or lessened by clipping the eyelids together before starting the operation. If this complication does occur it invariably heals if the eye is kept clean by bathing. The gangrene of the skin, as stated before, only occurs if the skin is dissected from the deeper fascial planes, but if the primary incision is clean and deep through skin and fascia and if the skin is kept moist throughout the operation, healing will occur with little difficulty. Infection of the head wound occurs easily unless rigid aseptic precautions are taken. The wound made for the insertion of the tracheal cannula was infected rarely. As the operation includes removal of one mandibular joint, mastication necessarily becomes asymmetrical, though only to a slight degree, owing to the fact that one-half to two-thirds of the ramus of the mandible and the corresponding internal pterygoid muscle are left intact. Normal chewing can, and indeed does occur, for the animal will masticate green food in a comparatively normal fashion within 24 hours of the operation. Milk should be supplied in the diet for the first 7 days. After several months the aperture in the skull becomes filled with partly calcified fibrous tissue and the pterygoid region filled with scar tissue. In one animal an attempted reformation of the jaw joint was noticed; a spicule of bone left in the wound had united with the ramus of the mandible and grown back to the skull just anterior to the bullat ympani, where a joint capsule had formed.

The advantage of this operation lies in the fact that *every stage of the operation is clearly visible to the operator*. The brain in the rabbit is small, the temporo-sphenoidal groove (middle fossa) is shallow, so that a good view can be obtained of the hypothalamic region. By this method also a greater variety of experiments can be performed than is possible by other methods. The hypothalamus may be stimulated electrically (for another method of performing this, see Harris, 1937), hypothalamic lesions may be made, various substances may be injected into the third ventricle, section of the hypophysial stalk and hypophysectomy may be performed. When performing hypophysectomy additional care is required to avoid haemorrhage from the cavernous sinus.

RESULTS

We have used this technique in two sets of experiments, first, for sectioning and making lesions in the pituitary stalk, and secondly, for compressing the stalk (without cutting it).

Lesions of varying extent were made in the stalks of twenty-six rabbits. The results of these operations may be grouped:

(i) Nine animals died during or immediately after the operation, the main cause of death being intracranial haemorrhage with resultant medullary anaemia.

(ii) Two rabbits lived for 3 days.

(iii) Seven rabbits lived between 5 and 50 days.

(iv) Whilst six rabbits lived for longer than 50 days, i.e. for periods of 55, 70, 92, 100, 125 and 218 days.

Seven of the animals in groups (ii) and (iii) appeared to have died from infection, as the conditions for asepsis were not good. It is, however, possible that their deaths were in part due to damage to the tuber cinereum, for the majority of these animals had convulsions prior to death. Bailey & Bremer (1921) noted in dogs that damage to the tuber often caused epileptiform convulsions.

As an example of our results, we quote here the case of rabbit 112, which lived for 70 days after the operation. From serial sections through the hypothalamus and pituitary, the stalk was seen to be entirely transected (Pl. I, fig. 1). The line of the lesion can be seen passing from one edge of the stalk to the other, the two cut ends having come into juxtaposition and united with fibrous tissue. This attempt at recovery is not functional however, for the nerve tracts and blood vessels in the stalk are interrupted by the scar tissue. In the sections it was found that on the pituitary side of the lesion, the stalk and posterior lobe were shrunken and very cellular (Pl. I, figs. 1 and 2). Also in some cases a large accumulation of colloid was observed in the posterior lobe. Crowe *et al.* (1910), Cushing & Goetsch (1910), noted similar effects. The cells of the anterior lobe appeared to have lost most of their cytoplasm and become rather atrophic.

In other experiments the stalk was compressed with a view to seeing on which side of the point of compression the blood would accumulate in the hypophysio-portal vessels. The operation was successfully performed in ten rabbits. In seven cases the stalk was pressed alone and in three cases the stalk and the internal carotid artery were taken together. Pl. I, figs. 3 and 4 show two such specimens—(the hypothalamus, stalk and pituitary gland having been fixed in situ and dissected out)—and it may be observed that the stalk is tense and swollen on the pituitary side of the point of compression. The detailed results of this operation will be included in a paper to be published by one of us (Gr. T. P.) in collaboration with Miss Una Fielding.

Fig. 2.

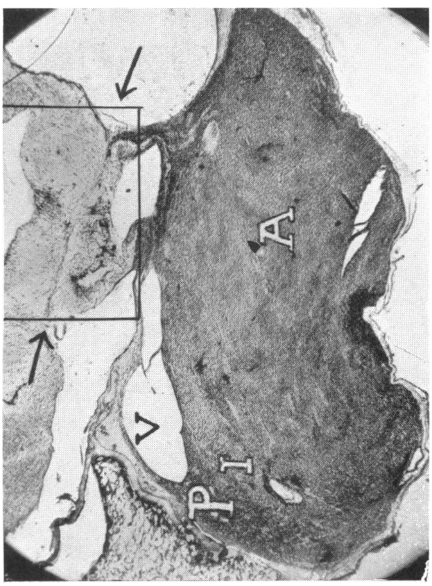


Fig. 1.

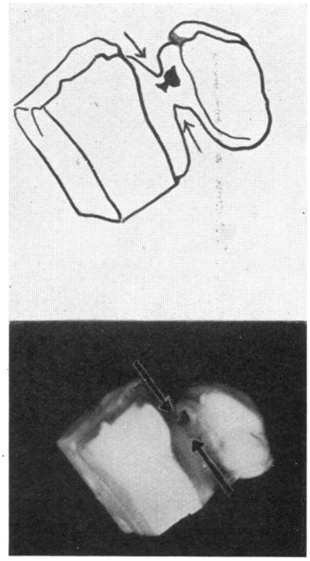


Fig. 4.

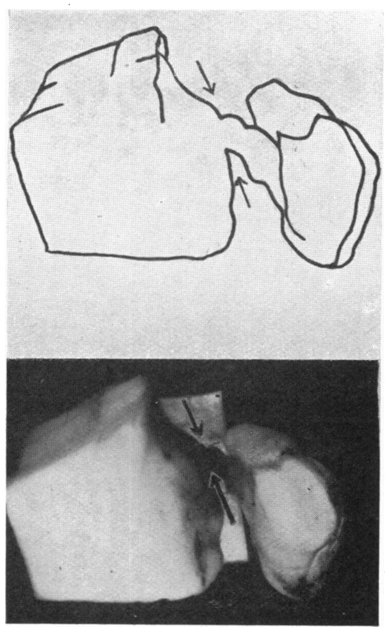


Fig. 3.

HARRIS AND POPA—HYPOTHALAMO-HYPOPHYSIAL REGION OF THE RABBIT.

SUMMARY

A description of a technique for operations on the hypothalamo-hypophysial region of the rabbit, with a criticism of the technique. Some experimental results, obtained by means of this operation, are briefly described.

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EXPLANATION OF PLATE I

Fig. 1. Microphotograph of a sagittal section through the pituitary gland, stalk and hypothalamus of rabbit 112, whose stalk was transected 70 days previously. Note, atrophic appearance of pituitary gland; line of lesion (indicated by two arrows), and vacuoles in posterior lobe and stalk (previously filled with colloid). ($\times$16.) *A*. anterior lobe; *I*. intermediate lobe; *P*. posterior lobe; *V*. vacuoles (previously filled with colloid).

Fig. 2. Line of lesion (in Fig. 1) under higher power. Note fibrous tissue "healing" of the stalk and slight accumulation of basophilic cells on the pituitary side of the lesion, *B*. ($\times$40.)

Fig. 3. Photograph and diagram of hypothalamus, stalk and pituitary gland, the stalk having been compressed immediately prior to death. Note the swelling of the stalk below the point of compression (indicated by arrows). ($\times$5.)

Fig. 4. Photograph and diagram of a specimen similar to that in Fig. 3. Note again the enlargement of the stalk below the line of compression. ($\times$3.)

(Figs. 1 and 2 are reproduced here by kind permission of the Royal Society from *Proc. roy. Soc.* B, vol. CXXII, p. 374, 1937.)