THE CONDUCTION OF PAIN IN THE FIFTH NERVE AND ITS BEARING ON THE TREATMENT OF TRIGEMINAL NEURALGIA*

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All of the various procedures which hitherto have been practised in the surgical treatment of major trigeminal neuralgia have —with the possible exception of the operation of Dandy[3]—the same disadvantage, that of being followed by a more or less permanent anesthesia for all qualities of sensation within part of the face. The studies to be reported here, and which were carried out during the years 1936-1938, are an attempt to map anatomically the course of fibers transmitting painful stimuli in the fifth nerve. They are based on the information gained from work performed during the last 10 or 12 years on the morphological characters of nerve fibers having different physiological functions. The evolution of our ideas in this field cannot be considered here, except with the utmost brevity. The investigations of Gasser and Erlanger[8] during the years 1924-1927 are of fundamental importance, even though some correlation between fiber size and functional activity had been vaguely suggested previously. From these investigations and from experience gained with his pyridine-silver stain Ranson[13] concluded that all of the pain-conducting fibers would be unmyelinated. Yet Zotterman,[17] working with the technic elaborated in conjunction with Adrian,[1] was unable to confirm this. Leading off action potentials from very slender branches of the lingual nerve of the cat he was able to obtain typical C potentials which, according to the view held by Gasser and Erlanger, should derive from unmyelinated fibers. Nevertheless, the preparations, each of which consisted of only 75 to 100 nerve fibers, did not contain unmyelinated fibers on microscopical examination (Zotterman,[17] plate 1).

A more extensive use of the Alzheimer-Mann stain also seems to change in some degree our opinion of the occurrence, in general of unmyelinated fibers in the central, the peripheral, and in the autonomic nervous systems. It is, however, of less importance

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from a functional point of view whether pain fibers are myelinated or not. One thing is certain, namely, that they have a very minute diameter. Table I, which is compiled chiefly from the work of

TABLE I

RELATIVE DATA* CONCERNING SENSORY NERVE FIBERS CONDUCTING DIFFERENT MODALITIES OF SENSATION

	Relative spike height	*Relative conduction rate*	*Relative diameter*
Touch	10	100	10
Taste	6–4	60–40	7–6
Heat	4–2	40–20	6–5
Cold	2–1.5	20–15	5–4
Pain	1 and less	10 and less	4 and less

Zotterman, consists of hitherto known *relative* data concerning different sensory nerve fibers. An attempt was made to "translate" these relative values of the diameter size into absolute ones, using the two fixed points on the scale which we have, namely, the largest fibers in the posterior roots and the taste fibers in the chorda tympani, the latter of which were identified and distinguished from pain and touch fibers by Zotterman[17] by electrophysiological methods. The following schedule was arrived at:

	Max. diameter in μ
Muscle sense	15
Touch	12
Pressure	8
Taste	6
Heat	5
Cold	5
Pain	4

This schedule is, of course, only approximate and may be modified by further investigations; it served only as a working hypothesis and, as such, was found useful. When nerve fiber diameters are measured in formalin-fixed and paraffin-embedded material the shrinkage of the fibers caused by the fixing and embedding proce-

* Calculated on the basis of an arbitrary spike height of 1 for the pain fibers.

dures also must be considered. This shrinkage, recently studied by Arnell,[2] is found to be very constant (28 to 29 per cent).

The present investigation on the fifth nerve root was originally undertaken to determine whether a neuro-anatomical basis could be found for the well-known opinion of Dandy[4]—which, however, has been questioned by others[5]—that partial section of the fifth nerve root at the pons could be followed by a dissociated anesthesia of the face. In serial sections of a specimen of a trigeminal nerve stained by a slight modification (mordanting in chromic acid, embedding in paraffin) of the Alzheimer-Mann method the distribution of fibers of different caliber was studied. The measurements were undertaken in photomicrographs, the section in question being simultaneously observed under the microscope. This technic, which was evolved by Häggqvist[9] and termed *fiber analysis*, is, indeed, an extremely useful method for studying the function of nerves and tracts. The results, of course, must be manipulated in accordance with general statistical rules, otherwise, they may easily be misleading. The standard deviation of the method of measuring (an especially designed pair of compasses is used) is small and amounts only to 0.26μ when the magnification is 750 times. The fiber analysis, however, has one drawbrack; it is an extremely time-consuming procedure. As the number of sensory fibers in the trigeminal nerve is about 140,000, the entire square of the root could not, of course, be analyzed, but the fiber diameters in a large number of sections taken at random and grouped around four different levels of the root were measured. The number of fibers measured was around 16,000, which from a statistical standpoint was found sufficient to give a true picture of the composition of the root.

Graphs of the percentual occurrence of fibers of different caliber in the peripheral divisions and at two of the four levels studied are shown in Fig. 1 (I, II, III). In the figures are inserted photomicrographs from the three different portions of the root—upper, middle, and lower. The pattern is very similar at all levels of the root. As seen from the graphs, the fibers less than 3μ in diameter are relatively most numerous in the upper portion of the root throughout its entire length. This part of the root corresponds to the ophthalmic division and the prevailing number of small fibers may be explained by the specific sensory supply to the eye where tactile sensation is missing. The fiber analysis also indicates that the upper portion of the root holds its position and individuality

throughout the entire length of the extracerebral part of the root and contradicts the opinion held by Davis and Haven[5] that the root itself should rotate as much as 180° during embryonic life. With regard to the question from which the investigation originated, the result was entirely negative, *i.e.*, no rearrangement of the smaller fibers was found which could possibly explain a dissociated anesthesia produced by partial section of the root itself. Within the glial cone of the fifth nerve, the apex of which is situated as far as 9 mm. from the pons,[14] a fiber analysis as outlined above could not be made. The interstitial tissue of the cone is of a very friable consistency and the nerve fibers do not retain their position after mordanting in chromic acid when the sections are as thin as 5μ. Thin section constitutes a proper condition for accurate measurement. Within the cone the fiber distribution was studied by ordinary methods after silver impregnation, and the findings of Davis and Haven,[5] namely, that there is no accumulation of smaller fibers in the inferoposterior portion of the root, was confirmed.

The fiber analytic studies were then extended to the bulbospinal trigeminal tract. For technical reasons these studies were carried out on brain stems of monkeys (*Macaca mulatta*). The mordanting in chromic acid gives the sections a tendency to loosen from the slides and wrinkle, and this tendency is much more marked when the pieces to be examined are large and of the size of the human medulla. By sample sections from human material it could, however, be ascertained that the fiber distribution of the tract in man fully corresponds to the distribution in monkeys. The fiber analytic pattern in the bulbospinal fifth tract is entirely different from the pattern of the nerve root, as is seen in Fig. 1 (IV). Fibers more than 4μ occur only to an insignificant degree and their percentage gradually decreases in the caudal direction. It must, therefore, be concluded that the fibers of the bulbospinal tract mainly serve to transmit painful and thermal stimuli. Some, but by no means all, of these fibers are unmyelinated. The fiber analytic pattern of the tract is thus in full accordance with clinical experience. Softenings of the medulla oblongata involving the bulbospinal trigeminal tract give, among other symptoms, analgesia and thermal anesthesia of the ipsilateral half of the face. Cases of this kind, with autopsy findings, were first published by Hun[11] in this country and by Wallenberg[15, 16] in Germany in the nineties, and a great number of similar cases have since been described.[10] Fiber analysis gave an

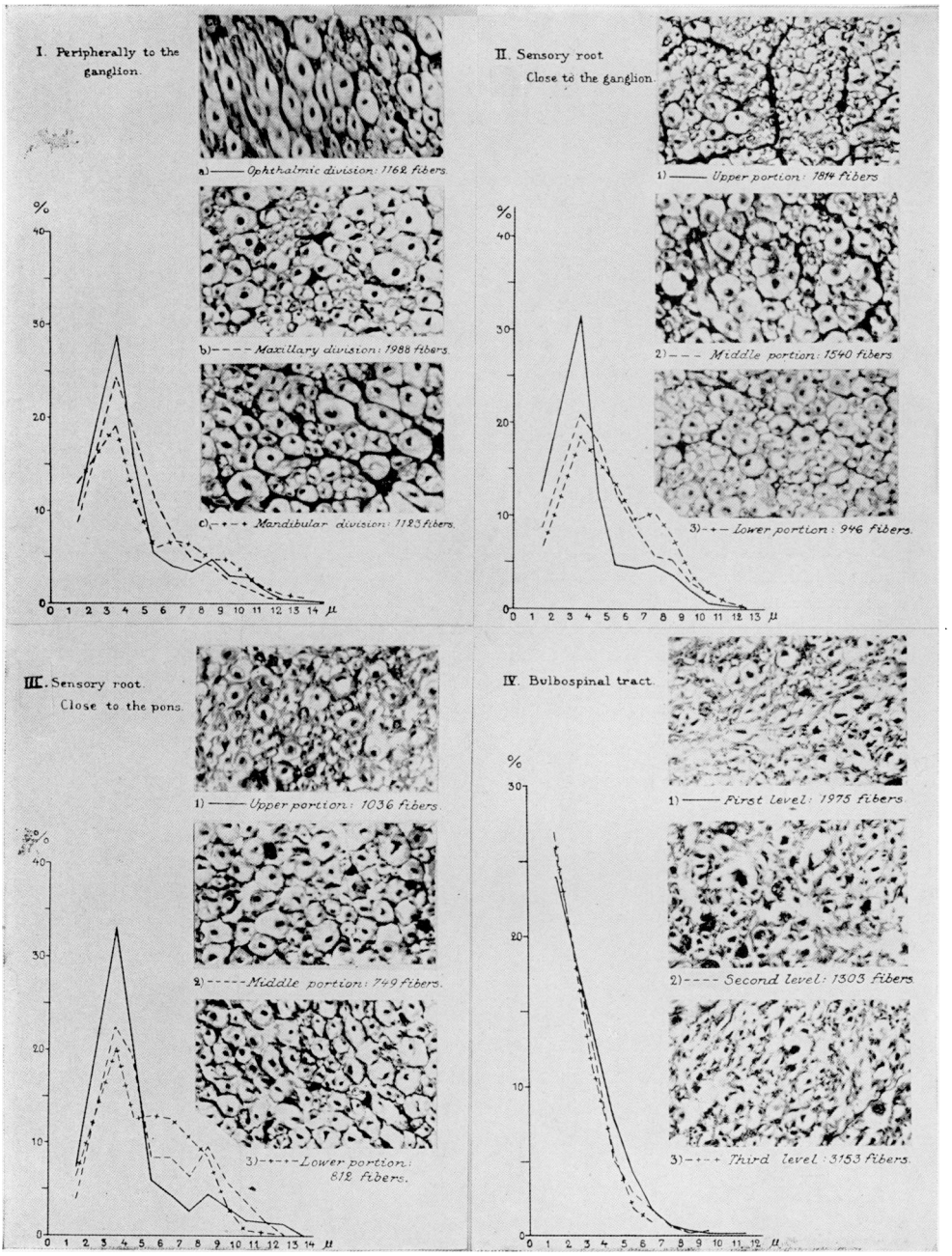

FIG. 1. Graphs showing the distribution of fibers of different caliber in the peripheral divisions (I), at two levels of the sensory fifth nerve root (II and III), and at three levels of the bulbospinal tract (IV). First level = level of superior olive; second level = immediately cranially to the upper pole of the inferior olive; third level = most caudal part of the inferior olive. Photomicrographs from the corresponding portions are inserted. The fiber pattern is very similar all over the root. The small fibers are most numerous in the upper portion of the root (uninterrupted line) which corresponds to the ophthalmic division. There is no accumulation of small fibers in the inferoposterior portion. The difference in occurrence of fibers less than 3μ and less than 4μ at the various levels of the tract is slight, but statistically proven.

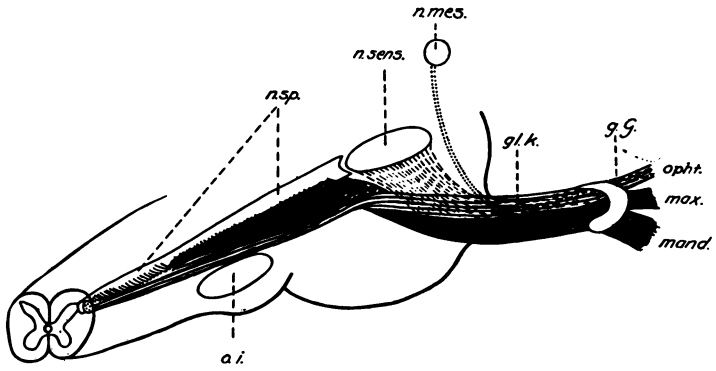

FIG. 2. Diagram of the conduction of different modalities of sensation in the fifth nerve. opht. = ophthalmic division, max. = maxillary division, mand. = mandibular division, g.G. = Gasserian ganglion, gl.k. = glial cone, n.mes. = mesencephalic nucleus, n.sens. = main sensory nucleus, n.spin. = bulbospinal nucleus. The touch fibers from the entire root are marked with interrupted lines, the pain and temperature fibers from the ophthalmic division are marked with single lines and the pain and temperature fibers from the maxillo-mandibular divisions with a dark toning. The former are situated in the ventral portion of the tract and pass further caudally, whereas the latter are situated in the dorsal portion of the tract and end more cranially in the medulla. The mesencephalic tract is marked with dotted lines. The fibers of this tract have a very big average diameter and consequently they most probably transmit proprioceptive impulses.

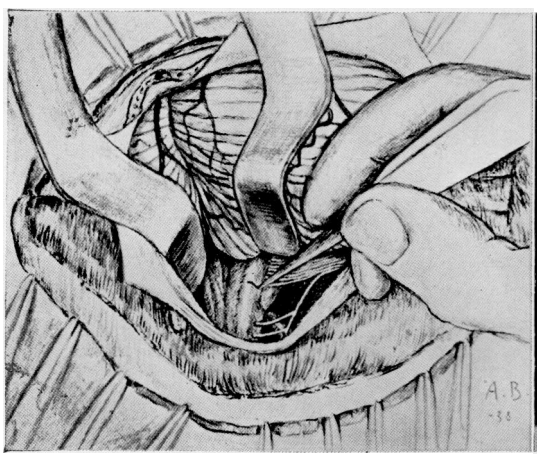

FIG. 3. Sectioning the bulbospinal fifth tract in man. For details in the operative technic see Sjöqvist, 1938, pp. 95-100.

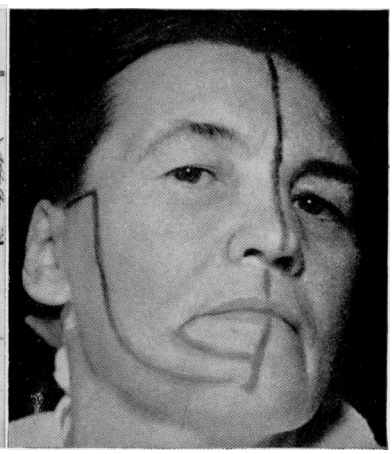

FIG. 4. The sensory defect produced by tractotomy in case 5 of the series. In this case a thermal anesthesia and a marked hypalgesia in almost half of the face ensued. In a small area on the lower lip there was thermal hypesthesia and slight but evident hypalgesia. The patient's paroxysmal pain was relieved.

obvious anatomical correlation to these pathophysiological findings and served to support the average correctness of the original working hypothesis.

In this connection, opportunity was given by Dr. Olivecrona to study three specimens from patients operated on for trigeminal neuralgia by section of the root. The degeneration in these rather unique specimens allowed certain anatomical conclusions which can be briefly summarized as follows: (i) the postero-inferior part of the root which is cut in the Dandy operation corresponds to the dorsal portion of the tract and must consequently be composed of maxillomandibular fibers; (ii) the bundles of the tract are more scattered in the upper part of the medulla and fuse gradually in the caudal direction. The topography of the tract also could be studied with great accuracy in one of the specimens in which the degeneration could be traced by the Marchi method. An attempt to summarize diagrammatically our present knowledge of pain conduction in the fifth nerve is given in Fig. 2. There must be a considerable rearrangement of fibers during the passage of the nerve through the middle cerebellar peduncle corresponding to the rearrangement of fibers in the entrance zone of the dorsal roots, but the details of this rearrangement are so far largely unknown.

It may easily be understood that we, at this stage, began to consider the possibilities of severing the tract in man for therapeutic purposes. As a matter of fact this possibility had been discussed in 1931 at the New York Neurological Society,[12] although the discussion did not lead to any actual surgical attempts. There was one point in favor of the operation, namely, that an isolated analgesia and thermal anesthesia with preservation of tactile sensibility could be predicted with considerable probability, but there were also several objections to the new operation, *i.e.*, the risk of accessory lesions, and also the fact that root sections *ad modum* Spiller and Frazier[7] has proved to be a safe procedure for the relief of major trigeminal neuralgia.

The first patient operated on, in May, 1937, was a case of atypical neuralgia persisting after root section and cervical sympathectomy. The operation was undertaken in the belief that painful impulses transmitted by the sensory portion of the seventh nerve, the pars intermedia of Wrisberg, might play a rôle in this type of neuralgia and that these fibers might run centrally within the bulbospinal tract. The latter of these two assumptions later proved to be

correct (Sjöqvist,[14] p. 120), the former did not. The patient was told of the possible risks of the operation and the fact that it had not been done before, but was still eager to be operated on as she considered her state unbearable.

The technic of the operation is comparatively simple. After a suboccipital exposure one of the cerebellar tonsils is gently elevated and an incision is made on the lateral surface of the medulla at the level of the caudal third of the eminentia olivaris (Fig. 3). The point of incision may be difficult to choose and when the operation is performed for the first time a guide consisting of a formalin-fixed specimen of the human medulla oblongata in which needles have been inserted along the substantia gelatinosa of Rolando may be useful.

Consideration of the clinical results obtained by this technic need not be detailed here. The first 9 cases have already been reported,[14] and the results in the subsequent cases will be dealt with later when the material has become more extensive. Only this much may be said, section of the bulbospinal fifth tract, or *tractotomy* as we have called it, gives an impairment or loss of sensation for painful and thermal stimuli with complete preservation of tactile sensibility (Fig. 4). The analgesia and thermal anesthesia are usually not complete—although they occasionally may be so—but are sufficiently deep to suppress the paroxysms of pain in major trigeminal neuralgia. The sensory loss, as a rule, is most marked in the first and second fifth nerve divisions, less in the third. The corneal reflex, being a nociceptive reflex, is invariably absent when the tract has been severed. The sensibility for deep pressure pain in the face is impaired or gone, contrary to the situation after root section. There has been no fatality in the series so far, but in two of the earlier cases the incisions apparently were made in wrong places, since no sensory loss ensued and the corneal reflexes were preserved. A recurrent nerve paresis may follow the operation if the most caudal tenth nerve rootlets are traumatized during the exposure.

It should be pointed out that tractotomy is a procedure directed toward the primary neurone. Non-paroxysmal facial neuralgias, which might be supposed to be nuclear in origin, could therefore not be expected to be relieved by it. "Further experience will allot to it its proper place in the increasing repertory of the neurological surgeon"[6] and enable judgment of its eventual value.

Summary and Conclusions

1. Fibers conducting pain and temperature in the fifth nerve are scattered evenly in the sensory root, but form the vast majority of fibers in the bulbospinal tract.

2. Impairment or loss of sensibility for pain and temperature in half of the face is produced in man by section of the ipsilateral bulbospinal fifth tract.

3. This procedure (tractotomy) can be used for the relief of trigeminal neuralgia.

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