DO THE MOTOR NUCLEI OF THE CRANIAL NERVES RECEIVE CORTICOFUGAL FIBRES? AN EXPERIMENTAL STUDY IN THE CAT

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INTRODUCTION

IN most textbooks of neuroanatomy pyramidal tract fibres are said to pass to the motor nuclei of the cranial nerves. Thus, Krieg (1947) and Mettler (1948), who experimentally have studied corticofugal fibres in more detail, both state in their textbooks that the fibres actually go to the nuclei in question.

On the other hand, Levin (1949), who also has contributed much to our knowledge of the connexions of corticofugal fibres, in a review of the efferent fibres of the precentral region states emphatically that most workers have agreed that the fibres to the tegmentum seem to terminate ventral to the cranial nerve nuclei.

In practically all studies of corticofugal fibres to the motor nuclei of the cranial nerves, the Marchi method has been used. However, this method is not well suited to solve the question whether pyramidal tract fibres virtually terminate in the nuclei under consideration or not, since it does not permit the determination of the ultimate endings of nerve fibres. A perusal of the relevant literature leaves one with the impression that the discrepancies are due to different interpretations of the findings made in Marchi material, since all authors seem to agree that fibres from the pyramidal tract can be followed through the reticular formation towards the motor nuclei of the various cranial nerves.

Positive statements that corticofugal fibres terminate in the motor nuclei of the cranial nerves were given by Muratoff (1893), Weidenhammer (1896), Hoche (1898), Romanow (1898), Piltz (1902), Probst (1903), Mettler (1935*a*, 1935*b*, 1935*c*, 1935*d*, 1947), Hirasawa and Kariya (1936) and Krieg (1954). On the other hand, the existence of such fibres was denied by Boyce (1894), Redlich (1897), Mellus (1899), Kosaka (1904) Lewandowsky (1904), Simpson and Jolly (1907), Poljak (1927), Levin (1936) and Combs (1949), who in Marchi sections of various animals were able to trace fibres from the pyramidal tract to the reticular formation ventral to the motor cranial nerve nuclei only.

Finally it should be recalled that Ramón y Cajal (1909) in his Golgi material never succeeded in following fibres from the pyramids into the motor nuclei of the cranial nerves, saying: "... il est démontré que les collatérales de la voie pyramidal n'ont pas de connexions directes avec les noyaux moteurs bulbaires" (loc. cit. p. 957), a conclusion also reached by Lorente de Nó (1924).

Since experimental studies with silver impregnation methods do not appear to have been made of this problem, a re-investigation of the question appears justified in order to see whether terminal degeneration occurs in the motor cranial nerve nuclei following lesions of the cerebral cortex or not. This was found to be of interest also because in the spinal cord it has been shown with a modified Bielschowsky method that the pyramidal tract fibres terminate, not on the motor cells, but on intercalated neurons only (Szentágothai-Schimert, 1941). A silver method also is the only way to decide whether fibres passing towards a nucleus, virtually terminate there or not.

Observations and Comments

My attention was directed to this problem when studying corticofugal fibres in three cats originally prepared for other purposes. In all of them (*see* fig. 1), extensive lesions of the cerebral cortex had been made

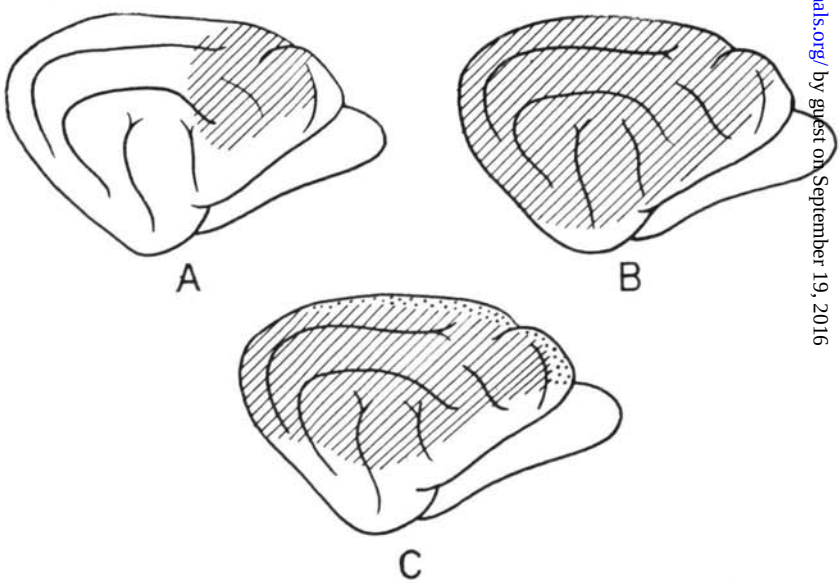

Fig. 1.—Diagrams showing the lesions (hatchings) of the cerebral hemisphere in cats B.St.L. 114 (A), 112 (B) and 113 (C). The dots in figure C indicate areas the fibres from which have been interrupted. Although in these cats various nuclei of the brain-stem show terminal degeneration, no degeneration is present in the motor nuclei of the cranial nerves.

on the right side. In the first cat (B.St.L. 114, killed after twelve days, fig. 1A) only the sensorimotor and adjacent parts of the cerebral cortex were destroyed, in the second (B.St.L. 112, killed after fifteen days, fig. 1B) and the third (B.St.L. 113, killed after seven days, fig. 1C) the cortex was damaged on almost the entire convexity of the hemisphere.[1] Histological control of the lesions shows that in none of the animals the destruction reached the basal ganglia or the thalamus.[2] After perfusion with formalin intravitally and subsequent fixation, the brain-stem was cut in horizontal (cat B.St.L. 112) or in transverse frozen sections (cat B.St.L. 113 and 114) and stained according to Glees' (1946) modification of the Bielschowsky silver method.

Even if in these cats there was abundant terminal degeneration in various nuclei of the brain-stem, e.g. in the pontine nuclei, the inferior olive, the dorsal column nuclei and the nucleus raphe, none of them showed any sign of terminal degeneration in the nuclei of the 3rd, 4th, 6th and 12th nerves, the motor nucleus of the 5th, and the nucleus ambiguus. This means that the termination of the corticofugal fibres, which are supposed to act on the motor nuclei of the cranial nerves, has to be looked for elsewhere, presumably in the reticular formation surrounding these nuclei. No systematic work has been done to locate this termination, but in none of my series did the regions immediately adjacent to the various nuclei show any evidence of terminal degeneration.[3]

It is well known that a localizatory pattern exists in the motor nuclei of the 3rd (Szentágothai, 1942; Warwick, 1953), 5th (Szentágothai, 1949), 7th (Vraa-Jensen, 1942; Szentágothai, 1948), and 12th (J. W. Barnard, 1940, and others) nerves, and in the nucleus ambiguus (Szentágothai, 1943) fibres passing to various muscles of the eye, head, tongue, and larynx, respectively, having their perikarya in different parts of these nuclei. Since it seems far-fetched to assume that fibres from the motor cortex ending diffusely in the brain-stem might convey localized effects to the topically arranged cells in the motor nuclei of the cranial nerves, one might, therefore, expect to find a localization within the termination of corticofugal fibres to the reticular formation. Rossi and Brodal (1956), however, in a recent study of corticoreticular fibres in the cat, found no evidence of such a localization. Regardless of their source within the cortex the fibres were found to terminate in identical parts of the reticular formation. In their study, localized lesions in the motor cortex were not made. It is possible, therefore, that future investigations,

[1]Because of some bleeding in the white matter underneath the lesion, in the latter two cats fibres from the suprasplenial, splenial and cingulate gyri also have been cut.

[2]In cats B.St.L. 112 and 113 the lesions approach the caudate nucleus, without, however, affecting this.

[3]This is of particular interest, since Golgi-studies have shown, that a few dendrites of the cells in the motor nuclei of the cranial nerves penetrate beyond the limits of these nuclei (Cajal, 1909).

where such discrete destructions are made, may nevertheless reveal that a certain localizatory pattern exists within the termination of cortico-reticular fibres. The recent Golgi-studies of A. B. Scheibel (1955) show that the potential pathways for transmission of impulses in the reticular formation are practically unlimited.

Most reticular neurones sending their axons to the various motor nuclei of the cranial nerves, must be supposed to have very short axons. This is learned from the findings in the various Marchi-studies, in which fibres from the pyramidal tract have been followed to the reticular formation in the neighbourhood of these nuclei. However, some of

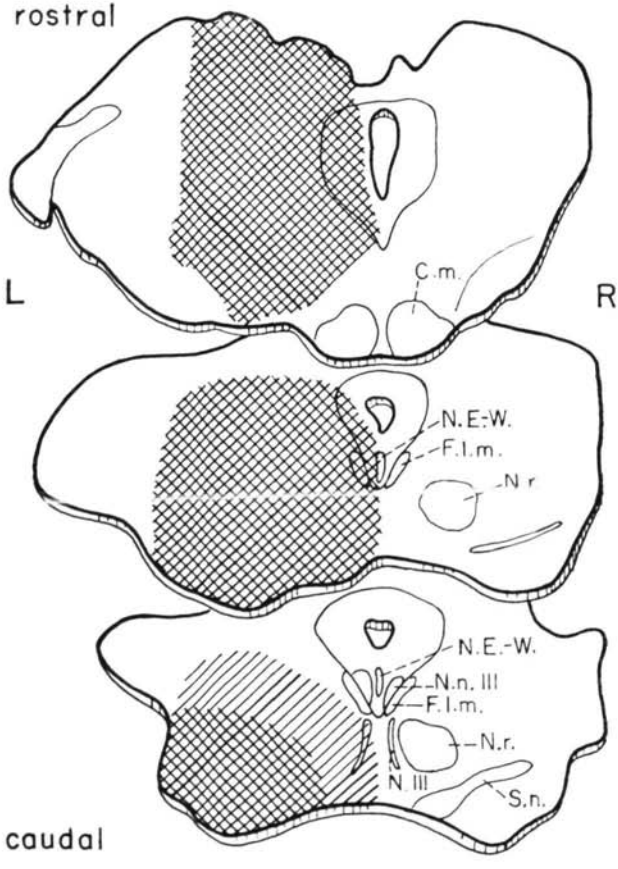

FIG. 2.—Diagrammatic presentation of the lesion in cat B.St.L. 127 with an almost complete hemisection of the mesencephalon on the left side. In this animal some of the motor nuclei of the cranial nerves show terminal degeneration (cp. text). Abbreviations: C.m.: nucleus of the mammillary body. F.l.m.: fasciculus longitudinalis medialis. L: left. N.E.-W.: nucleus of Edinger-Westphal. N.III: 3rd cranial nerve. N.n.III: Nucleus of the 3rd cranial nerve. N.r.: red nucleus. R: right. S.n.: substantia nigra.

the intercalated neurones may also have their perikarya in more remote situations. Thus, in cat B.St.L. 127 (fig. 2, killed ten days after the operation, perfused intravitally), subjected to an almost complete hemisection of the brain-stem on the left side at the level of the oculomotor nucleus, terminal degeneration is present in the facial and trigeminal nuclei on both sides, and in the hypoglossal nucleus on the ipsilateral side. Even if in this animal the lesion includes more than one fibre system and a large area of the brain-stem, the destruction of the reticular formation is so extensive that it might be surmised that part of the terminal degeneration in the motor cranial nerve nuclei is due to damage of cells of this structure, since it is known from Golgi-studies that many cells in the reticular formation send long axons in a caudal direction, some even to the spinal cord, and during their course emit frequent collaterals (M. E. Scheibel, 1955). Such collaterals have been traced to the cranial nerve nuclei. My findings of terminal degeneration in the nuclei of the cranial nerves on the right side, contralateral to the lesion (cat B.St.L. 127, fig. 2), is an indication that axons or collaterals of such intercalated reticular neurones may even cross the mid-line. This is in agreement with observations made in Golgi material.

The findings presented here parallel those made in the spinal cord. Hoff (1932, 1935) and Hoff and Hoff (1934) in their studies with the Cajal method of corticospinal fibres in monkey and cat claim that a few degenerating boutons were found on ventral horn cells. However, later investigations (Phalen and Davenport, 1937; Schimert, 1938; R. I. Barnard, 1940; Szentágothai-Schimert, 1941, and others) have made clear that for judging terminal degeneration in the spinal cord, changes in the boutons are no reliable criteria, since the structure of the boutons may differ considerably in normal preparations. The great variations among normal boutons in the reticular formation have been commented upon by Rossi and Brodal (1956). Furthermore, there may be regional variations even within an apparently uniformly structured nucleus. Thus Blackstad, Brodal and Walberg (1951) in Glees-stained material from the inferior olive in the normal cat found a great proportion of solid boutons in a particular region of the nucleus. Therefore, only when terminal fibres are found in a state of degeneration, should a region containing "degenerating" boutons be considered as showing terminal degeneration.

Employing this criterion, Szentágothai-Schimert (1941) in the cat never found any signs of terminal degeneration on the motor cells of the ventral horns following lesions of the cerebral cortex or the pyramidal tract in the mesencephalon and the medulla. The terminal degeneration was always confined to the cells in the intermediate part of the grey matter of the spinal cord. Lloyd (1941), on the basis of electrophysiological studies in the same animal, likewise concluded that pyramidal

tract fibres do not establish synaptical contact with the ventral motor horn cells. Recently, however, Bernhard, Bohm and Petersén (1953*a*, 1953*b*), and Bernhard and Bohm (1954*a*, 1954*b*) report electrophysiological findings in the monkey (Macaca mulatta) which they interpret as evidence that in this animal fibres from the pyramidal tract end directly around motor cells of the ventral horns. Such a direct pathway has not been convincingly demonstrated by anatomical methods in monkeys. While it is possible, although not likely, that there may exist species differences with regard to the synaptical connexions of the pyramidal tract fibres in the cord, it is clear that anatomical experiments, in which due regard is taken to changes not only in boutons, but terminal fibres as well, is the only way to settle this question.

My findings also have some bearing on the problem of the tonic innervation of the muscles of the head. The presence in the motor nuclei of the cranial nerves of cells other than those of the large motor type was emphasized by Marinesco (1898) and Ramón y Cajal (1909). Since these cells all show retrograde changes following transection of the facial nerve (Vraa-Jensen, 1942, and others) they cannot be considered as intercalated neurons. However, in the light of the recent findings of an efferent gamma system controlling the tonic activity of the muscle spindle afferents (Leksell, 1945; Hunt and Kuffler, 1951*a*, 1951*b*; Kuffler, Hunt and Quilliam, 1951; for details see also Granit, 1955, pp. 205–210), it seems reasonable to assume that the smaller cells in the motor nuclei of the cranial nerves may belong to this system.

In the literature two routes have been mentioned as possible pathways for the corticofugal fibres to the motor nuclei of the cranial nerves, namely fibres reaching the nuclei directly from the pyramidal tract, and aberrant pyramidal tract fibres descending in the medial lemniscus. These aberrant fibres are said to be distributed mainly to the facial and hypoglossal nuclei.

A certain intermingling of pyramidal tract fibres and fibres of the medial lemniscus at pontine levels was observed by Flechsig (1876). Schlesinger (1896) in human cases of syringomyelia with lemniscal degeneration noted that a bundle of fibres was not degenerated. This bundle joined the fibres of the cerebral peduncle. It was interpreted as the central pathway of the cranial nerves and called the "lateral pontine bundle." A few years later, however, von Bechterew (1899), judging from observations in cases with cortical lesions, produced evidence that the lateral pontine bundle of Schlesinger is a descending tract passing in the medial lemniscus. This observation has subsequently been confirmed and extended by many others. Thus, following lesions of various parts of the cerebral cortex in animals and man, fibres have been described which leave the pyramidal tract and enter the medial lemniscus (Weidenhammer, 1896; Hoche, 1898; Mellus, 1899; Dejerine,

1901; Sand, 1903; Kosaka, 1904; Simpson and Jolly, 1907; Mettler, 1935*a*, 1935*b*, 1947; Hirasawa and Kariya, 1936; Levin, 1936; Kanki and Ban, 1952; Krieg, 1954; and others). These descriptions have all been based on Marchi material.

Even if, as mentioned, the facial and hypoglossal nuclei are said to be the main terminal areas for these fibres, it is, nevertheless, evident that no one has been able to follow them into the nuclei themselves, the fibres in Marchi-preparations becoming scattered, dwindling at the level of the trapezoid body. In a recent study with the Glees method in the cat (Walberg, 1957) it has, however, been possible to follow these descending degenerating fibres in the medial lemniscus and to establish their area of termination, which was found to be the nuclei of the dorsal columns. In the first part of their course the fibres descend in the pyramidal tract from which they enter the medial lemniscus. Most of these descending fibres in the medial lemniscus which reach the dorsal column nuclei in the cat are very thin. This probably explains why they have not been followed in Marchi material to their ultimate point of destination.

Judging from the findings in the cat it seems reasonable to assume that also in monkey and man corticofugal fibres may reach the nuclei of the dorsal columns via the medial lemniscus, which would explain the findings of previous authors of fibre degeneration in the medial lemniscus following lesions of the cerebral cortex. It appears from my findings that there is no reason to assume that the fibres of the "lateral pontine bundle" end in the motor cranial nerve nuclei.

Though the findings presented in this paper are made on cats, it is likely that also in man the motor nuclei of the cranial nerves receive their impulses from the cerebral cortex via intercalated neurones. Symptoms from the motor cranial nerves accompanying a capsular hemiplegia, therefore, are probably due to interruption of fibres to certain areas of the reticular formation. This should be kept in mind in future studies of pathological human cases.

The findings presented here furnish another example that further studies on the connexions of corticofugal fibres most likely will bring our concept of the function of the pyramidal system into better accordance with clinical observations in man, still poorly understood (for an account on the many problems regarding the anatomy and physiology of the pyramidal tract, *see* Brodal, 1953). For example, the finding of pyramidal tract fibres from the temporal and occipital lobes (Walberg and Brodal, 1953) may explain the presence of so-called pyramidal signs in lesions of the cerebral cortex outside regions considered as the only origin of pyramidal tract fibres. In future investigations of the pyramidal system it is important to use methods which permit the study of details in its anatomical organization.

SUMMARY

In three cats subjected to extensive cortical ablations, the motor nuclei of the cranial nerves show no signs of terminal degeneration in Glees-stained silver sections. No detailed mapping of terminal degeneration in the reticular formation was undertaken, but it was found that also the region just adjacent to the motor nuclei of the cranial nerves is devoid of corticofugal fibres.

Impulses from the cerebral cortex, therefore, must be assumed to reach these nuclei by way of intercalated neurones lying in the reticular formation. Most of these neurones presumably have short axons, but observations have been made which indicate that some of them may have long axons. Some of the axons of the intercalated neurones probably cross the raphe before they terminate in the motor cranial nerve nuclei.

The anatomical findings made in this study parallel those made in the spinal cord by Szentágothai (1941). The functional significance of the findings is briefly discussed.

REFERENCES

BARNARD, J. W. (1940) *J. comp. Neurol.*, **72**, 489.

BARNARD, R. I. (1940) *J. comp. Neurol.*, **73**, 235.

v. BECHTEREW, W. (1899) "Die Leitungsbahnen im Gehirn und Rückenmark. Ein Handbuch für das Studium des Aufbaues und der inneren Verbindungen des Nervensystemes." Leipzig.

BERNHARD, C. G., and BOHM, E. (1954*a*) *Arch. Neurol. Psychiat., Chicago*, **72**, 473.

——, —— (1954*b*) *Acta physiol. scand.*, **31**, 104.

——, ——, and PETERSÉN, I. (1953*a*) *Experientia*, **9**, 111.

——, ——, —— (1953*b*) *Acta physiol. scand., Suppl.* **106**, **29**, 79.

BLACKSTAD, T., BRODAL, A., and WALBERG, F. (1951) *Acta anat.*, **11**, 461.

BOYCE, R. (1894) *Proc. roy. Soc.*, **56**, 305.

BRODAL, A. (1953) *Irish J. med. Sci.*, p. 289.

COMBS, C. M. (1949) *J. comp. Neurol.*, **90**, 373.

DÉJERINE, J. (1901) "Anatomie des centres nerveux." Paris, vol. II.

FLECHSIG, P. (1876) "Die Leitungsbahnen im Gehirn und Rückenmark des Menschen auf Grund entwicklungsgeschichtlicher Untersuchungen dargestellt." Leipzig.

GLEES, P. (1946) *J. Neuropath.*, **5**, 54.

GRANIT, R. (1955) "Receptors and sensory perception. A discussion of aims, means, and results of electrophysiological research into the process of reception." New Haven.

HIRASAWA, K., and KARIYA, K. (1936) *Okajimas Folia anat. jap.*, **14**, 603.

HOCHE, A. (1898) *Arch. Psychiat. Nervenkr.*, **30**, 103.

HOFF, E. C. (1932) *Proc. roy. Soc., B*, **111**, 226.

—— (1935) *Arch. Neurol. Psychiat., Chicago*, **33**, 687.

——, and HOFF, H. E. (1934) *Brain*, **57**, 454.

HUNT, C. C., and KUFFLER, S. W. (1951*a*) *J. Physiol.*, **113**, 283.

—— (1951*b*) *J. Physiol.*, **113**, 298.

KANKI, S., and BAN, T. (1952) *Med. J. Osaka Univ.*, **3**, 201.

KOSAKA, K. (1904) *Mitt. med. Fak., Tokio*, **5**, 77.
KRIEG, W. J. S. (1947) "Functional Neuroanatomy." Philadelphia.
—— (1954) "Connections of the Frontal Cortex of the Monkey." Springfield, Ill.
KUFFLER, S. W., HUNT, C. C., and QUILLIAM, J. P. (1951) *J. Neurophysiol.*, **14**, 29.
LEKSELL, L. (1945) *Acta physiol. scand., Suppl.* **31.**
LEVIN, P. M. (1936) *J. comp. Neurol.*, **63**, 369.
—— (1949) "Efferent Fibers." *In* Bucy, P. C. "The precentral motor cortex." 2nd edition. Urbana, Ill.
LEWANDOWSKY, M. (1904) *Denkschr. med.-naturw. Ges. Jena*, **10**, 63.
LLOYD, D. P. C. (1941) *J. Neurophysiol.*, **4**, 525.
LORENTE DE NÓ, R. (1924) *Trab. Lab. Invest. biol. Univ. Madr.*, **22**, 51.
MARINESCO, G. (1898) *Rev. neurol.*, **6**, 30.
MELLUS, E. L. (1899) *J. nerv. ment. Dis.*, **26**, 197.
METTLER, F. A. (1935*a*) *J. comp. Neurol.*, **61**, 221.
—— (1935*b*) *J. comp. Neurol.*, **61**, 509.
—— (1935*c*) *J. comp. Neurol.*, **62**, 263.
—— (1935*d*) *J. comp. Neurol.*, **63**, 25.
—— (1947) *J. comp. Neurol.*, **86**, 119.
—— (1948) "Neuroanatomy." 2nd edition. St. Louis.
MURATOFF, W. (1893) *Arch. Anat. Physiol. (Anat. Abt.)*, 97.
PHALEN, G. S., and DAVENPORT, H. A. (1937) *J. comp. Neurol.*, **68**, 67.
PILTZ, J. (1902) *Neurol. Zbl.*, **21**, 482.
POLJAK, S. (1927) *J. comp. Neurol.*, **44**, 197.
PROBST, M. (1903) *Jb. Psychiat. Neurol.*, **23**, 18.
REDLICH, E. (1897) *Neurol. Zbl.*, **16**, 818.
RAMON Y CAJAL, S. (1909) "Histologie du système nerveux de l'homme et des vertébrés." Paris, vol. I.
ROMANOW, M. P. (1898) *Neurol. Zbl.*, **17**, 593.
ROSSI, G. F., and BRODAL, A. (1956) *J. Anat., Lond.*, **90**, 42.
SAND, R. (1903) *Arb. neurol. Inst. Univ. Wien.*, **10**, 185.
SCHEIBEL, A. B. (1955) *Anat. Rec.*, **121**, 361.
SCHEIBEL, M. E. (1955) *Anat. Rec.*, **121**, 362.
SCHIMERT, J. (1938) *Z. Anat. EntwGesch.*, **108**, 761.
SCHLESINGER, H. (1896) *Neurol. Zbl.*, **15**, 146.
SIMPSON, S., and JOLLY, W. A. (1907) *Proc. roy. Soc. Edinb.*, **27**, 281.
SZENTÁGOTHAI, J. (1942) *Arch. Psychiat. Nervenkr.*, **115**, 127.
—— (1943) *Z. Anat. EntwGesch.*, **112**, 704.
—— (1948) *J. comp. Neurol.*, **88**, 207.
—— (1949) *J. comp. Neurol.*, **90**, 111.
SZENTÁGOTHAI-SCHIMERT, J. (1941) *Z. Anat. EntwGesch.*, **111**, 322.
VRAA-JENSEN, G. (1942) "The Motor Nucleus of the Facial Nerve. With a Survey of the Efferent Innervation of the Facial Muscles." Copenhagen.
WALBERG, F. (1957) *Brain*, **80**, 273.
——, and BRODAL, A. (1953) *Brain*, **76**, 491.
WARWICK, R. (1953) *J. comp. Neurol.*, **98**, 449.
WEIDENHAMMER, W. (1896) *Neurol. Zbl.*, **15**, 191.