

Citation:

G.C. Heringa, On the Peripheral Sensitive Nervous System, in:
KNAW, Proceedings, 21 I, 1919, Amsterdam, 1919, pp. 26-35

Physiology. — "*On the Peripheral Sensitive Nervous System.*"

By Dr. G. C. HERINGA. (Communicated by Prof. J. BOEKE).

(Communicated in the meeting of February 23, 1918).

When we endeavour to summarize our knowledge of the peripheral sensitive nervous system, which is a time-consuming experience as it involves the perusal of an enormous number of periodicals, we shall find amidst a mass of controversial matter a number of facts received by various controversialists, which, when put together, make up a gratifying whole.

In the neurological clinic the doctrine of neurons is still all but paramount, but in the neuro-anatomic literature it is quite a different thing. There, in spite of this same doctrine of neurons, experiences come to the front pointing to the existence of a very extensive continuous retiform structure of sensory nerves close to the periphery. As has been insisted upon by APATHY there exists a highly delicate texture of anastomotic nerve-fibers close under the surface of the body of invertebrates. This view has hardly been disqualified. It is now getting more and more evident that such a network is also to be found in vertebrates.

Many data regarding the "*rete amielinica subpapillare*" we owe especially to RUFFINI and his school, who based upon them his theory of the "*circuito chiuso delle neurofibrille.*" According to the descriptions given by RUFFINI himself, the fibers of this network spring from different sources:

1. end-branches of the ordinary medullated fibers;
2. ultraterminals of endorgans;
3. sympathetic fibers;
4. ultraterminals of fibers belonging to the TIMOFEEW-system.

From all sides (BOTEZAT, LEONTOWITCH, PRENTISS, SFAMENI, DOGIEL) much evidential matter tending in the same direction, has been brought forward, so that no room is left for any doubt as to the principal facts, though there remains some difference of opinion regarding the components of the network, and though several inquirers will not go the length of subscribing to all the inferences of RUFFINI's "*teoria unitaria.*"

Two recent publications from the Italian school seem to me to be

interesting in this connection. STEPHANELLI¹⁾ describes an extensive network of nerve-fibers, which he found in the skin of reptiles. This network built up of non-medullated fibers is easily distinguishable from the familiar subepithelial *plexus*, which lies deeper and in which only an interlacement of nerve-fibers, for the greater part still medullated, takes place. The relations of the non-medullated network to the subepithelial plexus are also described minutely by him. In the former, which spreads diffusely as a true network of nerves in the skin, he describes by the side of very few other endings an "organo di senso in stato diffuso," a conception which is the more plausible since the network is immediately connected with an intrapapillary extension of the same nature.

Here lies the link that joins STEPHANELLI'S publication to that of VITALI.²⁾

VITALI examined the skin of the nail-bed also after RUFFINI'S galvano-chloride method. His results correspond completely with those of similar researches by RUFFINI and others. In succession he describes the presence of many free endings easy to differentiate by the various melodious Italian names: gomitoli, alberelli, espansioni ad arborvoiticciati, fiocchetti papillari, grappoli, and also of RUFFINI'S, MEISSNER'S and VATER-PACINI'S corpuscles. The principal interest now hinges about the fact that he lays particular stress upon the occurrence of anastomoses between the terminals reciprocally and upon their contact, as a whole, with the rete amyelinica subpapillare, therewith emphasizing the importance attached by RUFFINI long since to the ultraterminals as expounded in his *teoria unitaria* previously mentioned.—Finally VITALI comes to the conclusion that all those terminals together with the rete subpapillare form one connected amyelinic meshwork. When following up the Italian school a little further, we shall see that this meshwork must be placed on a level with STEPHANELLI'S diffuse network. Then also the various endorgans of the higher vertebrates will be found to be points of differentiation amidst less developed surroundings. "Eche cos'altre sono," as Simonelli puts it rhetorically, "quello che noi denominiamo espansioni, se non il condensarsi in punti limitati di un simile reticolo diffuso periferico: in altri termini se non punti nodosi

¹⁾ AUGUSTO STEPHANELLI. Nuovo contributo alla cognoscenza della espansione sensitiva dei Rettili e considerazioni sulla tessitura del sistema nervoso periferico. Intern. Monatschrift. f. Anat. u. Phys. XXXII 1916. — Sui dispositivi microscopici della sensibilità cutanea e nella mucosa orale dei Rettili. (Ibid. XXXII 1916).

²⁾ G. VITALI. Contributo allo studio istologico dell'unghia. Le espansioni nervose del derma sotto ungueale dell'uomo. (Ibid. XXXII 1915).

maglie piu serrati di una rete generale, che intimamente involge e compenetrá i tessuti, per meglio localizzare e precusare gli stimoli periferici?"

Thus, according to this view an unbroken series of anastomoses must be traceable in numerous varieties of free endings from the rete amielinica on the one side to the tactile corpuscles inserted in a rete intrapapillare on the other.

It would perhaps be premature to consider this highly pregnant hypothesis as proven. Still, undoubtedly it is equally true that anyone who will take the trouble to look into the literature, will find attestations from other authors also pointing unmistakably in the same direction. It is evident that the border-lines demarcating the various forms of end-organs, classified into various-groups, are by no means established. Nearly coeval with the study of the end-organs itself are the efforts to establish a phylogenetic pedigree of the various end-organs, in which the intricate forms are reduced to more primitive types (MERKEL, KRAUSE, and others). Certain it is also that the more forms are brought to light by modern researchers, the more the border-lines between the various groups are fading out.

With this we are impressed forthwith when looking at the illustrations accompanying the several publications (see e.g. CECCHERELLI ¹⁾ v. D. VELDE). ²⁾ The leading modern authors (BOTEZAT, DOGIEL, SFAMENI and followers of RUFFINI) endeavour to demonstrate anastomoses between the various endings. DOGIEL ³⁾ says in his article about nerve-endings in the external genitalia: "Wenn wir die Beschreibung der Nervenendigungen in den verschiedenen Nervenapparaten, den Genitalkörperchen, den Endkolben und den Meissnerschen Körperchen, welche in der Haut der äusseren Genitalorgane gelegen sind, vergleichen, und zugleich die beigegebenen Zeichnungen betrachten, so müssen wir zu dem Schluss kommen, dass zwischen ihnen kein wesentlicher Unterschied besteht".

SFAMENI ⁴⁾ also describes the relationship between the genital corpuscles and KRAUSE's end-bulbs, GOLGI-MAZZONI's corpuscles and VATER-PACINI's corpuscles on the one side and RUFFINI's corpuscles on the other.

BOTEZAT ⁵⁾ has written a long and comprehensive paper on the system and the interrelationship of the nerve-endorgans.

¹⁾ Intern. Monatschr. XXV 1908.

²⁾ Intern. Mon. XXVI 1909.

³⁾ Arch. Micr. Anat. XLI.

⁴⁾ Arch. di fisiol. I 1904.

⁵⁾ Zeitsch. Wiss. Zool. LXXXIV. 1906.

But what seems to me to be more important than all this, as it falls in with RUFFINI's views, is that also the border-lines between the corpuscles and the "free" endings are gradually falling away. Here the only differential diagnostic is whether or not a capsule is present. The same characteristics of the nerve-fibers, of the supporting tissue, "tactile-cells" or whatever name may be given to the cells found in the endorgans are equally peculiar to either group of end-organs. This may be gathered from the illustrations and the descriptions in all papers. BOTEZAT makes particular mention of this, adding that a capsule round a nerve-ending is not a question of vital importance for it, either functionally or morphologically. On the contrary BOTEZAT very often finds by the side of a capsuled ending its fellow deprived of a capsule. Thus the free "Knäuel" are found side by side with the capsuled "Knäuel" and the bulbs of KRAUSE; side by side with MERKEL's cells GRANDRY's and MEISSNER's corpuscles etc. Moreover BOTEZAT distinguishes all sorts of gradations between the free and the capsuled endings.

In other authors we find the same again. RUFFINI's corpuscles are according to VITALI¹⁾ nothing else but capsuled "alberelli".

DOGIEL²⁾ also speaks of non-capsuled corpuscles of RUFFINI. SFAMENI³⁾ asserts that non-capsuled varieties occur of the same Genital corpuscles, which, as has been observed, are allied to all sorts of tactile-corpuscles. Of MEISSNER's corpuscles there seems to exist a large variety of simple modifications.

SFAMENI describes intermediate forms between MEISSNER's corpuscles and "fochetti papillare" i. e. free endings. DOGIEL's modifications of MEISSNER's corpuscles (RUFFINI calls them DOGIEL's corpuscles) are non-capsuled at the upper-pole from which the axis-cylinders are branching off into free endings. They are types of RUFFINI's "espansione misti". Other modifications again of MEISSNER's corpuscles (DOGIEL, v. D. VELDE) are characterised by their having a slightly developed capsule and a simplified nervecourse. DOGIEL's "eingekapselte Knäuel" described by him in 1903 as modified MEISSNER's corpuscles must therefore be closely allied to the free endings, perhaps identical with them (see supra). It seems, then, that MEISSNER's corpuscles are, in a higher degree than many other forms, closely allied to free nerve-endings. So when observing the several findings concerning the capsule of these corpuscles, we shall see that LAN-

¹⁾ Int. Mon. XXXI. 1915.

²⁾ Arch. f. Micr. Anat. 1903.

³⁾ l.c.

GERHANS¹⁾ absolutely disproves its existence. He says: "Es besitzt *der Zellhaufen*²⁾ den man Tastkörper nennt, nicht einmal eine eigene umschliessende Membran. Ueberal stossen die peripheren Zellen direct an das umgebende Bindegewebe, und nur nach längerer Einwirkung eines Reagenzes kann es vorkommen, dasz das starre Aussehen der Bindegewebsschichten eine eigene Membran vortäuscht".

Likewise ROUGET, TAFANI, IZQUERDO, HOGGAN, LEONTOWITCH absolutely deny the existence of a capsule. MEISSNER, RENAUT, KRAUSE, WOLFF, KOLLMAN and LEFEBURE consider it as a single endothelial membrane. LEFEBURE³⁾: "une simple lame conjoncture doublée sur une face profonde par un feuillet endothelial". From all this it follows that the hypothesis brought forward by DOGIEL, RUFFINI, THOMSA and KOLLIKER that the corpuscles are provided with a true lamella-capsule, is hardly tenable. The very gradations (and they are many) between MEISSNER's corpuscles and the free endings go far to substantiate a priori the opinion of LANGERHANS, who appears to have studied the organs under consideration thoroughly. They also support BOTEZAT's view when he puts MEISSNER's corpuscles on a level with the complicate, non-capsuled MERKEL's corpuscles. In virtue of my personal inquiry I incline to LANGERHANS's view, as will appear lower-down.

Finally let us bestow consideration upon the problem of the genetic connections between the free endings and the tactile bodies with the subpapillary network.

If we confine ourselves to the more modern authors, we mention the names of BETHE, PRENTISS, BOTEZAT, LEONTOWITCH, SFAMENI and DOGIEL⁴⁾, who have, all of them, discussed more or less minutely the subepithelial network and its connections with the nerve-endorgans.

BOTEZAT differs from the other investigators in that he considers the network to be independent of tactile corpuscles. This follows from his opinion that the rete amielinica, is built up of fibers of the so-called 2^d sort⁵⁾. But for the rest, he sides with the Italian School,

1) Arch. f. Micr. Anat. IX 1873.

2) The italics are mine.

3) Revue gen. d'histol. 1909.

4) BETHE. Allgemeine Anat. und Phys. des Nervensystems. Leipzig 1903

PRENTISS. Journ. of Comp. neur. XIV 1904.

BOTEZAT l.c.

LEONTOWITCH Int. Mon. XVIII 1901.

SFAMENI, DOGIEL l.c.

5) Medullated fibers losing their myelin already in the nerve-trunk. It seems doubtful whether these fibers are still to be considered as a separate group.

our starting point, when in speaking about certain free endings, he says that through anostomoses they form a widely spread end-structure, "welcher in der Form eines im allgemeinen weitmaschigen varikösen Netzes von weithin ausgebreiter Ausdehnung erscheint", which continues into the papillae, and there adheres to ordinary medullated fibers. He looks upon this nerve-complex as a "für sich bestehender sensibeler Apparat der Lederhaut". He finds it again in fishes and amphibia, so it is beyond doubt that he describes the very network which STEPHANELLI discusses in his publication.

DOGIEL, an authority on end-organs, concurs with RUFFINI that the lateral branches of the free papillary endings blend with the rete amielinica: "Wie aus dem mitgeteilten hervorgeht, so hat das aus Marklosen Aestchen und Faden zusammengesetzte subpapillare Nervenengeflecht, die uneingekapselte Nervenknäuel sowie die Schleifenförmig gebogene Bündel und das intrapapillare Fadennetz einen und denselben Ursprung". Also the TIMOFEEV fibres of the MEISSNER-corpuscles, which DOGIEL reckons among the sensory system, go to make up according to him, the intrapapillary nerve-complex by means of their ultraterminals.

SFAMENI, though far from adhering to the *teoria unitaria* gives a description of the subepithelial plexus and of its connection with tactile corpuscles and free endings, that accords fairly with RUFFINI's. Nor is it on the whole contradicted by PRENTISS and LEONTOWITCH in their publications respectively of *Rana* and the human skin.

It surely will not do to ignore the many differences between the various authors, differences in theoretical conception, in appreciation and in interpretation of their observations. Opposed to DOGIEL, who still holds that interlacement of the fibers is the fundamental principle governing the structure of the network, are BOTEZAT, BETHE, RUFFINI, LEONTOWITCH, and SFAMENI, who are convinced of the fusion of the fibers. PRENTISS wavers. It is a fact that the network is built up of sensitive fibers. However, the question whether also sympathetic elements are fused with it, is as yet unsettled. This depends in some degree on the doubtful character of the TIMOFEEV fibers. Still, though the origin of the sensory part of the network is still uncertain, there is no denying that, also in this respect, observers concur more and more. As we observed before BOTEZAT considers the whole network to be made up of anastomotic free nerve-endings. DOGIEL also looks upon them as the principal components, but according to him also ultraterminals of the TIMOFEEV system of the tactile corpuscles unite with it. SFAMENI believes there is *also* some connection with the genital corpuscles; LEONTOWITCH, BETHE, and PRENTISS assume an

immediate connection of the network with the free endings as well as with corpuscles. All these authors, though theoretically far removed from RUFFINI's neurogenetic conceptions, have brought forward a number of facts corresponding satisfactorily with those insisted upon most emphatically by the Italian school.

In short there is in the literature about the subject a tendency towards the hypothesis that there is, generally speaking, interconnection and coherence in the whole peripheral sensory nervous system.

It is these facts, derived from the literature, that enhance the significance of recent personal studies made by the BIELSCHOWSKY method on the sensory nerve-endings.

The BIELSCHOWSKY method differs from the methylene blue- and the gold-chloride method in that it affords another view of the problems. It does not present those typical appearances, which, when comparatively slight magnifications of rather thick sections are examined, yield a clear survey of the relations. Its efficiency lies in the fact that when preparations counterstained in haem. eosin, are examined under a microscope of the highest power, it brings out in strong relief the relations between the fibrils and their surroundings.

Along this totally different path I arrived at conclusions which, as I hope, will contribute to lend support to the hypothesis that the MEISSNER corpuscles are more related to the free endings than is commonly believed.

In a paper read at last year's Congress for Physics und Medicine at The Hague (1917) (see also: Verslagen Kon. Ak. v. Wetensch. 27 April 1917) I recorded some morphological data, hitherto unknown, concerning the structure of the axis-cylinder. In that paper I set forth that, when tracing an ordinary nerve-fiber from centre to periphery, the following changes in the structure are to be observed in a transverse section. First we find in the medullary sheath the axoplasm, which (in a transverse section) seems to be vacuolar in structure and embraces the neurofibrils in the protoplasmatic septa between the vacuoles. As known, the medullary sheath is surrounded by the protoplasmatic sheath of SCHWANN with its nucleus. More towards the periphery the medullary sheath splits up into several tubes. The always vacuolar axoplasma material with its fibrils spreads over the daughter medullary sheaths. Together they remain embedded in one undivided protoplasmatic mass, which must be considered as a continuation of the sheath of SCHWANN. Still further towards the terminus of the course of the nerve the medullary sheaths disappear from the section, so that the neurofibrils lie free in the protoplasmatic envelopment which, now being of vacuolar structure like

the primitive axis-cylinder, must be assimilated to the sheath of SCHWANN blended with the axoplasm. These formations are seen to get thinner and thinner and their meshes to get ever wider according as they approach the terminus of the nerve. To all appearance they ultimately blend or unite with the connective tissue plasmoderms in which we find the neurofibrils in the ultimate tract of their course¹⁾.

At first I was disposed to think that the described vacuolar dissolution of the axis-cylinder was characteristic of the so-called free nerve-endings, because I saw the medullated nerves force their way into the MEISSNER corpuscles without having undergone any modification.

I can go a step farther this time, and assert on the basis of a profound investigation of MEISSNER'S corpuscles that the axis-cylinders inside these corpuscles pass through precisely the same disintegration process, previously described by me for the so-called free nerve-endings, and just now designated as a vacuolar dissolution.

Whereas nowadays it is maintained by many inquirers that the axis-cylinder loses its medullary sheath, before it enters into the corpuscles, I side with ENGELMANN²⁾, LANGERHANS, FISCHER³⁾ KEY—RETZIUS⁴⁾ and LEFEBURE⁵⁾, having been able to ascertain, in preparations treated with Osmic acid, that the medullary sheath, just as the sheath of SCHWANN, is prolonged into the intracorpuseular course of the nerves. Moreover my preparations also proved distinctly that those medullary sheaths split up inside the sheath of SCHWANN exactly as has been indicated above.

I hold with LEFEBURE that most likely the fact that the Osmium method has been abandoned for the modern fibril staining methods, is responsible for the erroneous opinions about the presence or the absence of medullary sheaths, prevailing in the neurological literature.

As to the sheath of SCHWANN, it goes without saying that I must contest the hypothesis that it passes into the formation of the capsule, since to me it is an intrinsic part of the lemmoblastic sheath. (DOGIEL and others⁶⁾). My preparations, which are well impregnated and of good fixation also enable me to ascertain the fate of the axiscylinders

¹⁾ Cf. J. BOEKE. Studien zur Nervenregeneration I, Verh. Kon. Ak. v. Wet. A'dam 2e Sectie Deel, XVIII n^o. 6.

²⁾ Zeitschr. Wiss. Zool. XII 1863.

³⁾ Arch. f. Mikr. Anat. XII.

⁴⁾ Arch. f. Mikr. Anat. IX 1873.

⁵⁾ Revue génér. d'histologie 1909.

⁶⁾ With more justice LANGERHAUS, KRAUSE and others assert that the sheath of SCHWANN passes into the inner capsule of the corpuscles.

inside the MEISSNER corpuscles. For among the cells filling up the core of the MEISSNER-corpuscles we find many of the same vacuolar non-medullated nerve-sections, which we have described, with the fibrils, scattered over the spongy protoplasm.

Now it was but another step to establish in well-chosen objects that those vacuolar axis-cylinders maintain their course in the cells of the core itself. In tangential sections we were in a position to observe with absolute certainty that from the axis-cylinder the fibrils pass *into* the protoplasm of those cells, where they may aid in making up a regular network of the fine fibrils, and where, as a continuation of the vacuolar structure of the axis-cylinder in transverse section, a reticular protoplasm serves as a substratum to the neurofibrils. Just as I observed previously in the corpuscles of GRANDRY, I saw also here a similar diffuse expansion of the network over the cell-protoplasm, as well as the mechanical traction phenomena between protoplasm and fibril-system, so that my interpretation leaves hardly any room for doubt. It is beyond all question that the core cells are indeed parts of the nerve-course itself; consequently it fits in with my view ¹⁾ to term them lemmoblasts *together with* the other elements, building up the course of the nerve. The fibrillar networks described, are by no means terminal. As a rule the fibrils are seen to unite again and pursue their way as a new axis-cylinder. This is an additional argument for classing those cells among the structural elements of the nerve-course itself. In this way I came to the conclusion that *the entire MEISSNER corpuscle is built up of compact lemmoblast cords in structure completely similar to the free nerve-endings*. Now this appears to me to be an important conclusion, the more so when correlated with the above data regarding the connection between the tactile corpuscles and the free endings, as discussed in the literature.

In conclusion I will impart that in the MEISSNER corpuscles I found hardly anything that reminded me of a capsule, certainly not a fine fibrillary texture proper, still less a lamellar system. The enveloping connective tissue is rather of a loose spongy structure. I found in it vacuolar nerve-sections as well as "free" fibrils invested in the plasmoderms. I often despaired that the contours of MEISSNER-corpuscles are very indistinct. Especially in the tactile balls of the cat's paw I rarely found typical MEISSNER corpuscles; often, however, in the papillary connective tissue I found detached groups

¹⁾ Cf. G. C. HERINGA. Le développement des corpuscules de GRANDRY et de HERBST (Arch. néerl. des Sc. Exactes et nat. Serie III B. tome III 1917).

of nerve-sections of the familiar appearance in various sizes. Together they presented precisely the appearance of a transverse section of a MEISSNER corpuscle. Only by studying serial sections it can be ascertained whether we have to do with a MEISSNER corpuscle or rather with some detached axis-cylinders of free endings. Such forms, which must no doubt be classed as modified MEISSNER corpuscles, are in my judgment, as many proofs of the close relationship there is indeed between tactile corpuscles and free endings.

My conclusions, therefore, are the following:

1. the cells found by all inquirers¹⁾ except DOGIEL in the MEISSNER corpuscles are elements of the nerve-course itself, lemmoblasts, as I have endeavoured to demonstrate for GRANDRY-corpuscles.

2. As to structure and behaviour, the nerves in the MEISSNER-corpuscles correspond exactly with those of the so-called free-endings.

3. so that it is very likely that the terminal branches of the MEISSNER corpuscles (ultraterminals) form one connected whole with the free papillary endings.

¹⁾ THOMSA, LANGERHANS, RANVIER, MERKEL, KRAUSE, LEONTOWITCH SPAMENI, RUFFINE, LEFEBURE, VAN DE VELDE and others.