Anatomy. — *"Once more the innervation and the tonus of the striped muscles"*. By Dr. J. G. DUSSER DE BARENNE. (Communicated by Prof. J. BOEKE)[1]).

(Communicated in the meeting of January 29, 1919).

In continuation of a previous communication[2]), to which I think I may refer by way of introduction, I want briefly to revert to this question.

In the first place to communicate some further experimental facts and in the second place to recall my criticism on a communication by G. MANSFELD and A. LUCÁKS[3]), now that I have come to the conclusion that the former is not sound.

In that previous paper I have proved that S. DE BOER's opinion, that the tonus of the striped muscles should be governed by the sympathetic nervous system, is incorrect. That further neither the cadaveric-rigidity, nor, as has already been shown by me[4]) before and has been confirmed by VAN RIJNBERK[5]) since — the decerebrate rigidity have anything to do with sympathetic innervation. Only a slight, though clear hypotonus of the muscles of the hindleg was perceptible with warm-blooded animals and frogs, after unilateral resection of the abdominal sympathetic.

The result with my cats was that this symptom only disappeared in the course of 5 to 8 weeks. So I thought I had better not consider it a shock-phenomenon and as none of the other, in my opinion plausible explanations were decisive[6]), I had to leave

[1]) The experiments communicated here, were partly performed by Mr. H. J. HAVIK, med. stud. at Leiden, during my stay at Delft in the winter of 1917/1918.

[2]) Ueber die Innervation und den Tonus der quergestreiften Muskeln. Pflüger's Archiv, Band **166**, 1916, p. 145.

[3]) Untersuchungen über den chemischen Muskeltonus. I. Pflüger's Archiv, Band **161**, 1915, p. 467.

[4]) Ueber die Enthirnungsstarre (Decerebrate rigidity Sherrington's) in ihrer Beziehung zur efferenten Innervation der quergestreiften Muskulatur. Folia Neurobiologica, Band **7**, 1913, p. 651.

[5]) Recherches sur le tonus musculaire et son innervation, II. tonus musculaire et rigidité de décérébration. Archives néérlandaises de physiologie de l'homme et des animaux, tome I, 1917/1918, p. 726.

[6]) Cf. for l.c (Pflüger's Archiv.), Bd. 166, p. 166 and 167.

this experimental fact unexplained for the present. For this reason I thought I was right in not rejecting absolutely the supposition that the sympathetic nerve would partially influence the tonus of the striped muscles. Since that time two communications by E. Th. von Brücke[1]) have been published from which it appears that he too has been able to observe initial hypotonus of the same kind in the acute experiment as was evident in my animals; but only during some days, after which the hypotonus disappeared altogether.

If this result should prove to be right in the greater number of the cases, the long duration of that initial hypotonus in my experiments would certainly have to be made dependent on other factors, which however would have nothing to do with the tonus as such.

With this the last support of de Boer's theory would drop.

For not only it has been proved that neither rigor mortis nor decerebrate rigidity are due to the sympathetic nervous system but besides this it has become evident to me that another phenomenon — mentioned by de Boer as being governed by the sympathetic — has nothing to do with it.

The "nose of Funke" occurring again and again in the muscle contraction curve was to disappear after extirpation of the sympathetic nerve chain.

After this resection I very often distinctly observed the "nose of Funke" in the muscle nerve of the frog, both with electrical and mechanical stimulation of the spinal cord, not only in the acute experiment, but also if the extirpation of the sympathetic chain, was done 2 months before the actual experiment and the post-ganglionic sympathetic nervefibres had degenerated.

This positive fact is of course decisive in face of the negative one of de Boer.

Three curves stating this experimental fact follow below. [2])

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[1]) J. Negrin y. Lopez and E. Th. von Brücke. Zur Frage nach der Bedeutung des Sympathicus für den Tonus der Skelettmuskulatur. Pflüger's Archiv, Band 166. 1916, p. 55.

E. Th. von Brücke. Neuere Anschauungen über den Muskeltonus. Deutsche medizinische Wochenschrift, 1918, N°. 5 and 6.

[2]) In order to prevent a possible misunderstanding, I want to make the following remarks. The appearance of the "nose of Funke" in the muscle curve is often very variable. Sometimes it appears very distinctly as a second top in the curve. As is visible in fig. 1, very often its presence is only obvious from the fact that the duration of the muscle contraction curve is much longer than the duration of the single muscle contraction as in fig. 2 and 3. Between these all kinds of transition forms are to be found, also with respect to the place in the curve, where

When I published this communication [1]) à propos of VAN RIJNBERK's tabular scheme [2]) the latter [3]) maintained that the fact of the "nose of FUNKE" still occurring after extirpation of the sympathetic does not prove in the least that the stimulations which cause this phenomenon, do not travel by the sympathetic fibres, when they are uninterrupted.

Little is to be said against this argument, but on examining it closely, it is yet somewhat sophistical. I am of the opinion that, when during an experiment a phenomenon occurs, notwithstanding the experimental circumstances and conditions, one has a right provisionally to draw the conclusion that the phenomenon concerned is not dependent on those experimental circumstances and conditions.

What value VAN RIJNBERK attaches to his own objection is evident from the fact, that, if he had thought it serious, he would have left his own essay on the connection between sympathetic innervation and decerebate rigidity unwritten. Furthermore does he himself sin against it in the same table, a few lines higher. For he ought at least to have put a? after the sympathetic genese of the second veratrine top. This one indeed is also present after extirpation of the sympathetic.

VAN RIJNBERK does not however infer from this, as one might expect from his above-mentioned reasoning that therefore stimulations causing the second veratrine top under normal innervation conditions might travel along the sympathetic fibre, but he concludes that the sympathetic has nothing to do with the second top.

This last reasoning and experimental fact are quite in harmony with my own opinion and experience. For it has been proved that both during the acute experiment and the chronic, when the sympathetic nerve fibres are degenerated, the second veratrine top still occurs in the muscle contraction, caused by stimulation of the spinal cord, either electrical or mechanical.

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the nose occurs Cf. for this viz. T. GRAHAM BROWN. Pflüger's Archiv. Band 125, 1908, p. 491. We do not know yet what is the meaning of the "nose of Funke". In my opinion it is not impossible that several different phenomena are hidden behind this. For the sake of brevity I used the term "nose of Funke" without pronouncing as my opinion that this is a well known single phenomenon.

[1]) Spiertonus en ontherseningsstijfheid. Nederl. Tijdschrift voor Geneeskunde, 1917, I, p. 1756.

[2]) VAN RIJNBERK Spiertonus en ontherseningsstijfheid. Nederl. Tijdschr. voor Geneeskunde, 1917, I. p. 1634.

[3]) Answer of VAN RIJNBERK to the remark cited Nederl. Tijdschrift voor Geneeskunde, 1917, I, p. 1757.

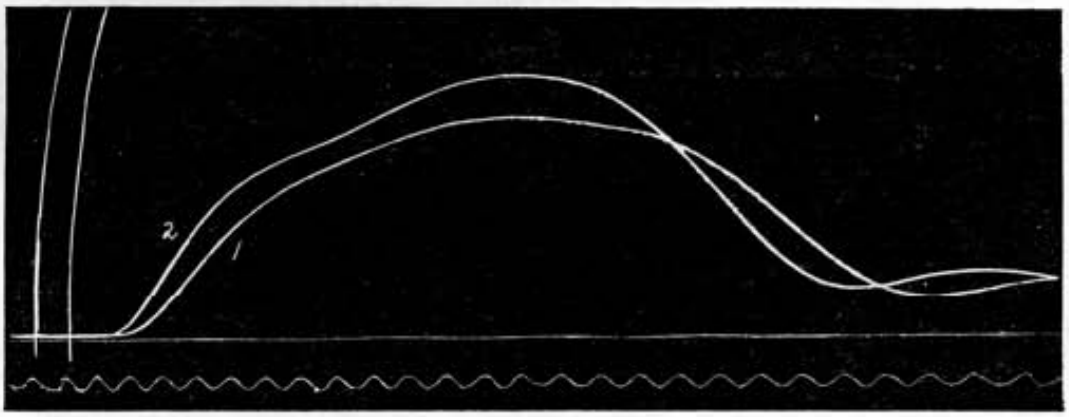

Fig. 1. Experiment B_1.

Frog. Acute experiment. *Right* sympathetic chain extirpated (under narcosis of ether) from N. V. to N. XI inclusive. Curves registered half an hour after the resection. Electrical stimulation of the cross section of the caudal part of the spinal cord with "make induction shock". In primary circuit $3^1/_2$ volts. In secondary circuit, except the resistance of the substance of the spinal cord, a resistance of 60.000 ohm, distance of coils 50.5 mm., small inductorium. Loading of the muscles about 12 grams. Curve 1 of *left* gastrocnemius. Curve 2 registered by *right* gastrocnemius.

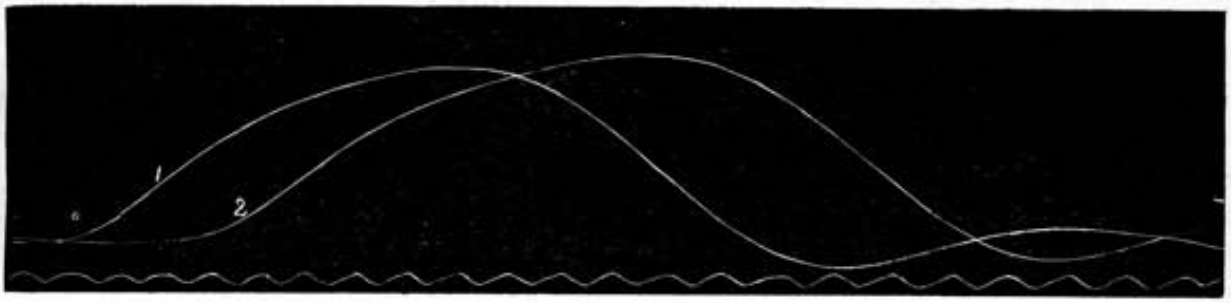

Fig. 2. Experiment C 28.

Frog. Acute experiment. *Right* sympathetic chain extirpated (under narcosis of ether) from N. IV to N. XI inclusive. Curves registered 45 minutes after resection. Temperature room $11^3/_4$° C. Mechanical stimulation of the spinal chord several segments above the origin of the roots of the Nn. ischiadici by the prick of a pin. Time curve $= {}^1/_{50}$". Loading of the muscles about 12 grams. Curve 1 of *right* leg, curve 2 of *left* leg.

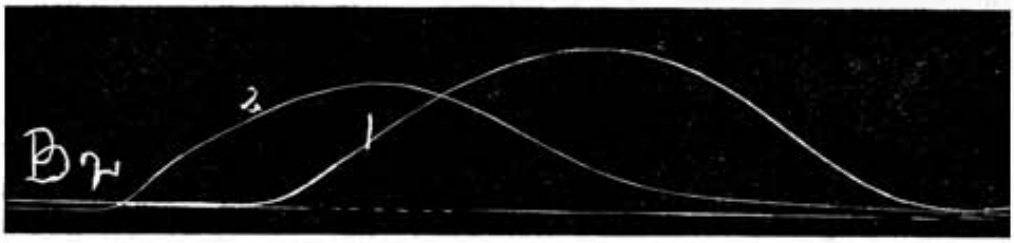

Fig. 3. Experiment B 2.

Frog. Acute experiment. *Right* sympathetic chain extirpated under narcosis of ether from N. IV to N. XI inclusive. Curves registered 32 minutes after resection. Mechanical stimulation of the spinal cord far above the origin of the roots of the legnerves. Loading of the muscles about 12 g. Curve 1 of *left* gastrocnemius, curve 2 of *right* gastrocnemius.

Wherever it occurs with degenerated endplates, at the same time another plausible genese of that top, to which I alluded [1]) before but which I already thought improbable, appears to be inconsistent.

In the acute experiment one might always suppose that owing to the muscle contraction indicated by the first top, the undegenerated sympathetic endplates in the acute experiment are stimulated in the muscle itself and thus cause the second top by secondary peripheral stimulation.

When we take into consideration all the facts published until now on the tonus question in connection with the double innervation of the striped muscles — which VAN RIJNBERK neglected — we come to quite a different view from the one VAN RIJNBERK has given us in his table. I will first reproduce the table of VAN RIJNBERK, then a similar one, which in my opinion offers the right data in this respect. Several of the extraordinary altogether enigmatical contradictions from VAN RIJNBERK's table have disappeared in my table.

Table of VAN RIJNBERK on p. 740, Archives néerlandaises l.c.

	Chimisme, augmentation de créatine.	Innervation.		Type du tonus.	
		Sympatique.	Muscolo-motrice	Plastique.	Contract
Rigidité de décérébration	+	cert. pas	+	cert. pas	+
Rigidité cadavérique	+	+		+	
Tonus de Brondgeest	+	+		+	+
Tonus de raidissement	+	?	+		+
2e sommet de vératrine.	+	cert. pas	+	cert. pas	+
Contract, chaleur.—Ca Cl_2 . . .	+	pas examiné.			
Tonus du froid	+				
Nez de Funke	pas examiné.	+		+	

Right table in my opinion.

	Chimisme, augmentation de créatine.	Innervation.	
		Sympatique.	Musculo-motrice.
Rigidité de décérébration	+	—	+
Rigidité cadavérique	+	—	+
Tonus de Brondgeest (*tonus méchanique*)	+	—(?)	+
Tonus de raidissement (tonus volontaire)	+	pas examiné.	+
Nez de Funke	pas examiné.	—	+

I left out the other facts, mentioned in the columns of the table of VAN RIJNBERK,

[1]) D. DE B. Ueber die Enthirnungsstarre u.s.w. Folia Neurbiologica, Band 7, 1913, p. 653 and 654

which I reproduced here. The forms of muscle-shortening indicated in these, perhaps or even probably arise from stimulation of the muscle-substance itself, so they have a muscular origin, in which the nervous system does not play any part. I left out the columns on the two types of tonus after LANGELAAN, because his division does not agree in my opinion, with several physiological facts. (See the criticism in my communication on muscletonus in PFLUGER's Archiv, Bd. 166, p. 163—165). I put the? in the second column of my table referring to the initial hypotonus in the acute experiment (DUSSER DE BARENNE—VON BRÜCKE).

Although it has appeared that none of the views uttered by DE BOER in this question is right, I have still tried in some other experiments to obtain proofs in favour of the supposed connection between muscle tonus and sympathetic innervation. My reasoning was the following: Supposing that the sympathetic nervous system has something to do with the mechanical muscle tonus, with the inward support of the muscles, then we might expect that some proof of this will appear in the musclecurves of fatigue or in curves illustrating the origin of tetanus by stimulation of increasing frequency. The result of these experiments was however quite a negative one, i.e. neither in the acute experiment, nor in the chronic one with degenerated sympathetic endplates, was there any essential difference in the muscle curves of the 2 gastrocnemii, of which one was deprived of its sympathetic innervation.

In the acute experiments the two largest ventral roots of the Nn. ischiadici were put on the electrodes, to stimulate the nerves centrally of the sympathetic chain aiming to avoid the post ganglionic neurones from being stimulated. In the chronic experiments the Nn. ischiadici were stimulated in the abdomen.

Small differences between the 2 curves of fatigue were perceptible, but these did not point in all cases in the same direction. In some cases the "Verkürzungsrückstand" in the muscles deprived of their sympathetic innervation was less evident than in the normal gastrocnemius. In other cases just the opposite took place. Besides, curves, taken as a test, of the 2 gastrocnemii of normal frogs, often showed similar small differences. It is noteworthy that all precautions were taken in these experiments to obtain a great regularity and equal intensity of the stimulations. I used therefore an induction apparatus with the usual waterwashed mercury contacts after KRONECKER. A very considerable resistance was interpolated in the secondary circuit (120.000—150.000 Ohm). The stimulations were given by a metronome. Thanks to all these precautions the curves generally showed a beautiful regularity. The stimulations were always either make — or break — induction shocks; the impulses of contrary direction were eliminated by the well-known method of PFLÜGER.

Also in similar experiments on the genese of tetanus, no essential differences pointing in one special direction between normal frog muscles and those deprived of their sympathetic innervation, could be observed.

We come therefore to the conclusion that until now not a single experimental fact exists, pointing clearly to a direct connection between the mechanical tonus of the muscles in the sense of BRONDGEEST, and the sympathetic nervous system. As regards to the initial hypotonus occurring in my experiments, the solution of this question ought to be given by further experiments. Special attention ought to be drawn to the fact already mentioned, that this hypotonus in the experiments of v. BRÜCKE disappears already some days after the extirpation of the sympathetic. At all events the communication of VON BRÜCKE has considerably weakened DE BOER's theory. This as regards the mechanical muscle tonus.

I have now to refer briefly to the chemical muscle tonus. G. MANSFELD and A. LUKÁCS [1]) communicated experimental facts from which they derive the existence of a so-called chemical muscletonus, by which term is expressed the view that striped muscles would have a certain amount of metabolism, also when they are at rest. This metabolism would be under the influence of the sympathetic nervous system. At first I thought [2]) that the experiments, published by these investigators, were not convincing, and lately I briefly explained [3]) my former objections against them

Since I have come to the conclusion that the criticism given by me is not sound, I recall it. All the same, the authors might have based their result even better, if they had made direct gasanalyses of the blood streaming to and from the muscles concerned. If the result of these analyses should confirm their former results, only then there could be no more doubt with regard to the accurateness of their result [4]).

The objection might yet always be raised against the respiratory analyses executed on the whole animal, that their result might be dependent on the fact, that by the extreme vaso-dilatation in the hind part of the body of their animals, too little blood remained in the fore part of the body, to preserve a fit exchange of gas in the muscles there, so that the respiratory metabolism might

[1]) l.c.

[2]) Pflüger's Archiv. Bd. **166**, 1916, p. 152.

[3]) Archives Néerlandais de Physiologie, tome II, 1918, p. 177.

[4]) A similar method as the one used by LANGLEY and ITAGAKI for their experiments on the oxygen use of denervated muscle, came into consideration (Journal of Physiology, **51**, 1917, p. 202).

considerably be lessened by too small an exchange of blood within these muscles. This factor eventually might have lowered the total gasexchange of their animals, as has been shown by their experiments.

Whether this objection has any ground cannot be made out without experiment, but it proves anyhow, that the experiments by MANSFELD and LUKÁCS are as yet not indisputable.

Until now we always accepted as a fact in all the experiments and speculations communicated, that the sympathetic nervefibres of BOEKE are centrifugal sympathetic nervefibres, a supposition for which several very evident histological arguments might be cited, but which has not been proved, as I said already once more.

This has been proved lately by a research ad hoc by Prof. BOEKE and me and besides by some similar experiments, made independently of us by AGDUHR.

If those nervefibres of BOEKE were indeed centrifugal sympathetic nervefibres, then it ought to be possible to preserve these in "pure culture" in the striped muscles, by section of the ventral nerve roots leading to one or more muscles, and extirpation of the corresponding spinal ganglia. After this section all the cerebro-spinal motor nervefibres with their so-called endplates of KÜHNE together with all the sensory fibres and organs in the muscles concerned ought to degenerate.

Granting that BOEKE's fibres are centrifugal sympathetic nervefibres, whose praeganglionic neurones have their origin in the spinal cord, leave the cord with the ventral root and terminate round the cells of the post-ganglionic neurones in the ganglia of the sympathetic chain those fibres of BOEKE ought to remain unaltered in a similar experiment. A look on the following scheme illustrates the conception on which these experiments are based. (Fig. 4).

The intercostal muscles of dog and cat have served as object for this experimental histological investigation, because the metameric arrangement has been best preserved in these muscles. There is no fear here for confusion caused by the plurisegmental innervation. The result of these experiments has been, that the nervefibres and endplates of BOEKE remained intact in the muscles between the ribs. All the motor cerebro-spinal nervefibres and endplates, as well as the sensory muscle-organs had disappeared.

Numberless amyelinic axiscylinders were preserved in the peripheral nerves (intercostal nerves) and beautiful accessory nervefibres and endplates of BOEKE in the muscles. By this result it has been proved that these nervefibres are indeed *centrifugal* sympathetic nervous systems.

AGDUHR obtained the same result with the muscles of the hindleg of the cat by section of the peripheral nerves distal of the spinal

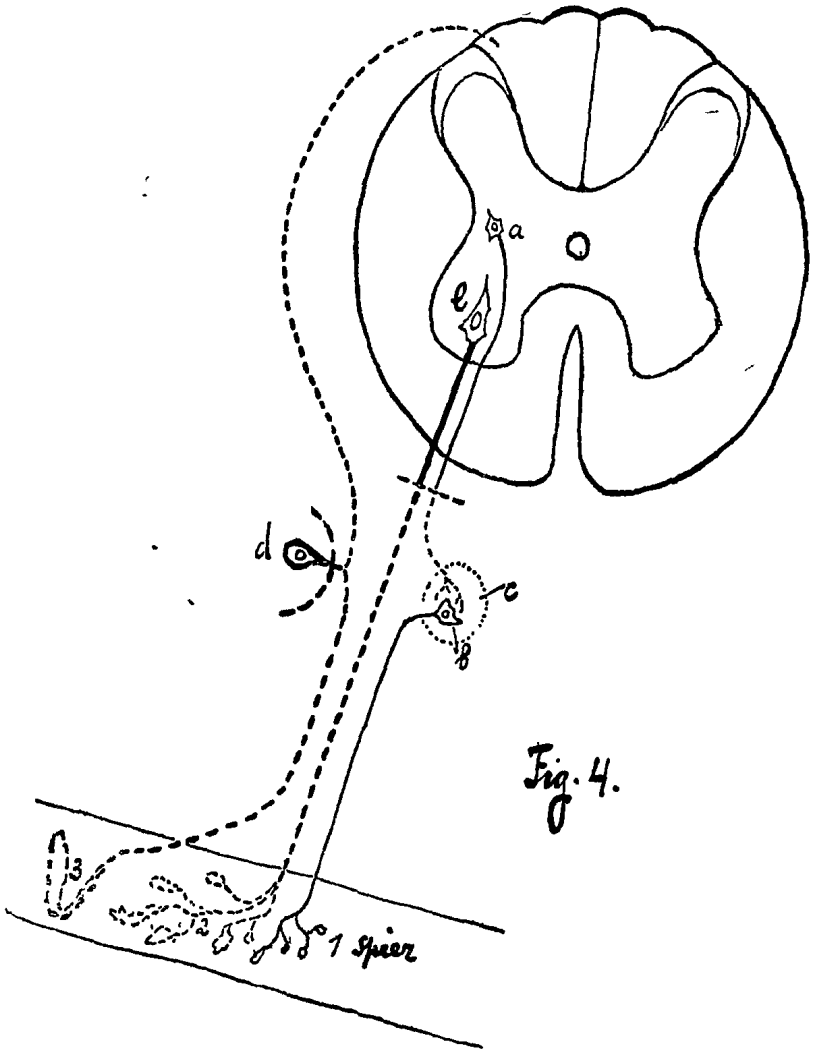

Fig. 4.

a = nervecell of the praeganglionic sympathetic neurone.
b = nervecell of the postganglionic sympathetic neurone.
c = ganglion of the sympathetic chain.
d = the spinal ganglion cell.
the degenerated nervefibres have been drawn in a blocked line.
1 = accessory endplate of BOEKE, preserved in "pure culture".
2 = degenerated endplate of KÜHNE (the ordinary motor endplate) (disappeared).
3 = degenerated sensory organ in the muscle (disappeared).

ganglia, but central of the origin of the rami communicantes grisei. [1])

The question that arises is consequently: What is the function of the fibres and accessory endplates of BOEKE?

[1]) See the foregoing communications.

After all we know about it, it is very improbable that they have anything to do with the mechanical muscletonus, known as the BRONDGEEST tonus. It is very probable that this one is exclusively due to the simple motor nervefibres. While considering this, the "chemical muscletonus" occurs to us, the existence of which and its dependence on the sympathetic nervous system, if not proved, is certainly not made unplausible by MANSFELD and LUKÀCS. When we realize these two hypotheses, most of the difficulties and strange contradictions, created by DE BOER's theory, which are evident in VAN RIJNBERK's table, disappear.

By the formula, just mentioned, the mechanical muscle tonus being governed by the cerebro-spinal nervefibres, the chemical one by the centrifugal sympathetic system of BOEKE, these difficulties disappear altogether and with them an important factor of confusion has been done away with. VAN RIJNBERK reproached me for having contributed only critical work with negative results; nobody better than I myself realize this; yet I believe that this work was necessary and I find the best argument for this in the two preceding hypotheses. I hope that these hypotheses will shortly be based on indisputable experimental facts. In my opinion everything points to it that this will be highly probable. I shall be the last to maintain that by these facts our knowledge of the nature of the tonus of the striped muscles has been much deepened. What the tonus really is, is as obscure and mysterious as before.