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AFFERENT IMPULSES IN THE CAROTID SINUS NERVE (NERVE OF HERING) DURING ASPHYXIA AND ANOXÆMIA.

By J. YULE BOGUE and G. STELLA.

(*From the Department of Physiology, University College, London.*)

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The reflex enhancement of respiration observed by Heymans, Bouckaert and Dautrebande [1930] when the blood in the carotid sinus was hypercapnic or anoxæmic, makes it very probable that under such conditions, augmentor impulses pass up to the respiratory centres. Up to the present, however, in Hering's nerve (whose section abolishes these reflexes) only impulses coming from the stretch receptors of the sinus have been definitely observed [Bronk, 1931; Bronk and Stella, 1932 *a*, *b*; Heymans and Rijlant, 1933]. Afferent discharges which could not be ascribed to the action of endosinual pressure and appeared in circumstances in which the augmentor impulses would have been expected, were sometimes noticed. Thus Bronk [1931 (personal communication)], while recording from the intact nerve of the rabbit, occasionally observed a discharge produced as the result of anoxæmia, which persisted after death of the animal, *i.e.* when the systemic blood-pressure had dropped to zero. Recently Heymans and Rijlant [1933] also described an increased activity in Hering's nerve during asphyxia of the rabbit, which they were unable to attribute to any difference in the blood-pressure. In neither case was any evidence given which excluded the possibility that these discharges were merely indicative of an irregular activity of the stretch receptors themselves, abnormally excited by the conditions of the blood. This objection is a very serious one, especially in view of the work of Matthews [1933], who found that the stretch end-organs of mammalian muscle discharge spontaneously, often at a very high frequency as the result of occlusion of the circulation. He also observed that such a spontaneous discharge could be obtained in the decerebrate animal by occluding the trachea long enough for convulsions

to set in. Matthews is inclined to ascribe these results to lack of oxygen in the end-organs, and it will be seen that the conditions under which Bronk, Heymans and Rijlant observed the discharges referred to above might have been such that the stretch receptors of the carotid sinus were reacting in a similar manner.

In spite of these previous observations, it was still quite possible that the augmentor impulses were not easily measurable. A hint of this possibility can be gathered from the work of Bronk and Stella [1932 *a*, *b*] on the carotid sinus nerve of the rabbit, when all the single fibre preparations studied happened to be of the stretch-receptor type. One of us (G. S.) obtained similar findings in the case of the dog. The carotid sinus

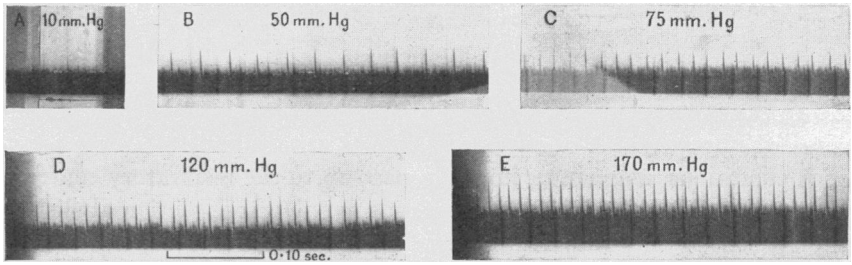

Fig. 1. Carotid sinus preparation of the dog, artificially perfused with acapnic blood. The nerve has been cut down to a few fibres, one of which gives well-measurable impulses. It shows the rhythm of the discharge in a single end-organ for five increasing degrees of sustained intrasinual pressure. Time marker, 0·10 sec.

was then removed from the animal and artificially perfused [Stella, 1931][1]. In severing most of the terminal subdivisions of the nerve of Hering the latter remained in connection with only a few end-organs of the sinus; such end-organs always happened to belong to the stretch type, *i.e.* gave responses which were in direct relationship with the endosinual pressure, as shown in Fig. 1. The appearance or disappearance of impulses associated with alterations in the blood perfusing the sinus which was either acapnic or in equilibrium with 10 p.c. CO_2 in air, was therefore not observed.

In view of the scanty and conflicting evidence we attempted to reinvestigate the question. A preliminary note has already been published [Bogue and Stella, 1934].

[1] Unpublished experiments carried out at the Physiological Laboratory, Cambridge, during the tenure of the George Henry Lewes Studentship (1931), and under the supervision of Prof. E. D. Adrian [see also Adrian, 1931].

Method.

It follows from what has been said above that the presence of fibres in the nerve of Hering, connected with the stretch receptors, whose behaviour in asphyxia and anoxæmia is not clearly known, makes it very difficult to analyse and interpret any changes in the total activity of the nerve which might be recorded in an animal under such conditions (*i.e.* asphyxia and anoxæmia). If, on the other hand, the stretch receptors could be disconnected from the nerve, without interfering with the innervation of the chemical receptors, the research would be greatly simplified.

Heymans and Bouckaert [1932] verified the prediction of De Castro [1928] that chemical end-organs might be found in the carotid body. According to them the chemical sensitivity of the sinus is in fact due mainly, at any rate, to the carotid body. If this is the case, then section of all the terminal branches of the nerve beyond the region of the carotid body should abolish most of, if not all, the impulses coming from pressure, and leave unaltered those elicited by the respiratory variations of the blood. Such experimental conditions were actually obtained in the present investigation. Cats were used under chloralose (0·085 g. per kg. intravenously), the carotid sinus was prepared, and the nerve of Hering freed from adherent tissue and cut centrally just below its junction with the glosso-pharyngeal.

By stripping the carotid at the bifurcation into internal and external, it was found that only one or two active fibres in the nerve were still connected with the stretch receptors. It might have been possible to go still further and cut off the few remaining fibres, but this would have been at the risk of damaging the chemical receptors and possibly disturbing their blood supply. On the other hand, the results obtained when there was still the moderate discharge of one or two end-organs responding to pressure, seemed clear enough to allow us to dispense with more drastic handling of the region.

The impulses were recorded in the usual way with a resistance-capacity amplifier and a Matthews' oscillograph. The asphyxia was caused by discontinuing the artificial respiration on animals with the chest open, or on animals deeply anæsthetized in which the breathing was very poor. Acute anoxæmia was induced by inhalation of pure nitrogen.

Results.

Anoxæmia and asphyxia were found to cause a discharge which under extreme conditions became very considerable. Fig. 2 A shows an example of this discharge. The discharge from the stretch receptors

consisted of only a few impulses appearing in rhythmic groups, coincident with the passive expansion of the sinus at each heart beat, as is also shown in Fig. 3 A. The magnitude of the discharge and its character indicate that many fibres were active, and there is no doubt that the largest action potentials were due to several fibres firing nearly synchronously. Therefore the possibility that this activity recorded during asphyxia or anoxæmia might be due to an irregular activity of the sinus, is very improbable.

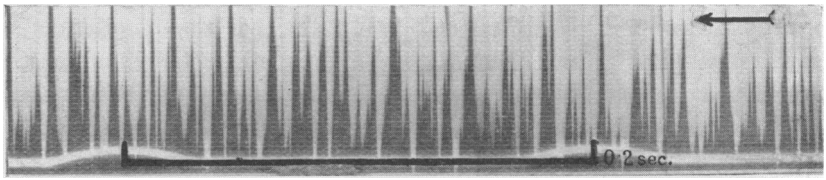

Fig. 2. Afferent discharge in the carotid sinus nerve of a cat during acute anoxæmia. The stretch receptors had all been denervated except one, whose discharge is not recognizable in the record. Time marker, 0·2 sec.

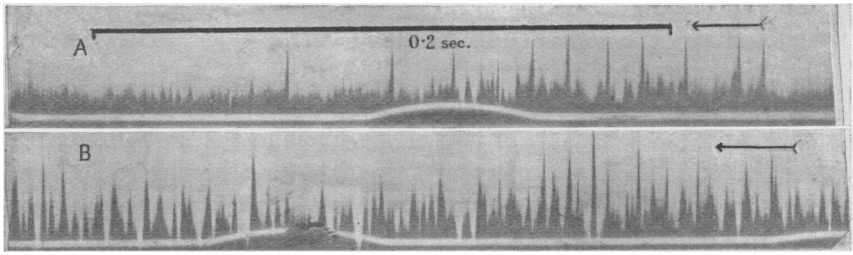

Fig. 3. In A the cat is well ventilated and there is a small outburst of fast impulses coinciding with the expansion of the sinus at the systole of the heart. In B the artificial respiration had been discontinued (chest open) and the animal was asphyxiating. It shows a large discharge of slightly slower impulses, besides those caused by the heart beat. Time marker, 0·2 sec.

The independence of the asphyxial discharge from the activity of those stretch receptors which were still connected with the nerve is still clearer when the discharges in Fig. 3 are examined, these having been recorded during an earlier stage of asphyxia. The fast impulses are seen in record A, and represent a systolic outburst from the stretch receptors, they are still recognizable in record B among a great number of new action potentials provoked by asphyxia. From Fig. 3 it appears that the impulses elicited by asphyxia have a slightly different appearance from

those coming with an increase in the endosinual pressure; the former appear to be slower. It is this difference in the appearance of the impulses caused by two different stimuli, namely, pressure and asphyxia, that makes it possible to follow the rhythm of those caused by pressure in record B. The difference is still more marked when listening to the loud-speaker, when the pressure impulses could be distinctly heard as sounds of higher pitch coming in groups at each cardiac systole. A still more marked difference in the two types of impulses can be seen in Fig. 4.

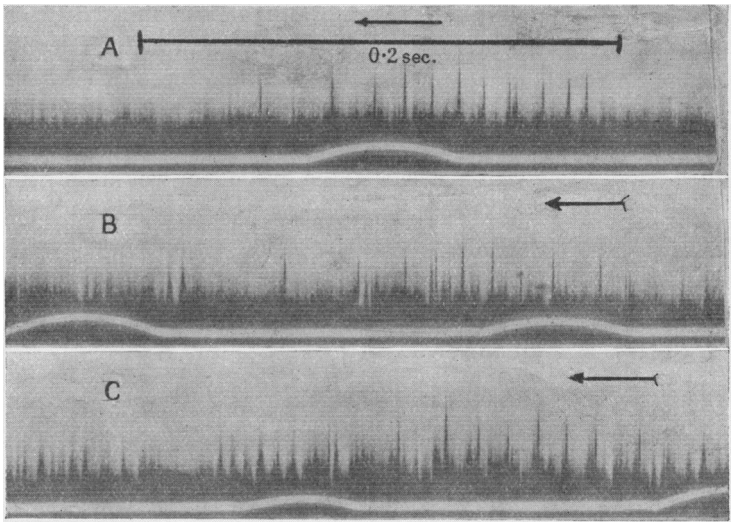

Fig. 4. A, taken while the cat was well ventilated, shows only impulses coincident with the heart beat. B and C were taken after discontinuing the artificial respiration and while the asphyxial discharge was just beginning to develop. A fresh type of impulse is now appearing in no relation with the heart cycle. Time marker, 0·2 sec.

In record A the animal is being well ventilated, under artificial respiration.

Apart from a group of fast impulses which were coincident with each cardiac systole, there is no sure sign of any other measurable activity in the nerve. The artificial respiration was then discontinued, and as soon as the first signs of fresh activity were noticed record B was taken, and immediately afterwards record C. The impulses caused by asphyxia are definitely smaller and of longer duration than those from pressure. This same difference between the two types has been observed in all records in which the discharges were small. There is no doubt, however, when the

discharge is larger, that some of the impulses caused by asphyxia and by anoxæmia are much bigger than those shown in Fig. 4, perhaps of the same order as those caused by pressure.

No definite difference could be found between the effect of asphyxia, as compared with that resulting from anoxæmia, either at the onset or in the later stages.

The character of the discharge during asphyxia and anoxæmia is entirely unaffected by variations in the endosinual pressure. Partial obstruction as well as complete occlusion of the common carotid artery had also no appreciable effect. If the animal was killed (by cutting through the heart) while the "chemical" discharge was on, it continued for a long time without any noticeable modification. In two cases in which observations were continued for 20–30 min. after death, it still continued practically undiminished. If, on the other hand, the animal was killed while being well ventilated, the first effect was simply a cessation of the systolic groups of single impulses; then small impulses began to appear of the type shown in Fig. 1 B, C. These gradually increased in number until within ½–1 min. the discharge became about as great as that produced by acute anoxæmia in the living animal.

Discussion.

With the above experimental conditions the possibility that the asphyxial discharges represented an irregular activity of the stretch receptors in the sense described by Matthews [1933] for the nerve-endings of mammalian muscle was definitely excluded. Moreover the peripheral ends of the cut fibres (from the stretch receptors) were, of course, superficially placed, practically in contact with air, and it seems difficult to believe that the asphyxia or lack of oxygen of the circulating blood might have caused them to give injury impulses [see Adrian, 1930]. Besides, the dropping of warm Ringer on the preparation had no evident effect on the discharge.

The impulses apparently originate in the carotid body, a fact which, when taken together with their appearance when the conditions of the blood were such as would have produced a more active respiration, point in favour of the assumption that they are the impulses responsible for the reflex increase of respiration found by Heymans, Bouckaert and Dautrebande [1930]. In the light of the present work, there seems to be little doubt that part, if not all the discharges observed by Bronk [1931], and by Heymans and Rijlant [1933] were actually of the same

nature as those observed here, as the authors had suggested. The absence of impulses on the other hand, other than those elicited by pressure in the single-fibre preparation by Bronk and Stella [1932 *a*, *b*], and by one of us in the dog (G. S.), may be explained by assuming that, in the process of cutting down to a single fibre, the chemical receptors were denervated.

Summary.

1. The afferent activity caused by some chemical respiratory conditions of the blood has been investigated in the nerve from the carotid sinus (nerve of Hering), after severing most of its connections to the end-organs sensitive to stretch.

2. Asphyxia and anoxæmia, cause the appearance of a fresh type of impulses. The significance of these impulses, *i.e.* their relation to the reflex increase in respiration described by Heymans, Bouckaert and Dautrebande is discussed.

3. The origin of these impulses is apparently in the carotid body.

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