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Effect of Vagus on the Monophasic Action Potential of Auricular Muscle.

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A turtle auricular strip is deeply immersed in a large volume of Ringer's solution. Arrangements are made for unipolar recording of the action potentials. Non-polarizable electrodes are used in conjunction with a Cambridge All-Electric Electrocardiograph. A drop of mecholyl (acetyl-beta-methylcholine chloride; $1:10^4$) is placed on the tissue near the tip of the recording electrode. A stimulus is now applied to one end of the strip and a triphasic curve is recorded which looks like the membrane current curve of nerve. If one performs two successive integrations on this curve, or uses the graphical method recently described (Churney, Ashman, and Byer[1]), the monophasic action potential curve may be obtained. This monophasic curve resembles that of nerve and differs from that of the uninhibited auricle in at least two respects: (1) the descending limb characterizing the repolarization process is convex towards the time axis rather than concave; and, (2) its duration is shorter. By means of the suction electrode[2] one can experimentally verify this theoretically derived monophasic curve.

Another method for studying these phenomena, and one which yields additional information, is as follows. A cotton wick electrode soaked in isosmotic potassium chloride solution is fixed to the apex of the left auricle. The other electrode is placed either on the surface of the left auricle, or in the body cavity. The left vagus is exposed in the neck and prepared for stimulation.

Recording with the KCl-treated electrode on the auricle in conjunction with a remote electrode lends itself, we believe, to a very simple interpretation. Almost surely we are recording the potential changes of a ring of injured cells whose inner surfaces are in electrical communication with the KCl-treated lead. We find a ready interpretation of our results by treating the situation as though it were a single spherical cell, one side of which has its charges partially or entirely wiped out. On, or close by, this latter surface is the recording electrode; the other being remote.

The result of vagal stimulation on the auricular monophasic curve is shown in Fig. 1. In addition to showing clearly the effects mentioned already, the "spike" voltage is seen to be greatly reduced. (The quantitative aspects of the fall and recovery in the magnitude of the spike are of no consequence for the moment). So, even though there is only a very slight increase in the threshold of excitation (Ashman and Garrey[3]), provided the inhibition is partial, the action currents originating in the sinus give rise to potentials in the auricle which are below normal. This record, as well as others obtained from linear strips treated with mecholyl, shows that the monophasic action potential during vagal stimulation is not associated with a change in the level of polarization of the resting membranes. We have never observed a Gaskell effect.

The question now confronting us is this. Is the decrease in spike voltage real, or only apparent? More specifically, is it associated with a partial depolarization of the individual auricular muscle fiber, or does it result from the irresponsiveness of various fibers? Early investigators (Gaskell,[4] Rossbach,[5] and oth-

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1 Churney, L., Ashman, R., and Byer, E., *Am. J. Physiol.*, 1948, **154**, 241.

2 Wiggers, H. C., *Am. J. Physiol.*, 1937, **118**, 333.

3 Ashman, R., and Garrey, W. E., *Am. J. Physiol.*, 1931, **98**, 109.

4 Gaskell, W. H., *J. Physiol.*, 1880, **3**, 48.

5 Rossbach, M. J., *Arch. f. ges. Physiol.*, 1882, **27**, 197.

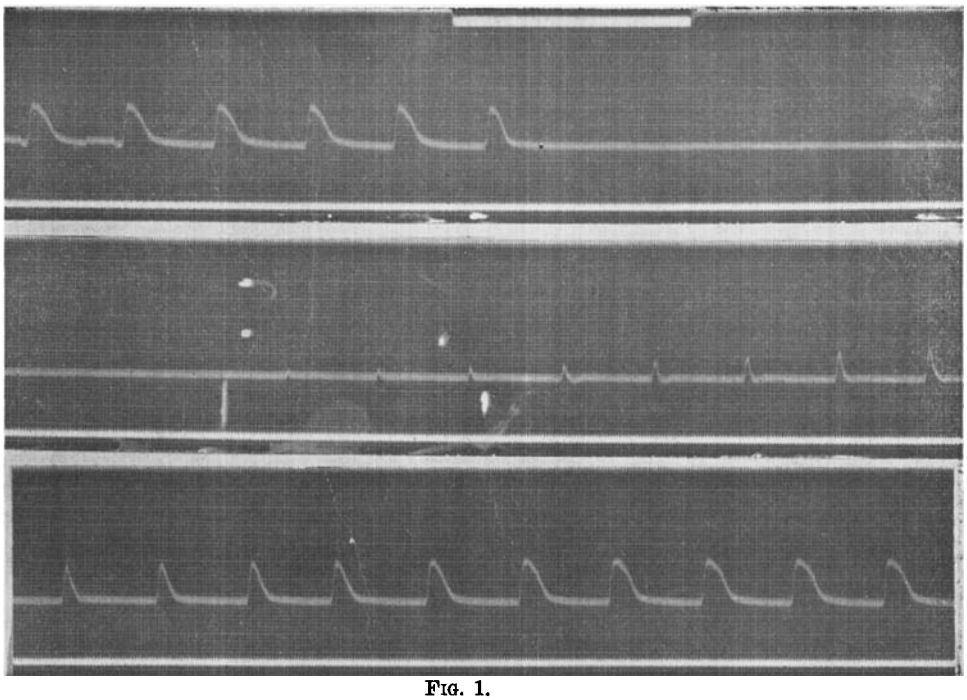

FIG. 1.

Effect of vagal stimulation on the monophasic action potential records of turtle auricular muscle. One electrode is on the KCl-treated apex of the left auricle, the other on the uninjured surface. The ventricle has been tied off to prevent its beating. Upper signal: left vagus stimulated faradically. Calibration: 3 millivolts.

ers) definitely assumed that the negative inotropic effect is the result of the diminished force of contraction of the entire syncytium, but without any real proof. See, too, the review of Adrian.[6] Concerning the reality of the modified spike potential itself there can be no doubt, since the theoretically predicted triphasic volume conductor curve is experimentally recorded.

Now there is no doubt that under some conditions mecholyl can cause blocking, and so the decrease in spike magnitude could be apparent only. However, at least four lines of evidence support the alternative viewpoint and are incompatible with the blocking concept. First, we recall the observation that there is a drastic change in the *form* of the monophasic action potential curve. Furthermore, there appears to be a strict association between the spike height and the shape of the recovery limb (Fig. 1). Not only is the convexity (towards the time axis) the more pronounced the less the apparent degree of depolarization, but the convexity appears *pari passu* with the decrease in spike magnitude following vagal stimulation, and does not become reversed during recovery until the spike is of full height, or very nearly so (Fig. 1). Secondly, we have confirmed the well known observation that vagal stimulation shortens the absolute refractory period of partially inhibited auricular muscle (Gilson[7]). There is some evidence that the less the spike height, or the shorter the duration of the electrical complex, the greater the percentage shortening of the absolute refractory period. With a decrease in spike amplitude to 17.9% of the original value, the "absolute refractory period" (as measured from the beginning of the spike to the signal of the applied stimulus) fell to at most 35.4% of its value for the unatropinized muscle. According to Asher and Scheinfinkel,[8] acetylcholine also shortens the absolute refractory period of nerve.

[6] Adrian, E. D., *Ergeb. d. Physiol.*, 1933, **35**, 744.

[7] Gilson, A. S., Jr., *Am. J. Physiol.*, 1935, **112**, 610.

Thirdly, we cite the finding of Gilson[9] that there is a very great increase in accommodation of turtle auricular muscle following vagal stimulation. If one defines accommodation in the most general terms: namely, as an active resistance of the tissue to depolarization, then this phenomenon may be the excitation counterpart of the decrease in spike voltage and accelerated repolarization seen in the electrograms.

Finally, insofar as the duration of the monophasic action potential curve and the absolute refractory period are measures of the length of the depolarized zone,[10] we should expect this length to be considerably reduced by vagal stimulation. Some idea of the order of magnitude of this reduction may be calculated as follows. From diphasic records of linear strips in air the speed of conduction may be taken, roughly, as 0.5 m./sec., though this may be a slight underestimate. At room temperature (30°C) the duration of the monophasic curve of the uninhibited muscle is about 0.8 sec. The depolarized area, by far the greater part of which is in the state of repolarization, is therefore 40 cm long. The duration of the shortest monophasic curve following vagal stimulation is 0.04 sec. (Fig. 1), and, since there is no apparent change in conduction speed, its length is 2 cm.

Now, if the decrease in spike amplitude is real, the degree of depolarization of the inhibited muscle, as well as its length, must be very much less than that of normal, uninhibited muscle. If the extent of depolarization is not different, then, leading from the injured to the uninjured surface, a decrease in the diameter of the electrode on the uninjured surface should give a considerable increase in the percentage amplitude of the spike of the inhibited muscle. The fact that no such increase was found may be taken as further evidence that the decrease in spike height following vagal stimulation is associated with a partial depolarization of the individual heart muscle fiber.

Summary. The effects of vagal stimulation on the form of the monophasic action potential of auricular muscle are listed along with the technics for demonstrating them. Evidence is presented for the viewpoint that auricular muscle, following vagal stimulation, acts like a single cell capable of giving graded electrical, as well as mechanical, responses.

8 Asher, L., and Scheinfinkel, N., *Z. Biol.*, 1929, **88**, 540.

9 Gilson, A. S., Jr., *Am. J. Physiol.*, 1939, **127**, 333.

10 Lloyd, D. P. C., in Fulton's revision of Howell's Textbook of Physiology, Philadelphia, 1941.

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Failure of Rutin to Decrease the Mortality of Acute Ionizing Radiation Illness in Mice.*

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Rutin, a crystalline rhamnoglucoside of quercetin, has been reported to influence favorably the hemorrhagic syndrome of acute ionizing radiation illness in dogs.[1] It has been found to accelerate the healing of the skin lesions of rats induced by localized radiation injury.[2] It seemed desirable, therefore, to study the effect of rutin on the mortality of

* Project NM 007 039, Report No. 16, Naval Medical Research Institute, Bethesda, Md., August 19, 1948.

† The opinions or assertions contained herein are the private ones of the authors and are not to be considered as official or reflecting the views of the Navy Department or the naval service at large.

1 Rekers, P. E., and Field, J. B., *Science*, 1948, **107**, 16.