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VAGAL NERVE FIBRE ACTIVITY FOLLOWING MULTIPLE PULMONARY EMBOLISM

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A striking increase in the rate of breathing of goats commonly follows the intravenous injection of a suspension of potato starch, the grains of which lodge in the small vessels of the lung (Dunn, 1919). This respiratory acceleration is absent if the vagi have been divided, and Christie (1938) suggested that it might be caused by an increase in the activity of the fibres that respond to pulmonary inflation. The experiments described in this paper were designed to discover, first, whether an increased discharge of vagal stretch receptors did in fact follow the injection of potato starch; and secondly, whether the discharge of any other group of vagal afferent fibres was modified.

METHODS

Eight cats and one rabbit, prepared as indicated in Table 1, were used for the first series of experiments. The animals were artificially ventilated and were placed in a warm moist chamber. The cervical vagus was cut across and its peripheral end was dissected until only one active fibre remained. The second series of experiments was conducted on three spontaneously breathing decerebrate cats and one spontaneously breathing anaesthetized rabbit. The animals were placed in an airtight box maintained at constant temperature and fitted with a tracheal tube and venous cannula leading to the outside. The changes in chest volume were registered kymographically by a volume recorder connected with the inside of the box. The connective tissue sheath of one vagus was removed and strands dissected from the side of the nerve were placed on the recording electrodes.

A differential amplifier and cathode-ray tube of conventional design were employed. Arterial and venous pressures were recorded optically by a liquid filled system.

Starch, prepared by filtering a suspension of minced potato through four layers of surgical gauze, was mixed with 20 times its volume of 0·9% NaCl and was injected into a femoral or jugular cannula.

RESULTS

The vagal afferent fibres encountered most frequently in this work were those responding to inflation of the lungs by discharging a steady series of action potentials. In the first series of experiments the peak frequencies of discharge of these stretch endings were measured in animals artificially ventilated by constant volumes of air, and were found to be sensibly constant during control periods. Table 1 shows the results of measurements of peak frequencies before and after injections of potato-starch suspensions. No consistent changes were detected, and it is clear that the small random variations observed are insignificant.

TABLE 1. The effect of starch embolism on the activity of vagal stretch receptors

Preparation	Dose of starch (ml.)	Peak frequency Before	Peak frequency After	Difference
Cat-nembutal	10	87·7±4·6 (7)	84·2± 0·83 (3)	− 3·5
Do.	10	53·0±2·6 (3)	65·2±64·3 (3)	+12·2
Cat-chloralose	20	122·6±4·3 (6)	115·9± 9·7 (9)	− 6·7
Cat-decapitate	15	99 (1)	106 (1)	+ 7
Do.	5	152 (1)	169 (1)	+17
Do.	5	123 (1)	100 (1)	−23
Do.	5	98·3 (2)	89·5± 6·7 (4)	− 9·3
Cat-decerebrate	15	91 (1)	99 (1)	+ 8
Rabbit-nembutal	5	156 (1)	149 (1)	− 7
			Mean difference	−0·44±4·2 (9)

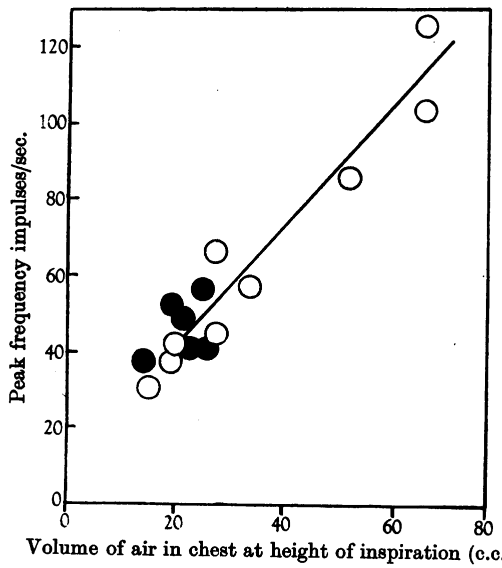

Fig. 1. Relationship between frequency of discharge of stretch receptor and height of inspiration. Spontaneously breathing decerebrate cat. Hollow circles before, black circles after starch injection.

In the second series of experiments the animals breathed spontaneously. Deep breaths were induced by the inhalation of carbon dioxide so that the rate of discharge of a stretch ending could be measured under widely varying degrees of chest expansion (Fig. 1). In conformity with the findings of Adrian (1933), a linear relation was found to exist between the volume of air in the lungs at the peak of inspiration and the maximum frequency of discharge. In the experiment represented by Fig. 1, the respiratory rate rose from 26 to 52/min., and the functional residual air decreased, following the injection of starch, but the properties of the ending did not change. Likewise in three similar experiments, one of which is represented by Fig. 2, there was no change in the sensitivity of the endings.

The stretch receptors are characteristically silent during expiration, but, in some, a few impulses are discharged at each heart beat. After the injection of starch, the stretch receptors frequently adopt such a rhythm, discharging 1–5 impulses at each heart beat throughout expiration.

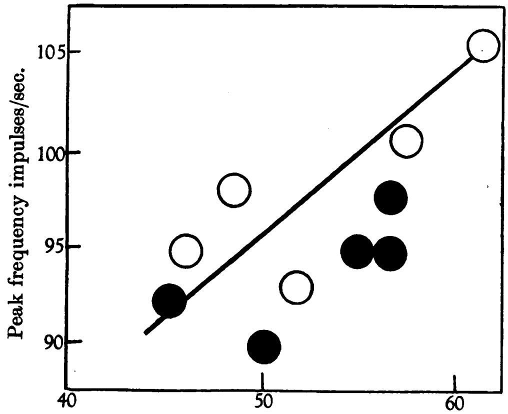

Fig. 2. Relationship between frequency of discharge of stretch receptor and height of inspiration. Another spontaneously breathing decerebrate cat. Hollow circles before, black circles after, starch injection.

A few fibres were encountered which discharged discrete volleys of impulses at each heart beat during both inspiration and expiration. Unlike the stretch receptors these endings do not respond to an artificial inflation by discharging a continuous series of action potentials, and their behaviour suggests that they are located on the walls of blood vessels. One bundle of fibres encountered in an artificially ventilated cat probably had a depressor function, for its behaviour suggested that the endings were located on the walls of a *systemic artery*. The discharge was systolic, paralleled the systemic arterial pressure, and was uninfluenced by respiration. After the injection of starch, the blood pressure fell and the activity of the bundle decreased. One fibre encountered in a freely breathing decerebrate cat appeared to correspond to an ending on the wall of a *great systemic vein*. Three volleys of impulses, apparently corresponding to the three waves of the venous pulse, were discharged at each heart beat. The discharge varied with the effective venous pressure, increasing with normal inspiration and artificial deflation, decreasing during normal expiration, and vanishing with positive pressure inflation. A great increase in the *a* and *v* wave volleys occurred after starch embolism corresponding perhaps to an increase in the venous pressure. The problem is complicated however by the fact that the venous pressure sometimes rose and sometimes fell. Two other venous fibres were encountered in cats and their discharge too was increased by the injection of starch. One fibre encountered in a freely breathing decerebrate cat seemed to respond to the *pulmonary arterial pressure*. A volley of 7 impulses

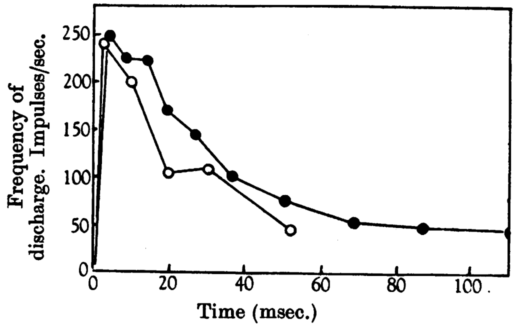

Fig. 3. Discharge of pulmonary arterial pressure receptor. The frequency of discharge declines in any given volley. Hollow circles before, black circles after injection of starch. The frequencies were calculated from the intervals between successive action potentials.

were discharged at each heart beat during inspiration, but only 1–3 impulses per beat during expiration. After the injection of starch the number of impulses in a volley, and the duration of each volley increased (Fig. 3). Such increases were probably related to a rise in pulmonary arterial pressure.

DISCUSSION

The only other direct study of vagal activity following pulmonary embolism of which the author is aware is that of Partridge (1935). In her paper the behaviour of two stretch endings was illustrated. One of these showed no increase in the rate of discharge, whilst the discharge of the other increased from 63 to 100 impulses/sec. As the activity of 13 endings investigated in the present work did not change significantly, it is difficult to believe that the rapid breathing that follows the injection of starch can be due to changes in stretch receptor sensitivity. Further evidence indicating that afferent fibres, other than those responding to pulmonary inflation, were responsible for the rapid breathing was obtained by Torrance (1947). He found that cooling the vagus until the stretch fibres were blocked, did not abolish the reflex respiratory acceleration of starch embolism. It is possible that fibres arising from endings on the walls of blood vessels may be important in this connexion. Three fibres were encountered which appeared to arise from endings on the walls of great systemic veins, a group for which Gernandt & Zotterman (1945) searched unsuccessfully. The discharge of this group and of a fibre apparently arising from an ending on a branch of the pulmonary artery was increased after the injection of starch. Nevertheless the problem cannot be regarded as solved. Unmyelinated fibres may be important, and the impulses produced would be too small to be detected by present techniques.

SUMMARY

The behaviour of single vagal afferent fibres has been investigated in cats and rabbits, in an attempt to discover the group responsible for the rapid breathing that follows potato starch embolism of pulmonary capillaries. It has been shown that, following embolism:

(1) The peak frequencies of discharge of single stretch endings in artificially ventilated animals show no significant changes.

(2) Stretch ending sensitivity in spontaneously breathing animals is unchanged.

(3) The discharge of some endings, apparently situated on the walls of blood vessels, is increased.

Many of these experiments were performed in collaboration with Dr D. Whitteridge with whom a short preliminary note was published (Walsh & Whitteridge, 1944). The author is indebted to Dr Whitteridge for many suggestions and much practical assistance, to Prof. Liddell for laboratory facilities, to the Christopher Welch Trust for a grant for electrical equipment and to Mr W. Austin for much technical assistance.

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