J. Physiol. (1952) 118, 509–519

A COMPARISON OF THE EFFECTS OF PULSATILE AND NON-PULSATILE BLOOD FLOW THROUGH THE CAROTID SINUS ON THE REFLEXOGENIC ACTIVITY OF THE SINUS BAROCEPTORS IN THE CAT

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(*Received* 3 *June* 1952)

It is not known whether the reflex inhibition of the vasomotor centre exerted by the carotid sinus nerves is solely dependent on the mean systemic blood pressure, or whether pulsations about this mean pressure themselves modify this afferent inhibition. As the intact circulation is pulsatile it seems important to answer this question, and the present experiments were performed with this purpose.

METHODS

Forty cats were used anaesthetized by intraperitoneal administration of chloralose and urethane (50 mg of chloralose + 250 mg of urethane/kg body weight) or of sodium pentobarbitone (60 mg/kg body weight). The trachea was cannulated. All animals were given heparin intravenously (5 mg/kg body weight).

Three types of experiment were performed.

Group I. One common carotid was dissected clear of the surrounding tissues from the level of the superior thyroid artery to that of the subclavian artery. The superior thyroid artery and the r. musculus dorsalis were tied but not cut; the presence of these arteries served to 'splint' the peripheral end of the common carotid artery and thus prevented drag on the carotid sinus during later manipulations. A specially shaped Y cannula was inserted into the common carotid artery and connected to a 20 ml. syringe containing 5 ml. of blood and 10–15 ml. of air, as shown in Fig. 1A. The syringe acted as an elasticity chamber; it could be excluded from the cannula system by means of a Halstead clip.

The carotid sinus nerve on the same side was dissected and cut centrally. A peripheral twig containing a few or one active baroceptor fibre was placed on saline-wick electrodes. By means of a resistance-capacity coupled amplifier the baroceptor impulse activity was registered on a cathode-ray oscillograph. The ipsilateral external carotid artery was cannulated and the end-pressure in the artery recorded by means of a condenser-manometer (devised by H. W. Ead) coupled to a second cathode-ray tube. Simultaneous photographic records were taken of the electroneurogram, sinus blood pressure and time marker. As the connexion between artery and manometer was of lead tubing, care was taken to avoid any stretch of the sinus by the cannula

system. Impulse activity in the baroceptor fibre was examined under conditions of pulsatile flow (elasticity chamber excluded) and non-pulsatile flow (elasticity chamber included), both types of flow occurring at the same mean blood pressure. By graded haemorrhages, the systemic blood pressure was lowered and the above comparison made at various levels of mean blood pressure. By altering the volume of air contained in the syringe, the degree of pulsation transmitted via the cannula to the carotid sinus could be varied.

Group 2. Both common carotid arteries were prepared and cannulated as in group 1. Both cervical vagosympathetic trunks were separated from the arteries between the superior thyroid and subclavian arteries. The aortic and vagosympathetic nerves were cut if required. In some experiments the carotid sinuses were not dissected; in others both external carotid arteries and both ascending pharyngeal arteries were tied, in order to exclude the entire contribution of the carotid arteries to the cerebral circulation. In all cases the carotid sinus nerves were kept intact. The systemic blood pressure was recorded from the femoral artery by means of a mercury manometer system arranged to write on a smoked drum. The reflex response of the systemic blood pressure was examined when the pulsatile flow through both sinuses was converted to a steady flow.

Group 3. One carotid sinus was isolated and perfused by means of a Dale-Schuster pump with oxygenated Ringer-Locke's solution at 38° C. The carotid sinus nerve was kept intact. An elasticity chamber was attached to the stem of a T-tube connected to the inlet cannula in the common carotid artery (Fig. 3A). By switching the elasticity chamber into the perfusion system, the pulsatile flow provided by the pumps could be converted at will into a steady flow at the same mean pressure. Sinus perfusion pressure (transmitted via a cannula in the external carotid artery) and systemic blood pressure from the femoral artery were graphically recorded via mercury manometer systems on a smoked drum. A comparison was made of the reflex effects on the systemic blood pressure of pulsatile and non-pulsatile sinus perfusion at the same mean pressure.

RESULTS

I. *Comparison of baroceptor activity during pulsatile and non-pulsatile flow in the carotid sinus*

Thirty preparations of few or single fibres of the sinus nerve were made and the effects of pulsatile and non-pulsatile blood flow on the electroneurogram were studied (Fig. 1B). The sinus blood pressure was recorded simultaneously. Different types of response were obtained. The details of the pattern of the discharge varied with the height and form of the sinus pressure. In general, with pulsatile flow through the sinus the baroceptor discharge was limited to the period of systole and early diastole. The frequency and number of the impulses set up during this period varied with the height of the blood pressure and the value of the pulse pressure. With the non-pulsatile flow the discharge was uniform and showed a lower frequency of impulses maintained steadily throughout the cardiac cycle. At certain levels of low blood pressure the pulsatile flow set up a sparse discharge but the non-pulsatile flow set up no discharge at all. These features are illustrated in Fig. 1C–H.

Fig. 1C shows the effects on the sinus pressure and the electroneurogram of transition from a pulsatile to a non-pulsatile flow. Inclusion of the elasticity chamber in the cannula system produced a marked reduction in the pulsations of the sinus pressure but the mean sinus pressure was maintained. A con-

spicuous change in the pattern of the electroneurogram occurred simultaneously. With the pulsatile flow the impulse discharge was restricted to groups of action potentials during systole and early diastole; with the non-pulsatile flow the discharge lasted throughout the cardiac cycle. The frequency

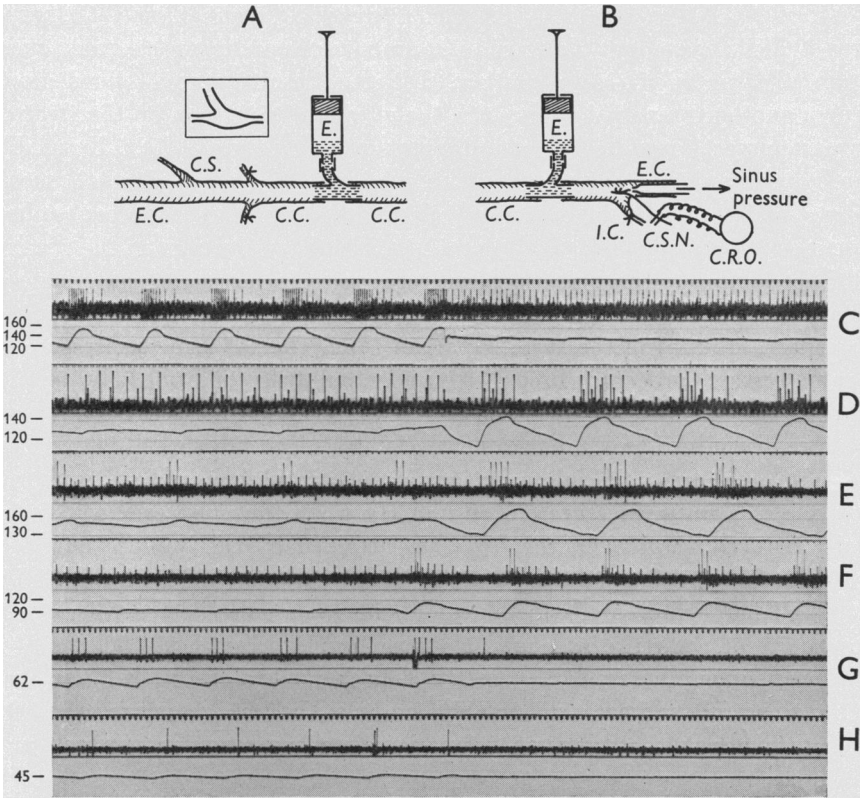

Fig. 1. A: the arrangement of cannula and syringe system in the common carotid artery. *E* = elasticity chamber represented by the syringe containing air. The plunger of the syringe is heavily greased to make the system leak proof. *C.C.* = common carotid artery; *C.S.* = carotid sinus; *E.C.* = external carotid artery. The inset figure shows the shape of the cannula employed. B: the type of experiment described in § I. *C.S.N.* = carotid sinus nerve; *I.C.* = internal carotid artery. Recording electrodes connected with cathode-ray oscilloscope (*C.R.O.*). Sinus pressure registered from external carotid artery. Each film strip shows time (50 c/s) sinus electroneurogram and sinus pressure, from above downwards. C: effect of transition from pulsatile to non-pulsatile sinus blood flow at a mean pressure of 140 mm Hg (animal 1). D: transition from non-pulsatile to pulsatile state at mean sinus pressure of 130 mm Hg (animal 2). E and F: both obtained from another animal (animal 3) and show transitions at mean sinus pressures of 150 and 95 mm Hg respectively. G and H: both obtained from animal 4 and show transitions at mean sinus pressures of 62 and 45 mm Hg respectively. The sinus blood-pressure calibrations in mm Hg for each record are shown on the left.

of the impulse discharge attained with the pulsatile flow during the systolic part of the cycle exceeded that obtained with the non-pulsatile flow. This was invariably the case with other fibre preparations.

The *total* number of impulses per cardiac cycle occurring during non-pulsatile flow through the sinus bore no constant relationship to that during pulsatile flow. In Fig. 1 C and D (obtained from two different animals) the nerve fibres studied show about the same total number of impulses per cardiac cycle during pulsatile or non-pulsatile flow. Different results were obtained, however, in another preparation in which the effects of transition on the electroneurogram were examined at two different mean pressures (Fig. 1 E and F). Two baroceptor units were discharging, one large and one small. At a mean pressure of 150 mm Hg the large baroceptor discharged 3–4 times per cardiac cycle during pulsatile flow. Inclusion of the elasticity chamber in the system failed to damp out the pulsations entirely, and the noticeable but reduced pulsations which resulted were each associated with two discharges from the baroceptor, grouped in the systolic part of the cycle. At a mean pressure of 95 mm Hg this baroceptor fired twice under pulsatile conditions and ceased to fire at all when the elasticity chamber was included in the system. Thus this fibre discharged two impulses per cycle at a mean pressure of 95 mm Hg during its exposure to the full pulsations of the carotid flow, and two impulses per cycle at a mean pressure of 150 mm Hg when the pulsations were artificially reduced. Moreover, the *frequency* attained by the impulse bursts is greater at 95 mm (full pulsation) than that at 150 mm (reduced pulsation). The small baroceptor fired steadily at about 14 impulses per cardiac cycle irrespective of the pulse pressure at a mean sinus pressure of 150 mm Hg. At a mean sinus pressure of 95 mm Hg it discharged in groups of 8 impulses limited to systole and early diastole during pulsatile flow, changing to steady firing throughout the cycle of 9 impulses per cycle under non-pulsatile conditions.

At mean pressures below 80 mm Hg, transition from pulsatile to steady flow caused a great reduction or total disappearance of impulse discharge. Fig. 1 G and H show this feature at mean sinus pressures of 62 and 45 mm Hg respectively.

II. *Reflex effects of pulsatile and non-pulsatile carotid sinus flows upon the systemic blood pressure*

Animals with both cervical vagosympathetic nerves intact. If both vagi and aortic nerves were intact, conversion of the pulsatile flow into a steady flow in both carotid sinuses produced no demonstrable change in the systemic blood pressure. If the aortic nerves were cut, however, leaving the vagosympathetic nerves intact, alteration from pulsatile to non-pulsatile conditions in the sinuses caused a reflex rise of systemic blood pressure. In the experiment

illustrated by Fig. 2B the rise was about 20 mm Hg. No perceptible change of heart rate or respiration occurred.

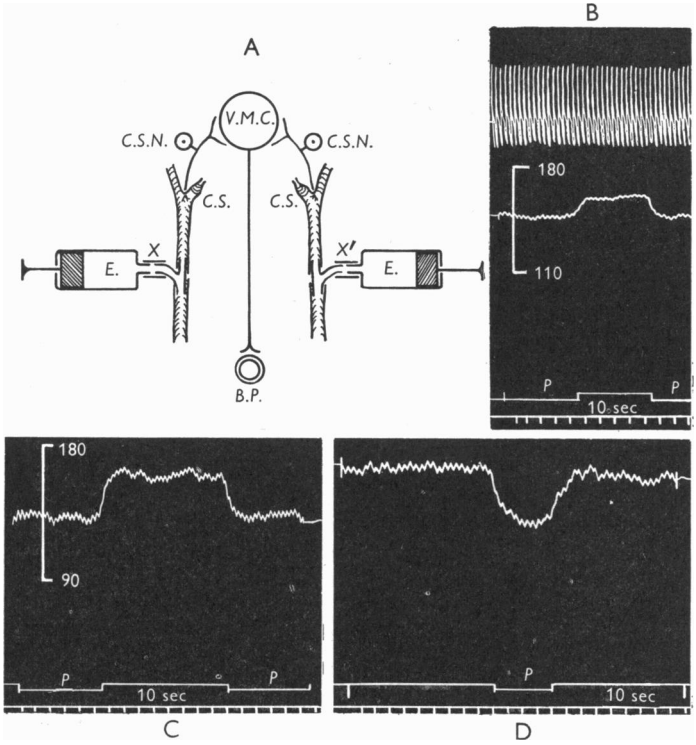

Fig. 2. A: scheme of the experiments described in § II. Both common carotid arteries were cannulated and the cannulae attached to syringes containing air. When the syringes were excluded by clips at the points X and X' the blood flow through the carotid sinuses was pulsatile. Removal of the clips converted the sinus blood flow to a non-pulsatile flow. Both sinus nerves were intact and exerted afferent inhibition of vasomotor discharge. Changes of peripheral resistance thereby induced caused changes of systemic blood pressure. *C.S.* = carotid sinus; *C.S.N.* = carotid sinus nerve; *V.M.C.* = vasomotor centre; *B.P.* = blood pressure. B: cat, 3·6 kg, sodium pentobarbitone anaesthesia. Both aortic nerves cut, vagi intact. Common carotid arteries cannulated as shown in A. Records from above downwards: respiration, systemic blood pressure, signal marker and time in 10 sec intervals. Note that the systemic blood pressure is maintained at a higher level when sinus flow is non-pulsatile (as shown by signal marker) than when it is pulsatile (*P*). Respiration is unaffected. C: cat, 3·3 kg, chloralose–urethane anaesthesia. Aortic nerves and vagi cut. Arrangements as in A. Note that the systemic blood pressure is higher during non-pulsatile sinus flow (shown by signal marker) than that during pulsatile flow (*P*). D: obtained from the same preparation, 30 min later. During this period the carotid sinuses were exposed to non-pulsatile flow, The high level of systemic pressure was maintained (cf. C), but conversion to pulsatile sinus flow (*P*) lowered the systemic pressure.

Animals with both cervical vagosympathetic nerves (including aortic nerves) cut. In this series, conversion of the pulsatile sinus flow into a non-pulsatile flow

caused a pronounced reflex effect on the systemic blood pressure, which rose 35–40 mm Hg (Fig. 2C). The higher level of systemic blood pressure thus produced was well maintained. Thus Fig. 2D was recorded 30 min after Fig. 2C was obtained; the sinuses were subjected to conditions of steady flow, throughout this period. Conversion to pulsatile flow lowered the systemic blood pressure to a level similar to that obtained under similar conditions in Fig. 2C.

In experiments in which respiration was also recorded slight stimulation of breathing was occasionally noted when the pulsatile flow through the sinuses was converted into a non-pulsatile flow. Such effects were inconstant, however. No changes of heart rate were observed and were not expected as the vagal efferent pathway had been cut.

The reflex effects on systemic blood pressure of altering the pulse pressure in the carotid sinuses were equally well marked whether the animal breathed air or oxygen. Animals in which both external carotid and ascending pharyngeal arteries were tied gave responses identical with those obtained when these arteries were patent.

III. *Reflex effects of pulsatile and non-pulsatile perfusion of one carotid sinus*

Fig. 3 shows the results of comparison of the reflex response of systemic blood pressure to pulsatile and non-pulsatile sinus perfusion at a series of mean perfusion pressures. The results are summarized in Table 1.

TABLE 1

Mean sinus perfusion pressure (mm Hg)	Mean systemic blood pressure (during non-pulsatile sinus perfusion) (mm Hg)	Mean systemic blood pressure (during pulsatile sinus perfusion (mm Hg)
0	160	160
15	160	130
80	160	110
135	115	88
240	83	83

Two main points arise from a consideration of Table 1 and Fig. 3: (1) at any given mean sinus perfusion pressure below 240 mm Hg, pulsatile perfusion is more effective in causing reflex hypotension than is non-pulsatile perfusion; (2) the threshold pressure within the sinus that will cause a reflex hypotension is less in the case of pulsatile perfusion than with non-pulsatile perfusion (see Fig. 3B–D).

At high sinus perfusion pressures (about 250 mm Hg) the two types of perfusion produced almost identical reflex responses (E, F).

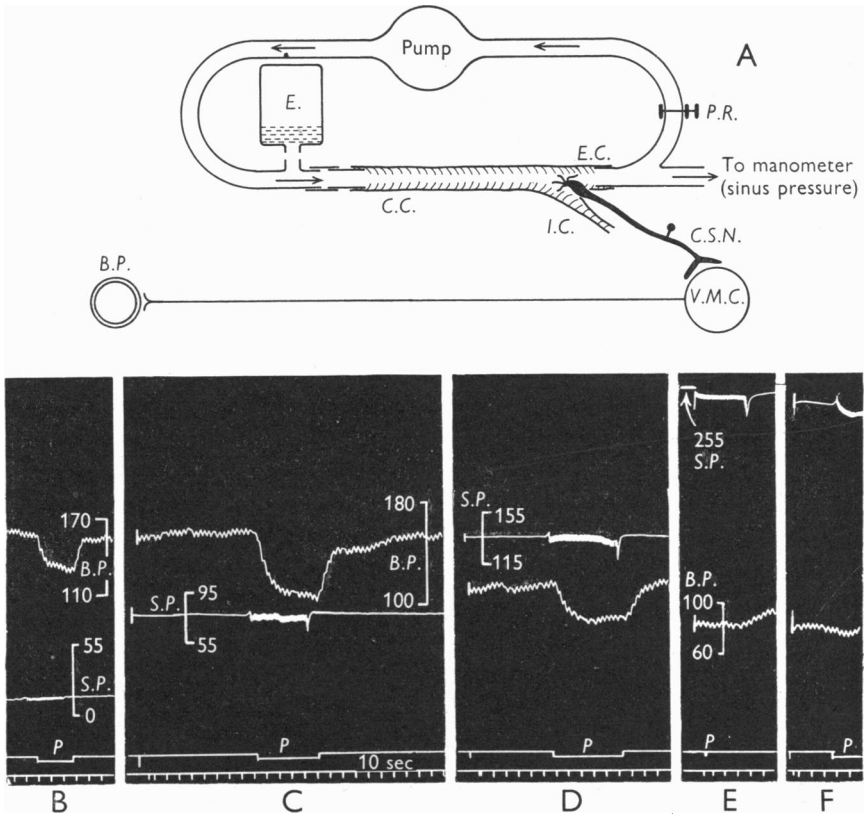

Fig. 3. A: scheme of the experiments described in § III. One carotid sinus was isolated and perfused by a pump. An elasticity chamber (*E.*) was placed on the inlet side of the perfusion circuit. Sinus pressure was recorded by a mercury manometer. Changes of sinus pressure caused reflex changes of vasomotor discharge and hence systemic blood pressure. *C.C.*, *E.C.* and *I.C.* = common carotid, external carotid and internal carotid arteries; *C.S.N.* = carotid sinus nerve; *V.M.C.* = vasomotor centre; *P.R.* = resistance on pump perfusion circuit; *B.P.* = systemic blood pressure. B–F: cat, 3·4 kg, chloralose–urethane anaesthesia. Right carotid sinus isolated and perfused. Left carotid sinus and both aortic nerves cut. Records from above downwards: systemic blood pressure, sinus perfusion pressure, signal marker, time in 10 sec intervals. Records show comparison of reflex effects of pulsatile and non-pulsatile sinus perfusion at mean pressures of 15, 80, 135, 240 and 235 mm Hg. *B.P.* = systemic blood pressure; *S.P.* = sinus pressure.

DISCUSSION

When a pulsatile flow through the innervated sinus regions is converted to a steady flow, the systemic blood pressure rises and remains at its higher level. This effect can only be shown clearly when the aortic nerves have been cut and is most evident when the remainder of the aortic arch afferent nerves have

been severed by section of the vagosympathetic trunks. The rise of systemic blood pressure which occurs on switching from a pulsatile to a steady flow through the sinuses is the reflex response to an alteration in the pattern of the impulse activity in the sinus baroceptor fibres. It is not due to concomitant changes in the cerebral blood flow as it occurs when such alterations have been prevented by tying the external carotid and ascending pharyngeal arteries. Similarly, the carotid chemoceptors are unlikely to contribute to the rise of systemic blood pressure produced by the alteration of conditions of flow in the sinus regions, for the effect can be equally well produced in animals breathing oxygen, when chemoceptor discharge is minimal. The change of systemic blood pressure probably represents an alteration in vasomotor discharge and therefore of peripheral resistance, as Kenney, Neil & Schweitzer (1951) have shown that sinus reflexes do not modify cardiac output significantly.

There are good reasons for believing that the difference between the reflexogenic activity of the baroceptors in the two conditions of sinus flow is even more striking than we have demonstrated. Introduction of the cannula into the carotid artery reduces the pulse pressure and smoothes the pulse wave-form in the pulsatile state. In addition, it is difficult to eradicate all traces of pulsation from the sinus blood pressure record by inclusion of the elasticity chamber in the system (e.g. Fig. 1E).

Our investigations of baroceptor impulse activity show that the impulse *frequency* occurring during pulsatile flow exceeds that seen during non-pulsatile flow, whatever may be the mean blood pressure at which the comparison is made. It appears, therefore, that the vasomotor centre is more effectively inhibited by the higher impulse frequency. Our results show that at mean pressures of 100–160 mm Hg the total number of impulses per cycle is approximately the same in the two conditions. The total number, however, is less important than the grouping of the impulses in bursts attaining a high frequency; and the latter are more capable of affecting the vasomotor centre than a steady discharge of an equal number of impulses at a lower frequency. In experiments with a natural circulation through the carotid sinuses, the rise of blood pressure which follows on switching from a pulsatile to a non-pulsatile flow stimulates the sinus baroceptors and so increases this discharge. In spite of this factor a higher level of blood pressure is maintained when the blood flow is non-pulsatile.

Sinus perfusion alone allows a strict comparison of the respective effects of pulsatile and steady flow at the same mean pressure, in producing reflex inhibition of the vasomotor centre. Experiments of this latter type confirmed that pulsatile flow caused a greater reflex inhibition of the vasomotor centre than a steady flow at the same mean pressure. Several additional points of interest also emerged.

(*a*) The reflex inhibition of the vasomotor centre exerted by steady sinus

perfusion pressures of about 250 mm Hg is unaffected by introducing pulsations into the perfusion system. Thus the high impulse frequency set up by non-pulsatile perfusion at such pressures itself produces maximal reflex inhibition of the vasomotor centre.

(*b*) The 'threshold of the sinus reflex effect' (Koch, 1931) is the level of sinus blood pressure below which the sinus baroceptor fibres produce no reflex effect on systemic blood pressure. Thus Fig. 3 shows that with a non-pulsatile flow, raising the sinus pressure from 15 to 80 mm Hg had no effect on systemic blood pressure; the 'threshold' under these conditions was, therefore, above 80 mm Hg. Using a pulsatile flow, however, a fall of systemic blood pressure was produced even at a mean sinus pressure of 15 mm Hg and a still greater fall at a sinus pressure of 80 mm Hg. Hence the 'threshold of the sinus reflex effect' is much lower when the sinuses are exposed to a pulsatile flow than when they are subjected to steady flow. Koch determined the 'threshold of the sinus reflex effect' by using the Moissejeff (1926) technique of producing changes of static pressure in the isolated sinus. He found under these conditions that a sinus pressure of 60–80 mm Hg was necessary to elicit any reflex fall of blood pressure. His conclusions have been widely quoted in the literature, and almost equally widely misquoted. Thus many authors have referred to Koch's 'threshold' as 'the threshold of baroceptor discharge', despite the published records of Bronk & Stella (1935) which show that baroceptors may fire at much lower pressures. However, it appears that Koch's conclusions, which were based on the results of steady sinus perfusion, are inapplicable to the conditions seen in the natural intact pulsatile circulation.

(*c*) Similarly, the 'Blutdruckcharakteristik' curves of Koch (1931) cannot be considered to express the 'buffer activity' of the sinus nerves in the intact circulation. Much prominence has been given to these curves in text-books of physiology, because they seemed to demonstrate that the sinus baroceptors exerted a 'buffer action' on the systemic blood pressure which was most efficient at or about the normal arterial blood pressure of the animal. These curves again are derived from the results of static perfusion pressure of the sinus.

(*d*) The greatest difference between the reflex effects produced by pulsatile and steady perfusion pressures respectively occurs at a mean pressure of 80 mm Hg. The explanation of this lies in the difference in impulse activity in the two conditions at such a mean pressure. It has already been noted that switching a mean pressure of 80 mm Hg from pulsatile to steady flow led to a marked reduction or complete disappearance of the baroceptor impulses. This effect would, therefore, be marked at a perfusion pressure of 80 mm Hg and is probably responsible for the small difference in the reflex response to pulsatile and steady perfusion pressures at a mean pressure of 15 mm Hg. At

such low pressures the impulse activity even during pulsatile flow must be very moderate.

Comparison of the reflex effects of sinus perfusion by pulsatile and non-pulsatile flows has previously been undertaken by Strauss (1940) and Bárány (1942). Strauss found that a rise of mean sinus perfusion pressure caused the same absolute fall of systemic blood pressure whether the sinus perfusion was pulsatile or steady. He claimed that the only difference in the reflex response to the two types of perfusion lay in the fact that pulsatile perfusion was more effective in maintaining the reflex hypotension. We cannot agree with his findings. Bárány reported that a sudden transition from steady sinus perfusion to pulsatile perfusion at the same mean sinus pressure caused no difference in the reflex response of the arterial blood pressure. The published record is unconvincing.

The present results indicate that the carotid baroceptor areas do not respond only to the mean systemic blood pressure. Changes of pulse pressure which do not alter the mean blood pressure must generally affect the afferent inhibition of the vasomotor centre. It seems very probable that changes of heart rate by altering the pulse pressure and the number of pulsations in unit time will thereby modify the reflex effects exerted by the carotid area. It may also be safely assumed that the aortic baroceptor activity is similarly affected by pulsatile changes.

SUMMARY

1. Carotid baroceptor impulse activity has been examined during pulsatile and non-pulsatile blood flow at the same mean pressure. During pulsatile flow the impulse discharge is grouped, the bursts occurring in systole and early diastole of each cardiac cycle. During non-pulsatile flow the impulse discharge occurs steadily throughout the cardiac cycle. The impulse frequency attained during pulsatile flow exceeds that seen during non-pulsatile flow.

2. In vagotomized cats conversion of the blood flow through both intact carotid sinuses from pulsatile to non-pulsatile causes a rise of systemic blood pressure which maintains this higher level as long as non-pulsatile sinus flow is continued. It seems that the sinus afferent impulse activity engendered by steady flow through the sinus is less effective in causing inhibition of vasomotor discharge than that occurring during pulsatile flow at the same mean pressure.

3. Perfusion of one sinus with pulsatile flow caused greater reflex effects on the systemic blood pressure than perfusion with steady flow at the same mean perfusion pressure.

We wish to thank Prof. Samson Wright for helpful advice and criticism.

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