THE BARORECEPTOR REFLEX EMANATING FROM THE CAROTID SINUS AND COMMON CAROTID ARTERY OF THE SHEEP

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Abstract of a Thesis Presented in Partial Fulfilment of the Requirements for the Degree of Master of Science

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by Karen T. Ball

The aim of this project was to improve understanding of the role of the common carotid arterial baroreceptor mechanism in controlling peripheral blood pressure in the sheep. The responses to clamping of one or both common carotid arteries were examined under chloralose anaesthesia with the vagus nerves intact and after they had been sectioned.

Unilateral clamping of a common carotid artery immediately reduced the mean blood pressure and pulse pressure in the ipsilateral carotid sinus and raised the peripheral mean blood pressure and pulse pressure. The failure of sinus pressures to show any recovery in the clamped vessel suggests that there was minimal flow through anastomoses into the occluded artery. Bilateral clamping of the common carotid arteries reduced the mean blood pressure within both carotid sinuses to a lower level than unilateral clamping, but raised the peripheral mean blood pressure and pulse pressures to a greater degree. This pressor response was interpreted as being due to the larger population of baroreceptors detecting the low carotid sinus pressures during bilateral occlusion.

To test whether there was a tendency for common carotid arterial clamping at different levels to produce different reflex responses of peripheral blood pressure, the carotid arteries were occluded at the caudal, mid- and cranial cervical levels. There was a trend towards a greater rise in peripheral mean blood pressure during caudal clamping compared with cranial clamping. This too may be due to a larger population of baroreceptors detecting the low carotid sinus and common carotid arterial pressures and suggests baroreceptors are distributed in regions of the common carotid artery caudal to the sinus.

In one third of the sheep, clamping the left common carotid artery caused a greater rise in peripheral mean blood pressure than clamping of the right vessel. Possible reasons for this include the presence of a larger population of baroreceptors in the left artery than the right and differences in the sensitivity of receptors in the two vessels.

The variability of responses to clamping and vagotomy was emphasised by the responses of two sheep in which section of the right vagus nerve totally abolished the reflex response to right common carotid arterial occlusion. Since in these animals neither the size of the baroreceptor population nor its sensitivity appeared to be responsible, a conclusion consistent with the evidence is that the baroreceptors in the vessel were innervated by the recurrent laryngeal or vagus nerves. Overall in the experiments, bilateral vagotomy enhanced the peripheral mean blood pressure and pulse pressure responses to clamping the common carotid arteries in keeping with a loss of the input from the aortic arch and cardio-pulmonary baroreceptors.

Histological evidence of the distribution of sensory areas along the common carotid artery was obtained for three discrete areas (A, B and C). It is suggested that baroreceptors located in the common carotid artery may be less sensitive than those in the carotid sinus region because of the low elastin content and lack of tunica medial thinning at the sites of carotid arterial baroreceptor innervation.

This thesis is dedicated to those persons who
thrust challenges upon me, and also those
who gave me support; but most of all to
those rare and precious individuals who
provide both caring and challenge.

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LIST OF ABBREVIATIONS

A	Arterial
BSA	Bovine serum albumin
CCA	Common carotid artery
Cd	Caudal position (middle of fifth cervical vertebra)
Cn	Cranial position (cranial pole of second cervical vertebra)
DAB	Diaminobenzidine
ECA	External carotid artery
fp	Facing page
G	Ganglion
Int	Intact
L	Left
Md	Mid position (caudal pole of third cervical vertebra)
N	Nervus
n	Number of animals, unless otherwise stated
NFA	Nerve fiber area
NNFA	Non-nerve fiber area
No.	Number
NSE	Neuron specific enolase
OG	Occipital group
PBS	Phosphate buffered saline
R	Right
SPG	Sucrose-potassium-phosphate glyoxylic acid
Vn	Vagus nerve

Only simpletons find things absolutely clear.

Alexander Solzhenitsyn
August 1914

CHAPTER 1

INTRODUCTION

The concept that the cardiovascular system is regulated by neural reflexes originating from the great vessels and heart is more than 100 years old, but its importance was probably not fully appreciated until Hering discovered the carotid sinus baroreceptor reflex in 1923. Subsequently, intense study of this subject has led to the present recognition of the central role of the arterial baroreflexes in circulatory control.

Baroreceptors are stretch receptors predominantly located in the adventitia of the carotid sinus and aortic arch, and the frequency of firing of these receptors varies directly with both the mean blood pressure and the rate of change of blood pressure. Afferent signals pass to nuclei in the floor of the fourth ventricle, where, by a system of interneurons, an increase in baroreceptor impulses results in reflex inhibition of sympathetic adrenergic efferents to the cardiovascular system and reflex stimulation of the cardiac vagus nerve, leading to a decrease in systemic pressure. Baroreceptors are tonically active when blood pressure is normal and, therefore, a decrease in blood pressure causes a reduction of baroreceptor impulses and a rise in blood pressure to its normal level (Kircheim, 1976).

Heymans and Neil (1958) commented that "the temporary and incomplete loss of baroreceptor activity caused by carotid occlusion causes such an obvious hypertension that it is used all over the world to demonstrate the sinus reflexes to students". This is the case at Massey University, where the dog was initially the subject of the physiology student. During an acute experiment on these animals, clamping of both the left and right common carotid arteries caused regular and reproducible moderate increases in blood pressure and heart rate. In addition, bilateral section of the vagus nerves could be relied on to enhance these responses significantly. These results are similar to those observed by other workers in this animal.

Difficulty in obtaining dogs caused the Physiology Department to substitute the sheep in this experiment. The change of species presented a major problem : unusual cardiovascular responses began to emerge from this experiment. In particular, sheep displayed poor blood pressure and heart rate rises upon bilateral common carotid arterial occlusion, a significant fall in basal blood pressure upon section of both the left and right vagus nerves and the failure of bilateral vagotomy to enhance the clamping response.

Since such atypical observations do not appear to have been reported in other species, the present project was instigated in order to explain these findings and improve the knowledge of the basic mechanisms involved in the control of blood pressure in sheep. This initially involved an anatomical review of the arterial supply of blood to the ovine cephalic circulation. The students' physiological observations were then examined and repeated under more suitable conditions of anaesthesia and further clamping protocols were subsequently undertaken in an attempt to clarify the carotid sinus baroreceptor mechanism in the sheep. The results from these latter experiments were suggestive of baroreceptors down the length of the common carotid artery and, because of this, the final component of this project was to study histologically the innervation of the ovine common carotid artery.

CHAPTER 2

THE ANATOMY OF THE CAROTID BIFURCATION OF THE SHEEP

2.1 INTRODUCTION

As this study was to require a detailed knowledge of the anatomical organisation of the common carotid artery, its branches and anastomotic connections, the first stage of the project involved anatomical dissection of the arterial supply to the head and neck. Publications have previously appeared on this topic, but there remain points of contention.

The preparation of a corrosion cast, and the dissection of embalmed specimens were undertaken to demonstrate the anatomy of the arterial branches of the aorta to the head and neck and the gross innervation of the carotid bifurcation of the sheep. This preliminary work was carried out to provide a detailed knowledge of the carotid bifurcation, its structure and innervation, so that the subsequent physiological and histological studies of the baroreceptor mechanism could be accomplished.

2.2 MATERIALS AND METHODS

The solutions used below are described in Appendix 1.

2.2.1 Preparation of the Corrosion Cast of the Arteries of the Head and Neck

2.2.1.1 Preparation of the sheep for resin injection

An adult sheep was anaesthetised with sodium pentobarbitone (Anathal, V.R. Laboratories Pty Ltd, Australia, 30 mg/kg body weight in a 6% solution) injected into an external jugular vein. With the sheep placed in dorsal recumbancy, the left and right common carotid arteries were catheterised using vinyl tubing (OD 4.5 mm, ID 3.0 mm, Dural Plastics and Engineering, Australia) and the catheter tips passed toward the head and positioned at the point of the bicarotid trunk bifurcation. The vessels of the head and neck were perfused through the right carotid catheter with Kaiserling's fixing fluid (Solution I) - the left carotid catheter allowed a free escape of blood and perfusate from the circulation. The body, with the head and neck outstretched, was stored overnight at about 4°C in a chiller.

The following morning (within 12 hours of death), the vessels of the head and neck were flushed through the right carotid catheter with 100 ml physiological saline at a rate of 20 ml/min, to remove blood clots which, although not restricting the flow of resin, do produce points of weakness in the cast. Restraint in the flushing rate avoids swelling and waterlogging of the tissues which may make a satisfactory resin injection impossible. A further period of one hour was allowed for excess saline to diffuse out of the tissue before starting the resin injection.

2.2.1.2 Injection of the resin

Taking care to avoid bubble formation, the resin mixture was prepared in a glass beaker by addition of enough mercuric sulphide to 200 ml Tensol cement No. 7 component A resin (I.C.I. New Zealand Ltd) to form a distinct vermillion colour; 10 ml Tensol cement No. 7 component B catalyst (I.C.I. New Zealand Ltd) was added to the pigmented resin and quickly, but thoroughly, mixed with a strip of perspex. The resin prepared was immediately poured into the barrel of a 60 ml hypodermic syringe; insertion of the plunger enabled injection under a constant 1500 mmHg pressure into the right carotid catheter.

The left carotid catheter was clamped when resin began to flow from it. The perfusion was stopped when the flow of resin into the right carotid cannula had almost ceased and a scalpel incision into the external nares showed a pink flush - reliable indicators that an optimum volume of resin had been injected. (Excessive perfusion results in resin soaking into the walls of the vessels and into the tissues - resin impregnated tissue cannot usually be detached from the cast without breaking off parts of the cast.) A 1800 mmHg injection pressure was applied just before the resin gelled, when it was too viscous to flow into small arteries. This additional pressure distends, but does not unduly enlarge the principal arteries, the cast of which is strengthened. Injection pressure was sustained until the resin remaining in the syringe reached a temperature of 40°C and had gelled.

Twenty four hours after the resin injection, polymerisation was sufficiently advanced that, for ease of handling, the animal's head and neck could be severed from the body just cranial to the thoracic inlet.

The perfused head and neck were placed in a colony of domestid beetles (Dermestes vulpinus) and left until the bones of the skull, cervical vertebrae, and corrosion cast were stripped of tissue (approximately 7 days).

2.2.2 Preparation of Specimens for the Gross Anatomical Dissection of the Arterial Branches of the Aorta to the Head and Neck and Nerves of the Carotid Bifurcation of the Sheep

Three mature sheep were anaesthetised with sodium pentobarbitone (30 mg/kg body weight) before euthanasia with 30 ml saturated magnesium sulphate injected into an external jugular vein. With the animal lying on its back, the left and right common carotid arteries were catheterised as in Section 2.2.1.1.

With the animal placed in lateral recumbancy, the head and neck outstretched, Kaiserling's fixing fluid (Solution I) was infused by gravity into the right carotid catheter. The left carotid catheter was clamped when clear fixing fluid began to flow from it. The infusion was taken as complete when the flow of the fixing fluid had ceased. Cadavers were kept at about 4°C in a chiller for 7 days; for ease of handling the animal's head and neck were severed just cranial to the thoracic inlet prior to dissection.

For better differentiation of nerves and their surrounding tissues, the specimens when not being worked on, were kept in Solution F (Solution II). The specimens were kept in this solution for months without becoming distorted or unduly hardened.

2.3 LITERATURE REVIEW AND RESULTS

2.3.1 Arterial Branching in the Head and Neck

In the last two decades, the descriptions of the arterial branching in the head and neck of the sheep (Ovis aries) became available from the work of Heeschen (1958), May (1964, 1965), Popesko (1970), du Boulay and Verity (1973), Ghoshal and Nanda (1975), Nickel, Schummer and Sieferle (1967, 1976), and Simoens, de Vos and Lauwers (1978-1979).

There has been interest in the region for much longer, however. Almost 100 years ago Chauveau (1891) described the sheep common carotid arteries as furnishing a thyroid branch, a laryngeal branch, and a slender occipital artery. Since then more detailed descriptions of the common carotid bifurcation have been given by Baldwin and Bell (1963a), May (1964, 1965) and Sha-Ban (1974).

Figures 2.1, 2.2 and 2.3 are sketches of the arterial branches of the aorta to the head and neck drawn from the corrosion cast and gross anatomical dissections. Each artery is referred to in the text by a number following the vessel nomenclature of the World Association of Veterinary Anatomists (1972), the number corresponding to that used in the figures of this chapter. Although there are some differences in detail, these figures agree with the general features of earlier work. This chapter will review the literature and illustrate the anatomy of the region by referring to the diagrams prepared during the initial part of this project. The description includes the origin of the cephalic vessels from the aorta but the dissection was undertaken cranial to the fifth cervical vertebra.

The vertebral artery (Arteria vertebralis - 1) arises from the brachiocephalic or subclavian artery in common with the deep cervical and costocervical arteries. The right costo-cervico-vertebral trunk (Truncus costocervico-vertebralis) arises from the brachiocephalic artery (A. brachiocephalica), the left costo-cervico-vertebral trunk arises from the left subclavian artery (A. subclavia) soon after the origin of the latter artery. The trunk (in each case) passes rostro-dorsally in the intercostal space towards the thoracic inlet, medial to the first rib or endothoracic fascia. The costocervical artery (A. costocervicalis) arises about 10 mm from the origin of the trunk and turns cranio-dorsally towards the second thoracic vertebra. As they continue rostro-dorsally, the cervico-vertebral trunk (Truncus cervicovertebralis)

FIGURE 2.1

Arterial branches of the aorta to the neck in relation to the first five cervical vertebrae, lateral aspect. The deep vessels are indicated by dotted lines.

Key

1 Vertebral artery

2 Muscular branch of the vertebral artery

5 Common carotid artery

6 Muscular branch of the common carotid artery

7 Caudal thyroid artery

8 Cranial thyroid artery

9 Caudal laryngeal artery

10 Lateral retropharyngeal lymph node branch of the common carotid artery

11 Cranial laryngeal artery

14 Occipital artery

15 Occipital carotid sinus

16 Muscular and glandular branch of the occipital artery

17 Ascending pharyngeal artery

18 Ascending palatine artery

23 External carotid artery

24 Lingual artery


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passes over the lateral surface of the vagosympathetic trunk and the trachea on the right and the oesophagus on the left at a point some 20 mm rostral to the first rib. As the trunk reaches the intertransversales colli muscle, the deep cervical artery (A. cervicalis profunda) separates and turns more dorsally between the transverse processes of the seventh cervical and first thoracic vertebrae, whereas the vertebral artery bends more rostrally, as the continuation of the original trunk, to pass ventral to the transverse process of the seventh cervical vertebra. It lies between the parts of the intertransversales colli muscle which originates from the transverse process of the sixth cervical vertebra. The vertebral artery enters the caudal foramen transversarium of the sixth cervical vertebra and continues cranially through the foramina transversaria of each of the preceding vertebrae to the axis. On reaching the axis, the vertebral artery leaves the foramina transversarium to enter the spinal canal and, at the level of the arch of the atlas, anastomoses with branches of the occipital artery. Cranial to the axis, it turns more dorsally to terminate in the obliquus capitis caudalis, rectus capitis dorsalis major, semispinalis, and spinalis muscles in the atlantal region.

Branches arising from the vertebral artery are:

Muscular branches of the vertebral artery (Rami musculares - 2) arise at each intervertebral junction and pass dorsally (larger vessels), laterally, or ventrally (smaller vessels). At the third cervical vertebra, a large muscular branch turns dorsally and is distributed to the omotransverse, omohyoid, longissimus atlantis, longissimus capitis and longissimus cervicis muscles. Other muscular branches terminate in the splenius longissimus capitis, longissimus atlantis, longissimus cervicis, cleidocervical, omotransverse, intertransversales colli, spinalis dorsi, spinalis cervicis, ventral serratus, trapezius, rhomboideus, multifidus dorsi, obliquus capitis caudalis, and rectus capitis dorsalis major muscles. Anastomoses occur between these branches and the muscular branches of the omocervical, deep cervical, common carotid and occipital arteries.

Spinal branches of the vertebral artery (Rami spinales - 3) arise as the vertebral artery leaves the cranial foramen transversarium of each vertebra or midway across the intervertebral space as far forward as the axis. They enter the vertebral canal, either through the intervertebral foramina or at the intervertebral spaces, and pass into the subdural space by penetrating the dura mater at, or medial to, the intervertebral foramen. On entering

this space, each branch divides into cranial and caudal branches. From the sixth to the second cervical vertebra, the cranial and caudal branches form a series of diamonds with the widest part at the intervertebral space where the spinal branches arise from the vertebral artery. This is shown diagrammatically in Figure 2.2. Adjacent diamonds are connected by a single artery (4) which lies on the dorsal surface of the body of the vertebra. The cranial branch of the second cervical vertebra anastomoses only with the caudal branch of the ipsilateral occipital artery. No connection occurs between contralateral vessels in the region.

Ventral spinal branches of the vertebral artery (Rami spinalis ventrale) two branches arise from the vertebral artery at each intervertebral space and pass on to the ventral surfaces of the vertebrae on each side of the space. These vessels lie between the ventral surface of the vertebrae and the longus colli muscle at the vertebral body and send branches to the muscle and bone. The cranial and caudal branches of each vertebra anastomose with corresponding branches from the opposite vertebral artery. A single median artery, the ventral spinal artery (A. spinalis ventralis) joins the union of branches at the caudal end of one vertebra with the union of branches of the cranial end of the same vertebra. No union occurs across the intervertebral space, although, in some regions, median vessels extend towards each other but do not meet.

Baldwin and Bell (1963a) did not show the anastomotic chain between the spinal branches of the vertebral artery and the occipital artery in their figure of the cephalic arterial system of the sheep. Their figure shows direct anastomoses between the vertebral and occipital arteries at the atlas, and the ventral spinal branches of the vertebral artery form the ventral spinal artery directly without any intervening system.

The right and left common carotid arteries (A. carotis communis) arise from the bicarotid trunk (Truncus bicaroticus) which in turn arises from the brachiocephalic artery near the thoracic inlet, medial and slightly caudal to the first rib. The 20 mm long trunk lies slightly to the left of the median plane. In its passage cranially, the bicarotid trunk lies dorsal to the oesophagus, dorsal and to the right of the trachea, ventral and to the right of the innominate vein and the deep cervical lymph nodes, ventral and to the left of the left thoracic duct as it joins the left external jugular vein or the origin of the innominate vein, and to the left of the subclavian artery, the

FIGURE 2.2

Spinal branches of the vertebral artery in relation to the cervical vertebrae, dorsal aspect. The dorsal and lateral parts of the vertebral arches have been removed.
Adapted from May (1965)

Key

I Fourth cervical vertebra

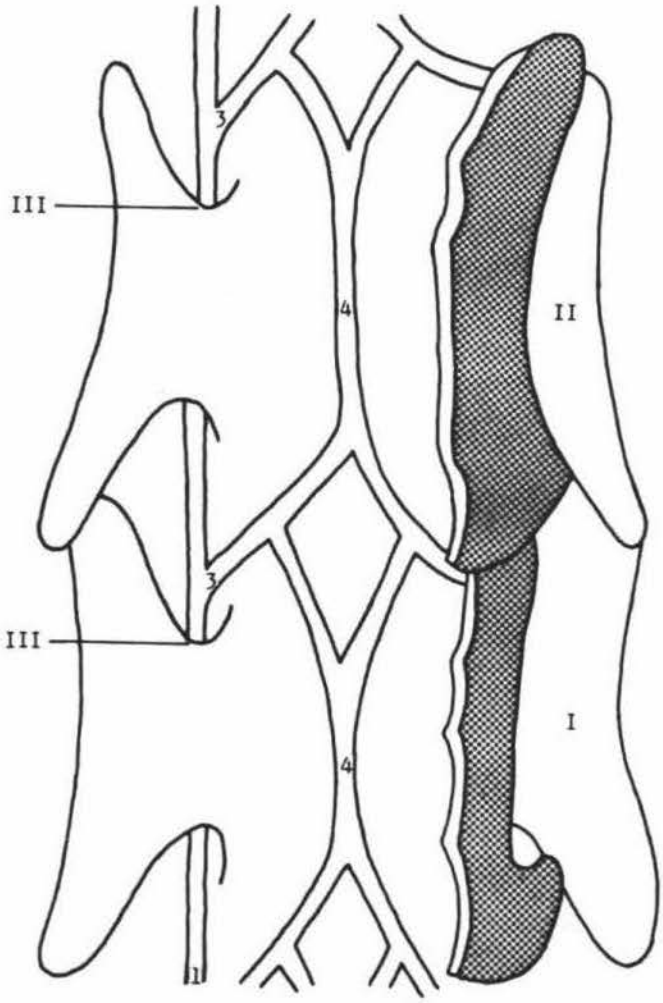
II Third cervical vertebra

III Foramen transversarium

1 Vertebral artery

3 Spinal branch of the vertebral artery

4 Arterial chain formed by the anastomoses of the spinal branches of the vertebral artery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left vagus and caudal laryngeal nerves. The relationship of the right and left carotid arteries differs slightly as they pass cranially along the neck.

The right common carotid artery passes towards the right, and cranially to ascend the neck at first on the ventro-lateral surface of the trachea, then obliquely across the lateral face of the trachea to the dorso-lateral surface at the level of the third cervical vertebra. The vagosympathetic trunk is related to the dorsal (or dorso-lateral) surface, and the caudal laryngeal nerve is related to the ventro-medial surface of the carotid artery. The relationship to the latter nerve terminates in the region of the third cervical vertebra. The nerve continues cranially along the ventro-lateral aspect of the trachea, and the artery becomes more dorsal. When present, the internal jugular vein lies on the lateral surface of the artery but is of variable relationship. The lymph duct (or ducts) lies dorsal and lateral to the common carotid artery. Laterally, the artery is covered superficially by the sternocephalic and scalenius muscles as far as the third cervical vertebra, and then by the omohyoid muscle. At the level of the third cervical vertebra these muscles separate the artery from the cranial end of the external jugular vein, and the aponeurotic insertion of the sternomandibular muscle of the level of the atlas.

The left common carotid artery (5) is related to the lateral surface of the oesophagus. More caudally, the artery is related ventrally to the trachea but this relationship terminates in the region of the fifth or sixth cervical vertebra. The vagosympathetic trunk is dorsal and the caudal laryngeal nerve is medial to the artery. The lymph duct (or ducts) is lateral to the origin of the artery, but for the major part of its course, the duct is related to the ventral surface of the artery. The lateral relation is to the sternocephalic muscle (caudally), the scalenius muscle in the region of the fifth and sixth cervical vertebrae, and then to the omohyoid muscle at the level of the third cervical vertebra. These muscles separate the artery from the cranial end of the external jugular vein. The dorsal relation is to the longus capitis muscle from the third cervical vertebra cranially.

In the atlantal region both common carotid arteries are related dorsally to the oesophagus and combined tendon of the sternomastoid, cleidomastoid and longus capitis muscles. Ventro-laterally the arteries are covered by fat which surrounds the lateral retropharyngeal lymph nodes. In some cases, the ventral relationship in this region may include the thyroid gland. The common carotid

artery, the vagosympathetic trunk and the caudal laryngeal nerve are included in a common fascial sheath, formed by the development of the deep fascia of the neck.

Branches arising from the common carotid artery are:

Muscular branches of the common carotid artery (Rami musculares - 6). A variable number of branches (in the majority of cases there are four or five branches) arising at uneven intervals along the course of the common carotid artery and pass laterally to divide into dorsal, lateral and ventral branches. These branches terminate in the skin and muscles of the lateral and ventral cervical region. Some of the dorsal branches extend dorsally to the level of the transverse processes of the cervical vertebrae. Branches in the atlanto-axial region terminate in the omotransversarius, splenius, longus colli, intertransversales colli, obliquus capitis, longus capitis, cleidocervical, omotyoid, cleidomastoid, sternomastoid, sternomandibular and cutaneous muscles.

Caudal thyroid artery (A. thyroidea caudalis - 7). A very small vessel arising from the ventral surface of the common carotid artery, a short distance caudal to the thyroid gland and ventral to the fourth cervical vertebra, usually arising as a branch of the cranial thyroid artery. The artery turns rostrally from its origin, and enters the caudal pole of the thyroid gland. When an independent vessel, it gives tracheal and muscular (sternomastoid, sternothyroid and sternohyoid) branches along its course.

Cranial thyroid artery (A. thyroidea cranialis - 8) arises slightly caudal to the laryngeal region and medial to the omohyoid muscle. The artery curves ventrally and enters the cranial pole of the thyroid gland to form the main blood supply to the thyroid gland. Branches of this vessel pass to the trachea, oesophagus, and the cricothyroid, sternothyroid, sternohyoid, omohyoid, and cricopharyngeal muscles.

Caudal laryngeal artery (A. laryngea caudalis - 9) arises as one, two or three branches of the cranial thyroid artery (it may arise as a single branch from the common carotid artery, May 1964, 1965). The vessel passes rostrally along the lateral surface of the trachea, to enter the larynx at the junction of the lamina and arch of the cricoid cartilage. Muscular branches pass to the sternohyoid, sternothyroid, cricothyroid, cricopharyngeal, and lateral and dorsal cricoarytenoid muscles. A branch

passes deeply caudally with the caudal laryngeal nerve, medial to the cricopharyngeal muscle, and terminates in the thyroarytenoid muscle and mucosa of the larynx.

Glandular branches of the common carotid artery (Rami glandulares - 10). Small vessels arise from the ventral surface of the common carotid artery and enter the caudal border of the mandibular salivary gland. A small branch passes caudo-dorsally, and enters the lateral retropharyngeal lymph node (or nodes). In the very young animal, branches also enter the cranial end of the thymus gland.

Oesophageal and tracheal branches of the common carotid artery (Rami oesophagei et tracheales) arise from the medial surface of the common carotid artery and ramify in the oesophagus and trachea.

In the absence of the extracranial part of the internal carotid artery in the adult, the termination of the common carotid artery is accepted as the point of origin of the occipital artery. This occurs ventral to the paramastoid process and 10 mm caudal to the muscular angle of the great cornu of the hyoid bone. The termination lies deep to the mandibular and parotid salivary glands, lateral to the retropharyngeal lymph nodes, and medial to the caudal belly of the digastric muscle. Dorsally it is related to the combined tendon of the sternomastoid, cleidomastoid, and longus capitis muscles. The external jugular vein is separated from the termination by the parotid and mandibular salivary glands.

The internal carotid artery arises from the common carotid artery in common with, or medial to, the occipital and ascending pharyngeal arteries in the foetus, and at times, in the newborn lamb. Shortly after birth, the extracranial segment (which, after passing rostro-dorsally, medial to the tympanic bulla, enters the cranial cavity through the foramen lacerum) degenerates and is represented by a thin fibrous cord. However, Baldwin (1960) found the extracranial segment of the internal carotid artery in a few animals up to nine months old.

It is probable that in the development of the occipital and temporal bones around the foramen lacerum, the foetal internal carotid artery is slowly occluded by convergence of the basilar occipital and temporal bones in the closure of the greater part of the foramen lacerum (May, 1965; Gadzhev, 1982). May (1965) states that by this occlusion, the extracranial part of the

internal carotid artery could remain and would then probably supply the longus capitis muscle, enlarging with the development of this muscle. As the pharynx is related to the ventral surface of this muscle, branches could also develop to supply this structure. In the adult sheep, May (1965) described the course of the caudal pharyngeal artery (A. pharyngea caudalis) as arising a short distance from the origin of the external carotid artery and passing rostro-dorsally over the dorso-lateral wall of the pharynx, although he reported that in 30% of animals it arose from the terminal part of the common carotid artery and passed rostro-medially, ventral to the longus capitis muscle, on to the dorsal surface of the pharynx) to terminate in the longus capitis muscle and the muscles of the pharynx. At the origin of the oesophagus, branches passed to the muscles of the mucosa. A small branch followed along the medial side of the tympanic bulla to enter the foramen lacerum and join the caudal part of the rete mirabile cerebri. This vessel followed the same course and has the above distribution in the region of the foramen lacerum and May (1965) stated it might be the extracranial part of the internal carotid artery. However, neither Chauveau (1891), Heeschen (1958), Baldwin and Bell (1963a), May (1964), Popesko (1970), du Boulay and Verity (1973), Ghoshal and Nanda (1975), Nickel, Schummer and Sieferle (1967, 1976), Simoens, de Vos and Lauwers (1978-1979), nor this study describe a caudal pharyngeal artery.

The intracranial part of the internal carotid artery remains in the adult as the communicating vessel between the rostral epidural rete mirabile and the rostral cerebral and caudal communicating arteries to form the circle of Willis of the brain (Daniel, Dawes and Prichard, 1953). The union of the caudal communicating arteries rostral to the pons forms the unpaired median basilar artery (A. basilaris). The basilar artery passes caudally to the foramen magnum, decreasing considerably in size rostro-caudally to join the ventral spinal artery at the foramen magnum.

The carotid sinus (Sinus caroticus - 15) is a dilatation at the origin of the internal carotid artery in many species though Binswanger (1879), Adachi (1928) and Boyd (1937) demonstrated conclusively that the dilatation was not always situated at the commencement of the internal carotid artery, but that it might include the termination of the common carotid artery or might be limited to the latter situation. The carotid sinus has been described in the rat (Rees, 1967a), rabbit (Rees, 1966, 1967a; Muratori, 1967), cat (Addison, 1944; Rees, 1966, 1967a; Muratori, 1967), dog (Addison, 1939, 1944; Rees, 1966, 1967a;

Muratori, 1967; Ábráham, 1969) and human (Rees, 1966, 1967a; Muratori, 1967; Ábrahám, 1969). In species in which the extracranial part of the internal carotid artery is absent (the guinea-pig, pig, sheep, horse and cow), de Castro (1928) made the following observation: 'The homologue of the sinus is to be found on the vessel which supplants the internal carotid artery in supplying the brain.' The carotid sinus is situated at the undilated origin of the occipital artery (de Castro, 1928; Sunder-Plassman, 1930; Heymans, Bouckaert and Regniers, 1933; Rees, 1966, 1967a; Muratori, 1967; Ábráham, 1969; Kondo, 1971; Aumonier, 1972; Sha-Ban, 1974) or the occipito-ascending pharyngeal trunk (Sha-Ban, 1974) and is generally referred to as the occipital, occipito-carotid, or occipito-internal carotid sinus (Adams, 1958; Muratori, 1967) in these species. Figure 4.1 compares the morphology of the carotid sinus in the human and sheep. Schäefer (1877), Adachi (1928) and Boyd (1937) found that, in humans, the left carotid sinus was better developed than the right. Schäefer considered that this was because of a greater blood supply being required by the left side of the brain. Adachi suggested that this might be explained by the fact that the left common carotid artery originates directly from the aortic arch.

Branches arising from the termination of the common carotid artery are:

Cranial laryngeal artery (A. laryngea cranialis - 11) arises from the medial surface of the common carotid artery close to the origin of the occipital artery (it may arise in common with the ascending pharyngeal or occipital and ascending pharyngeal arteries, Sha-Ban, 1974; Simoens, de Vos and Lauwers, 1978-1979), ventral to the muscular angle of the great cornu of the hyoid bone. The vessel passes ventrally, with the cranial laryngeal nerve, across the thyropharyngeal muscle, the pharyngo-oesophageal nerve and the dorso-lateral surface of the larynx to the ventral side of the cranial cornu of the thyroid cartilage. It then disappears in the foramina formed by the thyroid cornu of the hyoid bone, the lamina of the larynx thyroid cartilage, and the thyrohyoid muscle. The vessel ramifies in the mucosa of the larynx and the cricothyroid, throarytenoid, and transverse arytenoid muscles.

Branches arising from the cranial laryngeal artery are:

Muscular branches of the cranial laryngeal artery (Rami musculares - 12)

1. A small vessel arises as the cranial laryngeal artery crosses the thyropharyngeal muscle and ramifies in the thyropharyngeal and chondropharyngeal muscles.

FIGURE 2.3

Arterial branches of the aorta to the head in relation to the skull, lateral aspect. The deep vessels are indicated by dotted lines.

Key

5 Common carotid artery

11 Cranial laryngeal artery

12 Muscular branch of the cranial laryngeal artery

13 Glandular branch of the cranial laryngeal artery

14 Occipital artery

15 Occipital carotid sinus

16 Muscular and glandular branch of the occipital artery

17 Ascending pharyngeal artery

18 Ascending palatine artery

19 Condyloid artery

20 Middle meningeal artery

21 Caudal meningeal artery

22 Muscular branches of the caudal meningeal artery

23 External carotid artery

24 Lingual artery

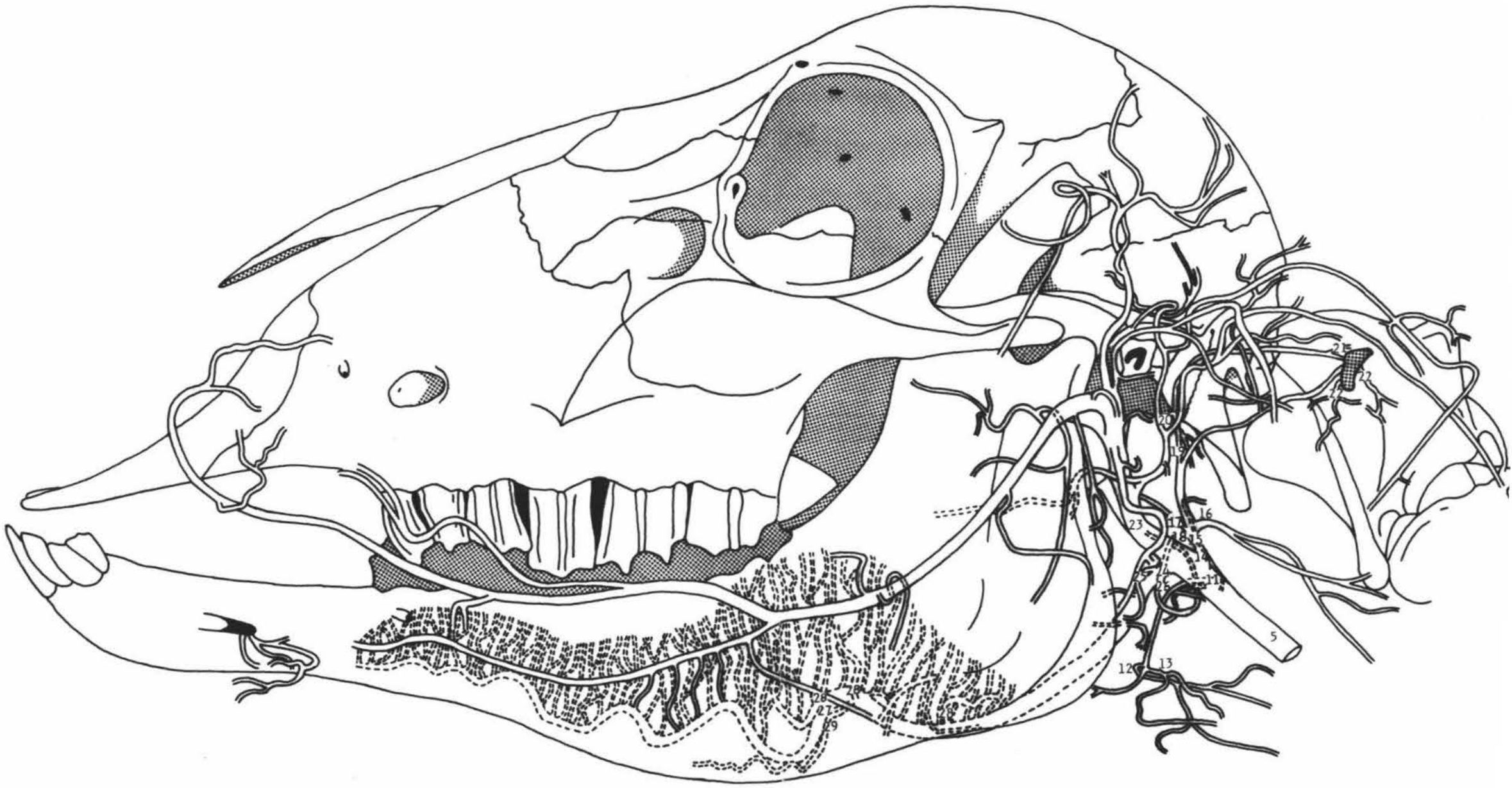
25 Mandibular branch of the lingual artery

26 Pharyngeal branch of the lingual artery

27 Deep lingual artery

28 Dorsal branches of the deep lingual artery

29 Sublingual artery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2. A large vessel arises as the cranial laryngeal artery passes medial to the thyrohyoid muscle, and divides immediately. The rostral branch passes medial to the thyrohyoid muscle and ramifies in this muscle, the glossoepiglotic muscle and fold, and the mucosa of the larynx. The ventral branch ramifies in the thyrohyoid, omohyoid and sternohyoid muscles.

Glandular branches of the cranial laryngeal artery (Rami glandulares - 13) generally comprise two or more branches; one of which arises near the origin of the cranial laryngeal artery and enters the caudal part of the mandibular salivary gland whilst the other arises more ventrally from the cranial laryngeal artery and enters the medial face of the main part of the mandibular salivary gland and the rostral end of the oesophagus.

Muscular and membraneous branch of the cranial laryngeal artery passes rostro-ventrally to disappear medial to the thyrohyoid muscle, and terminate in the region of the small cornu of the hyoid bone.

Pharyngeal branch of the cranial laryngeal artery (Ramus pharyngeus) arises from the larger muscular branch to terminate in the ventral and lateral pharyngeal wall in the epiglottic region.

Occipital artery (A. occipitalis named 'Ramus descendens' by Popesko, 1961 - 14) arises from the medial side opposite (or rostral) to the cranial laryngeal artery, 10 mm caudo-medial to the muscular angle of the great cornu of the hyoid bone, medial (or slightly caudal) to the caudal belly of the digastric muscle, and covered laterally by the parotid and mandibular salivary glands. Although the base of this artery has no dilatation, it appears to be the physiological homologue of the carotid sinus. The vessel passes caudo-dorsally and medially to the wing of the atlas (when the common carotid artery is more dorsal in position the occipital artery arises rostral to the dorsal end of the great cornu, turns caudally shortly after its origin and passes medial to the paramastoid process towards the alar foramen to pass through the rectus capitis ventralis muscle, May, 1964) and enters the alar foramen on the ventral surface of the wing of the atlas uniting with a branch from the vertebral artery to form a well-developed occipito-vertebral anastomosis.

Branches of the occipital artery are:

Ascending pharyngeal artery (A. pharyngea ascendens named 'ascending palatine artery' by Appleton and Waites, 1957 - 17) arises cranio-medially by a common trunk (the occipito-ascending pharyngeal trunk, it may arise in common with the cranial laryngeal, occipital and cranial laryngeal, or directly from the common carotid artery, Sha-Ban, 1974). The vessel passes rostrally, medial to the hyoid bone, between the external carotid artery and the glossopharyngeal nerve (lateral) and the pharyngeo-oesophageal nerve and the medial retropharyngeal lymph node (medial). Its course is then somewhat dorsally across the pterygopharyngeal and palatopharyngeal muscles, deep to the dorsal lingual vein, to pierce the levator veli palatini muscle near the Hamulus of the pterygoid bone and terminate in the mucosa of the pharynx in the region of the dorsal border of the caudal nares. Branches arise along the vessel's course and pass to the pterygopharyngeal, palatopharyngeal, stylopharyngeal, chondropharyngeal, thyropharyngeal, keratopharyngeal, occipitohyoid, levator veli palatini and tensor veli palatini muscles, and the medial retropharyngeal lymph node.

In the foetus, the ascending pharyngeal artery enters the cranium through the foramen lacerum to join the interior surface of the rostral epidural rete mirabile. In the adult sheep, the artery has no major communication with the rete (Daniel, Dawes and Prichard, 1953). Baldwin (1960) therefore stated that the ascending pharyngeal artery was a misnomer for the internal carotid artery.

A branch arising from the ascending pharyngeal artery is:

Ascending palatine artery (A. palatina ascendeus - 18) which arises from the origin of the ascending pharyngeal artery, but may arise directly from the common or external carotid artery (Heeschen, 1958) or the occipital artery (Simoens de Vos and Lauwers, 1978-1979). The vessel terminates in the soft palate and the medial retropharyngeal lymph nodes.

Muscular and glandular branches of the occipital artery 16 - most of these vessels are large and extend considerable distances cranially, caudally and dorsally:

1. arises from the caudal wall of the occipital artery and passes caudally to the caudal end of the wing of the atlas. At this point the vessel turns dorsally to terminate in the deep surface of the cleidomastoid muscle. Along its course branches are given off to the cleidocervical, cleidomastoid, splenius, longissimus capitis, rectus capitis lateralis, and intertransversales colli muscles, and the caudal end of the mandibular salivary gland,

2. two or three small muscular branches arise from the caudal wall of the occipital artery and terminate in the longus capitis, rectus capitis lateralis and obliquus capitis cranialis muscles,

3. arise at the intervertebral foramen of the atlas, and emerge through the alar foramen. Branches pass cranially and caudally to the muscles (including the splenius, obliquus capitis caudalis, rectus capitis dorsalis, semispinalis capitis and superficial caudal auricular muscles) and skin over the occipital bone, atlas and axis.

Condyloid artery (A. condyloidea named 'meningeal branch' by Daniel, Dawes and Prichard, 1953 - 19) is a relatively large vessel (may arise directly from the external carotid artery May, 1965; Sha-Ban, 1974; Simoens, de Vos and Lauwers, 1978-1979). The vessel passes dorsally over the lateral (or medial) surface of the vagus, accessory, hyoglossal and sympathetic trunk, and medial to the paramastoid process (may arise in the fossa atlantis, and pass rostro-dorsally across the lateral surface of the paramastoid process) to enter the cranial cavity through the condyloid foramen. As the artery passes through the foramen, it enters the condyloid canal along which it passes to reach the temporal canal.

Branches arising from the condyloid artery are:

Middle meningeal artery (Ramus meningea media - 20) arises near the condyloid foramen and passes rostro-dorsally to enter the cranial cavity through the caudal foramen lacerum where it is encircled by the basilar venous plexus. The vessel passes along the lateral wall of the vertebral canal of the atlas and through the foramen magnum to ramify in the meninges dorsal to the foramen.

Caudal meningeal artery (A. meningea caudalis named 'occipital branch' by Heeschen, 1958 - 21) arises medial to the paramastoid process as the condyloid artery crosses the longus capitis muscle (may arise as a common trunk with the condyloid artery, Sha-Ban, 1974). The vessel has a sinuous course, passing caudally around the base of the paramastoid process to ascend the caudal wall of the skull lying parallel with the lateral border of the occipital condyle and deep to the rectus capitis lateralis and obliquus capitis cranialis muscles. It enters the cranial cavity through the mastoid foramen, passing along the mastoid canal to enter the temporal canal and ramify in the subarachnoid space. Branches arising from the caudal meningeal artery are:

Muscular branches of the caudal meningeal artery (Rami musculares - 22) pass dorsally along the temporal crest to the occipitohyoid, obliquus capitis cranialis, rectus capitis lateralis, and rectus capitis dorsalis major and minor.

Laryngeal branch of the caudal meningeal artery (Ramus laryngeus) arises from the caudal surface of the condyloid artery, between the origin of the condyloid artery and its second muscular branch. The vessel passes ventrally over the lateral surface of the pharynx, lateral to the cranial laryngeal artery and ramifies in the muscles and mucosa of the pharyngeal and laryngeal walls, and in the muscles of the lateral aspect of the cranial end of the neck.

Muscular branches of the condyloid artery (Rami Musculares). Small branches arise from the condyloid artery between the origin and condyloid foramen to enter the occipitotyoid, longus capitis, rectus capitis, and rectus capitis lateralis.

Spinal branches of the condyloid artery (Rami spinalis) pass ventrally and caudally along the ventrolateral wall of the vertebral canal. In the vessel's course, they detach a small branch which passes ventrally, then cranially, to anastomose with the corresponding branch from the opposite side. The conjoined vessel joins the ventral spinal artery.

The external carotid artery (A. carotis externa - 23) is the continuation of the common carotid artery. The vessel's course is dorsal, medial, rostral, and parallel with the internal maxillary vein. It is related superficially to the mandibular and parotid salivary glands, the digastric and stylohyoid muscles, and the ventral buccal nerve. The artery passes between the caudal belly of the digastric muscle (lateral) and the great cornu of the hyoid bone (medial) and turns more dorsally to divide into the superficial temporal and internal maxillary arteries 20 mm caudo-ventral to the temporo-mandibular articulation and medial to the parotid salivary gland.

A branch arising from the origin of the external carotid artery is:

Lingual artery (A. lingualis - 24) which arises from the rostral surface 10 mm caudo-ventral to the muscular process of the great cornu of the hyoid bone near the origin of the external carotid artery, medial to the caudal belly of the digastric muscle. The vessel passes rostro-ventrally along the medial surface of the medial pterygoid muscle and along the dorsal border of the digastric and stylohyoid muscles. The course is almost parallel with the ventral border of the great cornu of the hyoid bone. It passes over the lateral wall of the larynx and pharynx, between the styloglossal muscle and the cranial belly of the digastric muscle, and then across the lateral surface of the small cornu of the hyoid bone between the chondropharyngeal and hyoglossal muscles. The deep lingual artery (A. profunda linguae - 27) is the continuation of the lingual artery beyond the origin of the sublingual artery (Simoens, de Vos and Lauwers, 1978-1979) along a flexuous course towards the apex of the tongue. The vessel turns slightly rostro-dorsally between the hyoglossal and genioglossal muscles to enter the tongue. It continues rostrally within the tongue towards the tip lateral to the genioglossal muscle. The artery terminates in relation to the venous plexus in the tip of the tongue. Dorsal lingual branches of the deep lingual artery (Rami dorsales linguae - 28) arise within the tongue and pass dorsally and ventrally to terminate in the intrinsic and extrinsic muscles of the tongue, the genioglossus, hyoglossus, styloglossus, myoglossus, geniohyoid and mylohyoid muscles, and the mucosa of the dorsal and lateral surfaces of the tongue. The more caudal branches of the lingual artery terminate in the digastric, stylohyoid, chondropharyngeal, keratopharyngeal and medial pterygoid muscles, the mucosa of the pharynx, and the mandibular and sublingual salivary glands.

Branches arising from the lingual artery are:

Mandibular branch of the lingual artery (Ramus mandibularis - 25) arises a short distance (15 mm) from the origin of the lingual artery. The vessel bends laterally, then ventrally across the internal maxillary vein, and passes along the caudal surface of the masseter muscles, slightly rostro-medial to the caudal border of the mandible. In this part of the course, small branches arise and ramify in the parotid salivary gland. The artery divides 25 mm above the ventral border of the mandible. The medial branch passes a short distance along the medial border of the mandible to turn medially, and divide into numerous branches which ramify in the mandibular salivary gland. The lateral branch passes ventrally, and divides into rostral and caudal branches which enter the digastric, masseter, stylohyoid, sternohyoid, sternomandibular and medial pterygoid muscles.

Pharyngeal branches of the lingual artery (Rami pharyngeii - 26) arise as the lingual artery passes the middle of the great cornu of the hyoid bone (may arise from the mandibular branch, May, 1965). The vessels cross the ventral surface of the great cornu to divide and ramify on the dorsal and lateral surfaces of the pharynx.

Sublingual artery (A. sublingualis - 29) arises a short distance rostral (or lateral) to the small cornu of the hyoid bone on the deep surface of the hyoglossal muscle. The vessel passes rostro-ventrally between the mylohyoid and geniohyoid muscles, accompanied by the sublingual vein and a branch of the mandibular nerve, towards the symphysis of the mandible to terminate in the mucosa of the floor of the mouth in the incisor teeth region. Branches arising from the sublingual artery also supply the hyoglossal, geniohyoid and mylohyoid muscles, the cranial belly of the digastric muscle, the sublingual salivary gland, the skin of the mandibular space, and the mucosa of the floor of the mouth. The sublingual artery of one side may be very slender, or even absent, and in that case is compensated by the deep lingual or sublingual artery of the opposite side (Heeschen, 1958).

Anastomoses are extensive and occur in all parts of the arterial branches of the aorta to the head and neck. Table 2.1 lists the more extensive anastomotic connections between the arterial branches of the aorta to the head and neck. These vary in calibre and range from vessels of arteriolar dimensions to arteries of relatively large [1 mm] diameter).

2.3.2 Gross Innervation of the Carotid Bifurcation

Chauveau (1891) observed nerves in the region of the carotid bifurcation and described the carotid sinus nerve branching from the glossopharyngeal nerve, and the external carotid nerve branching from the cranial cervical ganglion to the carotid bifurcation. Dougherty, Habel and Bond (1958), Waites (1960), May (1964, 1965), Sha-Ban (1974), and Godinho and Getty (1975) later provided detailed accounts of the gross innervation of the carotid bifurcation.

Figure 2.4 is a sketch of the gross innervation of the carotid bifurcation from the anatomical dissections. Each nerve is referred to in the text by a letter following the nerve nomenclature of the Word Association of Veterinary Anatomists (1972), the letter corresponding to that used in Figure 2.4. Although the general features of this figure do not differ from the descriptions given by Chauveau (1981), Dougherty, Habel and Bond (1958), Waites (1960), May (1964, 1965), Sha-Ban (1974), and Godinho and Getty (1975), they are included here to emphasise the following features:

The **hypoglossal nerve** (Nervus hypoglossus - a) appears medial to the paramastoid process and ventral to the origin of the digastric muscle, between the vagus (deep) and the accessory (superficial) nerves to which it is attached by loose connective tissue. The nerve is related laterally to the occipitohyoid, digastric and stylohyoid muscles, and the parotid salivary gland. It passes caudo-ventrally to bend sharply rostrally as it passes between the latter two nerves, curving around the medial aspect of the occipital or condyloid artery to reach the lateral surface of the external carotid artery. The nerve passes rostro-ventrally between the digastric muscle and the muscles of the larynx and pharynx to become associated with the lateral aspect of the lingual artery near the level of the centre of the great cornu of the hyoid bone, and accompanies this vessel, parallel with the great cornu, as far as the hyoglossal muscle. It then passes along the ventral border of the hyoglossal muscle, deep to the mylohyoid muscle and the main branch enters the tongue between the hyoglossal (lateral) and genioglossal (medial) muscles. The nerve branches medial to the styloglossus muscle; the

TABLE 2.1 ARTERIAL ANASTOMOSES OF THE ARTERIAL BRANCHES OF THE AORTA TO THE HEAD AND NECK
Adapted from May (1965)

Main Artery	Anastomotic area or branch	Main artery
Vertebral artery	In the muscles ventral to the axis	Cranial thyroid artery
	In the muscles dorsal, lateral, and ventral to the atlas	Occipital artery
	In the muscles dorsal to the atlas	Caudal auricular artery
	In the muscles lateral to the cervical vertebrae	Common carotid artery
	Across the midline in the muscles of the neck	Vertebral artery
Common carotid artery	The muscular branch to the lateral and ventral neck muscles near the atlas	Occipital artery
	The muscular branches to the lateral and ventral neck muscles	Vertebral artery
	The dorsal and lateral muscular branches	Vertebral artery
Caudal thyroid artery	The muscular branches in the ventral neck muscles	Common carotid and occipital arteries
Cranial thyroid artery	The muscles of the larynx	Cranial laryngeal artery
	The muscular branches to the muscles ventral to the axis	Vertebral artery
	The muscular branches to the muscles ventral to the atlas	Occipital artery
	The muscular branches to the cricopharyngeal and cricothyroid muscles	Caudal and cranial laryngeal arteries
	The muscles of the oesophagus and around the larynx	Common carotid and caudal laryngeal arteries
	The vessels of the opposite side across the trachea	Cranial thyroid artery
Caudal laryngeal artery	The laryngeal branches of the same and opposite side	Cranial laryngeal artery
	In the Tracheal region	Common carotid and cranial thyroid arteries
	In the mandibular salivary gland	Mandibular branch of lingual artery
	The muscles of the larynx and around the oesophagus	Cranial thyroid artery
	The muscles ventral to the larynx and the mucosa of the larynx	Caudal laryngeal artery
	The mucosa lining of the trachea and oesophagus	Caudal laryngeal artery of opposite side and cranial laryngeal artery
Cranial laryngeal artery	The laryngeal branches to the same and opposite side	Caudal laryngeal artery
	The laryngeal branches	Cranial thyroid artery
	The caudal region of the pharynx	Ascending pharyngeal artery
	The pharyngeal branches	Lingual artery mandibular branch
	Through the ascending pharyngeal artery	Occipital artery
Occipital artery	The ventral surface of the wing of the atlas and the floor of the vertebral canal of the atlas	Vertebral artery
	The muscular branches to the muscles ventral to the atlas	Common carotid, condyloid, and caudal meningeal arteries
	In the muscles of the atlanto-occipital area	Caudal auricular and auriculopalpebral arteries

	The muscular branches	Caudal thyroid artery
	In the muscles dorsal and ventral to the atlas	Occipital artery
Ascending pharyngeal artery	Pharyngeal branches	Cranial laryngeal, condyloid cranial branch, external carotid, lingual, and caudal nasal arteries
Condyloid artery	Passing through the foramen magnum	Occipital artery
	In the temporal canal	Caudal meningeal and caudal meningeal branch of caudal auricular arteries
	Branch passing through the caudal foramen lacerum	Basilar artery
	Spinal branch at the atlanto-axial junction	Vertebral artery spinal branch
	Cranial branch on lateral wall of the foramen magnum	Occipital, condyloid, caudal meningeal, and caudal auricular arteries
	Cranial branch in the vertebral canal of the atlas	Occipital artery
	Small branch of the cranial branch	Basilar artery
Caudal meningeal artery	In the temporal canal	Caudal meningeal branch of caudal auricular artery
	Muscular branches	Occipital artery and caudal meningeal artery of the opposite side
	Foramen lacerum branch of the muscular branches	Basilar artery
External carotid artery	The pharyngeal branches	Lingual artery
	Through the ascending pharyngeal artery	Occipital artery
Lingual artery	Through the mandibular branch at various points in the mandibular space from the fifth cheek tooth	Sublingual artery
	In the parotid salivary gland	External carotid artery
	Through the mandibular branch in the caudal pharynx	Cranial laryngeal artery
	Through the ascending pharyngeal artery	Occipital artery
	Within the muscles of the mucosa of the tongue	Lingual artery
	Across the mid-ventral plane	Lingual artery of opposite side and buccinator artery
	Rostral branch of the lateral branch of the mandibular branch	Transverse facial artery ventral masseteric branches
Caudal auricular artery	The parotid gland branches	External carotid artery
Mandibular alveolar artery	The pharyngeal branches	Lingual artery
	Through the mental artery in the chin	Sublingual artery
Buccal artery	The rostral pharyngeal branches	Lingual artery
Lesser palatine artery	The pharyngeal branches	Lingual artery
Transverse facial artery	The parotid branches	External carotid artery
	Through the mandibular branch in the parotid salivary gland and masseter muscle	Lingual artery
Maxillary labial artery	Around the ventral border of the mandible	Sublingual artery

FIGURE 2.4

Gross Innervation of the Carotid Bifurcation, lateral aspect. The deep structures are indicaed by dotted lines.

Adapted from Dougherty, Habel and Bond (1958)

Key

5 Common carotid artery

11 Cranial laryngeal artery

12 Muscular branch of the cranial laryngeal artery

13 Glandular branch of the cranial laryngeal artery

14 Occipital artery

15 Occipital carotid sinus

16 Muscular and glandular branch of the occipital artery

17 Ascending pharyngeal artery

18 Ascending palatine artery

23 External carotid artery

24 Lingual artery

a Hypoglossal nerve

b Anastomotic branch of the hypoglossal nerve

c Accessory nerve

d Internal branch of the accessory nerve

e External branch of the accessory nerve

f Vagus nerve

g Anastomotic branch of the vagus nerve with the glossopharyngeal nerve

h Pharyngo-oesophageal nerve

i Anastomotic branch of the pharyngo-oesophageal nerve with the external branch of the cranial laryngeal nerve

j Anastomotic branch of the pharyngo-oesophageal nerve with the internal branch of the cranial laryngeal nerve

k Cranial laryngeal nerve

l Internal branch of the cranial laryngeal nerve

m External branch of the cranial laryngeal nerve

n Branch of the cranial laryngeal nerve to the cranial cervical ganglion

o Nodose ganglion

p Recurrent laryngeal nerve

q Glossopharyngeal nerve

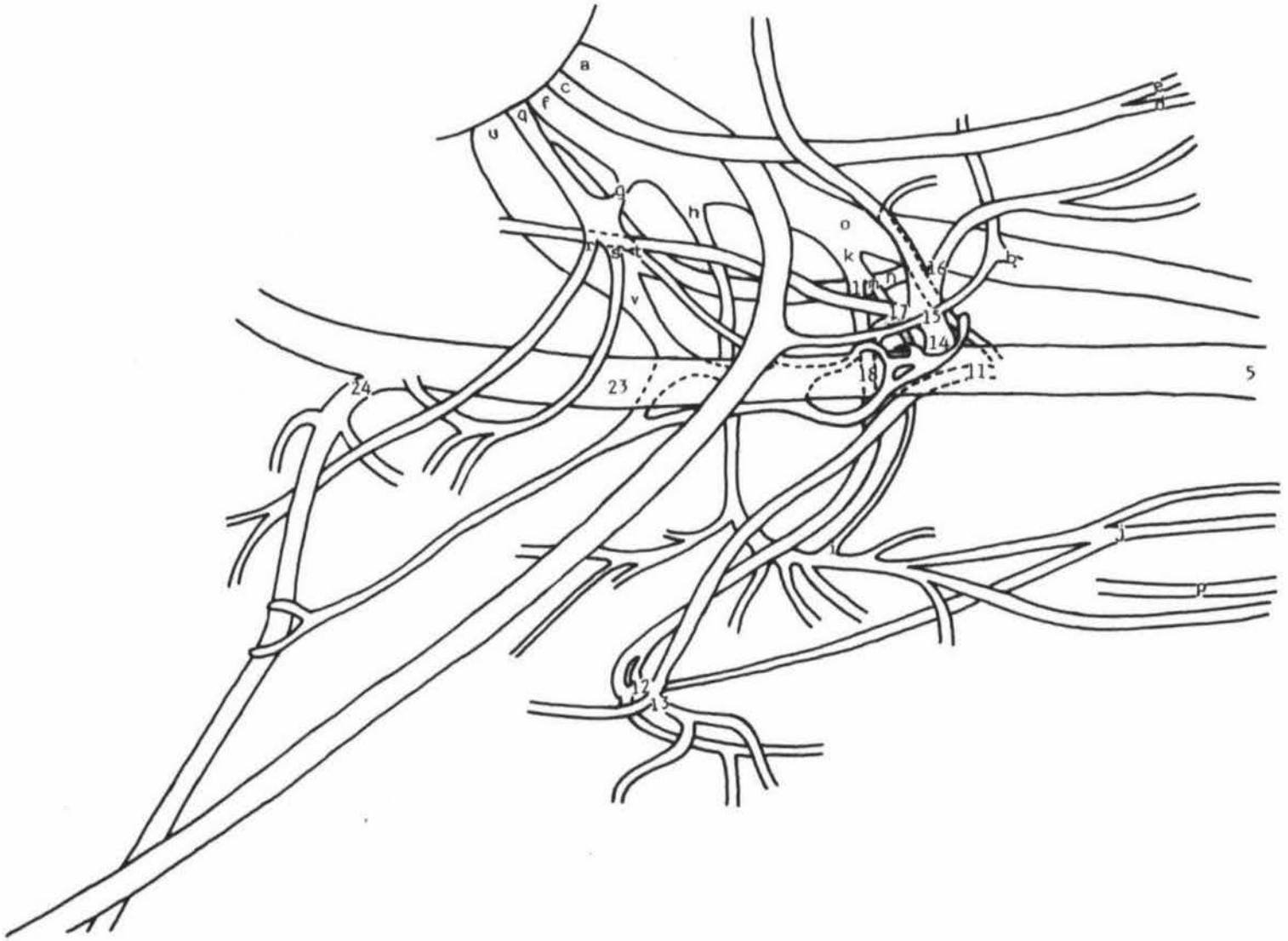
r Lingual branch of the glossopharyngeal nerve

s Pharyngeal branch of the glossopharyngeal nerve

t Carotid sinus nerve

u Cranial cervical ganglion

v External carotid nerve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branches pass rostrally, between the geniohyoid and genioglossus muscles to terminate in the genioglossal, hyoglossal, styloglossal, geniohyoid and thyrohyoideus muscles.

A branch arises from the hypoglossal nerve as the latter passes across the external carotid artery. The branch passes caudally for a short distance laterally along the common carotid artery to innervate the omohyoid, sternohyoid, and sternothyroid muscles (this branch may be joined by a branch from either the first or second cervical nerve, Ansa cranialis). Near the origin of this branch, an anastomotic branch of the hypoglossal nerve (Ansa n. hypoglossi - b) passes caudo-dorsally, between the accessory nerve (lateral) and the vagosympathetic trunk (medial), and across the lateral surface of the occipital artery. It accompanies the occipital artery and vein to the atlantal fossa to anastomose with the ventral branch of the first cervical nerve. Branches to the cranial cervical ganglion, the pharyngeal plexus, and the sternohyoid and omohyoid muscles, and an anastomotic branch to the lingual nerve may also arise in this region.

The spinal root of the accessory nerve (N. accessorius - c) passes ventrally on the medial aspect of the tympanic bulla. It is enclosed in a common fibrous sheath with the vagus nerve as far as the ventral end of the paramastoid process. In this region, the nerve is separated from the vagus nerve by the hypoglossal nerve and the occipital artery. It passes caudo-ventrally, accompanied by a muscular branch of the occipital artery, between the aponeurotic tendon of the sternomastoid and intertransversarius longus muscles to the atlantal fossa. The two structures pass caudo-dorsally for a short distance, 15 mm ventral to the wing of the atlas. On the medial aspect of the tendon of the sternomastoid muscle and lateral aspect of the longus capitis muscle the accessory nerve divides into internal and external branches. The internal branch of the accessory nerve (Ramus internus - d) passes to the vagus nerve. The external branch of the accessory nerve (Ramus externus - e) passes laterally, crossing the occipitohyoid muscle. At the level of the atlas it passes lateral to the rectus capitis ventralis muscle and divides into ventral and dorsal branches. The ventral branch (Ramus ventralis) passes caudo-ventrally to terminate in the sternocephalic, sternomastoideus, cleidomastoideus, and cleido-occipitalis muscles. The dorsal branch (Ramus dorsalis) passes, with a muscular branch of the occipital artery, caudo-dorsally between the tendon of the sternomastoid muscle and the intertransversarius longus muscle to exchange fibers with the first, second,

third, and fourth cervical nerves and terminates on the medial surface of the trapezius muscle.

The **vagus nerve** (N. vagus - f) passes caudo-ventrally, medial to the glossopharyngeal and accessory nerves. The latter is enclosed in a common fibrous sheath. The glossopharyngeal nerve then turns more rostrally, and the vagus and accessory nerves continue ventrally until separated by the hyoglossal nerve and the occipital artery immediately ventral to the paramastoid process and medial to the origin of the digastric muscle. The vagus nerve passes medially, and the accessory nerve laterally. The vagus nerve continues caudally, dorsal to the common carotid artery and lateral to the longus capitis muscle in the neck.

Branches arising from the vagus nerve in the retropharyngeal region are:

Anastomotic branch of the vagus nerve with the glossopharyngeal nerve (Ramus communicans cum n. glossopharyngea - g) arises just before the vagus nerve separates from the accessory nerve.

Pharyngo-oesophageal nerve (N. pharyngo-oesophageus - h) arises from the ventral edge of the vagus nerve medial to the paramastoid process and slightly caudal to the level of the cranial cervical ganglion. The nerve passes caudo-ventrally, between the mandibular salivary gland and the dorso-lateral surface of the larynx, medial to the ascending pharyngeal and external carotid arteries, to reach the dorsal surface of the pharynx, and at the level of the atlanto-occipital articulation, joins the pharyngeal branch of the glossopharyngeal nerve to form the pharyngeal plexus. It turns caudally, medial to the cranial laryngeal nerve and artery to give off a rostral branch which terminates largely in the chondropharyngeal region of the hyopharyngeus muscle.

The pharyngo-oesophageal nerve continues caudally to form:

Anastomotic branch of the pharyngo-oesophageal nerve with the recurrent laryngeal nerve (Ramus communicans cum n. laryngeus recurrens) arises at the level of the third cervical vertebra and the caudal end of the thyroid gland. The nerve passes across the cricopharyngeus muscle, to which it gives a branch, and then on to the trachea to anastomose with the cranial laryngeal nerve near the thyroid gland. As it crosses the cricopharyngeus muscle, it sends fibers to the cricopharyngeal,

thyropharyngeal, thyrohyoid, and cricothyroideus (probably the continuation of the external branch of the cranial laryngeal nerve) muscles, the thyroid gland, and oesophagus.

Anastomotic branch of the pharyngo-oesophageal nerve with the external branch of the cranial laryngeal nerve (Ramus communicans cum ramus externus n. laryngeus cranialis - i) arises as the pharyngo-oesophageal nerve crosses the cricopharyngeus muscle.

Anastomotic branch of the pharyngo-oesophageal nerve with the internal branch of the cranial laryngeal nerve (Ramus communicans cum ramus internus n. laryngeus cranialis - j) arises as the pharyngo-oesophageal nerve crosses the cricopharyngeus muscle.

Cranial laryngeal nerve (N. laryngeus cranialis - k) arises from the ventral surface of the vagus nerve, slightly caudal (10 mm) to the pharyngo-oesophageal nerve, medial to the origin of the occipital artery. The nerve passes rostro-ventrally, medial to the common carotid and cranial laryngeal arteries, across the lateral surface of the pharyngo-oesophageal nerve and the thyropharyngeal muscle. It accompanies the cranial laryngeal artery to the larynx, descending by the pharynx to divide into internal and external branches. The internal branch of the cranial laryngeal nerve (Ramus internus - l) passes rostro-ventrally, medial to the common carotid and cranial laryngeal arteries, to penetrate the larynx between the thyropharyngeus and hypopharyngeus muscles. As the branch passes the thyroid fissure, it divides into rostral and ventral branches. The rostral branch (Ramus rostralis) soon divides to innervate the laryngeal mucosa. The ventral branch (Ramus ventralis) passes caudally on the medial surface of the thyroid lamina to the cricoarytenoideus dorsalis muscle to innervate the pharyngeal mucosa and anastomose with the pharyngo-oesophageal and recurrent laryngeal nerves beneath the cricopharyngeal muscle. The external branch of the cranial laryngeal nerve (Ramus externus - m) passes ventrally with the pharyngo-oesophageal nerve to the cricothyroideus and thyropharyngeus muscles and the thyroid gland to anastomose with the pharyngo-oesophageal and recurrent laryngeal nerves. Fibers originating from the latter anastomosis innervate the cricoarytenoid and thyroarytenoid muscles.

Branches of the cranial laryngeal nerve to the pharyngeal and intercarotid plexuses.

Branches of the cranial laryngeal nerve to the cranial cervical ganglion - n.

Anastomotic branch of the cranial laryngeal nerve with the ansa hypoglossi.

Recurrent laryngeal nerve (N. laryngeus recurrens - p) separates from the vagus nerve in the thorax and emerges at the thoracic inlet. The right recurrent laryngeal nerve leaves the vagus in the area of the first intercostal space and passed around the right subclavian artery, medial to the costo-cervico-vertebral trunk, to reach the right ventral surface of the trachea. The left recurrent laryngeal nerve leaves the vagus at the aortic arch, passes around the caudal face of the arch, and then passes cranially along the left ventral surface of the trachea. At the entrance to the thorax the nerve is connected with the caudal cervical ganglion (Ganglion cervicale caudale). In the cervical region both recurrent laryngeal nerves pass along the ventro-lateral surface of the trachea, related dorsally on the left to the oesophagus and on the right to the common carotid artery. The nerve inclines more dorsally towards the cranial end of the trachea, to pass across the dorsal surface of the thyroid gland to the larynx and disappear beneath the cricopharyngeal muscles on the caudo-dorsal surface of the larynx. It passes between the cranial cornu of the thyroid cartilage and the cricoarytenoid muscle. At the caudal end of the larynx branches terminate in the cricoarytenoid, thyroarytenoid, transverse arytenoid, cricopharyngeal and thyropharyngeal muscles, and anastomose with the nerves supplying the cranial portion of the oesophagus.

A large branch passes from the recurrent laryngeal nerve to anastomose with the cranial laryngeal nerve medial to the cricopharyngeal muscle. Another branch arises to anastomose with the pharyngo-oesophageal nerve lateral to the cricopharyngeal muscle at the level of the second or third tracheal ring. From the latter branch fibers pass to the thyropharyngeal, cricothyroid, and thyrohyoid muscles. Branches are also given off to the cardiac, tracheal and oesophageal plexuses.

The nodose ganglion (G. distale - o) is indicated only by a slight broad, flattened enlargement of the vagus nerve in the region of the origin of the cranial laryngeal nerve.

The sympathetic trunk (Truncus sympathicus) joins the vagus nerve on the medial side in the atlantal region, medial to the parotid salivary gland. The two lie on the medial surface of the occipital artery, then descend the neck related to the dorso-medial (or dorso-lateral) surface of the common carotid artery in the common fibrous sheath. The nerves separate at the thoracic inlet.

The **glossopharyngeal nerve** (N. glossopharyngeus - q) lies medial to the tympanic bulla and on the internal surface of the cranial cervical ganglion. The nerve separates from the vagus and accessory nerves on its caudal side and crosses the lateral surface of the medial retropharyngeal lymph node and pharyngeal muscle medial to the great cornu of the hyoid bone and the keratopharyngeal muscle. In the region of the great cornu, the lingual artery lies ventral to the nerve.

Branches arising from the glossopharyngeal nerve slightly caudo-dorsal to the tympanic bulla on the medial surface of the occipitohyoideus muscle are:

Anastomotic branch of the glossopharyngeal nerve with the vagus nerve (Ramus communicans cum n. vagus - g) arises caudally.

Lingual branch of the glossopharyngeal nerve (Ramus linguales - r) passes down the stylohyoid bone to pass ventrally deep into the hypopharyngeus muscle and enter the tongue between the hyoglossal and chondropharyngeal muscles. The branch turns dorsally to innervate the caudal region of the body and root of the tongue, pharyngeal mucous membrane, and tonsils.

Pharyngeal branch of the glossopharyngeal nerve (Ramus pharyngeus - s) arises from the glossopharyngeal nerve near the medial retropharyngeal lymph node (may arise from the anastomotic branch to the vagus nerve or branch to the carotid sinus) and passes medial to this structure. The branch turns rostro-medial to the lingual branch to join the pharyngo-oesophageal and sympathetic nerves to form the pharyngeal plexus, and innervate the muscles of the pharynx. A second pharyngeal branch arises as the glossopharyngeal nerve passes medial to the keratopharyngeal muscle. This branch enters the chondropharyngeal muscle.

Carotid sinus nerve (N. sinus carotici, Hering, 1924; intercarotid nerve, de Castro, 1928; glossopharyngeal carotid branch, Drüner, 1925; nerve of Hering - t) may arise as two branches and pass caudo-ventrally to innervate the rostro-lateral aspect of the occipital artery. The name, carotid sinus nerve, is misleading in its implication as it has been found to innervate not only the carotid sinus and carotid body, but also the entire carotid bifurcation. Just before the carotid sinus nerve reaches the bifurcation it divides into three to five filaments: the medial filaments supply the medial aspects and the lateral filaments supply the lateral aspects of the carotid sinus, carotid body, occipital, ascending pharyngeal, cranial laryngeal, lingual, external carotid and common carotid arteries (Sha-Ban, 1974). A carotid sinus nerve filament receives an anastomotic filament from the external carotid nerve at the ventral (or lateral) aspect of the ascending pharyngeal artery origin.

Anastomotic branch of the glossopharyngeal nerve with the pharyngo-oesophageal nerve. These branches may arise as a common trunk.

The glossopharyngeal nerve continues rostrally, medial to the junction of the great and middle cornua of the hyoid bone, and the styloglossal and hyoglossal muscles to enter the tongue.

The **cranial cervical ganglion** (G. cervicale craniale - u) is a pale brown, fusiform structure that lies ventral to the cranial foramen lacerum and medial to the glossopharyngeal and vagus nerves and condyloid artery, ventro-medial to the paramastoid process, and lateral to the longus capitis muscle at the cranial end of the cervical sympathetic trunk.

The branch joining the ventral extremity of the cranial cervical ganglion is:

Sympathetic trunk (Truncus sympathicus) which separates from the vagus nerve at the cranial end of the atlantal fossa to pass medial to the common carotid and occipital arteries to join the cranial cervical ganglion.

The branch arising from the ventral extremity of the cranial cervical ganglion is:

External carotid nerve (N. aroticus externus - v) which passes caudo-ventrally to the origin of the occipital and external carotid arteries. Before reaching the medial aspect of the ascending pharyngeal artery, the nerve divides into three to five filaments. Just ventral to

the origin of the ascending pharyngeal artery, some filaments innervate the carotid body and anastomose with the carotid sinus branch. Other filaments follow the medial aspects of the occipital, cranial laryngeal, lingual, external carotid and common carotid arteries (Sha-Ban, 1974).

Fibers also connect the cranial cervical ganglion with the pharyngeal plexus, and the cranial laryngeal, hypoglossal, accessory, vagus, glossopharyngeal and first cervical nerves.

CHAPTER 3

THE PHYSIOLOGY OF THE CAROTID SINUS AND COMMON CAROTID ARTERY OF THE SHEEP

3.1 INTRODUCTION

The carotid sinus is a dilatation at the origin of the internal carotid artery in many species, including the rat, rabbit, dog and human. In the sheep, however, in which the extracranial part of the internal carotid artery is absent, the analogous baroreceptor area is located at the undilated origin of the occipital artery or the occipito-ascending pharyngeal trunk.

The integrity of the ovine common carotid arterial baroreceptor reflex was examined by the simple technique of cervical arterial clamping and compared with that described in other species with a true carotid sinus.

3.2 LITERATURE REVIEW

3.2.1 Discovery of the Carotid Sinus Baroreceptor Reflex

For many years it has been recognised that bradycardia can be produced by external pressure on the upper neck (the vagus pressure test or Vagusdruckversuch of Tschermak, 1866) and that tachycardia and systemic hypertension follow clamping of the common carotid arteries. The former was attributed to direct vagal stimulation (Tschermak, 1868) and the latter to cerebral ischaemia (Cooper, 1836; Landois, 1865; Sewall and Steiner, 1885; Hedon, 1910). Alternative views were put by Concato (1870) who stated that pressure on the carotid bifurcation seemed to be more effective than pressure on the vagus trunk. This interpretation became less tenable when Bayliss (1893) demonstrated that common carotid arterial occlusion did not appreciably decrease medullary blood flow because it was largely derived from the vertebral arterial system. Pagano (1900) and Sicilano (1900) discovered that, in the dog, the pressor effects of common carotid arterial clamping depended upon the integrity of nervous structures located near the carotid vessels. These findings, however, did little to alter the view held for three-quarters of a century that the circulatory changes were due to direct ischaemic stimulation of the medullary centers.

Sollman and Brown (1912) bordered on discovery of the carotid sinus reflex when they found that tugging the cephalic end of the common carotid artery, even if it had been previously ligated, caused bradycardia. Discovery of the carotid sinus reflex was made by Hering (1932) after sustained interest in the mechanism of the Vagusdruckversuch. In 1905, in performing this test on an elderly woman, he was struck by the fact that it was sufficient merely to press lightly on one of her common carotid arteries to evoke bradycardia. It seemed surprising to him that the vagus trunk could possibly be excited by such a delicate stimulus. In 1919, Hering demonstrated that direct mechanical stimulation of the vagal trunk did not provoke bradycardia in the rabbit or dog. On the contrary, he showed that compression of the larynx provoked bradycardia in the rabbit (1920); he surmised, therefore, that the Vagusdruckversuch might be a reflex phenomenon. Hering (1923) localised the origin of the reflex to nerve endings in the region of the carotid bifurcation, particularly that of the carotid sinus. In subsequent papers (1924, 1925, 1927) he demonstrated that the tonically active afferent pathway resided in the carotid sinus branch of the glossopharyngeal nerve and that stimulation of the nerve or the sinus produced reflex systemic hypotension and bradycardia.

De Castro (1926, 1928) was of the opinion that afferent impulses from the carotid sinus travelled partly in the glossopharyngeal nerve, but more particularly in the vagus nerve. Daniélopolu, Aslan, Marcu, Proca and Manesco (1927), Daniélopolu, Marcu, Proca and Aslan (1932) and Heymans, Brouckaert and Regniers (1933) stated that branches from the glossopharyngeal nerve, the cranial cervical ganglion and the vagus nerve take part in the transmission of the carotid sinus reflex. In addition, Wright (1932) proposed that the carotid sinus may also connect with the hypoglossal nerve. Gerard and Billingsly (1923) and Kahn (1929) found that only occasionally did fibers reach the carotid sinus through the vagus nerve in the dog.

In 1936, Code, Dingle and Moorehouse perfused the isolated carotid sinus at various pressures. Section or evulsion of the carotid sinus nerve prevented changes in either blood pressure or heart rate upon lowering or raising the pressure within the carotid sinus. Section of the external carotid nerve alone had little or no effect on the cardiovascular components of the carotid sinus reflex. From these observations, it was concluded that the sensory components of the carotid sinus reflex are conducted solely by the carotid sinus nerve.

3.2.2. Mechanical Aspects of Carotid Sinus Baroreceptor Stimulation

The carotid sinus nerve contains sensory nerve fibers of various sizes, activated at different pressure thresholds. These fibers may be grouped into two types:

3.2.2.1 Fibers Innervating Slowly Adapting Baroreceptors

These respond to changes in mean arterial pressure, i.e., static non-pulsatile pressure, and are not stimulated below a mean pressure of about 60 mmHg in most of the species studied (Hering, 1924; Koch, 1929, 1931; Heymans and Neil, 1958). Maximal sensitivity of the carotid sinus reflex occurs between 95 to 120 mmHg, i.e., near the normal blood pressure of mammals, and no further response occurs once the pressure has exceeded 195 to 200 mmHg (Koch, 1929; Aviado and Schmidt, 1955). For example, in the rabbit, the threshold of response was 25 mmHg, the maximal sensitivity was at 95 mmHg and there was no further response once the blood pressure exceeded 160 mmHg. In the cat, the comparable figures are 65, 145 and 230 mmHg and, in the dog, 60, 120 and 210 mmHg. The 'threshold' concept of Koch explains the lack of reflex response to carotid clamping when the systemic pressure is low.

Mean blood pressure and maximal sensitivity values have been determined using the appearance of reflex changes in blood pressure and heart rate to identify baroreceptor activation. These values are consistent with the observations of investigators who used neural recording techniques to identify baroreceptor activity (Koshanpour and Kelso, 1972) and imply a direct relationship of threshold and intensity of baroreceptor stimulation to changes in efferent activity.

3.2.2.2 Fibers Innervating Rapidly Adapting Baroreceptors

Fibers of this type respond to changes in pulse pressure. The neural responses demonstrated by Bronk and Stella (1932, 1935) indicated that the rate of baroreceptor change of discharge about a given mean involved:

1. increased frequency and duration of discharge,
2. recruitment of more baroreceptor units.

Thus, a volley of impulses discharges from the carotid sinus baroreceptors during each cardiac cycle with maximal activity at the rapid systolic rise and early diastolic fall in pressure. During the late diastolic phase, this is followed by a decline in activity to relative quiescence. Using a Dale-Schuster pump to provide pulsatile perfusion, Heymans, Bouckaert and Dautrebande (1931) repeated the experiments of Koch (1929) and observed that the threshold blood pressure for responses to carotid sinus perfusion was 65 mmHg, maximal sensitivity of the carotid sinus reflex occurred between 85 and 110 mmHg and no further response occurred once blood pressures exceeded 220 mmHg. These values are similar to those of Pelletier, Clement and Shepherd (1972) who used nerve recording techniques to identify baroreceptor activation with a pulsatile system. These authors, together with Gero and Gerová (1967), established a direct relationship of baroreceptor activity to systemic blood pressure. A systemic pressure response dependent on the pulsation frequency occurs up to a pulse amplitude of 45 mmHg - the pulsation frequency being most effective at the lowest amplitude of 20 mmHg. At a pulse amplitude of 90 mmHg, on the other hand, the frequency dependent systemic response increases up to 120 pulse cycles/min only, and any further increase of pulse frequency induces insignificant increases of systemic blood pressure (Gero and Gerová, 1967). A fall in pulse pressure without any change in mean pressure reduces baroreceptor stimulation even when the mean blood pressure is above threshold and conversely a rise in pulse pressure (especially when the rate of pressure change is greatest), without any change in mean blood pressure, increases baroreceptor stimulation.

This concept of both the mean blood pressure and the pulse pressure being significant variables that influence the gain of the baroreceptor reflex is supported by McCrea and Wiggins (1933), Ead, Green and Neil (1952), Schmidt, Kumada and Sagawa (1972) and Kenner, Baertschi, Allison and Ono (1974). Schmidt, Kumada and Sagawa (1972) designed a study to assess the relative importance of mean blood pressure, pulse amplitude and frequency on carotid sinus reflex activity. They found that increasing the pulse amplitude from 0 to 75 mmHg at a constant frequency of 2 Hz augmented the reflex response when the mean sinus pressure was less than 150 mmHg, but at higher mean sinus pressures the pulse pressure was not a significant variable. Changing the pulse frequency from 1 to 4 Hz did not alter the magnitude of the reflex responses in any of the stimulus mode combinations examined.

Nerve recordings support these reflex findings and show that a pulsatile endosinus pressure is more effective in exciting baroreceptor discharge than is a steady pressure with the same, or higher, mean value (Ead, Green and Neil, 1952; Heymans and Neil, 1958; Gero and Gerová, 1962, 1963).

It also appears that afferent activity engendered by steady flow through the carotid sinus is less effective centrally in inhibiting vasomotor discharge than that occurring during pulsatile flow at the same mean pressure (Ead, Green and Neil, 1952). The rate of change of pressure also seems to be important - at a mean intrasinus pressure of 70 mmHg, a small alteration in the rate of change of pulse pressure induced a considerable systemic response; doubling the rate of change of pulse pressure caused a five-fold increase in the systemic response.

Thus the normal regulation of systemic pressure involves both the mean blood pressure and the rate of change of blood pressure (Heymans and Neil, 1958; Scher, 1967).

3.2.2.3 Mode of Baroreceptor Stimulation

The baroreceptors of the carotid sinus are functionally three dimensional stretch (or mechano) receptors that are stimulated by any deformation of the adventitial tissue in which they reside - normally through altering intraluminal pressure. Shubrooks (1972), however, demonstrated in dogs that altering the transmural pressure across the carotid sinus wall, with a specially designed airtight cylinder around the neck, was an effective method of eliciting reflex responses. It was presumed that this technique induced

significant dimensional changes in the sinus wall, even though changes of endosinus pressure were minimal. Additional evidence that carotid sinus baroreceptor sensitivity is a function of dimensional alterations, and not solely the intraluminal pressure has come from experiments in which dimensions were maintained. One of the first of such demonstrations was conducted by Hauss, Kreuziger and Asteroth (1949) and was repeated by Wakerlin, Crandall, Frank, Johnson, Pomper and Schmid (1954) who showed that when the carotid sinuses were rendered nondistensible by embedding them in plaster, endosinal pressure changes failed to elicit reflex responses. Moreover, bilateral placement of rigid casts around the carotid sinuses have been reported to produce sustained hypertension, presumably also by abolishing baroreceptor mediated inhibition of sympathetic activity (Burnstyne, Horrobin and Lloyd, 1972).

3.2.2.4 Modification of the Mode of Baroreceptor Stimulation

It is possible that the baroreceptor reflex sensitivity may be modified by alterations in the tension or distensibility of the carotid sinus wall which result from catecholamine stimulation, acidosis, hypoxaemia or modifiers of vascular smooth muscle tone (Palme, 1943; Petersen, 1962a,b; Mills and Sampson, 1969; Knoche and Kienecher, 1977). One mechanism that has aroused considerable interest is the autonomic regulation of sinus compliance through the sympathetic efferent pathways. Palme (1936), Heymans and van den Heuvel-Heymans (1950, 1951), Landgren, Neil and Zotterman (1952) and Heymans, Delaunois and van den Heuvel-Heymans (1953) demonstrated that the local application of adrenaline or noradrenaline to the wall of the carotid sinus caused contraction of the vascular smooth muscle. This in turn increased the longitudinal tension and decreased the distensibility of the arterial wall in the vicinity of the baroreceptor fibers and enhanced the excitability of the terminals to stimuli provided by the blood pressure. Heymans and Delaunois (1955) and Heymans, Delaunois and Rovati (1957) took the view that the effectiveness of the baroreceptor mechanism was dependent on the degree of tension in the carotid sinus wall itself. The fact that sympathomimetic drugs induced large systemic pressure changes when applied to the walls of the empty carotid sinus (Heymans, 1952) suggests that the tension of vascular muscle in or around the sinus might be important in modifying the baroreceptor afferent activity independent of the endosinal blood pressure.

Kezdi (1954), Sampson and Mills (1970), Bagshaw and Peterson (1972) and Bolter and Ledsome (1976) demonstrated that electrical stimulation of the nerves from the superior cervical sympathetic ganglion supplying the carotid sinus caused hypotension similar to that following the topical application of catecholamines to the sinus wall. They argued that there may be a local efferent sympathetic control of baroreceptor output by inducing contraction of the sinus wall muscular tissue. Further, Wurster and Trobiani (1973) demonstrated that sympathetic stimulation may reduce the hypertensive response to bilateral common carotid arterial clamping by more than 50% - a result that implies a smaller reduction of baroreceptor impulse activity during occlusion and is consistent with the increase of this activity by administration of catecholamines. On the other hand, Code, Dingle and Moorehouse (1936) reported that the depressor responses to stimulation of the carotid sinus sympathetic supply were greatly reduced, or abolished, by section of the carotid sinus nerve. They suggested, therefore, that any depressor effects produced by stimulation of the sympathetic nerves were the result of activating depressor fibers carried in the sympathetic nerve after communication with the sinus nerve, or were caused by the spread of the stimulating current along the numerous communicating branches to the glossopharyngeal trunk, the adjacent nodose ganglion, or vagus nerve. Others (Floyd and Neil, 1952; Carlston, Folkow, Grimby, Hamberger and Thulesius, 1958; Heymans and Neil, 1958; Moncada and Scher, 1963), however, were able to confirm that stimulation of the local sympathetic supply to the carotid sinus caused hypotension and concluded that under physiological conditions the sympathetic innervation of the sinus region was of little practical importance in modifying the baroreceptor sensitivity.

It should be remembered that the muscularity of the tunica media in the carotid sinus region is both sparse and eccentric. If sympathetic fibers do cause any effect on the tone of the arterial musculature in this area, it is likely to be exerted in adjacent parts of the vessel wall rather than in the sinus itself. As a result, there may be slight distortion of the sinus, which could in turn increase the activity of the baroreceptors. Perhaps the best interpretation is offered by Folkow and Neil (1971) who suggested that catecholamines given exogenously or released from sympathetic nerves may stimulate smooth muscle contraction and 'so deform the wall that the baroreceptors become excited'. The physiological significance of this proposed mechanism for sympathetic regulation of baroreceptor function has not, as yet, been fully assessed.

3.2.3. Comparison of the Carotid Sinus and Aortic Arch Baroreceptor Reflexes

Electrical stimulation of the central end of the carotid sinus nerve produces hypotension and bradycardia (Cyon and Ludwig, 1866), a response that is quantitatively identical to that seen upon electrical stimulation of the aortic arch recurrent laryngeal nerve (Hering, 1924, 1927). Kendrick and Matson (1973) further demonstrated that, in the dog, the maximal changes in blood pressure and heart rate accompanying carotid sinus nerve stimulation do not differ quantitatively from those accompanying stimulation of the recurrent laryngeal nerve. More recently, however, Samodelov, Godehard and Arndt (1979) compared in the decerebrate cat the response characteristics of two groups of carotid sinus and aortic arch baroreceptors to inflating and deflating a balloon. They concluded that carotid sinus and aortic arch baroreceptors differ neither in their sensitivities nor in their working blood pressure ranges when in their physiological environment. It is, therefore, possible that the carotid sinus and aortic arch baroreflexes are functionally equivalent. This has, however, been questioned by a considerable number of workers.

The potential for reflex circulatory regulation by the carotid sinus and aortic arch baroreceptor systems may not differ with maximal stimulation, but there are important differences in the level of excitation achieved by a given pressure stimulus. This has been demonstrated in a study reported by Edis (1971), which showed that, in vagotomised dogs selective cold blockade of the recurrent laryngeal nerves resulted in a trivial increase in blood pressure and heart rate, thus suggesting minimal tone in the laryngeal nerves at normal pressure levels. Selective cold blockade of the carotid sinus nerves produced a marked rise of blood pressure and heart rate. When this was followed by recurrent laryngeal nerve blockade, a still greater increase of blood pressure and heart rate was observed. Similarly, Pelletier, Clement and Shepherd (1972) and Pelletier and Shepherd (1973) undertook a study that permitted a comparison of the carotid sinus nerve and recurrent laryngeal nerve activity in the dog. These workers found that the threshold blood pressure sufficient to elicit a change in afferent impulse activity in the carotid sinus nerve was 62 mmHg, whereas that of the recurrent laryngeal nerve was much higher, averaging 95 mmHg. Moreover, the curve relating arterial pressure to the integrated activity of the recurrent laryngeal nerve constructed by Donald and Edis (1971) and Pelletier, Clement and Shepherd (1972) was not as steep and substantially displaced to the right except at the lowest and highest

pressures, indicating that over a broad range the functionally significant aortic arch baroreceptors have a relatively high pressure threshold and are less sensitive to normal blood pressures than are the carotid sinus baroreceptors. There may, however, be important differences between species. In the rabbit, for example, Bloor (1964), Aars (1968) and Angell-James (1971, 1973) have shown that recurrent laryngeal nerve activity increases in a linear fashion from aortic pressures as low as 40 mmHg, with an average threshold of about 55 mmHg. The response curves of Donald and Edis (1971) and Pelletier, Clement and Shepherd (1972) closely resemble those obtained in the dog by Kendrick and Matson (1973) from step increases in nerve stimulus frequency. This study revealed that a higher frequency of 60 to 80 Hz is necessary to produce maximal depression of blood pressure and heart rate during recurrent laryngeal nerve stimulation than is required during carotid sinus nerve stimulation (10 to 20 Hz). These frequency response characteristics are similar to the findings in the rabbit (Neil, Redwood and Schweitzer, 1949a,b,c; Douglas, Ritchie and Schaumann, 1956), cat (Neil, Redwood and Schweitzer, 1949a,b,c; Douglas, Ritchie and Schaumann, 1956; Douglas and Schaumann, 1956) and pig (Schmidt, 1968). These results suggest that increasing the frequency of baroreceptor discharge is of greater importance than baroreceptor recruitment in response to raising the pressure in the aortic arch and the rate of baroreceptor discharge frequency is of less importance than recruitment for the carotid sinus reflex. Pelletier, Clement and Shepherd (1972) concluded that differences in the receptors themselves were responsible for the differences in reflex effects. Kendrick and Matson (1973), however, suggested that the differences in reflex effects may be related to the proportion of large and small depressor fibers in the two nerves and the fiber terminations on the medullary neurons. The major depressor effects of recurrent laryngeal nerve stimulation may be mediated by the large depressor fibers, which have fewer terminations on the medullary neurons than the small depressor fibers that constitute the major depressor component of the carotid sinus nerve. In addition, the carotid sinus baroreceptor reflex appears to be more sensitive to dynamic stimulation (Angell-James and de Burgh Daly, 1970) and to exhibit more pronounced effects on peripheral vascular resistance than on heart rate when compared with the aortic arch baroreceptor reflex (Glick and Lovell, 1968; Hainsworth, Ludsome and Carswell, 1970).

3.2.4 Influence of the Carotid Sinus Baroreceptor Afferents on the Cardiovascular Effector Organs

The glossopharyngeal carotid sinus nerve baroreceptor fibers enter the brainstem and synapse in the nucleus of the solitary tract, from where secondary fibers travel to the medulla oblongata reticular formation and enter the vasomotor and cardioinhibitory centers. It is the discharge from these centers that the carotid sinus baroreceptors modify.

1. The Vasomotor Center

The vasomotor center is a large diffuse area extending from just below the obex to the vestibular nuclei and from the floor of the fourth ventricle almost to the pyramids in the reticular formation. Within the vasomotor center there exist separate pressor and depressor regions that overlap in the rostro-caudal and lateral directions (Alexander, 1946). These two regions exert influence solely through variations in the rate of tonic discharge in the sympathetic vasoconstrictor and cardiac nerves.

The preganglionic sympathetic vasoconstrictor and cardiac fibers pass from the vasomotor center to the intermedio-lateral gray matter of the spinal column upper five thoracic vertebrae before running to the cervical and cranial thoracic ganglia, from which the postganglionic vasoconstrictor and cardiac nerves originate.

2. The Cardioinhibitory Center

The cardioinhibitory center is an area of the medulla oblongata nucleus ambiguus and exerts influence solely through variations of the tonic inhibitory discharge in the parasympathetic vagal cardiac nerve.

The preganglionic cardiac fibers pass from the cardioinhibitory center to the dorsal motor nucleus of the vagus and descend in the vagal trunk to ganglia in the cardiac plexus and possibly the atrial wall. It is from here that the parasympathetic postganglionic vagal cardiac nerves originate.

3.2.4.1 Regulation of Vascular Tone by the Carotid Sinus Baroreceptor Reflex

3.2.4.1.1 Reflex Effects on Regional Arterial Blood Flow

In the conscious animal, carotid sinus hypotension induces remarkably transient changes of cardiac output, however, during the steady state of the reflex, approximately two-thirds of the rise in systemic pressure can be attributed to an increased total peripheral resistance (Kircheim and Gross, 1971). These reflex responses involve several vascular beds.

1. Mesenteric Blood Flow

The splanchnic vascular bed is thought to play an important role as a blood depot in the carotid sinus reflex adjustment of blood pressure (Izquierdo and Koch, 1930; Heymans and Neil, 1958; Grayson and Mendel, 1965; Rowell, Detry, Blackmon and Wyss, 1972). Alterations in baroreceptor output produced by common carotid arterial clamping or by increased perfusion pressure in the isolated carotid sinus induces reflex sympathetic mesenteric vasoconstriction or vasodilation, respectively (Driver and Vogt, 1950; Folkow, 1962; Vatner, Franklin, Van Citters and Braunwald, 1970; Johnson, Rowell, Niederberg and Eisman, 1974). The most convincing evidence in support of a reflex vasoconstriction is found only in studies performed in vagotomised animals - results obtained in intact animals can be interpreted as showing increased resistance in the mesenteric vascular bed is due to autoregulation (Polosa and Rossi, 1961; Bond and Green, 1969; Resnicoff, Harris, Hampsey and Schwartz, 1969). Interruption of the cervical vagi may eliminate a continuous inhibitory influence on sympathetic efferents (Guazzi, Libretti and Zanchetti, 1962; Pillsbury, Guazzi and Freis, 1969; Öberg and White, 1970a,b; Mancia, Donald and Shepherd, 1973). The vagal afferents not only demonstrate a central interaction with carotid sinus baroreceptor afferents, but also - like the baroreceptors - seem to have a differential inhibitory effect on the output to the various parallel-coupled vascular beds (Öberg and White, 1970a,b; Mancia, Donald and Shepherd, 1973). A reasonable postulate may be that carotid baroreceptor activation induces only mesenteric vasoconstriction when the simultaneous inhibitory afferent vagal influences from the low pressure system receptors in the cardiopulmonary region are eliminated (Kircheim, 1976).

2. Skeletal Muscle Blood Flow

There is convincing evidence derived from cardiovascular experimentation that the carotid sinus baroreceptors reflexly control the sympathetic constrictor tone of the muscle resistance vessels, particularly sensitively. Reflex vasoconstriction in response to an unloading of the carotid baroreceptors is especially pronounced in skeletal muscle resistance vessels (Hartman, Orskov and Rein, 1937; Folkow, Ström and Uvnäs, 1950; Folkow, 1962; Kendrick and Matson 1973). Conversely, carotid sinus nerve stimulation induces reflex vasodilation (Carlsten, Folkow, Grimby, Hamberger and Thulesius, 1958; Vatner, Franklin, Van Citters and Braunwald, 1970; Guo and Richardson, 1984).

3. Kidney Blood Flow

Most of the early and more recent studies in the anaesthetised animal demonstrated that alterations of carotid sinus baroreceptor input produced by changing the intrasinus pressure induced changes in renal blood flow. Reflex sympathetic vasoconstriction has been reported upon common carotid artrial clamping and reflex vasodilation has been described during carotid sinus nerve stimulation (Hartmann, Orskov and Rein, 1937; Kramer, 1959; McGiff and Aviado, 1961; Iriuchijima, 1972).

4. Skin Blood Flow

Although carotid sinus baroreceptor reflex vasoconstriction has been observed in the skin vasculature of animals (Harlan, Smith and Richardson, 1967), there is good experimental evidence that the carotid baroreceptor reflex responses of the skin vasculature are very small compared with the reflex effects on skeletal muscle vessels (Roddie, Shepherd and Whelan, 1958; Lofving, 1961a,b; Folkow and Neil, 1971; Delius, Hagbarth, Hongell and Wallin, 1972).

3.2.4.1.2 Reflex Effects on the Venous System

The lack of a suitable, convenient and reliable method of measuring venous tone has prompted many investigators to explore the problem in quite different, but inconclusive, ways. Nevertheless, some generalisations on the degree of venous tone in response to the carotid sinus baroreceptor reflex can be formulated.

It has been suggested that sympathetic venous contraction plays an important part in the reflex response to carotid sinus hypotension (Daly and Luck, 1958; Hadjiminas and Öberg, 1968; Shoukas and Sagawa, 1973; Shoukas and Brunner, 1980) by its ability to mobilise blood from the venous system, thereby promoting venous return to the heart and thus increasing cardiac output (Landis and Hortenstine, 1950; Bartelstone, 1960; Öberg, 1964; Shoukas and Sagawa, 1973).

Changes in carotid baroreceptor activity under certain experimental conditions can alter the capacitance of vessels in different parallel-coupled vascular beds. The venous vessels of the intestine, with their relatively large blood content, seem to be engaged to a greater extent than those of the skeletal muscle vasculature (Browse, Donald and Shepherd, 1966). This is consistent with the lack of noteworthy reaction of the human venous vessels in the extremities in response to changes in posture (Gauer and Thron, 1962, 1965; Samueloff, Browse and Shepherd, 1966) and to transfer of blood to the legs by lower-body negative pressure (Samueloff, Browse and Shepherd,1966). The quantitative aspects of the venous vessels in the carotid sinus baroreceptor reflex remains to be elucidated, however.

3.2.4.2 Regulation of Cardiac Performance by the Carotid Sinus Baroreceptor Reflex

The significance of the carotid sinus baroreceptor reflex in cardiac regulation in the intact circulation is debated. There is controversy as to whether the haemodynamic changes responsible for the systemic hypotension or hypertension induced by baroreceptor impulses are due to changes in cardiac output, total peripheral resistance or both (Kircheim, 1976). Baskerville, Eckberg and Thompson (1979) and Borst (1979) suggest that a decrease in cardiac output is more likely to contribute to the early hypotensive effect of carotid sinus baroreceptor stimulation than to the later phase, when the blood pressure reduction seemed independent of cardiac phenomena. An increase in parasympathetic tone may also participate in the reflex bradycardia (Eastcott, Pickering and Rob, 1954; de Vleeschhouwer and Heymans, 1967; Pickering, Gribbin, Strange-Petersen, Cunningham and Sleight, 1972; Mancia, Bonazzi, Pozzoni, Ferrari, Gardumi, Gregorini and Perondi, 1979).

3.2.4.2.1 Reflex Effects on Heart Rate

In the anaesthetised dog, common carotid arterial clamping increased the steady-state heart rate (Kenney, Neil and Schweitzer, 1951; de Vleeschhouwer and Heymans, 1967; Kircheim and Gross, 1970; Constantine, McShane and Wang, 1971) with a greater rise under chloralose anaesthetic (Delaunois and Bernard, 1967; De Vleeschhouwer and Heymans, 1967; Thames and Kontos, 1970; Wang, Chai, Kuo and Wang, 1970) than pentobarbitone (Iriuchijima, Soulsby and Wilson, 1968; Bond and Green, 1969; Constantine, McShane and Wang, 1971). An important factor appears to be in the pre-existing level of activity in the sympathetic and parasympathetic branches of the autonomic nervous system. The high background level of vagal activity in the conscious dog results in a depressed cardiac responsiveness to sympathetic stimuli and vice versa (Kircheim, 1976).

Studies in the dog neither provide unequivocal evidence in favour of the classical viewpoint that heart rate responses result from reciprocal changes in the vagal and sympathetic motor discharges (Rosenblueth and Freeman, 1931; Heymans and Neil, 1958) nor do they support the experiments of Glick and Braunwald (1965) who suggested that responses to increased systemic blood pressure predominantly involved vagal compensation, whereas responses to decreased blood pressure were mediated by the sympathetic effector component.

The transient changes in cardiac output that are dependent on heart rate were shown to induce rapid changes in systemic blood pressure before an effect on total peripheral resistance (Kircheim and Gross, 1971).

3.2.4.2.2 Reflex Effects on Stroke Volume

The carotid sinus baroreceptor induced reflex effects on stroke volume differ in the anaesthetised and conscious dog; in the anaesthetised animal there is an insignificant increase or no change in stroke volume (Bond and Green, 1969; Constantine, McShane and Wang, 1971), whereas in the conscious animal stroke volume invariably decreases during common carotid clamping (Corcondilas, Donald and Shepherd, 1964; Olmsted, McCubbin and Page, 1966; Fronek, 1970; Kircheim and Gross, 1971). It remains to be elucidated, however, whether the Frank-Starling mechanism (Frank, 1895; Patterson, Peiper and Starling, 1914) or the after load (Anrep, 1912; Sarnoff, Mitchell, Gilmore and Remensnyder, 1960) are responsible for the increased work after reduction of carotid sinus pressures in the conscious dog.

3.2.5 Effects of Anaesthesia on the Carotid Sinus Baroreceptor Reflex

When administered in normal anaesthetic doses, chloralose, cyclopropane, Evipan and thiopentone appear to be the anaesthetics of choice for demonstrating the carotid sinus baroreceptor reflex because of their limited reductions of the cardiovascular responses to sinus pressure changes. However, these systemic responses may be slower to develop and disappear (Vatner, Franklin and Braunwald, 1971). Comroe and Schmidt (1940) and Schmidt (1940) reported that chloralose increases the sensitivity of the carotid sinus baroreceptors and the effectiveness of their reflex. Longer-acting barbiturates, notably barbitone and phenobarbitone, profoundly reduce the blood pressure response to the carotid sinus baroreceptor reflex (Bouckaert and Heymans, 1930; Heymans and Neil, 1958) while pentobarbitone appears to be intermediate in depressant activity between that of chloralose and barbitone (Heymans and Neil, 1958).

If anaesthesia with even the anaesthetic of choice for demonstrating the carotid sinus baroreceptor reflex is too deep, then there is a direct depression of the vasomotor and cardioinhibitory centers (Greisheimer, 1965; Korner, 1971; White and McRitchie, 1973; Zimpfer, Manders, Barget and Vatner, 1982). As a result, the blood pressure falls, partly due to a reduction in arteriolar resistance and partly due to decreased venous return subsequent to the loss of sympathetic venous tone. In such circumstances, the carotid sinus baroreceptor impulse activity is itself feeble and the sparse impulse discharge impinges little on the depressed centers.

Halothane's most impressive effect on the cardiovascular system is its depressant action on myocardial contractility and velocity of shortening (Vatner and Braunwald, 1975), but it also further produces a differential effect on regional vascular resistances. Vasodilation occurs to a greater extent in the renal, and to a lesser extent in the iliac bed, while the mesenteric bed responds with marked constriction (Vatner and Braunwald, 1975). Studies on the effect of halothane on the carotid sinus baroreceptor reflex have produced conflicting results. Several studies using the slope of blood pressure-heart rate interval relationships in humans and pressure-nerve activity relationships in the isolated carotid sinus preparation of animals have shown that halothane depresses the carotid sinus baroreceptor reflex (Price, Price and Morse, 1965; Bristow, Prys-Roberts, Fischer, Pickering and Sleight, 1969; Duke, Fownes and Wade, 1977; Wilkinson, Stowe, Glantz and Tyberg, 1980) though this finding has not been confirmed by others (Epstein,

Wang and Bartelstone, 1968; Bagshaw and Cox, 1977; Cox and Bagshaw, 1980b). Recently, however, Behnia and Koshanpour (1984) used a cross circulation technique that preserved the physiological integrity of the carotid sinus baroreceptor reflex and the sympathetic innervation of the sinus. They found that inspired halothane concentrations of 0.50 to 1.25% caused a dose dependent depression of the carotid sinus pressure-nerve activity relationship, whereas an increase in the inspired halothane concentration beyond 1.25% tended to increase the baroreceptor response towards normal.

3.3 MATERIALS AND METHODS

Ten of the ewes and wethers used in these experiments were 9 to 24 month old Romney or Romney crosses with an average weight of 20 kg. Four older sheep were also used.

3.3.1 Anaesthetic Protocol

In order to find the most suitable anaesthetic to demonstrate the carotid sinus baroreceptor reflex, two anaesthetic protocols were undertaken:

1. Anaesthesia was induced with sodium pentobarbitone (Anathal, V.R. Laboratories Pty Ltd, Australia, 30 m/kg body weight in a 6% solution) injected into an external jugular vein. Throughout the dissection and experimental procedure, anaesthesia was maintained with a sodium pentobarbitone infusion (5-10 mg/min in a 1% solution) into the venous catheter.

2. Anaesthesia was induced and maintained until the completion of dissections with Halothane (Fluothane, ICI England) in oxygen; for induction 5-7% and for maintenance 1-3% Halothane in oxygen was given via a Fluotec 3 anaesthetic vapouriser (Cyprane Keighley, England). Throughout the experimental procedure, anaesthesia was maintained with α-D(+)-gluco-chloralose reinst (E. Merck, Darmstadt, 70 mg/kg body weight in a 1% solution). The chloralose was dissolved by heating in deionized water to 70°C, and then injected into the left femoral vein catheter over about 20 minutes. This maintained general anaesthesia for approximately three hours.

   At the conclusion of the experiment, the sheep was euthanased with saturated magnesium sulphate injected rapidly into the venous catheter.

Anaesthetic protocol 1 was used in experimental series 1 only. Experimental series 2 to 4 were performed under anaesthetic protocol 2.

3.3.2 Dissection

The sheep were placed in dorsal recumbancy for all dissections.

3.3.2.1 Tracheal Cannula

A cannula was inserted into the trachea at the level of the third cervical vertebra to prevent the entrance of foreign material into the lungs, and when it was appropriate, to permit the administration of Halothane.

3.3.2.2 Femoral Venous Catheter

Sodium pentobarbitone, chloralose and magnesium sulphate were administered via a clear vinyl catheter (Dural Plastics and Engineering, Australia, O.D. 3.00 mm, I.D. 2.00 mm) placed in the left femoral vein, in its course beneath the sartorius muscle.

3.3.2.3 Femoral Arterial Catheter

A polyethylene catheter (Dural Plastics and Engineering, Australia, O.D. 3.00 mm, I.D. 2.00 mm) filled with heparinised saline (Multiparin, Weddel Pharmaceuticals Ltd, England, 50 units/ml) was similarly placed in the right femoral artery, in its course beneath the sartorius muscle, and advanced into the thoracic aorta. This was used to measure the peripheral blood pressure with the aid of a 4-327-1 physiological pressure transducer (Bell and Howell Co., U.S.A.) connected to a Neurolog System DC Amp (Digitimer Ltd., England). Permanent records were obtained on a strip chart recorder 2400S (Gould Inc., U.S.A.). At the beginning and end of the experiment, the transducer was calibrated with a manometer.

3.3.2.4 Lingual Arterial Catheters

A 50 mm skin incision was made along the ventral midline midway between the chin and the angle of the mandible. After retracting the mylohyoid and geniohyoid muscles, the lingual artery could be identified about 10 mm lateral to the midline, deep to the geniohyoid muscle, and running with the lingual nerve. The lingual artery was freed from underlying tissue to place a polyethylene catheter (Dural Plastics and Engineering, Australia, O.D. 1.50 mm, I.D. 1.00 mm) in the vessel with the tip lying at the origin of this vessel from the common carotid artery. The carotid sinus blood pressure was measured as described above.

3.3.2.5 Vagus Nerve Dissection

The vagus nerve was exposed at the level of the fifth cervical vertebra for sectioning.

3.3.2.6 Common Carotid Arterial Dissection

The common carotid artery was exposed at the level of the middle fifth, caudal third, and cranial second cervical vertebrae for occlusion with a bulldog clamp or blue monofilament nylon 000 (Davis and Geck, U.S.A.).

3.3.2.7 Carotid Sinus Area Dissection

A 60 mm skin incision was made extending along the ventral cervical midline from the ventral ends of the jugular processes of the occipital bone. After passing between the sternohyoid and thyrohyoid muscles, the mandibular salivary gland was freed from underlying tissue to enable the gland to be retracted laterally. The terminal portion of the common carotid artery could then be identified lateral to the thyroid cartilage, medial to the mandibular salivary gland, and dorsal to the laryngo-pharynx. The 'occipital group' (comprising the occipital, ascending pharyngeal and ascending palatine arteries) and external carotid artery were freed from underlying tissue for occlusion with a bulldog clamp, about 5 mm from their origins. Care was taken to minimise damage to the structures in this area. See Figure 3.1.

3.3.3 Experimental Protocol

Each experiment was performed on a different animal.

3.3.3.1 Series 1 - Bilateral Common Carotid Arterial Clamping Before and After Vagotomy

In this series the following dissections were undertaken:

1. cannulation of the trachea and catheterisation of the left femoral vein and right femoral artery,
2. exposure of the left and right vagus nerves at the level of the middle fifth cervical vertebra,
3. exposure of the left and right common carotid arteries at the level of the middle fifth cervical vertebra (caudal position) for occlusion with a bulldog clamp.

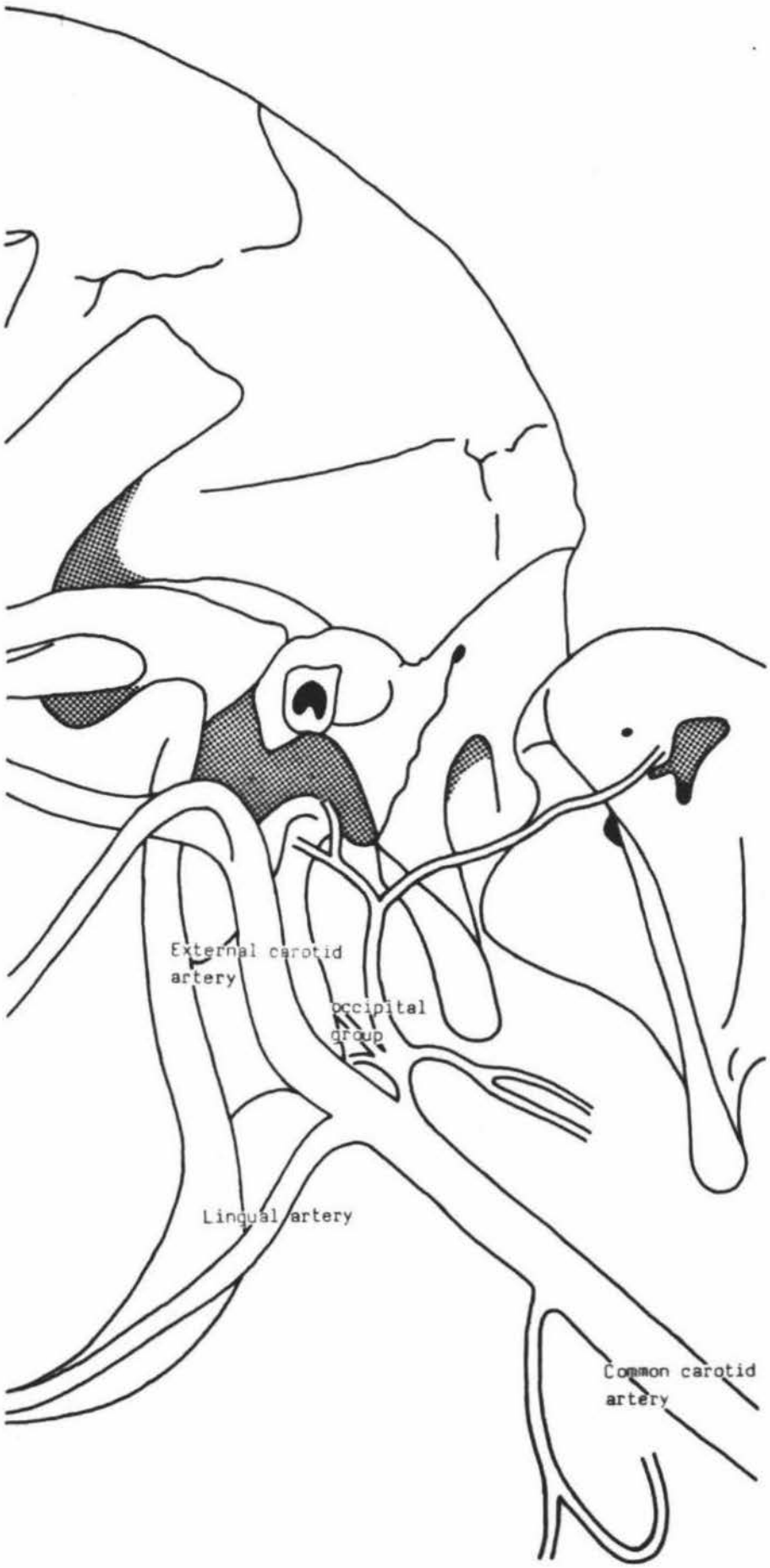

Figure 3.1 Arterial Branches of the Common Carotid Artery in Relation to the Base of the Skull

The clamping protocol involved repeated occlusion of both the left and right common carotid arteries simultaneously in the caudal position. This was repeated after bilateral section of the left and right vagi.

3.3.3.2 Series 2 - Common Carotid Arterial Clamping Before and After Vagotomy

In this series the following dissections were undertaken:

1. cannulation of the trachea and catheterisation of the left femoral vein and right femoral artery,
2. exposure of the left and right vagus nerves at the level of the middle fifth cervical vertebra,
3. exposure of the left and right common carotid arteries at the level of the middle fifth cervical vertebra (caudal position) for occlusion with a bulldog clamp.

The clamping protocol involved repeated occlusion of the left, right or both common carotid arteries in the caudal position. This was repeated after sectioning of the left or right vagus nerve, and then again after sectioning of the remaining intact vagus nerve.

3.3.3.3 Series 3 - Common Carotid Arterial Tying at Three Positions Before and After Vagotomy

In this series the following dissections were undertaken:

1. cannulation of the trachea and catheterisation of the left femoral vein and right femoral artery,
2. exposure of the left and right vagus nerves at the level of the middle fifth cervical vertebra,
3. exposure of the left and right common carotid arteries at the caudal position plus exposure of the left and right common carotid artery at the level of the caudal third (mid position) and cranial second (cranial position) cervical vertebrae for tying with monofilament nylon.

The occlusion protocol involved tying of the left, right or both common carotid arteries in the caudal, middle and then cranial positions. This was repeated after sectioning of the left or right vagus nerve, and then again after sectioning of the remaining intact vagus nerve.

3.3.3.4 Series 4 - Combined Common Carotid Arterial, Occipital Group and External Carotid Arterial Before and After Vagotomy

In this series the following dissections were undertaken:

1. cannulation of the trachea and catheterisation of the left femoral vein, right femoral artery, and left and right lingual arteries,
2. exposure of the left and right vagus nerves at the level of the middle fifth cervical vertebra,
3. exposure of the left and right common carotid arteries at the caudal and cranial positions for occlusion with a bulldog clamp,
4. exposure of the origin of the left and right occipital group and external carotid arteries for occlusion with a bulldog clamp.

The clamping protocol involved occlusion of the left, right or both common carotid arteries in the caudal and then cranial positions. The caudal position of the left, right or both common carotid arteries, along with the left, right or both occipital groups and external carotid arteries were then clamped, and released in the reverse order of occlusion. This was repeated after sectioning of both the left and right vagus nerves.

For more detailed information of the clamping protocol used in each experimental series, see Appendix 2.

3.3.4 Data Processing

In experimental series 1 to 4, the mean blood pressure was estimated as the diastolic pressure plus one-third of the pulse pressure recorded in each cardiac cycle. This estimate of the mean blood pressure was highly correlated (R^2 = 0.983) with the mean blood pressure calculated from twenty co-ordinates in each cardiac cycle (R.E. Munford, personal communication). [1]

The mean blood pressure, pulse pressure, heart rate and respiratory rate of experimental series 1 to 4 were translated from the permanent records into a numerical table (see Appendix 3, Tables 1 to 4). The errors inherent in this conversion are:

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[1] The mean blood pressure was obtained indirectly from the area under the blood pressure curve for each cycle which was approximated by the application of Simpson's rule.

Mean blood pressure and pulse pressure	± 1 to 3 mmHg (exact value dependent upon blood pressure calibration)
Heart rate	± 6 beats/min.
Respiratory rate	± 1 breath/min.

Changes in peripheral mean blood pressure, pulse pressure and heart rate in experimental series 2 to 4 were calculated from the basal values immediately before each clamping cascade. The significance of the clamping treatment upon these values was then examined by analyses of variance. The treatment main effects and interactions were partitioned into single degree of freedom contrasts using orthogonal polynomials (Cochran and Cox, 1960) which were constructed to test specific experimental hypotheses (Barrell and Lapwood, 1978-1979). In addition, t-tests were carried out on particular peripheral mean blood pressure responses of series 3 and the combined data of parts of series 2 to 4. In the statistical analysis tables, levels of significance are denoted thus:

* $P < 0.05$,

** $P < 0.01$,

*** $P < 0.001$.

3.4 RESULTS

3.4.1 Basal Peripheral Mean Blood Pressure, Pulse Pressure, Heart Rate and Respiratory Rate

The basal values of series 2, 3 and 4 are summarised in Table 3.1.

Prior to section of the vagi, the mean basal peripheral mean blood pressure during experimental series 2 and 3 was 111 mmHg and 108 mmHg respectively, but in series 4 the pressure was considerably lower at 90 mmHg. Unilateral section of the left or right vagus nerve in 7 of the 10 sheep in experimental series 2 and 3 caused a rapid decrease in the basal peripheral mean blood pressure of approximately 9 mmHg over a period of 25 to 35 seconds. A similar fall was seen in 10 of the 14 sheep upon cutting the remaining intact vagus nerve in experimental series 2 and 3 and during the section of at first the left, then the right vagus (when the peripheral blood pressure had stabilised) in series 4 (see Figure 3.2). In sheep number 5 of experimental series 2, sheep 3 and 4 of series 3 and sheep 1 of series 4, neither unilateral nor bilateral section of the vagi appeared to affect the basal peripheral mean blood pressure (see Table 3.2). With the exception of experimental series 4, the basal peripheral mean blood pressure tended to remain stable during the experimental period. In experimental series 4, bilateral carotid sinus isolation and successive bilateral occlusion of the common carotid artery, occipital group and external carotid artery clamping cascades elevated the basal peripheral mean blood pressure slightly.

In experimental series 2, 3 and 4, the basal peripheral pulse pressure and heart rate did not vary with the state of vagal innervation and remained stable at 32 mmHg and 143 beats/min respectively. Similarly, in 9 of the 14 sheep in these series, the respiratory rate was also stable at 20 breaths/min. However, upon bilateral section of the vagi, the respiratory rate decreased by approximately 9 breaths/min in sheep numbers 1 and 3 of experimental series 2 and sheep 2, 3 and 4 of series 4.

TABLE 3.1 BASAL PERIPHERAL MEAN BLOOD PRESSURE, PULSE PRESSURE, HEART RATE AND RESPIRATORY RATE (MEAN ± SEM) FOR EACH SHEEP OF EXPERIMENTAL SERIES 2, 3 AND 4

Experimental Series	Sheep No.	State of Vagal Innervation	Peripheral Mean Blood Pressure, mmHg	Peripheral Pulse Pressure, mmHg	Heart Rate Beats/min	Respiratory Rate Breaths/min
2($n^{\dagger}$ = 8)	1	Intact Vn	117 ± 2.2	27 ± 1.0	182 ± 8.5	21 ± 0.2
		Cut L Vn	111 ± 2.8	28 ± 1.0	192 ± 3.9	19 ± 0.2
		Cut LR Vn	108 ± 1.3	27 ± 0.4	164 ± 6.2	14 ± 0.2
	2	Intact Vn	122 ± 1.9	36 ± 0.7	130 ± 1.6	20 ± 0.2
		Cut L Vn	132 ± 3.8	38 ± 1.8	146 ± 3.0	18 ± 0.2
		Cut LR Vn	141 ± 2.7	40 ± 1.8	147 ± 2.5	16 ± 0.4
	3	Intact Vn	108 ± 0.1	33 ± 0.4	137 ± 1.5	25 ± 0.4
		Cut L Vn	103 ± 0.6	29 ± 0.5	137 ± 1.5	21 ± 0.2
		Cut LR Vn	101 ± 1.6	31 ± 0.5	138 ± 1.1	18 ± 0.2
	4	Intact Vn	120 ± 0.8	34 ± 0.3	164 ± 3.0	24 ± 0.4
		Cut R Vn	109 ± 0.8	32 ± 0.4	181 ± 2.1	21 ± 0.3
		Cut LR Vn	91 ± 1.7	31 ± 0.6	177 ± 2.5	21 ± 0.0
	5	Intact Vn	105 ± 1.2	34 ± 0.2	119 ± 2.4	30 ± 0.2
		Cut R Vn	95 ± 0.9	35 ± 0.3	122 ± 2.3	27 ± 0.5
		Cut LR Vn	97 ± 0.6	34 ± 0.7	127 ± 2.4	26 ± 0.3
	6	Intact Vn	91 ± 0.7	28 ± 0.7	113 ± 3.3	17 ± 0.5
		Cut R Vn	84 ± 0.9	27 ± 0.3	131 ± 1.0	15 ± 0.2
		Cut LR Vn	81 ± 2.1	29 ± 0.4	143 ± 3.3	16 ± 0.1
3($n^{\dagger}$ = 8)	1	Intact Vn	109 ± 1.0	35 ± 0.4	125 ± 2.1	18 ± 0.3
		Cut L Vn	94 ± 1.2	32 ± 0.6	120 ± 1.1	17 ± 0.2
		Cut LR Vn	86 ± 0.7	33 ± 0.6	120 ± 0.0	19 ± 0.2
	2	Intact Vn	128 ± 0.8	39 ± 0.3	132 ± 2.0	18 ± 0.3
		Cut L Vn	117 ± 1.0	37 ± 0.6	129 ± 2.0	17 ± 0.5
		Cut LR Vn	115 ± 1.0	35 ± 1.0	131 ± 2.5	15 ± 0.3
	3	Intact Vn	99 ± 2.1	37 ± 1.5	120 ± 3.2	18 ± 0.1
		Cut R Vn	89 ± 1.7	34 ± 0.5	135 ± 3.8	20 ± 0.2
		Cut LR Vn	83 ± 1.1	33 ± 0.5	149 ± 1.5	20 ± 0.2
	4	Intact Vn	95 ± 1.0	29 ± 0.5	146 ± 1.5	17 ± 0.2
		Cut R Vn	96 ± 1.1	30 ± 0.7	152 ± 1.0	19 ± 8.2
		Cut LR Vn	97 ± 0.8	31 ± 0.4	159 ± 1.1	19 ± 0.2
4($n^{\dagger}$ = 18)	1	Intact Vn	78 ± 2.9	30 ± 0.5	177 ± 1.8	23 ± 0.2
		Cut LR Vn	74 ± 1.1	32 ± 0.3	180 ± 1.3	19 ± 0.3
	2	Intact Vn	107 ± 0.6	34 ± 0.6	132 ± 1.3	31 ± 0.4
		Cut LR Vn	98 ± 2.3	36 ± 0.9	129 ± 4.2	14 ± 0.7
	3	Intact Vn	93 ± 1.4	31 ± 1.5	150 ± 2.3	17 ± 0.1
		Cut LR Vn	92 ± 1.4	33 ± 0.3	145 ± 0.8	11 ± 0.2
	4	Intact Vn	81 ± 0.6	29 ± 0.5	130 ± 0.8	23 ± 0.2
		Cut LR Vn	62 ± 1.3	30 ± 0.4	120 ± 1.3	16 ± 0.2

† Number of basal values between clamping cascades per sheep.

Figure 3.2 Peripheral blood pressure a. and left b. and right c. carotid sinus blood pressures prior to and following section of the left and right vagi in sheep number 4 of experimental series 4

Section procedure:

1. cut left vagus nerve,
2. cut right vagus nerve.

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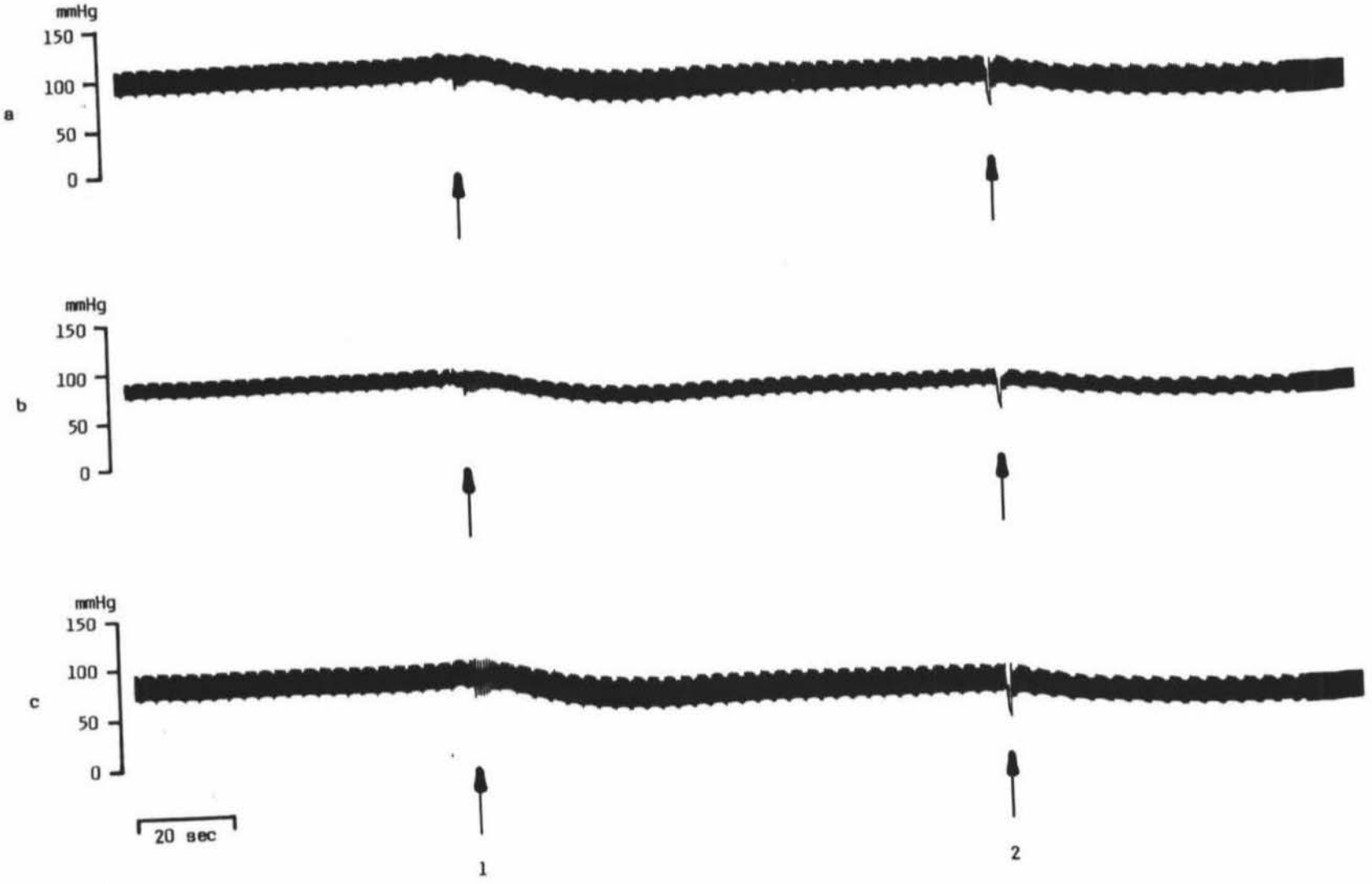
mmHg
150
100
50
0
a
mmHg
150
100
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b
mmHg
150
100
50
0
c
20 sec
1
2

TABLE 3.2 IMMEDIATE CHANGE OF THE BASAL PERIPHERAL MEAN BLOOD PRESSURE† (mmHg) UPON VAGOTOMY IN EACH SHEEP OF EXPERIMENTAL SERIES 2, 3 AND 4

Experimental Series	Sheep No.	State of Vagal Innervation		
		Cut L Vn	Cut R Vn	Cut LR Vn
2	1	-9		-12
	2	-1		-9
	3	-4		-9
	4		-4	-27
	5		-4	2
	6		-15	-14
3	1	-19		-15
	2	-9		-9
	3		1	7
	4		1	-4
4	1			0
	2			-10
	3			-10
	4			-28

† Basal peripheral mean blood pressure change from the value immediately before section of the vagus nerve(s).

3.4.2 Experimental Series 1 - Bilateral Common Carotid Arterial Clamping Before and After Vagotomy (under pentobarbitone anaesthesia)

The effect of bilateral clamping of the caudal common carotid artery on the peripheral mean blood pressure was examined in two sheep under pentobarbitone anaesthesia. Prior to vagotomy, simultaneous clamping of both the left and right common carotid arteries induced a peripheral mean blood pressure rise of 16 ± 3.9 mmHg (mean ± SEM), the response following vagotomy was similar at 20 ± 0.9 mmHg (mean ± SEM). For raw data see Appendix 3, Table 1. Similar experiments were also performed in six sheep under chloralose anaesthesia (experimental series 2) and the corresponding peripheral mean blood pressure values were 41 ± 6.5 mmHg (mean ± SEM) and 48 ± 7.0 mmHg (mean ± SEM). All further experimental series employed chloralose as the anaesthetic.

3.4.3 Experimental Series 2 - Common Carotid Arterial Clamping Before and After Vagotomy

The effect of unilateral and bilateral clamping of the caudal common carotid artery on the peripheral mean blood pressure, pulse pressure, heart rate and respiratory rate was examined in six sheep (for raw data see Appendix 3, Table 2). The changes in mean blood pressure, pulse pressure and heart rate, produced by carotid occlusion combined with vagotomy, were subjected to analyses of variance using orthogonal polynomials (see Tables 3.3, 3.4 and 3.5).

3.4.3.1 Effect of Common Carotid Arterial Clamping

Contrast numbers 1 and 2 in each of Tables 3.3, 3.4 and 3.5.

Bilateral clamping of the common carotid artery induced a significantly greater rise in peripheral mean blood pressure, pulse pressure and heart rate than did unilateral occlusion of a single carotid artery. An exception to this was heart rate upon section of a single vagus nerve. When both common carotid arteries were clamped, the rise in peripheral mean blood pressure was approximately four times greater (see Table 3.3), the rise in peripheral pulse pressure six-fold (see Table 3.4) and heart rate three-fold (see Table 3.5), compared with that seen when only one carotid artery was occluded. In addition, following unilateral section of the left or right vagus nerve, clamping of the left common carotid artery produced a rise in heart rate seven times greater than did contralateral right carotid arterial occlusion (see Part 2 of Table 3.5).

TABLE 3.3 PERIPHERAL MEAN BLOOD PRESSURE INCREASE (MEAN ± SEM, mmHg) AND SUMMARY OF ANALYSES OF VARIANCE FROM EXPERIMENTAL SERIES 2

(1) Experimental Series 2a, Intact and Bilateral Section of Vagi (n = 6)

Occlusion Number	Clamping Position	Number of Observations per Animal	State of Vagal Innervation	
			Intact Vn	Cut LR Vn
1	Cd L CCA	3	10 ± 1.0	13 ± 1.5
2	Cd R CCA	3	8 ± 1.0	8 ± 1.4
3	Cd LR CCA	2	41 ± 6.5	48 ± 7.0

Contrast Number	Source of Variation (Described by Occlusion Numbers)	Degrees of Freedom	Variance Ratio
	A. Clamping treatment	7	19.964***
1	Significant contrasts 1+2 versus 3	1	137.327***
	B. Vagi : intact versus bilateral section	1	1.032
	C. Animals	5	2.681*
	Interaction: AxB	7	0.308
	Residual mean square	75	1.579

(2) Experimental Series 2b, Unilateral Section of Left and Right Vagus (n = 3)

Occlusion Number	Clamping Position	Number of Observations per Animal	State of Vagal Innervation	
			Cut L Vn	Cut R Vn
4	Cd L CCA	3	18 ± 1.6	14 ± 2.2
5	Cd R CCA	3	12 ± 2.1	4 ± 1.6
6	Cd LR CCA	2	54 ± 9.2	25 ± 2.0

Contrast Number	Source of Variation (Described by Occlusion Numbers)	Degrees of Freedom	Variance Ratio
	A. Clamping treatment	7	5.574***
2	Significant contrasts 4+5 versus 6	1	35.503***
	B. Vagi : unilateral left versus right section	1	8.831**
	C. Animals	2	1.176
	Interaction: AxB	7	0.924
	Residual mean square	30	1.890

TABLE 3.4 PERIPHERAL PULSE PRESSURE INCREASE (MEAN ± SEM, mmHg) AND SUMMARY OF ANALYSES OF VARIANCE FROM EXPERIMENTAL SERIES 2

(1) Experimental Series 2a, Intact and Bilateral Section of Vagi (n = 6)

Occlusion Number	Clamping Position	Number of Observations per Animal	State of Vagal Innervation	
			Intact Vn	Cut LR Vn
1	Cd L CCA	3	3 ± 0.5	1 ± 1.1
2	Cd R CCA	3	2 ± 0.6	1 ± 0.5
3	Cd LR CCA	2	14 ± 3.2	12 ± 2.9

Contrast Number	Source of Variation (Described by Occlusion Numbers)	Degrees of Freedom	Variance Ratio
	A. Clamping treatment	7	8.242***
1	Significant contrasts 1+2 versus 3	1	56.554***
	B. Vagi : intact versus bilateral section	1	1.166
	C. Animals	5	0.648
	Interaction: AxB	7	0.155
	Residual mean square	75	0.386

(2) Experimental Series 2b, Unilateral Section of Left and Right Vagus (n = 3)

Occlusion Number	Clamping Position	Number of Observations per Animal	State of Vagal Innervation	
			Cut L Vn	Cut R Vn
4	Cd L CCA	3	4 ± 1.6	1 ± 0.3
5	Cd R CCA	3	2 ± 1.3	0 ± 0.2
6	Cd LR CCA	2	16 ± 4.7	3 ± 0.9

Contrast Number	Source of Variation (Described by Occlusion Numbers)	Degrees of Freedom	Variance Ratio
	A. Clamping treatment	7	2.450*
2	Significant contrasts 4+5 versus 6	1	15.661***
	B. Vagi : unilateral left versus right section	1	9.525**
	C. Animals	2	0.915
	Interaction: AxB	7	1.419
	Residual mean square	30	0.295

TABLE 3.5 HEART RATE INCREASE (MEAN ± SEM, BEATS/MIN) AND SUMMARY OF ANALYSES OF VARIANCE FROM EXPERIMENTAL SERIES 2

(1) Experimental Series 2a, Intact and Bilateral Section of Vagi (n = 6)

Occlusion Number	Clamping Position	Number of Observations per Animal	State of Vagal Innervation	
			Intact Vn	Cut LR Vn
1	Cd L CCA	3	4 ± 1.4	6 ± 2.2
2	Cd R CCA	3	3 ± 1.2	0 ± 1.4
3	Cd LR CCA	2	8 ± 3.5	24 ± 6.6

Contrast Number	Source of Variation (Described by Occlusion Numbers)	Degrees of Freedom	Variance Ratio
1	A. Clamping treatment	7	4.229***
	Significant contrasts 1+2 versus 3	1	24.169***
	B. Vagi : intact versus bilateral section	1	2.661
	C. Animals	5	1.035
	Interaction: AxB	7	1.759
	Residual mean square	75	1.240

(2) Experimental Series 2b, Unilateral Section of Left and Right Vagus (n = 3)

Occlusion Number	Clamping Position	Number of Observations per Animal	State of Vagal Innervation	
			Cut L Vn	Cut R Vn
4	Cd L CCA	3	7 ± 2.6	7 ± 1.9
5	Cd R CCA	3	0 ± 2.4	2 ± 1.7
6	Cd LR CCA	2	8 ± 5.9	5 ± 1.8

Contrast Number	Source of Variation (Described by Occlusion Numbers)	Degrees of Freedom	Variance Ratio
2	A. Clamping treatment	7	0.958
	Significant contrasts 4 versus 5	1	4.320*
	B. Vagi : unilateral left versus right section	1	0.007
	C. Animals	2	0.487
	Interaction: AxB	7	0.262
	Residual mean square	30	0.750

For all six sheep in experimental series 2, overall there was no difference in the peripheral mean blood pressure and pulse pressure effects of left or right common carotid arterial occlusion. However, examination of the responses of individual animals revealed that sheep number 2 consistently had lesser peripheral mean blood pressure rises upon right common carotid arterial clamping than on left carotid arterial occlusion (mean peripheral mean blood pressure 4 mmHg compared with 17 mmHg prior to vagotomy and 5 mmHg compared with 13 mmHg following bilateral vagotomy). The other five sheep showed no such differences between left and right common carotid arterial clamping. See Table 3.15.

3.4.3.2 Effect of Vagotomy

Bilateral section of the vagi did not alter the response of the peripheral mean blood pressure, pulse pressure or heart rate to common carotid arterial clamping (see Part 1 of Tables 3.3, 3.4 and 3.5). Unilateral section of the right vagus nerve gave a lesser rise of peripheral mean blood pressure and pulse pressure upon clamping than cutting the left vagus nerve (see Part 2 of Tables 3.3 and 3.4).

Sheep number 4 demonstrated an unusual response to unilateral section of the right vagus nerve. In this animal there was no longer a rise in peripheral mean blood pressure upon right common carotid arterial clamping, as demonstrated in Figure 3.3. In addition, bilateral common carotid arterial occlusion had the same effect as clamping of the left carotid artery alone. See Table 3.15.

3.4.4 Experimental Series 3 - Common Carotid Arterial Tying at Three Positions Before and After Vagotomy

In each of four sheep, the left or right common carotid artery was tied at the caudal, middle and cranial positions. In addition, bilateral tying of the common carotid artery was performed in the caudal position. For raw data see Appendix 3, Table 3. Of the resulting changes in peripheral mean blood pressure, pulse pressure, heart rate and respiratory rate only the rises in peripheral mean blood pressure, both prior to and following bilateral vagotomy, were analysed statistically by an analysis of variance using orthogonal polynomials. There was no significant difference between tying a single common carotid artery at the three different positions along the vessel. However, the peripheral blood pressure rise upon tying the caudal common carotid artery

Figure 3.3 Peripheral blood pressure upon unilateral clamping of the caudal common carotid artery prior to a., during b. and following c. section of the right vagus nerve in sheep number 4 of experimental series 2

Clamping and section procedure

↑ indicates when an artery was clamped or a vagus nerve cut and ↓ when an arterial clamp was removed:

1. clamp caudal left common carotid artery,
2. unclamp caudal left common carotid artery,
3. clamp caudal right common carotid artery,
4. unclamp caudal right common carotid artery,
5. cut right vagus nerve.

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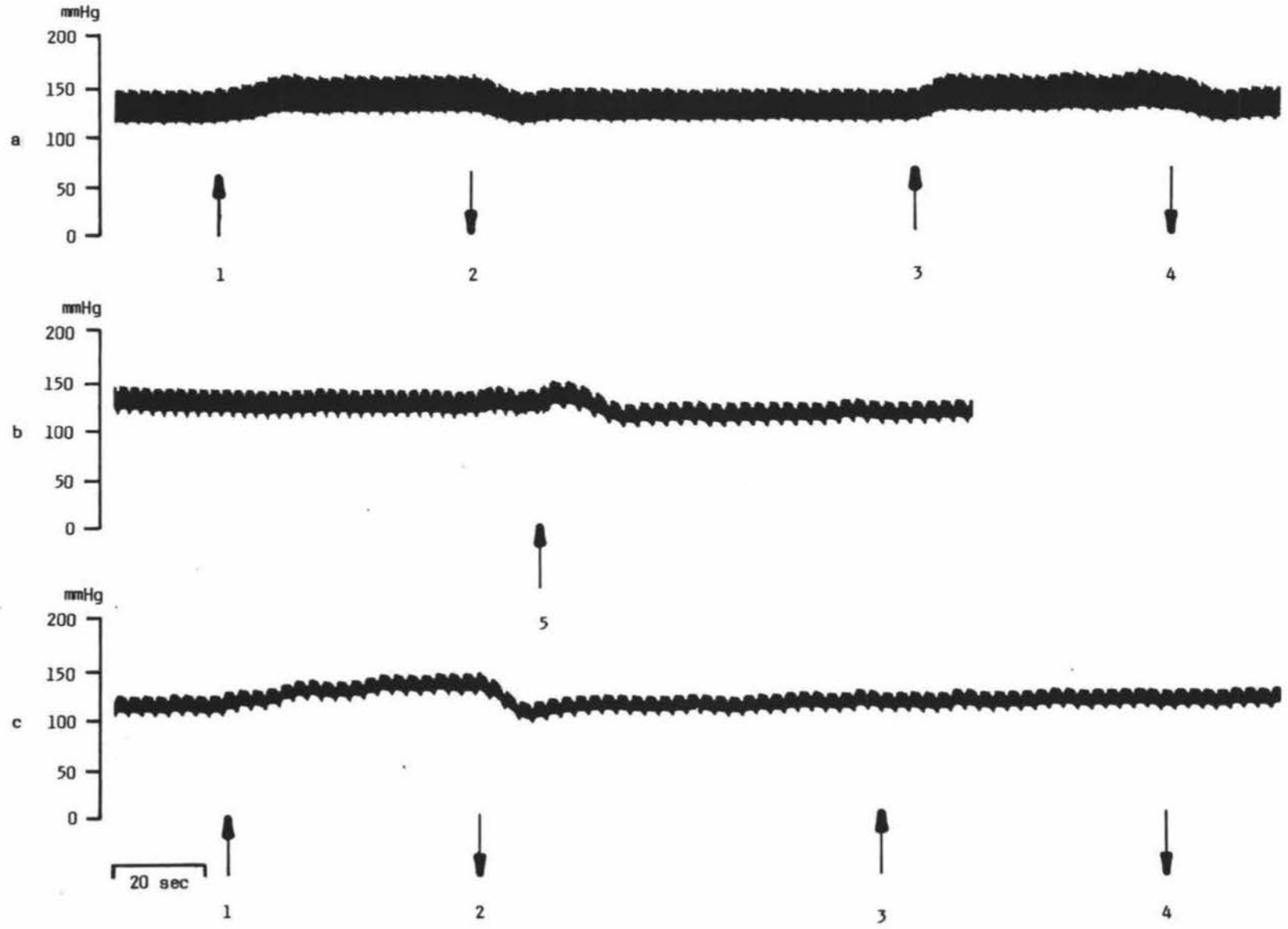
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tended to be greater than with occlusion of the cranial carotid artery. Bilateral vagotomy reduced the effect of tying the right common carotid artery, but not of tying the left carotid artery, although the left carotid arterial values were reduced somewhat but not to levels that were significantly different for the two sheep examined. See Table 3.6.

The effect of vagotomy was examined by subjecting to a paired t-test the data obtained from the two sheep in which one vagus nerve was cut and tying was repeated at three levels in the ipsilateral common carotid artery. In the animal in which the left common carotid artery was tied in three positions, left vagotomy reduced the peripheral mean blood pressure rise upon tying. In the other sheep, there was no demonstrable effect of right vagotomy on tying the right common carotid artery. See Table 3.7.

3.4.5 Experimental Series 4 - Combined Common Carotid Arterial, Occipital Group and External Carotid Arterial Clamping Before and After Vagotomy

In four sheep, prior to and following bilateral vagotomy, the clamping cascade of clamping up to six cervical blood vessels was examined for its effect on peripheral mean blood pressure, pulse pressure, heart rate and respiratory rate, while the left and right lingual blood pressure was monitored as a measure of carotid sinus mean blood pressure and pulse pressure. For raw data see Appendix 3, Table 4.

3.4.5.1 Carotid Sinus Mean Blood Pressure and Pulse Pressure

The carotid sinus pressure was measured in the four sheep of experimental series 4 via a lingual arterial catheter, the tip of which was situated at the origin of this vessel from the external carotid artery. It was unusual, however, for the pressure measured in the carotid sinuses to be exactly the same as that measured peripherally. In sheep number 1, the left carotid sinus mean blood pressure was 10 mmHg above the peripheral mean blood pressure, while the right sinus pressure was equal to that in the periphery. Both the left and right carotid sinus mean blood pressures were lower, 22 mmHg and 10 mmHg respectively, than the peripheral mean blood pressure in sheep number 2. Again, in sheep number 3 the mean blood pressure in the left and right carotid sinuses was 17 mmHg below the peripheral mean pressure. Both the left and right carotid sinus mean blood pressures in sheep number 4 were similar (5 mmHg below) to the peripheral blood pressure.

TABLE 3.6 PERIPHERAL MEAN BLOOD PRESSURE INCREASE (MEAN ± SEM, mmHg) AND SUMMARY OF ANALYSES OF VARIANCE FROM EXPERIMENTAL SERIES 3

(1) Experimental Series 3a, Clamping of Left Common Carotid Artery (n = 2)

Clamping Position	Number of Observations per Animal	State of Vagal Innervation	
		Intact Vn	Cut LR Vn
Cd L CCA	2	12 ± 1.4	10 ± 2.4
Md L CCA	2	13 ± 0.6	9 ± 1.3
Cn L CCA	2	10 ± 1.1	8 ± 1.1

Source of Variation	Degrees of Freedom	Variance Ratio
A. Clamping treatment	2	0.748
B. Vagi : intact versus bilateral section	1	4.285
Interaction: AxB	2	0.867
Residual mean square	18	3.514

(2) Experimental Series 3b, Clamping of Right Common Carotid Artery (n = 2)

Clamping Position	Number of Observations per Animal	State of Vagal Innervation	
		Intact Vn	Cut LR Vn
Cd R CCA	2	9 ± 1.1	6 ± 1.2
Md R CCA	2	7 ± 0.9	6 ± 0.9
Cn R CCA	2	6 ± 0.7	6 ± 1.0

Source of Variation	Degrees of Freedom	Variance Ratio
A. Clamping treatment	2	1.445
B. Vagi : intact versus bilateral section	1	6.482*
Interaction: AxB	2	0.576
Residual mean square	18	7.875

TABLE 3.7 PERIPHERAL MEAN BLOOD PRESSURE INCREASE (MEAN ± SEM, mmHg) AND RESULTS OF PAIRED t-TESTS FOR THE TWO SHEEP OF EXPERIMENTAL SERIES 3 IN WHICH IPSILATERAL COMMON CAROTID ARTERIAL TYING AND VAGUS NERVE SECTION WERE UNDERTAKEN

Sheep No.	Clamping Position	Occlusion Number and State of Vagal Innervation					
		Occlusion No.	Intact Vn	Occlusion No.	Cut L Vn	Occlusion No.	Cut R Vn
1	Cd L CCA	1	12 ± 3.0	4	7 ± 1.5		
	Md L CCA	2	12 ± 0.0	5	8 ± 1.5		
	Cn L CCA	3	11 ± 1.0	6	7 ± 0.0		
4	Cd R CCA	7	7 ± 1.0			10	7 ± 1.5
	Md R CCA	8	6 ± 0.5			11	9 ± 0.0
	Cn R CCA	9	7 ± 1.0			12	8 ± 1.0

Contrast Number	Source of Variation (Described by Occlusion Numbers)	$\underline{t}_{(4)}$
1	Sheep 1 : 1+2+3 versus 4+5+6	13.012***
2	Sheep 4 : 7+8+9 versus 10+11+12	1.511

The carotid sinus mean blood pressure and pulse pressure from the four sheep in this series are presented in Table 3.8. Both the peripheral and carotid sinus mean blood pressures fell 9 mmHg upon vagotomy, but the pulse pressures were unchanged. The carotid sinus mean blood pressure and pulse pressure in the clamping and unclamping sequence of these clamping cascades were similar both prior to and following vagotomy.

3.4.5.1.1 Unilateral and Bilateral Clamping of the Common Carotid Artery

Unilateral clamping of the left or right common carotid artery at the caudal or cranial position reduced the mean blood pressure and pulse pressure of the clamped carotid sinus by 34 mmHg and 17 mmHg to 49 mmHg and 5 mmHg, respectively. The pressures within the contralateral sinus were 84 mmHg and 20 mmHg, similar to the basal mean blood pressure and pulse pressure values. On the other hand, bilateral common carotid arterial occlusion substantially decreased the mean blood pressure of both the left and right carotid sinuses by 46 mmHg to 34 mmHg and virtually eliminated the pulse pressure. These changes in sheep number 4 are shown in Figure 3.4.

3.4.5.1.2 Unilateral Clamping of a Common Carotid Artery and Contralateral Clamping of the Occipital Group and External Carotid Artery

Clamping of the contralateral occipital group, in addition to a single common carotid artery, further lowered (5 mmHg) the mean blood pressure of both carotid sinuses slightly. When the contralateral external carotid artery was also occluded, the mean blood pressure of the afferently clamped carotid sinus fell a further 11 mmHg, while the pressure in the efferently clamped sinus increased toward the basal value. This rise, however, only occurred in three of the four sheep studied. In sheep number 3 the carotid sinus mean blood pressure suddenly decreased to 29 mmHg and the pulse pressure to 2 mmHg (for raw data see Appendix 3, Table 4).

The pulse pressure of the afferently clamped carotid sinus did not vary from the low level attained by occlusion of the common carotid artery. That in the efferently clamped sinus, with the exception of sheep number 3, remained at the basal value.

The responses of sheep number 4 are presented in Figure 3.5.

TABLE 3.8 MEAN BLOOD PRESSURE AND PULSE PRESSURE (MEAN ± SEM, mmHg) IN THE LEFT AND RIGHT CAROTID SINUSES PRIOR TO VAGOTOMY IN EXPERIMENTAL SERIES 4 (n = 4)

Clamping Position	Number of Observations per Animal	Mean Blood Pressure, mmHg		Pulse Pressure, mmHg	
		Left Carotid Sinus	Right Carotid Sinus	Left Carotid Sinus	Right Carotid Sinus
Basal	18	81±1.0	83±1.4	23±0.7	22±0.5
Unilateral and Bilateral Clamping of the Common Carotid Artery					
Cd or Cn L CCA	8	47±2.4	87±2.3	4±0.3	20±0.7
Cd or Cn R CCA	8	80±1.6	51±2.9	20±1.4	6±0.6
Cd or Cn LR CCA	4	32±0.3	35±4.2	2±0.2	4±1.9
Unilateral Clamping of the Common Carotid Artery and Contralateral Clamping of the Occipital Group and External Carotid Artery					
Cd L CCA	8	47±2.4	87±2.3	4±0.3	20±0.7
Cd L CCA, R OG	2	40±5.4	85±0.2	4±1.5	19±2.8
Cd L CCA, R OG, R ECA	2	28±6.7	75±15.7	2±0.6	22±7.3
Cd R CCA	8	80±1.6	51±2.9	20±1.4	6±0.6
Cd R CCA, L OG	2	74±3.9	47±8.4	20±2.7	5±1.9
Cd R CCA, L OG, L ECA	2	81±3.8	37±6.4	26±3.6	3±1.3
Bilateral Carotid Sinus Isolation					
Cd L CCA	8	47±2.4	87±2.3	4±0.3	20±0.7
Cd L CCA, L OG	3	43±5.0	82±3.4	3±0.5	20±1.0
Cd L CCA, L OG, L ECA	2	56±7.3	83±3.9	6±1.9	20±1.6
Cd L CCA, L OG, L ECA, Cd R CCA	1	42±15.1	30±8.0	5±2.3	2±1.1
Cd L CCA, L OG, L ECA, Cd R CCA, R OG	1	45±16.5	20±3.1	6±2.6	1±0.6
Cd L CCA, L OG, L ECA, Cd R CCA, R OG, R ECA	4	66±8.2	68±7.5	5±0.9	4±1.1
Cd R CCA	8	80±1.6	51±2.9	20±1.4	6±0.6
Cd R CCA, R OG	3	77±1.6	41±5.1	20±2.5	4±1.1
Cd R CCA, R OG, R ECA	2	78±2.2	60±5.7	18±3.5	8±2.5
Cd R CCA, R OG, R ECA, Cd L CCA	1	23±2.8	48±12.1	1±0.7	4±1.4
Cd R CCA, R OG, R ECA, Cd L CCA, L OG	1	21±3.9	56±9.1	1±0.7	4±1.7
Cd R CCA, R OG, R ECA, Cd L CCA, L OG, L ECA	4	66±8.2	68±7.5	5±0.9	4±1.1
Successive Bilateral Clamping of the Common Carotid Artery, Occipital Group and External Carotid Artery					
Cd L CCA	8	47±2.4	87±2.3	4±0.3	20±0.7
Cd L CCA, Cd R CCA	4	32±0.3	35±4.2	2±0.2	4±1.9
Cd L CCA, Cd R CCA, L OG	1	29±5.8	36±6.8	1±0.5	2±1.1
Cd L CCA, Cd R CCA, L OG, R OG	1	27±6.9	30±8.0	1±0.5	2±1.1
Cd L CCA, Cd R CCA, L OG, R OG, L ECA	1	58±15.0	21±7.6	5±1.3	2±1.1
Cd L CCA, Cd R CCA, L OG, R OG, L ECA, R ECA	4	66±8.2	68±7.5	5±0.9	4±1.1
Cd R CCA	8	80±1.6	51±2.9	20±1.4	6±0.6
Cd R CCA, Cd L CCA	4	32±0.3	35±4.2	2±0.2	4±1.9
Cd R CCA, Cd L CCA, R OG	1	26±5.1	27±1.3	3±0.4	2±0.9
Cd R CCA, Cd L CCA, R OG, L OG	1	26±5.3	26±1.4	2±0.5	3±2.1
Cd R CCA, Cd L CCA, R OG, L OG, R ECA	1	25±4.8	44±12.3	1±0.5	5±2.2
Cd R CCA, Cd L CCA, R OG, L OG, R ECA, L ECA	4	66±8.2	68±7.5	5±0.9	4±1.1

Figure 3.4 Peripheral blood pressure a. and left b. and right c. carotid sinus blood pressures upon unilateral and bilateral clamping of the caudal common carotid artery in sheep number 4 of experimental series 4

Clamping procedure

↑ indicates when an artery was clamped and ↓ when an arterial clamp was removed:

1. clamp caudal left common carotid artery,
2. unclamp caudal left common carotid artery,
3. clamp caudal right common carotid artery,
4. unclamp caudal right common carotid artery,
5. clamp caudal left and right common carotid artery,
6. unclamp caudal left and right common carotid artery.

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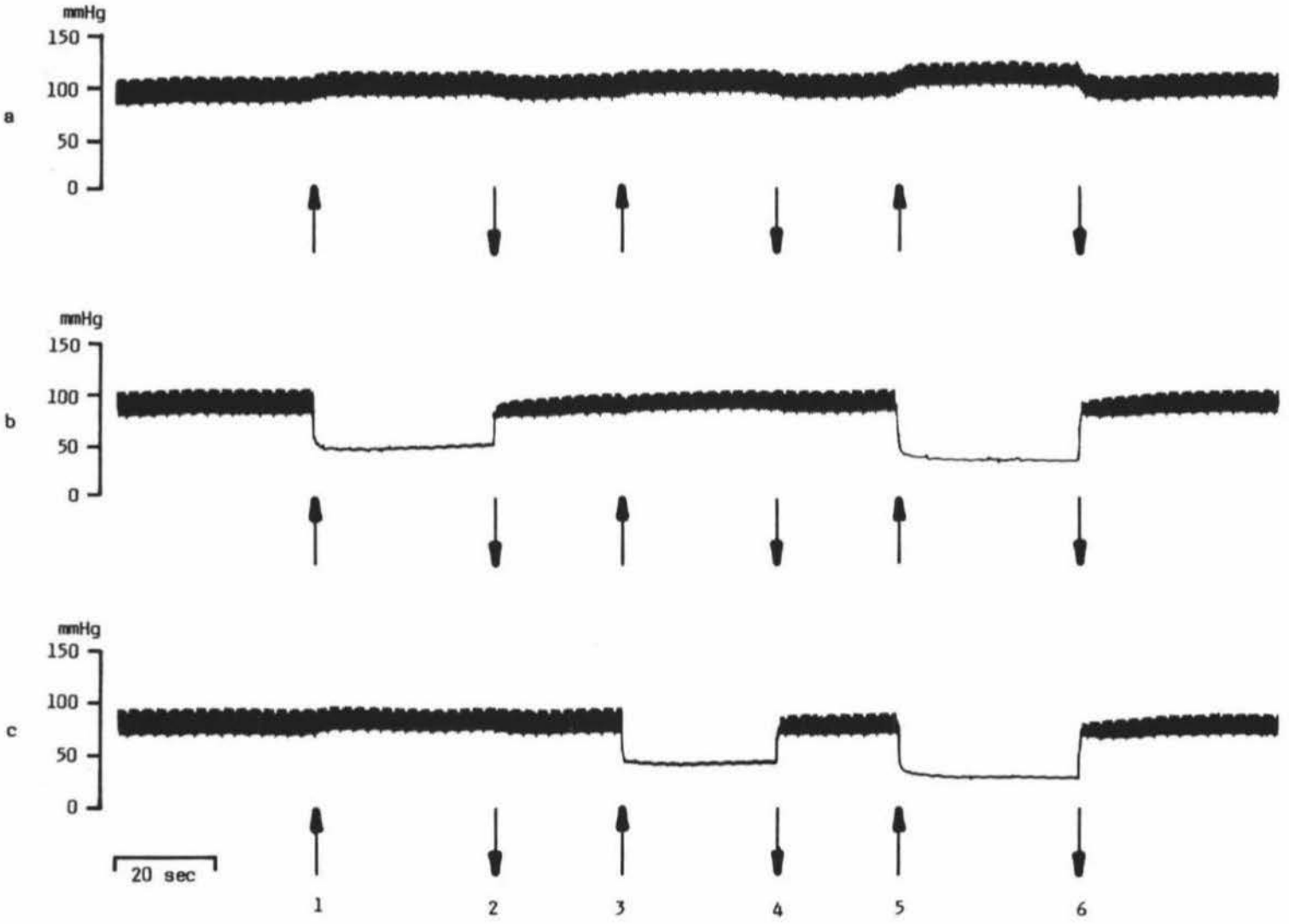
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Figure 3.5 Peripheral blood pressure a. and left b. and right c. carotid sinus blood pressures upon unilateral clamping of the left common carotid artery and contralateral clamping of the right occipital group and external carotid artery in sheep number 4 of experimental series 4

Clamping procedure

↑ indicates when an artery was clamped and ↓ when an arterial clamp was removed:

1. clamp caudal left common carotid artery,
2. clamp right occipital group,
3. clamp right external carotid artery,
4. unclamp right external carotid artery,
5. unclamp right occipital group,
6. unclamp caudal left common carotid artery.

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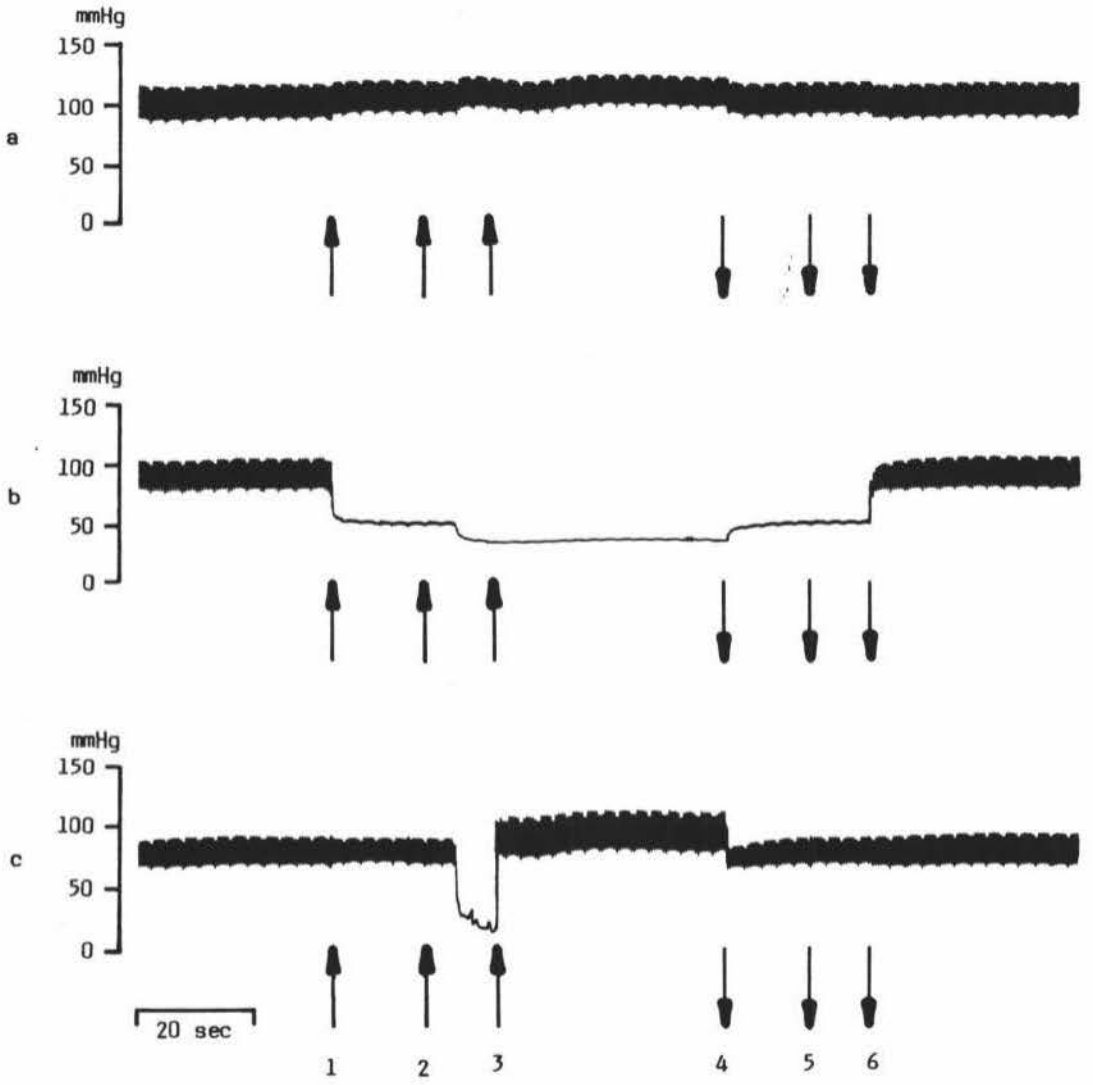
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3.4.5.1.3 Bilateral Carotid Sinus Isolation

During the isolation of a single carotid sinus, clamping the ipsilateral occipital group in addition to a single common carotid artery further lowered the clamped carotid sinus mean blood pressure by 7 mmHg. The blood pressure was increased 16 mmHg upon further occlusion of the external carotid artery. The progressive isolation of the second carotid sinus caused a similar ipsilateral carotid sinus mean blood pressure fall upon clamping the occipital group. However, occlusion of the external carotid artery caused a substantially greater (47 mmHg) rise in carotid sinus blood pressure.

The carotid sinus pulse pressures were virtually eliminated upon ipsilateral clamping of the common carotid artery and remained virtually unchanged as additional vessels were occluded.

These changes in sheep number 4 are shown in Figure 3.6.

3.4.5.1.4 Successive Bilateral Clamping of the Common Carotid Artery, Occipital Group and External Carotid Artery

In this clamping cascade, the clamping of each occipital group, in addition to both the common carotid arteries, lowered the mean blood pressure of the ipsilateral carotid sinus slightly (6 mmHg). The mean blood pressure of the carotid sinus rose 35 mmHg upon occlusion of the ipsilateral external carotid artery. Within the contralateral sinus, however, the blood pressure fell 5 mmHg upon occlusion of the first, then rose 16 mmHg following clamping of the second external carotid artery.

The very low pulse pressure within both carotid sinuses following bilateral clamping of the common carotid arteries was unchanged by the clamping of further vessels.

The responses of sheep number 4 are presented in Figure 3.7.

The changes in peripheral mean blood pressure, pulse pressure and heart rate (see Tables 3.9, 3.11 and 3.13) were analysed statistically by an analysis of variance using orthogonal polynomials, allowing the comparison of pairs and groups of data. For such comparisons, a number of statistically significant effects of the clamping combinations were demonstrated (see Tables 3.10, 3.12 and 3.14).

Figure 3.6 Peripheral blood pressure a. and left b. and right c. carotid sinus blood pressures upon bilateral carotid sinus isolation in sheep number 4 of experimental series 4

Clamping procedure and point to note

↑ indicates when an artery was clamped and ↓ when an arterial clamp was removed:

1. clamp caudal left common carotid artery,
2. clamp left occipital group,
3. clamp left external carotid artery,
4. clamp caudal right common carotid artery,
5. clamp right occipital group,
6. clamp right external carotid artery,
7. unclamp right external carotid artery,
8. unclamp right occipital group,
9. unclamp caudal right common carotid artery,
10. unclamp left external carotid artery,
11. unclamp left occipital group,
12. unclamp caudal left common carotid artery,
13. cessation of respiration.

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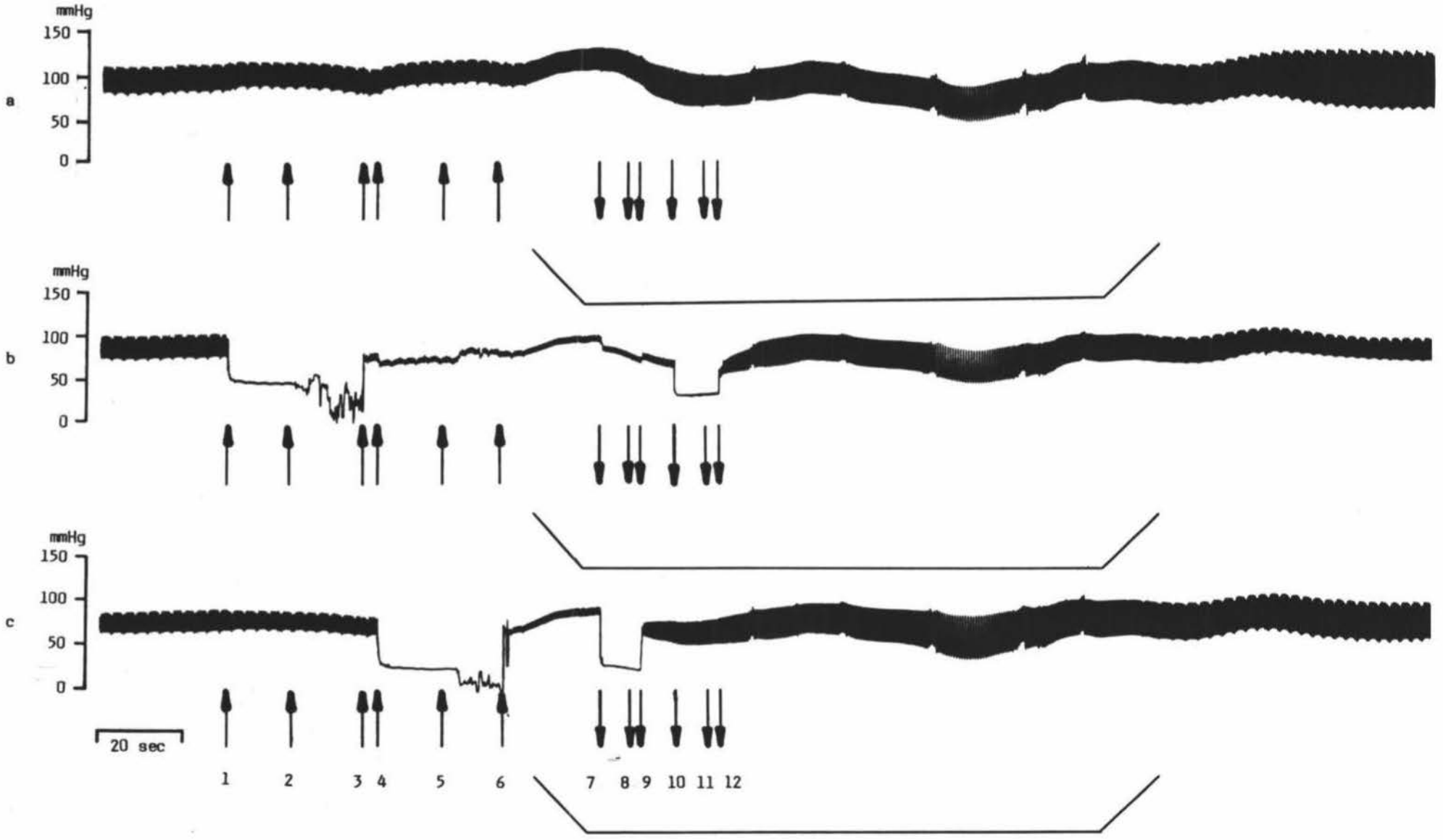
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Figure 3.7 Peripheral blood pressure a. and left b. and right c. carotid sinus blood pressures upon successive bilateral clamping of the caudal common carotid artery, occipital group and external carotid artery in sheep number 4 of experimental series 4

Clamping procedure

↑ indicates when an artery was clamped and ↓ when an arterial clamp was removed:

1. clamp caudal left common carotid artery,
2. clamp caudal right common carotid artery,
3. clamp left occipital group,
4. clamp right occipital group,
5. clamp left external carotid artery,
6. clamp right external carotid artery,
7. unclamp right external carotid artery,
8. unclamp left external carotid artery,
9. unclamp right occipital group,
10. unclamp left occipital group,
11. unclamp caudal right common carotid artery,
12. unclamp caudal left common carotid artery.

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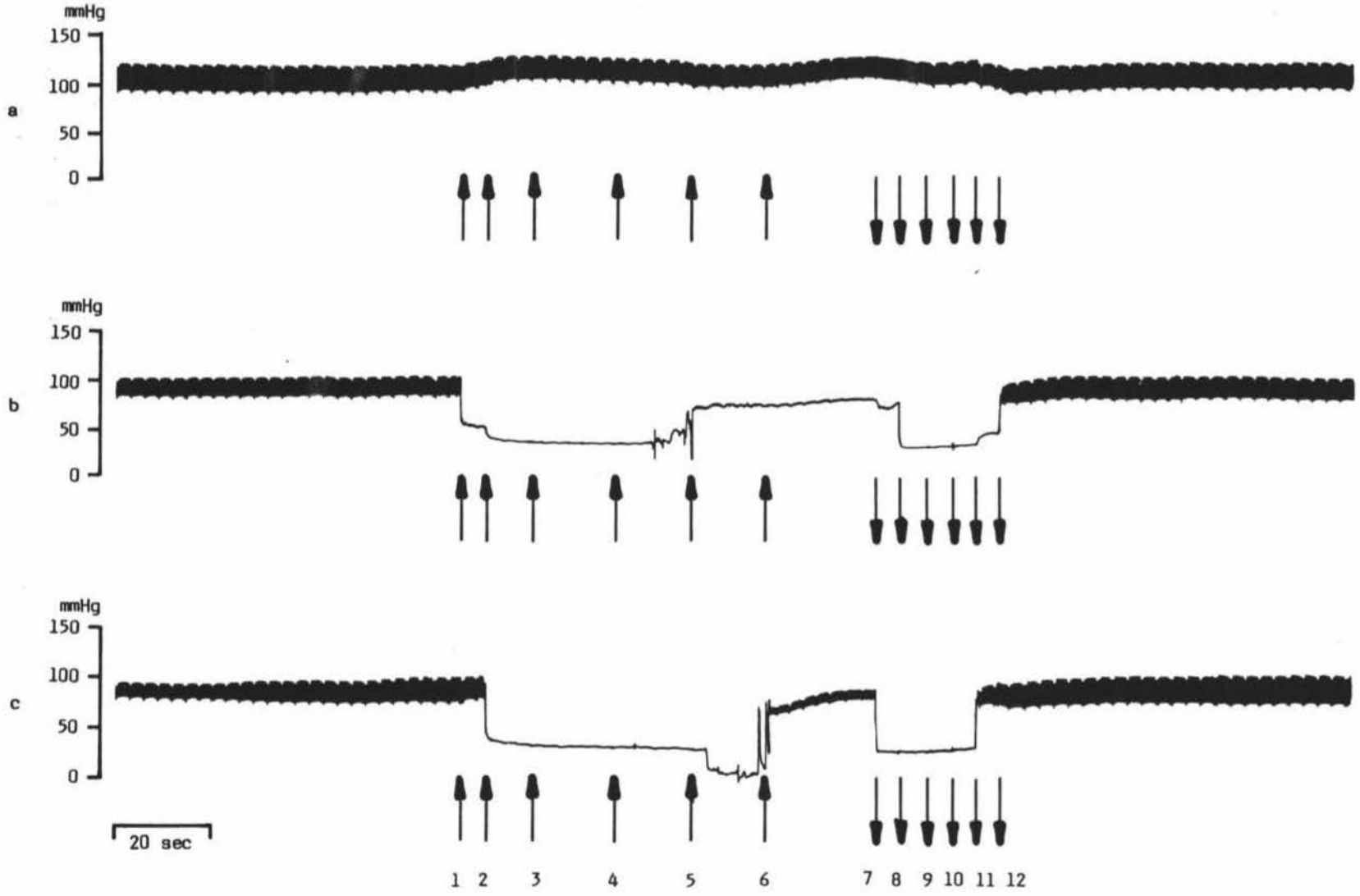
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3.4.5.2 Peripheral Mean Blood Pressure

3.4.5.2.1 Clamping Position

The following significantly different effects of clamping position on the peripheral mean blood pressure are summarised diagrammatically in Figure 3.8 and listed in Table 3.10:

1. Unilateral Versus Bilateral Clamping of the Common Carotid Artery
   Contrast numbers 1, 2, 7, 11, 16 and 19.
   Bilateral clamping of the common carotid artery in either the caudal or cranial position induced a peripheral mean blood pressure rise four times the magnitude produced by unilateral occlusion of a single carotid artery.

2. Unilateral Left Versus Right Clamping of the Common Carotid Artery
   Several observations indicate that unilateral clamping of the left common carotid artery alone, or in combination with other arteries, caused a greater rise of peripheral mean blood pressure than did occlusion of the contralateral vessels.

   (a) Left versus right common carotid arterial occlusion
   Contrast Number 22 and 23.
   Clamping the left common carotid artery in either the caudal or cranial position induced a peripheral mean blood pressure rise greater than that produced by clamping the right carotid artery.

   (b.i) Unilateral clamping of the left common carotid artery and contralateral clamping of the right occipital group and external carotid artery versus unilateral clamping of the right common carotid artery and contralateral clamping of the left occipital group and external carotid artery
   Contrast numbers 3 and 4.
   Clamping the left common carotid artery, in association with right occipital group and right external carotid artery occlusion, induced a peripheral mean blood pressure rise greater than that caused by right common carotid arterial clamping combined with left occipital group and left external carotid arterial occlusion. Examination of contrast number 4, comparing occlusion steps 39 and 44 involved in this cascade, further

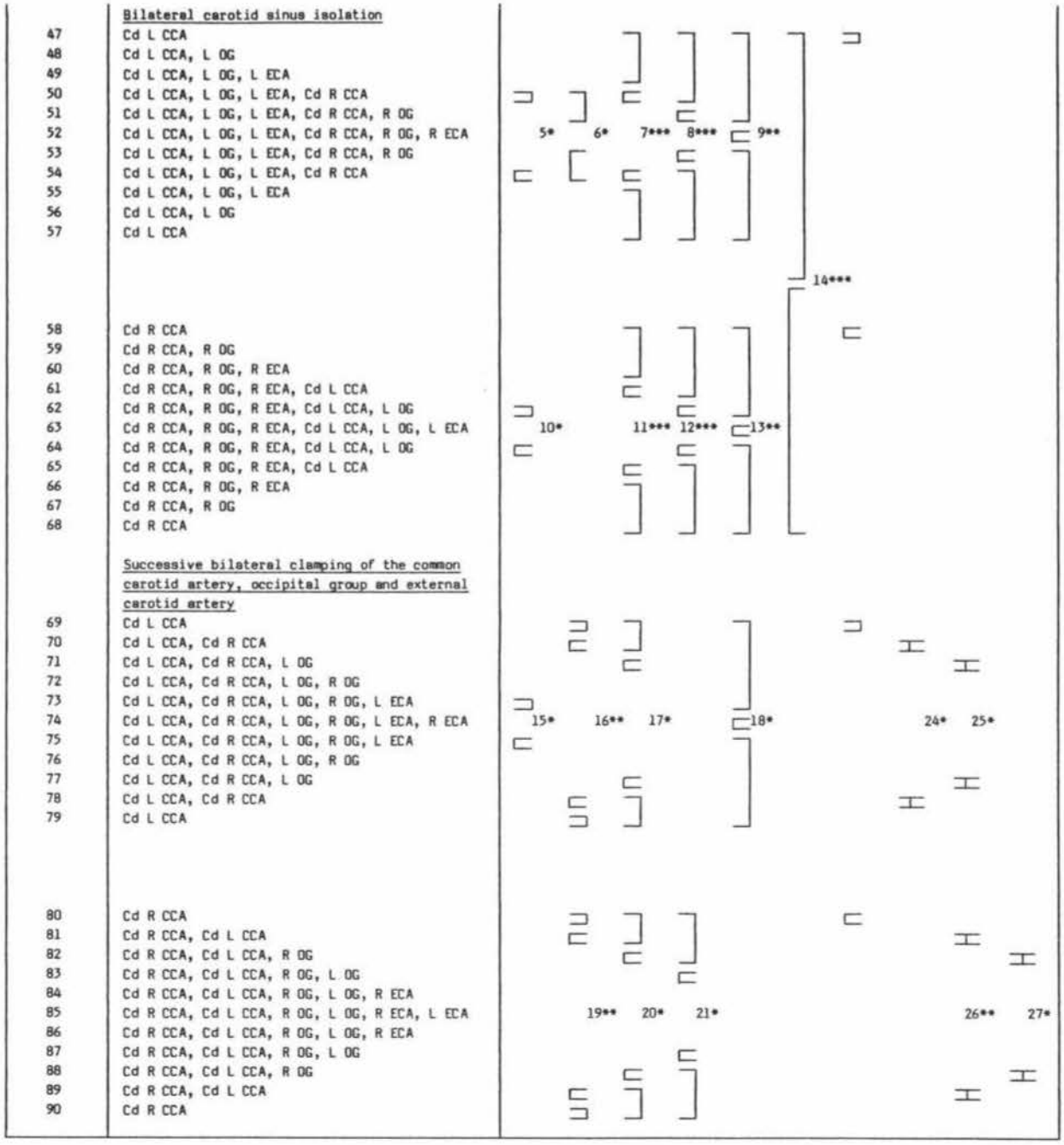
TABLE 3.9 PERIPHERAL MEAN BLOOD PRESSURE CHANGE (MEAN ± SEM, mmHg) FROM EXPERIMENTAL SERIES A (n = 4)

Occlusion Number	Clamping Position	State of Vagal Innervation	
		Intact Vn	Cut LR Vn
1	Cd L CCA	7 ± 0.9	8 ± 3.9
2	Cd R CCA	3 ± 0.3	6 ± 4.9
3	Cd LR CCA	19 ± 4.2	20 ± 4.9
4	Cn L CCA	10 ± 1.1	9 ± 4.9
5	Cn R CCA	4 ± 1.3	3 ± 1.2
6	Cn LR CCA	19 ± 5.3	21 ± 6.7
7	Cd L CCA	7 ± 2.1	8 ± 1.8
8	Cd L CCA, L OG	-6 ± 8.3	3 ± 5.5
9	Cd L CCA, L OG, L ECA	-5 ± 7.0	6 ± 2.0
10	Cd L CCA, L OG	5 ± 2.5	5 ± 1.1
11	Cd L CCA	-4 ± 5.8	8 ± 2.4
12	Cd R CCA	3 ± 2.3	6 ± 1.0
13	Cd R CCA, R OG	3 ± 3.3	0 ± 1.7
14	Cd R CCA, R OG, R ECA	2 ± 2.2	1 ± 2.4
15	Cd R CCA, R OG	2 ± 3.5	3 ± 2.2
16	Cd R CCA	3 ± 2.7	2 ± 2.3
17	Cd L CCA	7 ± 1.7	10 ± 4.9
18	Cd L CCA, R OG	-10 ± 8.5	10 ± 2.9
19	Cd L CCA, R OG, L ECA	5 ± 4.0	2 ± 6.7
20	Cd L CCA, R OG	6 ± 5.2	8 ± 7.7
21	Cd L CCA	5 ± 4.3	9 ± 7.9
22	Cd R CCA	0 ± 2.8	3 ± 3.3
23	Cd R CCA, L OG	-2 ± 3.4	2 ± 1.2
24	Cd R CCA, L OG, R ECA	3 ± 3.2	4 ± 1.4
25	Cd R CCA, L OG	1 ± 3.2	4 ± 1.1
26	Cd R CCA	-5 ± 4.6	3 ± 1.7
27	Cd L CCA	8 ± 3.5	13 ± 4.3
28	Cd L CCA, L OG	8 ± 3.5	13 ± 6.6
29	Cd L CCA, L OG, R ECA	15 ± 10.0	19 ± 4.0
30	Cd L CCA, L OG	8 ± 6.0	7 ± 6.7
31	Cd L CCA	13 ± 7.6	5 ± 9.4
32	Cd R CCA	3 ± 1.6	3 ± 1.1
33	Cd R CCA, R OG	1 ± 2.8	2 ± 6.3
34	Cd R CCA, R OG, L ECA	3 ± 2.4	11 ± 7.2
35	Cd R CCA, R OG	1 ± 3.1	-2 ± 2.5
36	Cd R CCA	0 ± 0.8	-1 ± 2.7
37	Cd L CCA	7 ± 5.5	15 ± 3.1
38	Cd L CCA, R OG	10 ± 7.2	19 ± 6.5
39	Cd L CCA, R OG, R ECA	13 ± 11.9	23 ± 7.3
40	Cd L CCA, R OG	8 ± 5.0	12 ± 7.5
41	Cd L CCA	10 ± 4.8	11 ± 8.5
42	Cd R CCA	8 ± 4.7	4 ± 2.7
43	Cd R CCA, L OG	12 ± 8.1	8 ± 3.8
44	Cd R CCA, L OG, L ECA	11 ± 3.8	6 ± 1.5
45	Cd R CCA, L OG	5 ± 4.0	-2 ± 1.5
46	Cd R CCA	6 ± 4.9	3 ± 1.1
47	Cd L CCA	7 ± 2.1	18 ± 9.1
48	Cd L CCA, L OG	8 ± 2.8	11 ± 9.2
49	Cd L CCA, L OG, L ECA	1 ± 4.5	8 ± 6.1
50	Cd L CCA, L OG, L ECA, Cd R CCA	13 ± 4.2	14 ± 8.9
51	Cd L CCA, L OG, L ECA, Cd R CCA, R OG	15 ± 11.7	24 ± 13.3
52	Cd L CCA, L OG, L ECA, Cd R CCA, R OG, R ECA	40 ± 10.8	31 ± 15.1
53	Cd L CCA, L OG, L ECA, Cd R CCA, R OG	34 ± 10.8	34 ± 9.9
54	Cd L CCA, L OG, L ECA, Cd R CCA	20 ± 3.7	30 ± 13.8
55	Cd L CCA, L OG, L ECA	5 ± 3.8	6 ± 11.2
56	Cd L CCA, L OG	-6 ± 5.9	5 ± 11.6
57	Cd L CCA	1 ± 4.9	3 ± 11.4
58	Cd R CCA	1 ± 2.6	4 ± 1.4
59	Cd R CCA, R OG	-4 ± 3.1	3 ± 0.8
60	Cd R CCA, R OG, R ECA	-4 ± 3.2	1 ± 0.3
61	Cd R CCA, R OG, R ECA, Cd L CCA	11 ± 2.3	20 ± 2.3
62	Cd R CCA, R OG, R ECA, Cd L CCA, L OG	8 ± 4.0	16 ± 3.6
63	Cd R CCA, R OG, R ECA, Cd L CCA, L OG, L ECA	16 ± 8.0	24 ± 7.1
64	Cd R CCA, R OG, R ECA, Cd L CCA, L OG	24 ± 6.4	29 ± 11.7
65	Cd R CCA, R OG, R ECA, Cd L CCA	17 ± 3.1	28 ± 11.1
66	Cd R CCA, R OG, R ECA	4 ± 2.0	9 ± 9.6
67	Cd R CCA, R OG	-1 ± 3.2	4 ± 8.9
68	Cd R CCA	-8 ± 1.4	2 ± 7.9
69	Cd L CCA	8 ± 3.4	7 ± 1.5
70	Cd L CCA, Cd R CCA	14 ± 1.8	26 ± 3.5
71	Cd L CCA, Cd R CCA, L OG	14 ± 3.5	31 ± 4.1
72	Cd L CCA, Cd R CCA, L OG, R OG	9 ± 9.4	19 ± 2.1
73	Cd L CCA, Cd R CCA, L OG, R OG, L ECA	8 ± 2.7	11 ± 5.5
74	Cd L CCA, Cd R CCA, L OG, R OG, L ECA, R ECA	29 ± 13.0	19 ± 4.2
75	Cd L CCA, Cd R CCA, L OG, R OG, L ECA	27 ± 6.2	17 ± 4.3
76	Cd L CCA, Cd R CCA, L OG, R OG	24 ± 7.9	14 ± 6.3
77	Cd L CCA, Cd R CCA, L OG	19 ± 6.9	7 ± 5.7
78	Cd L CCA, Cd R CCA	18 ± 7.3	4 ± 8.6
79	Cd L CCA	8 ± 5.5	-6 ± 11.1
80	Cd R CCA	2 ± 0.7	1 ± 4.5
81	Cd R CCA, Cd L CCA	12 ± 2.8	23 ± 5.9
82	Cd R CCA, Cd L CCA, R OG	9 ± 2.7	22 ± 5.2
83	Cd R CCA, Cd L CCA, R OG, L OG	9 ± 5.8	19 ± 3.7
84	Cd R CCA, Cd L CCA, R OG, L OG, R ECA	10 ± 4.9	15 ± 4.9
85	Cd R CCA, Cd L CCA, R OG, L OG, R ECA, L ECA	23 ± 6.3	15 ± 4.4
86	Cd R CCA, Cd L CCA, R OG, L OG, R ECA	25 ± 8.6	19 ± 4.8
87	Cd R CCA, Cd L CCA, R OG, L OG	26 ± 7.0	16 ± 3.9
88	Cd R CCA, Cd L CCA, R OG	23 ± 9.3	9 ± 7.2
89	Cd R CCA, Cd L CCA	22 ± 12.8	1 ± 10.0
90	Cd R CCA	15 ± 9.5	-12 ± 8.0

FIGURE 3.8 DIAGRAMMATIC SUMMARY OF THE SIGNIFICANT CONTRASTS FROM THE PERIPHERAL MEAN BLOOD PRESSURE ANALYSIS OF VARIANCE OF EXPERIMENTAL SERIES 4

Occlusion Number	Clamping Position	Contrast Number and Level of Significance
	Unilateral and bilateral clamping of the common carotid artery	
1	Cd L CCA	1**
2	Cd R CCA	
3	Cd LR CCA	
4	Cn L CCA	2**
5	Cn R CCA	
6	Cn LR CCA	
	Unilateral carotid sinus isolation	
7	Cd L CCA	
8	Cd L CCA, L OG	
9	Cd L CCA, L OG, L ECA	
10	Cd L CCA, L OG	
11	Cd L CCA	
12	Cd R CCA	
13	Cd R CCA, R OG	
14	Cd R CCA, R OG, R ECA	
15	Cd R CCA, R OG	
16	Cd R CCA	
	Clamping combinations to decrease the carotid sinus blood supply	
17	Cd L CCA	
18	Cd L CCA, R OG	
19	Cd L CCA, R OG, L ECA	
20	Cd L CCA, R OG	
21	Cd L CCA	
22	Cd R CCA	
23	Cd R CCA, L OG	
24	Cd R CCA, L OG, R ECA	
25	Cd R CCA, L OG	
26	Cd R CCA	
27	Cd L CCA	
28	Cd L CCA, L OG	
29	Cd L CCA, L OG, R ECA	
30	Cd L CCA, L OG	
31	Cd L CCA	
32	Cd R CCA	
33	Cd R CCA, R OG	
34	Cd R CCA, R OG, L ECA	
35	Cd R CCA, R OG	
36	Cd R CCA	
	Unilateral clamping of a common carotid artery and contralateral clamping of the occipital group and external carotid artery	
37	Cd L CCA	22** & 23*
38	Cd L CCA, R OG	
39	Cd L CCA, R OG, R ECA	
40	Cd L CCA, R OG	
41	Cd L CCA	3** 4*
42	Cd R CCA	
43	Cd R CCA, L OG	
44	Cd R CCA, L OG, L ECA	
45	Cd R CCA, L OG	
46	Cd R CCA	

Cont....



In this figure the 27 significant peripheral mean blood pressure contrasts in experimental series 4 are diagrammatically presented. Within each clamping cascade there is one contrast per column, with the exception of contrast number 14 which compares the two bilateral carotid sinus isolation cascades, and contrast numbers 22 and 23 which compare clamping the left with the right common carotid artery of all cascades, the latter contrast following vagotomy only.

Clamping Treatment Significant Contrasts

The left-pointing bracket(s) (]) indicate the clamping position(s) against which the right-pointing bracket(s)([) were compared.

Clamping Treatment and Vagotomy Significant Interactions

Each of these contrasts is indicated by a pair of I's.

Each contrast is denoted on the right-hand side by the contrast number and level of significance (as in Tables 3.9 and 3.10).

TABLE 3.10 PERIPHERAL MEAN BLOOD PRESSURE CHANGE - SUMMARY OF ANALYSIS OF VARIANCE FROM EXPERIMENTAL SERIES 4

Contrast Number See Figure 3.8	Source of Variation	Degrees of Freedom	Variance Ratio
	A. Clamping treatment	89	4.318***
	Significant contrasts, as numbered in Table 3.9		
1	1+2 versus 3	1	7.120**
2	4+5 versus 6	1	7.957**
3	37+38+39+40+41 versus 42+43+44+45+56	1	7.306**
4	39 versus 44 (Cut LR Vn)	1	4.308*
5	50 versus 54	1	4.424*
6	50+51 versus 53+54	1	6.237*
7	47+48+49+55+56+57 versus 50+54	1	17.104***
8	47+48+49+50+54+55+56+57 versus 51+53	1	29.147***
9	47+48+49+50+51+53+54+55+56+57 versus 52	1	29.293***
10	62 versus 64	1	6.459*
11	58+59+60+66+67+68 versus 61+65	1	29.378***
12	58+59+60+61+65+66+67+68 versus 62+64	1	18.126***
13	58+59+60+61+62+64+65+66+67+68 versus 63	1	7.696**
14	47+48+49+50+51+52+53+54+55+56+57 versus 58+59+60+61+62+63+64+65+67+68	1	10.138**
15	73 versus 75	1	4.700*
16	69+79 versus 70+78	1	8.210**
17	69+70+78+79 versus 71+77	1	4.877*
18	69+70+71+72+73+75+76+77+78+79 versus 74	1	5.653*
19	80+90 versus 81+89	1	10.384**
20	80+81+89+90 versus 82+88	1	5.161*
21	80+81+82+88+89+90 versus 83+87	1	4.332*
	Non-orthogonal contrasts		
22	1+4+7+17+27+37+47+69 versus 2+5+12+22+32+42+58+80	1	8.479**
23	1+4+7+17+27+37+47+69 versus 2+5+12+22+32+42+58+80 (Cut LR Vn)	1	6.567*
	B. Vagi : intact versus bilateral section	1	4.009*
	C. Animals	3	22.189***
	Interaction: A x B	89	0.943
	Significant contrasts, as numbered in Table 3.9		
24	70 (Intact Vn) + 78 (Cut LR Vn) versus 70 (Cut LR Vn) + 78 (Intact Vn)	1	5.192*
25	71 (Intact Vn) + 77 (Cut LR Vn) versus 71 (Cut LR Vn) + 77 (Intact Vn)	1	4.516*
26	81 (Intact Vn) + 89 (Cut LR Vn) versus 81 (Cut LR Vn) + 89 (Incact Vn)	1	8.618**
27	82 (Intact Vn) + 88 (Cut LR Vn) versus 82 (Cut LR Vn) + 88 (Intact Vn)	1	5.392*
	Residual mean square	537	1.302

clarifies the situation. This difference is not apparent when both the data prior to, combined with that following vagotomy, and the data only before vagotomy were examined. It is only after bilateral vagotomy that the systemic effects of the left common carotid arterial clamping cascade are greater than the right carotid arterial clamping cascade.

(b.ii) Bilateral carotid sinus isolation, left vessels clamped initially versus right vessels clamped initially

Contrast number 14.

Bilateral carotid sinus isolation was achieved by sequential isolation of firstly the ipsilateral common carotid artery, occipital group and external carotid artery and finally the contralateral vessels. Adding successive clamps to isolate the left, followed by the right, carotid sinus, progressively increased the peripheral mean blood pressure more than the rise upon isolating the right then left sinus.

3. Clamping Versus Unclamping During the Clamping Cascade

During the clamping cascade, unclamping many of the vessels did not result in the peripheral mean blood pressure returning to the same value as that recorded when the clamps were applied. On average, the peripheral mean blood pressure rise upon unclamping was twice that seen during clamping. Examples of this difference between clamping and unclamping are contrast numbers 5, 6, 10 and 15.

4. Effect of Additional Clamps Upon the Partial Clamping Cascade

Several comparisons indicate that during the clamping cascade, clamping additional vessels, especially the later clamps, elevated the peripheral mean blood pressure response above the progressively increasing systemic pressure prior to the additional occlusions. Examples of this elevation are contrast numbers 8, 9, 12, 13, 17, 18, 20 and 21.

3.4.5.2.2 Effect of Bilateral Vagotomy on the Clamping Cascade

Bilateral vagotomy increased the rise in peripheral mean blood pressure upon clamping the cervical blood vessels. This was demonstrated in the overall comparison of the rises in peripheral mean blood pressure with the vagi intact and upon bilateral vagotomy. A similar effect was seen with vagotomy on the peripheral pulse pressure, but not on the heart rate (see Tables 3.12 and 3.14).

One particular case illustrating the effect of vagotomy has previously been described. In section 3.4.5.2.1, part 2 b.i, bilateral vagotomy was shown to enhance the effect of unilateral clamping of the left common carotid artery and contralateral occlusion of the right occipital group and external carotid artery more than that of unilateral clamping of the right common carotid artery and contralateral occlusion of the left occipital group and external carotid artery.

A striking interaction is apparent between the effect of vagotomy, clamping and unclamping (see contrast numbers 24 to 27). Prior to vagotomy, the peripheral mean blood pressure rise upon unclamping was greater than that during clamping, whereas, following bilateral vagotomy, this rise was less during unclamping than clamping.

3.4.5.3 Peripheral Pulse Pressure

Cervical arterial clamping had very little effect on the peripheral pulse pressure. In a single clamping cascade, the unclamping phase of the caudal left and right common carotid artery and the left occipital group fell to lower values than recorded during the clamping phase.

As has been previously described in section 3.4.5.2.2, bilateral vagotomy significantly enhanced the overall peripheral pulse pressure rise upon clamping the cervical blood vessels.

See Table 3.12.

3.4.5.4 Heart Rate

Neither the clamping position nor state of vagal innervation are statistically significant sources of variation. The only significant contrast was the overall interaction between the treatment and state of vagal innervation such that vagotomy enhanced the rise of heart rate upon clamping.

See Table 3.14.

3.4.5.5 Respiratory Rate

Since the respiratory rate appeared to remain constant throughout many of the clamping combinations in this experimental series, the data was not analysed statistically. It should be noted, however, that in sheep number 1 prior to vagotomy, respiration ceased upon successive bilateral clamping of the common

TABLE 3.11 PERIPHERAL PULSE PRESSURE CHANGE (MEAN ± SEM, mmHg) FROM EXPERIMENTAL SERIES 4 (n = 4)

Occlusion Number	Clamping Position	State of Vagal Innervation	
		Intact Vn	Cut LR Vn
1	Cd L CCA	0 ± 0.3	-1 ± 0.9
2	Cd R CCA	-1 ± 0.8	-1 ± 0.4
3	Cd LR CCA	1 ± 1.4	0 ± 2.5
4	Cn L CCA	-1 ± 1.3	-1 ± 0.8
5	Cn R CCA	0 ± 0.3	-1 ± 0.3
6	Cn LR CCA	2 ± 1.2	-1 ± 1.8
7	Cd L CCA	-1 ± 0.9	0 ± 1.1
8	Cd L CCA, L OG	-1 ± 1.0	-3 ± 1.6
9	Cd L CCA, L OG, L ECA	0 ± 0.6	-1 ± 1.3
10	Cd L CCA, L OG	0 ± 0.3	-1 ± 1.7
11	Cd L CCA	-1 ± 0.3	-1 ± 1.7
12	Cd R CCA	0 ± 0.3	-1 ± 0.9
13	Cd R CCA, R OG	-1 ± 0.6	-2 ± 1.0
14	Cd R CCA, R OG, R ECA	0 ± 0.4	-2 ± 0.8
15	Cd R CCA, R OG	-1 ± 1.3	-4 ± 1.7
16	Cd R CCA	-1 ± 0.5	-1 ± 1.0
17	Cd L CCA	2 ± 1.2	-1 ± 0.9
18	Cd L CCA, R OG	-1 ± 1.1	-2 ± 1.0
19	Cd L CCA, R OG, L ECA	0 ± 0.3	1 ± 1.0
20	Cd L CCA, R OG	0 ± 1.3	2 ± 0.9
21	Cd L CCA	1 ± 0.5	1 ± 1.7
22	Cd R CCA	1 ± 0.9	-2 ± 0.5
23	Cd R CCA, L OG	1 ± 0.9	-2 ± 0.6
24	Cd R CCA, L OG, R ECA	1 ± 0.5	-2 ± 1.0
25	Cd R CCA, L OG	1 ± 0.8	-2 ± 0.9
26	Cd R CCA	1 ± 0.5	0 ± 1.3
27	Cd L CCA	-1 ± 2.4	-2 ± 0.7
28	Cd L CCA, L OG	-3 ± 1.7	-2 ± 1.9
29	Cd L CCA, L OG, R ECA	-2 ± 3.2	-4 ± 2.7
30	Cd L CCA, L OG	-1 ± 2.5	-3 ± 0.7
31	Cd L CCA	-2 ± 2.4	1 ± 0.3
32	Cd R CCA	-1 ± 0.3	-2 ± 0.6
33	Cd R CCA, R OG	-3 ± 0.9	-3 ± 0.5
34	Cd R CCA, R OG, L ECA	-4 ± 2.3	-6 ± 1.8
35	Cd R CCA, R OG	-4 ± 2.6	-4 ± 1.0
36	Cd R CCA	-2 ± 1.9	-2 ± 1.8
37	Cd L CCA	-1 ± 1.3	-2 ± 0.9
38	Cd L CCA, R OG	-2 ± 0.4	-4 ± 2.5
39	Cd L CCA, R OG, R ECA	-2 ± 1.0	-4 ± 1.8
40	Cd L CCA, R OG	-1 ± 1.8	-3 ± 1.0
41	Cd L CCA	-2 ± 1.3	-3 ± 1.1
42	Cd R CCA	-1 ± 0.4	-2 ± 0.9
43	Cd R CCA, L OG	-3 ± 1.3	-2 ± 1.0
44	Cd R CCA, L OG, L ECA	-3 ± 0.8	-4 ± 1.7
45	Cd R CCA, L OG	-2 ± 1.5	-3 ± 0.5
46	Cd R CCA	-2 ± 1.2	-3 ± 0.9
47	Cd L CCA	-2 ± 1.2	0 ± 1.1
48	Cd L CCA, L OG	-2 ± 1.0	-1 ± 1.2
49	Cd L CCA, L OG, L ECA	-2 ± 0.9	-2 ± 1.0
50	Cd L CCA, L OG, L ECA, Cd R CCA	-3 ± 0.9	-2 ± 1.5
51	Cd L CCA, L OG, L ECA, Cd R CCA, R OG	-2 ± 1.3	-3 ± 1.7
52	Cd L CCA, L OG, L ECA, Cd R CCA, R OG, R ECA	-2 ± 2.7	-3 ± 3.9
53	Cd L CCA, L OG, L ECA, Cd R CCA, R OG	-2 ± 2.7	-3 ± 3.2
54	Cd L CCA, L OG, L ECA, Cd R CCA	-1 ± 2.1	-2 ± 3.0
55	Cd L CCA, L OG, L ECA	0 ± 2.3	-1 ± 1.1
56	Cd L CCA, L OG	-1 ± 1.7	2 ± 3.2
57	Cd L CCA	-1 ± 1.3	1 ± 2.4
58	Cd R CCA	-1 ± 1.1	-1 ± 0.9
59	Cd R CCA, R OG	-1 ± 1.1	-2 ± 0.3
60	Cd R CCA, R OG, R ECA	-1 ± 1.1	-1 ± 0.5
61	Cd R CCA, R OG, R ECA, Cd L CCA	-3 ± 2.1	-4 ± 2.1
62	Cd R CCA, R OG, R ECA, Cd L CCA, L OG	-3 ± 0.9	-5 ± 2.9
63	Cd R CCA, R OG, R ECA, Cd L CCA, L OG, L ECA	-3 ± 1.7	-5 ± 4.0
64	Cd R CCA, R OG, R ECA, Cd L CCA, L OG	-3 ± 2.5	-2 ± 3.0
65	Cd R CCA, R OG, R ECA, Cd L CCA	-2 ± 1.4	-2 ± 2.5
66	Cd R CCA, R OG, R ECA	-3 ± 0.9	-3 ± 1.3
67	Cd R CCA, R OG	-2 ± 1.4	-3 ± 2.6
68	Cd R CCA	-1 ± 1.3	-2 ± 1.8
69	Cd L CCA	0 ± 0.6	-1 ± 1.5
70	Cd L CCA, Cd R CCA	1 ± 1.0	0 ± 2.9
71	Cd L CCA, Cd R CCA, L OG	0 ± 1.0	2 ± 2.6
72	Cd L CCA, Cd R CCA, L OG, R OG	-2 ± 0.9	-1 ± 1.4
73	Cd L CCA, Cd R CCA, L OG, R OG, L ECA	-2 ± 0.6	0 ± 0.3
74	Cd L CCA, Cd R CCA, L OG, R OG, L ECA, R ECA	-2 ± 2.5	-2 ± 2.5
75	Cd L CCA, Cd R CCA, L OG, R OG, L ECA	-4 ± 2.1	-5 ± 2.1
76	Cd L CCA, Cd R CCA, L OG, R OG	-2 ± 3.4	-4 ± 2.3
77	Cd L CCA, Cd R CCA, L OG	-1 ± 2.8	-5 ± 1.9
78	Cd L CCA, Cd R CCA	-2 ± 2.5	-4 ± 1.6
79	Cd L CCA	-3 ± 1.5	-2 ± 2.0
80	Cd R CCA	0 ± 0.4	-2 ± 0.0
81	Cd R CCA, Cd L CCA	-1 ± 0.8	-6 ± 0.6
82	Cd R CCA, Cd L CCA, R OG	-1 ± 0.5	-5 ± 1.2
83	Cd R CCA, Cd L CCA, R OG, L OG	0 ± 1.2	-4 ± 1.3
84	Cd R CCA, Cd L CCA, R OG, L OG, R ECA	-2 ± 0.6	-4 ± 0.9
85	Cd R CCA, Cd L CCA, R OG, L OG, R ECA, L ECA	-5 ± 1.3	-6 ± 1.9
86	Cd R CCA, Cd L CCA, R OG, L OG, R ECA	-5 ± 2.1	-7 ± 1.7
87	Cd R CCA, Cd L CCA, R OG, L OG	-3 ± 1.7	-5 ± 2.0
88	Cd R CCA, Cd L CCA, R OG	-2 ± 1.7	-7 ± 2.1
89	Cd R CCA, Cd L CCA	0 ± 1.3	-8 ± 4.2
90	Cd R CCA	-1 ± 2.1	-8 ± 4.4

TABLE 3.12 PERIPHERAL PULSE PRESSURE CHANGE - SUMMARY OF ANALYSIS OF VARIANCE FROM EXPERIMENTAL SERIES 4

Source of Variation	Degrees of Freedom	Variance Ratio
A. Clamping treatment	89	1.771*
Significant contrasts, as numbered in Table 3.11		
71 versus 77	1	7.755**
B. Vagi : intact versus bilateral section	1	18.367***
C. Animals	3	27.687***
Interaction: AxB	89	0.615
Residual mean square	537	0.098

TABLE 3.13 HEART RATE CHANGE (MEAN ± SEM, BEATS/MIN) FROM EXPERIMENTAL SERIES 4 (n = 4)

Occlusion Number	Clamping Position	State of Vagal Innervation	
		Intact Vn	Cut LR Vn
1	Cd L CCA	6 ± 6.0	0 ± 2.4
2	Cd R CCA	2 ± 2.9	0 ± 0.0
3	Cd LR CCA	0 ± 0.0	0 ± 2.4
4	Cn L CCA	0 ± 0.0	-3 ± 1.7
5	Cn R CCA	-3 ± 1.7	5 ± 4.5
6	Cn LR CCA	0 ± 2.4	2 ± 2.9
7	Cd L CCA	-2 ± 1.5	2 ± 1.5
8	Cd L CCA, L OG	-3 ± 3.0	0 ± 0.0
9	Cd L CCA, L OG, L ECA	-3 ± 1.7	-2 ± 2.9
10	Cd L CCA, L OG	-3 ± 1.7	0 ± 2.4
11	Cd L CCA	2 ± 1.5	8 ± 2.9
12	Cd R CCA	0 ± 2.4	-2 ± 1.5
13	Cd R CCA, R OG	-5 ± 3.8	-3 ± 3.9
14	Cd R CCA, R OG, R ECA	2 ± 3.8	-3 ± 1.7
15	Cd R CCA, R OG	0 ± 4.2	0 ± 2.4
16	Cd R CCA	0 ± 6.5	5 ± 1.5
17	Cd L CCA	-3 ± 3.0	6 ± 2.4
18	Cd L CCA, R OG	-6 ± 2.4	8 ± 2.9
19	Cd L CCA, R OG, L ECA	-5 ± 1.5	2 ± 1.5
20	Cd L CCA, R OG	-5 ± 1.5	8 ± 3.8
21	Cd L CCA	0 ± 2.4	8 ± 2.9
22	Cd R CCA	0 ± 2.4	3 ± 1.7
23	Cd R CCA, L OG	-3 ± 3.9	3 ± 1.7
24	Cd R CCA, L OG, R ECA	0 ± 2.4	3 ± 1.7
25	Cd R CCA, L OG	-2 ± 2.9	3 ± 3.0
26	Cd R CCA	2 ± 2.9	-2 ± 3.8
27	Cd L CCA	5 ± 2.9	0 ± 4.2
28	Cd L CCA, L OG	5 ± 2.9	8 ± 8.6
29	Cd L CCA, L OG, R ECA	5 ± 2.9	2 ± 2.9
30	Cd L CCA, L OG	-2 ± 2.9	3 ± 3.9
31	Cd L CCA	0 ± 2.4	6 ± 5.5
32	Cd R CCA	-1 ± 3.8	-2 ± 4.5
33	Cd R CCA, R OG	-6 ± 2.4	-6 ± 2.4
34	Cd R CCA, R OG, L ECA	-6 ± 4.2	2 ± 2.9
35	Cd R CCA, R OG	-8 ± 3.8	5 ± 8.3
36	Cd R CCA	-2 ± 3.8	0 ± 4.2
37	Cd L CCA	2 ± 3.8	3 ± 3.9
38	Cd L CCA, R OG	0 ± 2.4	5 ± 2.9
39	Cd L CCA, R OG, R ECA	2 ± 3.8	0 ± 5.5
40	Cd L CCA, R OG	3 ± 3.0	3 ± 5.7
41	Cd L CCA	11 ± 2.9	5 ± 8.3
42	Cd R CCA	3 ± 1.7	3 ± 3.9
43	Cd R CCA, L OG	3 ± 3.9	0 ± 2.4
44	Cd R CCA, L OG, L ECA	3 ± 1.7	-3 ± 1.7
45	Cd R CCA, L OG	3 ± 1.7	3 ± 1.7
46	Cd R CCA	5 ± 2.9	5 ± 3.8
47	Cd L CCA	5 ± 1.5	2 ± 2.9
48	Cd L CCA, L OG	6 ± 2.4	2 ± 4.5
49	Cd L CCA, L OG, L ECA	5 ± 2.9	2 ± 3.8
50	Cd L CCA, L OG, L ECA, Cd R CCA	5 ± 2.9	3 ± 3.9
51	Cd L CCA, L OG, L ECA, Cd R CCA, R OG	9 ± 3.9	-9 ± 5.7
52	Cd L CCA, L OG, L ECA, Cd R CCA, R OG, R ECA	12 ± 0.0	-2 ± 4.5
53	Cd L CCA, L OG, L ECA, Cd R CCA, R OG	17 ± 4.5	6 ± 10.1
54	Cd L CCA, L OG, L ECA, Cd R CCA	14 ± 6.2	11 ± 8.6
55	Cd L CCA, L OG, L ECA	11 ± 1.5	8 ± 5.7
56	Cd L CCA, L OG	5 ± 2.9	8 ± 9.6
57	Cd L CCA	15 ± 9.3	5 ± 7.5
58	Cd R CCA	-3 ± 3.0	2 ± 1.5
59	Cd R CCA, R OG	-3 ± 5.2	2 ± 2.9
60	Cd R CCA, R OG, R ECA	-5 ± 2.9	3 ± 1.7
61	Cd R CCA, R OG, R ECA, Cd L CCA	-2 ± 4.5	3 ± 1.7
62	Cd R CCA, R OG, R ECA, Cd L CCA, L OG	-6 ± 2.4	2 ± 1.5
63	Cd R CCA, R OG, R ECA, Cd L CCA, L OG, L ECA	0 ± 5.5	0 ± 0.5
64	Cd R CCA, R OG, R ECA, Cd L CCA, L OG	5 ± 5.7	11 ± 6.7
65	Cd R CCA, R OG, R ECA, Cd L CCA	2 ± 1.5	6 ± 4.2
66	Cd R CCA, R OG, R ECA	-2 ± 1.5	8 ± 3.8
67	Cd R CCA, R OG	-8 ± 2.9	-3 ± 3.9
68	Cd R CCA	-5 ± 2.9	-3 ± 5.2
69	Cd L CCA	8 ± 2.9	0 ± 2.4
70	Cd L CCA, Cd R CCA	0 ± 4.2	-5 ± 3.8
71	Cd L CCA, Cd R CCA, L OG	6 ± 2.4	-2 ± 2.9
72	Cd L CCA, Cd R CCA, L OG, R OG	2 ± 1.5	-2 ± 2.9
73	Cd L CCA, Cd R CCA, L OG, R OG, L ECA	2 ± 1.5	0 ± 5.5
74	Cd L CCA, Cd R CCA, L OG, R OG, L ECA, R ECA	8 ± 5.1	-8 ± 2.9
75	Cd L CCA, Cd R CCA, L OG, R OG, L ECA	23 ± 9.9	9 ± 7.9
76	Cd L CCA, Cd R CCA, L OG, R OG	17 ± 9.3	15 ± 11.6
77	Cd L CCA, Cd R CCA, L OG	18 ± 16.1	11 ± 10.5
78	Cd L CCA, Cd R CCA	12 ± 2.4	18 ± 14.5
79	Cd L CCA	12 ± 10.1	21 ± 15.2
80	Cd R CCA	0 ± 2.4	6 ± 3.5
81	Cd R CCA, Cd L CCA	-2 ± 2.9	-2 ± 3.8
82	Cd R CCA, Cd L CCA, R OG	-3 ± 3.9	-3 ± 7.5
83	Cd R CCA, Cd L CCA, R OG, L OG	-3 ± 5.7	5 ± 4.5
84	Cd R CCA, Cd L CCA, R OG, L OG, R ECA	-8 ± 4.5	2 ± 3.8
85	Cd R CCA, Cd L CCA, R OG, L OG, R ECA, L ECA	5 ± 1.5	11 ± 8.6
86	Cd R CCA, Cd L CCA, R OG, L OG, R ECA	21 ± 12.1	17 ± 15.0
87	Cd R CCA, Cd L CCA, R OG, L OG	15 ± 13.5	23 ± 12.6
88	Cd R CCA, Cd L CCA, R OG	14 ± 13.5	17 ± 15.0
89	Cd R CCA, Cd L CCA	12 ± 14.5	11 ± 9.0
90	Cd R CCA	-5 ± 2.9	23 ± 12.6

TABLE 3.14 HEART RATE CHANGE - SUMMARY OF ANALYSIS OF VARIANCE FROM EXPERIMENTAL SERIES 4

Source of Variation	Degrees of Freedom	Variance Ratio
A. Clamping treatment	89	1.006
B. Vagi : intact versus bilateral section	1	2.829
C. Animals	3	17.014***
Interaction : AxB	89	2.088***
Residual mean square	537	1.093

carotid artery, occipital group and external carotid artery, irrespective of whether the left or right vessels were occluded first. On the other hand, in sheep numbers 2 and 4 an apnoeic period occurred after vagotomy following bilateral carotid sinus isolation and successive bilateral clamping of the common carotid artery, occipital group and external carotid artery on occlusion of either the left or right vessels first. Respiration recommenced mainly upon unclamping all the occluded vessels. In addition, following vagotomy in sheep numbers 2 and 4, clamping of the unilateral external carotid artery in addition to the contralateral common carotid artery and occipital group decreased or completely abolished respiration until the release of the external carotid artery.

For raw data see Appendix 3, Table 4.

3.4.6 Comparison of the Relative Effects of Unilateral Left and Right Common Carotid Arterial Clamping on the Peripheral Mean Blood Pressure Using the Combined Data from Experimental Series 2 to 4

The data from all 14 sheep of experimental series 2 to 4 was subjected to a *t*-test to compare the peripheral mean blood pressure response of caudal left common carotid arterial clamping and caudal right common carotid arterial clamping prior to, and following, bilateral vagotomy. The analysis demonstrated that, overall, left common carotid arterial clamping had a greater effect on the peripheral mean blood pressure than did right carotid arterial occlusion. In addition, there was a significant interaction between treatment and vagotomy which increased the rise in peripheral mean blood pressure when the left common carotid artery was clamped, but not upon right carotid arterial occlusion.

The rise in peripheral mean blood pressure upon right common carotid arterial clamping did not appear to decrease upon vagotomy, except in experimental series 2, sheep number 4 and series 4, sheep 3, where bilateral vagotomy rendered the right vessel totally unresponsive to clamping.

Examination of the responses from individual sheep, however, showed that there appeared to be two groups of animals: those in which there is a similar response to both left and right common carotid arterial clamping (experimental series 2, sheep numbers 1, 3, 4 [prior to vagotomy], 5 and 6; series 4, sheep 2 and 4), and those in which the left vessel is approximately four times more responsive (or 9 mmHg greater) than the right (series 2, sheep 2 and 4

[following vagotomy, 20 times, or 20 mmHg more responsive], series 4, sheep 1 and 3 [20 times or 20 mmHg more responsive]). In none of the animals did left common carotid arterial clamping cause a lesser response than the right carotid artery. In addition, the peripheral mean blood pressure response appears to fall into two groups: the first low ranging group from 1 to 11 mmHg with a mean of 6 ± 2.9 mmHg (experimental series 2, sheep numbers 1, 2 [following vagotomy], 5 [prior to vagotomy], and 6; series 4, sheep 1, 2 and 4), and the second highest group ranging from 4 to 21 mmHg with a mean of 12 ± 6.4 mmHg (series 2, sheep 2 [prior to vagotomy], 3, 4 and 5 [following vagotomy]; series 4, sheep 3).

See Table 3.15.

TABLE 3.15 PERIPHERAL MEAN BLOOD PRESSURE CHANGE (MEAN ± SEM, mmHg) FROM EXPERIMENTAL SERIES 2, 3 AND 4 AND RESULTS OF t-TEST ANALYSES OF POOLED DATA

Clamping Position	Experimental Series 2 ($n^{\dagger}$ = 3) Sheep Number						Experimental Series 3 ($n^{\dagger}$ = 2) Sheep Number				Experimental Series 4 ($n^{\dagger}$ = 7) Sheep Number			
	1	2	3	4	5	6	1	2	3	4	1	2	3	4
							Intact Vn							
Cd L CCA	7±1.7	17±0.7	10±0.3	14±0.9	8±0.3	6±0.3	12±3.0		13±1.5		5±0.6	4±1.4	15±1.7	4±0.3
Cd R CCA	9±1.5	4±0.7	13±0.6	13±0.7	6±1.0	4±1.3		10±1.0		7±1.0	1±1.7	4±0.9	4±3.3	3±0.6
							Cut LR Vn							
Cd L CCA	8±0.9	13±7.4	17±1.5	20±2.1	12±0.6	10±1.9	11±2.0		8±5.0		9±1.5	11±3.7	21±3.2	4±1.6
Cd R CCA	8±0.3	5±2.9	16±4.4	0±0.6	11±0.3	6±1.8		7±0.5		5±2.5	2±0.7	4±1.6	1±3.1	6±0.9

Source of Variation	Degrees of Freedom	t
A. Clamping treatment L versus R	46	3.513**
B. Vagi : intact versus bilateral section	46	0.677
Interaction: AxB	44	2.385*
Error mean square	44	20.062

† Number of observations per sheep

3.5 DISCUSSION

3.5.1 Anaesthesia

The anaesthetic chosen to investigate the carotid sinus baroreceptor reflex in this research was chloralose.

In preliminary experiments (experimental series 1), the suitability of sodium pentobarbitone was examined but, after minimal dissection, bilateral clamping of the caudal common carotid artery induced a peripheral mean blood pressure rise of only 18 mmHg, about two and a half times less than that seen under chloralose anaesthesia in experimental series 2. Barbiturates appear to depress the response to the carotid sinus baroreceptor reflex (Bouckaert and Heymans, 1930; Heymans and Neil, 1958) whereas Comroe and Schmidt (1940) and Schmidt (1940) reported that chloralose increased the effectiveness of the carotid sinus baroreceptor reflex. Chloralose anaesthesia must not, however, be so deep that the vasomotor and cardioinhibitory centers are depressed (Greisheimer, 1965; Korner, 1971; White and McRitchie, 1973; Zimpfer, Manders, Barget and Vatner, 1982) for carotid sinus baroreceptor activity has little effect on these centers when they are affected by an anaesthetic overdose (Heymans and Neil, 1958).

Anaesthesia in experimental series 2 to 4 was induced by inhalation of halothane which proved to be quick and simple, and the decreased vascular resistance and myocardial depression (Vatner and Braunwald, 1975) produced a hypotensive animal which facilitated the dissection. After cessation of halothane administration and the commencement of chloralose anaesthesia, the basal peripheral mean blood pressure increased and stabilised at a higher level when the central and cardiovascular effects of halothane had worn off.

3.5.2 Basal Peripheral Mean Blood Pressure and Pulse Pressure

The mean basal peripheral mean blood pressure and pulse pressure of experimental series 2 and 3 were 110 mmHg and 32 mmHg, respectively. These values are comparable to those measured in three conscious sheep by G.V. Petersen, D.H. Carr, A.S. Davies and B.T. Pickett (personal communication) and indicate anaesthesia was at a suitable depth. In experimental series 4, however, the mean basal peripheral mean blood pressure was 20 mmHg lower than that in series 2 and 3 and in the conscious animal. This is attributed to the extensive carotid sinus dissection undertaken in these sheep. The mean basal peripheral

mean blood pressure and pulse pressure of experimental series 2 and 3 remained stable during the experimental period. A similar stability was seen in experimental series 4 until the multiple clamping cascades involving bilateral carotid sinus isolation and successive bilateral clamping of the common carotid artery, occipital group and external carotid artery increased the mean basal peripheral mean blood pressure. This latter elevation was probably the result of an adrenal medullary discharge accompanying cerebral anoxia due to a severe reduction in blood flow.

Vagotomy was performed during the experimental period and had the effect of inducing a rapid fall in basal peripheral mean blood pressure, averaging 12 mmHg in 10 of the 14 sheep in experimental series 2 to 4. In the remaining 4 sheep, vagotomy had no effect upon the peripheral blood pressure level. There appear to be no other reports of the effect of vagotomy on the basal peripheral mean blood pressure in the sheep. In the conscious dog, however, vagal section elevated the basal peripheral mean blood pressure by 40 mmHg (Stephenson and Donald, 1980). The available data support the concept that the blood pressure returns to near normal within 1 to 17 days (MacCanon and Harvath, 1957; Shephard and Whitty, 1964; McRitchie, Vatner, Heyndrickx and Braunwald, 1976; Ito and Scher, 1978). This systemic hypertension in the dog may have resulted from the interruption of tonically active vagal inhibitory afferents from extracarotid aortic and cardiopulmonary baroreceptors that caused an increase in sympathetic vasomotor activity or the elimination of vagal inhibitory efferents to the heart which cannot be completely compensated for by maximal activation of the carotid sinus baroreceptors (Koike, Mark, Heistad and Schmid, 1975; Bishop and Peterson, 1978; Ito and Scher, 1979; Stephenson and Donald, 1980).

The reason for the discrepancy in the response to vagotomy in the dog and sheep may be due to section of vagal afferents which, in the sheep, maintain a degree of vasoconstriction. It is possible that these afferents innervate the aortic arch and other peripheral chemoreceptors which are stimulated by the hypoxic, hypercapnic and acidaemic conditions caused by inadequate ventilation. Such impaired ventilation is likely in the sheep because, in dorsal recumbancy, the mass of abdominal contents restricts diaphragmmatic movement.

3.5.3 Unilateral and Bilateral Clamping of the Common Carotid Artery

Clamping of the common carotid artery in these animals induced a reflex rise in peripheral mean blood pressure, pulse pressure and heart rate. These results confirm the findings of Van Damme (1933) and Waites (1955, 1960) that carotid sinus baroreceptor reflexes are demonstrable in the sheep despite the lack of a morphological carotid sinus and oppose the contrary conclusion of de Boissezon (1941).

In the present experiments, bilateral common carotid arterial clamping produced a significantly greater rise in peripheral mean blood pressure, pulse pressure and heart rate than did unilateral carotid arterial occlusion. Measurement of lingual arterial blood pressures confirmed the expected fall in mean blood pressure and pulse pressure at the baroreceptor zone in the carotid sinus.

Clamping a single common carotid artery lowered the carotid sinus pressures by 40% - mean blood pressure by 33 mmHg and pulse pressure by 18 mmHg - no recovery of pressure occurred. There were no pressure changes in the contralateral carotid sinus. Baldwin and Bell (1963c) recorded the slightly lesser fall in mean blood pressure of 31% in the ipsilateral lingual artery, but some recovery of pressure occurred during the next few seconds, so that the average fall became 21%. The data of this present project are similar to those recorded in the rabbit, cat and dog (Chungcharoen, Daly, Neil and Schweitzer, 1952) and goat (Pyper, 1938), but greater than that seen in the dog (Schmidt, 1932; Von Euler and Liljestrand, 1936) and calf (Baldwin and Bell, 1963c). The recovery of mean blood pressure observed in the ovine carotid sinus reported by Baldwin and Bell (1963c) also occurs in other species (rabbit, cat, dog - Chungcharoen, Daly, Neil and Schweitzer, 1952).

Bilateral common carotid arterial clamping in the present study caused a fall in carotid sinus mean blood pressure in both arteries of an even greater magnitude (59%) and, as with unilateral occlusion, there was no secondary stabilisation. Waites (1960) did note a recovery in pressure upon bilateral common carotid arterial clamping which was, however, slower than when only one common carotid artery was occluded. The present data are of a similar order to those reported in the sheep (Linzell and Waites, 1957; Baldwin and Bell, 1963c), dog and cat (Schmidt, 1932), dog, cat and rabbit (Chungcharoen, Daly, Neil and Schweitzer, 1952), cat (Holmes and Wolstencroft, 1959) and calf (Baldwin and Bell 1963c).

The present observation of reflex systemic hypertension and tachycardia upon bilateral common carotid arterial clamping are of a similar order to those reported by Waites (1960) and Baldwin and Bell (1963c), and significantly greater than when one carotid artery was occluded. The effect on heart rate was more variable than the effect on peripheral mean blood pressure and pulse pressure.

Baldwin and Bell (1963a,c), however, found that usually no systemic hypertension occurred upon unilateral common carotid arterial clamping and frequently demonstrated only a small rise in systemic pressure during the period of bilateral carotid arterial occlusion. The explanation may lie in the anaesthetic used - sodium thiopentone. Although the baroreceptor system appears unaffected by thiopentone, there is a reduction of sympathetic nerve activity (Goodman Gilman, Goodman and Gilman, 1980) which may reduce the systemic blood pressure response to the carotid sinus baroreceptor reflex. On the other hand, chloralose, the anaesthetic used by Waites (1960) and in this research, has been reported to increase the sensitivity of the carotid sinus baroreceptors and the effectiveness of the reflex. Waites observed a baroreceptor reflex response to common carotid arterial clamping of a similar magnitude to that in this work. Baldwin and Bell (1963, 1963c) explained the lack of reflex effects and the recovery of the lingual blood pressure during unilateral common carotid arterial clamping by increased collateral flows in the contralateral carotid artery and the vertebral arteries. Waites (1960) was of the view that blood flow in the occipital artery during common carotid arterial occlusion was slow - a view supported by the present observation that adding occipital arterial clamps in addition to carotid arterial occlusion caused only a slight reduction in carotid sinus mean blood pressure.

The enhanced effect of bilateral compared with unilateral common carotid arterial clamping would be expected from the greater fall of mean blood pressure in both carotid sinuses and consequently the larger population of baroreceptors that are affected. The baroreceptors of the carotid sinus are three dimensional stretch receptors stimulated by deformation of the adventitial tissue in which they reside. Occlusion of the common carotid artery greatly reduces the endosinus mean blood pressure and pulse pressure which induces significant dimensional changes in the carotid sinus wall, and so the baroreceptors discharge at a decreased rate.

The carotid sinus nerve contains two types of sensory fibers which innervate slowly adapting and rapidly adapting baroreceptors. The fibers innervating slowly adapting baroreceptors respond to changes in mean blood pressure and are not stimulated below a blood pressure of 60 mmHg but, at least in the dog and cat, are maximally sensitive between 95 to 120 mmHg (Hering, 1924; Koch, 1929, 1931; Heymans and Neil, 1958; Koshanpour and Kelso, 1972). During the clamping cascades of this research, both unilateral and bilateral clamping of the common carotid artery decreased the mean blood pressure within the occluded carotid sinus well below 60 mmHg, and probably rendered the slowly adapting baroreceptor fibers silent. Fibers innervating the rapidly adapting baroreceptors, on the other hand, respond to the changes in pulse pressure; they are reported in the dog as being unstimulated below a mean blood pressure of 65 mmHg and are maximally sensitive between 85 and 110 mmHg (Heymans, Bouckaert and Dautrebande, 1931; Pelletier, Clement and Shepherd, 1972). As unilateral and bilateral clamping of the common carotid artery virtually eliminated the pulse pressure, these rapidly adapting baroreceptor fibers would also be silent. It, therefore, appears that in this study the sensory fibers of the carotid sinus nerve were likely to be silent during both unilateral and bilateral occlusion of the common carotid artery. Therefore, the greater effect of bilateral clamping was due to the greater number of baroreceptors involved.

The decreased inhibitory discharge in baroreceptor afferents enhances the vasomotor center mediated tonic discharge in the sympathetic vasoconstrictor and cardiac nerves and depresses the cardioinhibitory center discharge in the parasympathetic vagus nerve. There is controversy as to whether the haemodynamic changes responsible for the resultant hypertension are due to changes in total peripheral resistance, cardiac output or both. From experiments in anaesthetised animals in which the carotid sinus was isolated and perfused over a wide range of blood pressures, and also from the more limited studies in conscious animals, this matter still remains in dispute. Many workers, including Daly and Daly (1959), Sonnenblick (1962), Kircheim and Gross (1971), Vatner, Higgins, Franklin and Braunwald (1972), Stephenson and Donald (1980), Faris, Iannos, Jamieson and Ludbrook (1980) and Faris, Jamieson and Ludbrook (1981) have presented data suggesting that changes in carotid sinus pressure elicited important reflex modifications in peripheral vasomotor tone and that the contribution of cardiac output to the reflex rise in peripheral mean blood pressure was small. On the other hand, evidence for a reflex increase in cardiac output without a significant rise in peripheral resistance

has been described by Carlsten, Folkow, Grimby, Hamberger and Thulesius (1958), Sarnoff, Gilmore, Brockman, Mitchell and Linder (1960), Bevegard and Shepherd (1966) and Bjurstedt, Rosenhamer and Tyden (1977). In the present experiments on sheep there appeared to be both increased vasoconstriction and heart rate but the latter changes were demonstrated less consistently.

3.5.4 Unilateral Left and Right Clamping of the Common Carotid Artery

The present experiments suggest that there may not always be similar responses to occlusion of the left and right common carotid arteries in sheep. This does not appear to have been reported previously.

Comparison of the peripheral mean blood pressure data for all 14 sheep showed that left common carotid arterial clamping, overall, caused greater systemic effects than did right common carotid arterial occlusion. The same conclusion was reached in experimental series 4, where this was demonstrated both for single clamping and for some occlusion combinations. However, although this was the trend over the population of 14 sheep, it was not necessarily true for every individual. This can be seen in Table 3.15 where left and right common carotid arterial clamping produced equal responses in some animals, while in others occlusion of the left artery produced demonstrably larger reflex effects; but in no case was the converse true. The variation of responses means that when small groups of animals are studied, a difference between left and right common carotid arterial clamping is not necessarily present.

The difference in the reflex response of the peripheral mean blood pressure that is independent of the state of vagal innervation may reflect either the baroreceptor number, baroreceptor sensitivity, or both. It is possible that either the population of baroreceptors or their sensitivity within the left carotid sinus and common carotid artery is significantly different from that in the right sinus and carotid artery so that detection of a decreased intraluminal pressure induces a peripheral mean blood pressure response that is greater.

3.5.5 Unilateral Caudal and Cranial Tying of the Common Carotid Artery

Because of the possibility that baroreceptors are distributed more widely in the common carotid artery than the carotid sinus alone, a preliminary study was made of the responses to tying at specific regions. The carotid artery was occluded by tying rather than by clamping in order to minimise the amount of

damage to any vagal innervation during dissection and reduce the number of baroreceptors mechanically stimulated by the occlusion procedure. No other physiological studies appear to have been reported in the sheep on this aspect.

No significant difference was detected in the response to tying the left or right common carotid artery at the caudal, middle or cranial positions in the 4 sheep tested. Overall, however, there was a tendency for caudal tying to cause a greater rise in peripheral mean blood pressure than cranial tying. This suggests that, in the sheep, baroreceptors distributed along almost the entire length of the carotid artery may monitor mean blood pressure and pulse pressure within the vessel. This possibility warrants examination in a larger number of sheep.

Evidence to suggest that in other species common carotid arterial baroreceptors are functional has been presented in the cat by Green (1953) and Boss and Green (1956). The extensive distribution of baroreceptors which they demonstrated is shown in Figure 4.4. The electroneurogram of the common carotid baroreceptor nerve leaving the common carotid baroreceptor area (area 4) at the origin of the superior thyroid artery issued a burst of impulses when the pulse wave passed along the artery, activity comparable with that of the carotid sinus and aortic arch baroreceptor nerves. This activity ceased on clamping the common carotid artery immediately proximal to the baroreceptor area, and was enhanced by clamping distal to the area. Further reflex systemic responses were obtained by raising and lowering the pressure in the appropriate isolated short length of common carotid artery - these reflexes were lost after the nerve had been cut.

3.5.6 Effect of Cervical Arterial Clamping on Collateral Blood Flow

The effect of restricting collateral blood flow to the carotid sinus following common carotid arterial clamping was examined by multiple clamping cascades (experimental series 4) involving the occipital group and external carotid artery, in addition to the common carotid artery. Common carotid arterial clamping caused the major drop in carotid sinus mean blood pressure and almost completely removed the pulse pressure, but there was apparently a compensatory increase in flow in the occipital arteries which anastomose with muscular branches of the vertebral arteries as described by Baldwin and Bell (1963a).

Their direct measurements of flow in the vessels conveying blood to the brain of the sheep demonstrated that unilateral clamping of a common carotid artery caused an immediate 60% increase in flow in the contralateral carotid artery and a rise of 185% in the vertebral arteries. A similar enhancement of flow was seen in the dog (Rein, 1929; Gollwitzer-Meier and Eckardt, 1934; Schneider and Schneider, 1934; Bouckaert and Heymans, 1935).

In spite of reversed occipital flow to supply blood to the occluded common carotid artery, clamping the occipital group had only a small effect on carotid sinus pressure and provoked only a small additional reflex systemic hypertension. Bilateral common carotid arterial clamping may have entirely silenced the baroreceptors and collateral flow failed to reverse this. The fact that bilateral occlusion of the carotid artery does not abolish the electroencephalogram spontaneous electrical activity in the sheep, demonstrates that the volume of collateral blood is sufficient to maintain cortical activity (Linzell and Waites, 1957; Baldwin and Bell, 1963a,d).

This enhancement of flow upon common carotid arterial clamping is probably a reflection of the dependence of the sheep cerebral circulation on carotid flow, compared with other animals. In the sheep, apart from a small and variable area of the caudal medulla oblongata, the entire brain is supplied from the common carotid arteries and blood from a single carotid artery is restricted to an ipsilateral cerebral and extracerebral distribution (Baldwin and Bell, 1960a, 1963a). The vertebral arteries do not provide blood via the basilar artery to the circle of Willis and, therefore, do not form part of the cephalic vascular supply (Baldwin and Bell, (1960a,b). In the cat, dog, horse and man cerebral ischaemia could not occur on clamping the common carotid and occipital arteries because blood would flow directly to the circle of Willis from the vertebral arteries via the basilar artery which has been postulated to act as a potential antero-posterior anastomosis for blood from the internal carotid and vertebral arteries (Kramer, 1912; Rogers, 1947; McDonald and Potter, 1951).

Clamping the external carotid artery in addition to the common carotid artery and occipital group raised, rather than lowered, the carotid sinus mean blood pressure and further elevated the peripheral mean blood pressure. This was accompanied by inhibition of respiration. The rise in carotid sinus mean blood pressure after occlusion of the common carotid artery, occipital group and external carotid artery suggests that arterial branches of the common

carotid artery remain patent. Possibly it is the muscular branch of the common carotid artery, caudal thyroid artery, cranial thyroid artery, and cranial laryngeal artery whose anastomoses with several of the cervical vessels permit reversal of blood flow into the common carotid artery.

In spite of the carotid sinus mean blood pressure increasing from a mean of 28 mmHg to 61 mmHg, there was a marked rise in peripheral mean blood pressure. The coincidence of the onset of the enhanced rise in systemic pressure with the apnoeic period strongly suggests that the origin of the additional hypertension is cerebral and that it is probably caused by cerebral anoxia rather than by baroreceptor activity.

Similar systemic pressure and respiratory observations have been noted in the sheep by Baldwin and Bell (1963c) upon bilateral clamping of the common carotid arteries when both occipital arteries had been occluded previously. Baldwin and Bell (1963d) also observed apnoea during multiple clamping experiments and proposed that the coincidence of the onset of the rise in systemic pressure with the time at which the electroencephalogram was completely abolished, strongly suggested that the medullary centers became hyperactive because of asphyxial stimulation, while at the same time cerebral function was quiescent because of anoxaemia.

A consistent observation during the multiple clamping cascades of experimental series 4 was that during the unclamping procedure, the peripheral mean blood pressure remained elevated compared with the blood pressure at the corresponding clamping step. This phenomenon was seen only during the multiple vessel occlusions where at least both common carotid arteries, an occipital group and an external carotid artery were clamped. In these instances, the mean blood pressure and pulse pressure in the carotid sinuses were similar during the clamping and unclamping sequences (37 mmHg and 3 mmHg, respectively), so the underlying cause probably derived from arrest of the cerebral circulation, rather than peripheral effects on the baroreceptors.

3.5.7 The Effect of Vagotomy on the Cervical Arterial Clamping Response

Vagotomy altered the magnitude of the reflex systemic hypertension induced by clamping of the cervical arteries. The effect, however, was not identical for every individual sheep and suggests there may be considerable individual variation either in baroreceptor distribution or sensitivity and also in the course taken by the afferent nerves.

In various species, the ability of the carotid sinus baroreceptor reflex to increase the blood pressure above its basal level is significantly increased after vagotomy (Sagawa and Watanabe, 1965; Stinnett, Peterson and Bishop, 1979; Stephenson and Donald, 1980; Stinnett, Sepe and Mangusson, 1981). The results of experimental series 4 agree with these observations as, over the entire series, the peripheral mean blood pressure and pulse pressure response to clamping the cervical blood vessels was enhanced by bilateral vagotomy. This is further demonstrated in two separate contrasts where bilateral vagotomy increased the peripheral mean blood pressure rise to caudal bilateral common carotid arterial clamping and unilateral clamping of the left common carotid artery in association with right occipital group and external carotid arterial occlusion.

Although the cardiovascular changes after bilateral vagotomy vary between species (Korner, 1971; Kircheim, 1976) it is well recognised that vagotomy results in the removal of some of the cardiac parasympathetic components of the carotid sinus and aortic arch baroreflexes as well as interruption of the vagal afferent limb of reflexes originating in the aortic arch and cardiopulmonary regions (Koike, Mark, Heistad and Schmid, 1975; Mancia, Shepherd and Donald, 1976; Stinnett, Peterson and Bishop, 1976, 1979). Therefore, unilateral or bilateral common carotid arterial clamping, in lowering the carotid sinus blood pressure, elevates the peripheral mean blood pressure, pulse pressure and heart rate, though this pressor response is moderated by the aortic and cardiopulmonary baroreceptors which still function normally. Interruption of these baroreceptor afferents by sectioning both vagi eliminates any buffering action and the resulting reflex hypertension is of greater magnitude.

The sensory afferents from the aortic arch and cardiopulmonary baroreceptors may not be carried equally in the left and right vagus nerves of the sheep. such an observation has been made in dogs where section of the left vagus nerve interrupted 90% of the aortic arch barorereceptor reflex (Walgenbach, 1984). The observations in experimental series 2 suggest that this may also be the case in sheep since right vagotomy induced a lesser rise in peripheral mean blood pressure and pulse pressure than section of the left vagus nerve.

It is possible that the baroreceptor afferents from the aortic arch and cardiopulmonary regions do not, in every individual sheep, run predominantly in the left vagus nerve. This is suggested by the results of a paired t-test of

data from two sheep in experimental series 3 which compared the section of a vagus nerve and clamping the ipsilateral common carotid artery. In the animal in which the left vagus nerve was cut and the left common carotid artery occluded the overall peripheral mean blood pressure rise was lessened following vagotomy, but this was not the case with the right nerve and artery. This observation suggests that the aortic arch and cardiopulmonary baroreceptor afferent fibers were predominantly in the right vagus nerve of this sheep or that a significant number of baroreceptors cranial to the site of clamping in the left common carotid artery were innervated by the recurrent laryngeal or vagus nerves.

In the present study, two particular contrasts suggest that the recurrent laryngeal or vagal innervation of the left and right common carotid arteries may not be identical in the sheep. This is best illustrated in comparisons where afferents from the aortic arch and cardiopulmonary baroreceptors were interrupted by bilateral vagotomy. First, examination of the data from all 14 sheep revealed a significant interaction between clamping and vagotomy: bilateral vagotomy increased the peripheral mean blood pressure rise upon left common carotid arterial occlusion; however, no effect of vagotomy was seen on right carotid arterial occlusion. These results suggest that, following section of the left and right vagi, the baroreceptors in the left common carotid artery were more effective than those in the right carotid artery. This may be because vagotomy silences more common carotid arterial baroreceptors cranial to the clamp in the right carotid artery than it does in the left artery. Secondly, in experimental series 3, overall bilateral vagotomy reduced the rise in peripheral mean blood pressure on right common carotid arterial tying, but not on left carotid arterial tying. With only two sheep in each group, the results showed no statistically significant effect of vagotomy in the left common carotid artery, although the response following vagotomy tended to be lower at each tying position. These results provide further evidence that bilateral vagotomy may silence more common carotid arterial baroreceptors cranial to the clamp in the right carotid artery than it did in the left artery. Taken together, the preceding observations suggest that, in some sheep at least, there are likely to be baroreceptors in the common carotid artery with afferent fibers in the recurrent laryngeal or vagus nerves. There is also an indication that this is more so in the right than the left common carotid artery.

An extreme case of this indication was illustrated on two sheep where the peripheral mean blood pressure response to right common carotid arterial occlusion was totally abolished upon section of the right vagus nerve. Therefore, section of the right vagus nerve may have totally denervated the baroreceptors in both the right common carotid artery and carotid sinus in these animals. Previous workers have indicated that in the sheep, as in most other species, the carotid sinus receives its nerve supply from two major sources - the carotid sinus nerve and the external carotid nerve, whereas the contribution from the pharyngeal branches of the vagus nerve and the hypoglossal nerve is minor (Sha-Ban, 1974). One must, therefore, come to the unlikely conclusion that in these two animals the baroreceptors of the carotid sinus as well as the common carotid were innervated by the recurrent laryngeal or vagus nerves.

As has been inferred from the above observations, the affects of vagotomy on common carotid arterial clamping differ between individuals; this is further apparent in Table 3.15 which contains the rise in peripheral mean blood pressure upon unilateral occlusion of the left and right common carotid artery in each sheep prior to and following vagotomy. Examination of this data reveals that these animals may be divided into three groups of at least three individuals, depending on whether bilateral vagotomy had enhanced, had no effect, or depressed the reflex peripheral mean blood pressure response to left or right common carotid arterial clamping. Furthermore, there was often no correlation of this vagotomy effect between clamping the left and clamping the right vessel.

In summary, it is apparent that during unilateral clamping of the common carotid artery, clamping the left carotid artery induced a reflex systemic response that is equal to or greater than the right vessel response. The effects of vagotomy were variable, due to the extent of recurrent laryngeal or vagal innervation of the carotid sinus and common carotid arterial baroreceptors and the distribution of aortic arch and cardiopulmonary baroreceptor afferent fibers between the left and right vagi. If both vagi are sectioned, one can assume that all buffering action by the aortic arch and cardiopulmonary baroreceptors has been eliminated and all subsequent reductions in the reflex systemic response upon unilateral common carotid arterial clamping is due to the silencing of carotid arterial baroreceptors cranial to the clamp. Under these conditions, vagotomy enhanced, did not affect, or depressed the response to left common carotid arterial occlusion whereas, with the right carotid

artery, it did not affect, depressed or totally abolished the response. These observations indicated that the extent of recurrent laryngeal or vagal innervation varies between individual sheep, but that it was generally more extensive and may even totally innervate both the common carotid artery and carotid sinus in the right common carotid artery.

CHAPTER 4

HISTOLOGY OF THE CAROTID SINUS AND COMMON CAROTID ARTERY IN THE SHEEP

4.1 INTRODUCTION

In the many mammalian species in which the carotid sinus is located at the origin of the internal carotid artery, the structure and innervation of the sinus are well described, but few authors have studied the comparable area of the sheep which lacks an internal carotid artery. In view of this, the distribution of sensory and vasomotor nerves and the related structure of the carotid sinus have been investigated in the sheep using light microscopy. A similar study of the common carotid artery was also undertaken to examine the suggestion in Chapter 3 that there may be baroreceptors along the length of the common carotid artery in the sheep.

4.2 LITERATURE REVIEW

4.2.1 Structure of the Arterial Wall

Histologically, the arterial wall is composed of three tissue layers arranged in concentric sleeves:

1. The innermost tunica intima, composed of a single layer of endothelial cells lining the vascular wall, a thin basal lamina, and a subendothelial layer consisting of collagen bundles, elastic fibers, smooth muscle, and some fibroblasts. This layer constitutes a selective diffusion barrier against plasma lipids and lipoproteins (Rhodin, 1980).
2. The middle tunica media, composed of smooth muscle cells, a variable number of elastic laminae, bundles of collagen fibers and a network of elastic fibers. The arrangement of alternating elastic and muscular laminae in this layer gives mechanical strength to the media, adapting rapidly to conditions of altered pressure and flow because of the compliance and plasticity (Rhodin, 1980).
3. The outer tunica adventitia, composed of dense fibroelastic tissue without smooth muscle cells, and harbouring the sensory and vasomotor nerves. This gives mobility but also stability and strength to the wall and limits the degree of distension of the vessel (Rhodin, 1980).

These three layers are present in all the vessels of the carotid bifurcation, but there is some specialisation appropriate to the reflexogenic function of the carotid sinus.

4.2.1.1 Structure of the Wall of the Carotid Bifurcation

The most prominent feature of the vessels comprising the carotid bifurcation is the variability in the composition of the tunica media.

In all species so far studied, the tunica media of these vessels may be one of the three classical types (Arey, 1957) - muscular, elastic or musculoelastic. As their names imply, a muscular tunica media contains little elastic tissue, while an elastic tunica media contains predominantly elastic laminae with a single layer of circumferentially arranged smooth muscle cells between each succeeding elastic membrane. The smooth muscle cells in vessels both caudal and cranial to the sinus are helically arranged. A musculoelastic tunica media contains both elastic laminae and a thick muscular coat.

Rees (1966, 1967a), Rees and Jepson (1970) and Bagshaw and Fischer (1971) described the carotid bifurcation tunica media of the mature rat, guinea-pig, rabbit, cat, and dog and human foetus. The tunica media of the internal carotid, occipital and ascending pharyngeal arteries was predominantly muscular, that of the carotid sinus elastic and the media of the common and external carotid arteries musculoelastic.

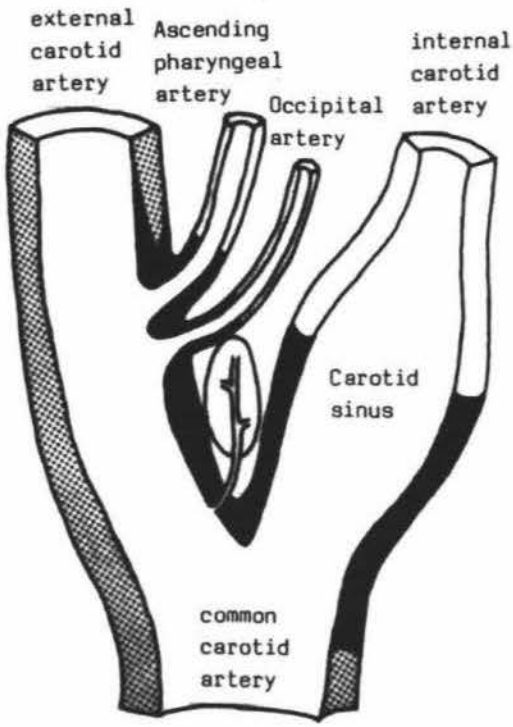
Rees (1966, 1967a) and Rees and Jepson (1970) reported that the carotid sinus tunica media contains more than twice as much elastic tissue per unit area as the media in the carotid vessel walls adjoining the sinus. Rees (1966, 1967a) referred to the specialised tunica media of the carotid sinus as the elastic segment, the extent of which varies in different species. Despite this species difference, the areas most densely supplied with receptor endings are of elastic structure.

The structural transition from the carotid sinus to the adjoining internal carotid, occipital and ascending pharyngeal arteries is abrupt - the elastic membranes of the sinus wall diverge and become confluent with the internal and external elastic laminae and the deep adventitial elastic fibers of its more muscular continuation. In contrast, the structural transition between the junction of the common and external carotid arteries is gradual and extends over a distance of approximately 0.5 mm (Addison, 1939; Rees, 1966, 1967a).

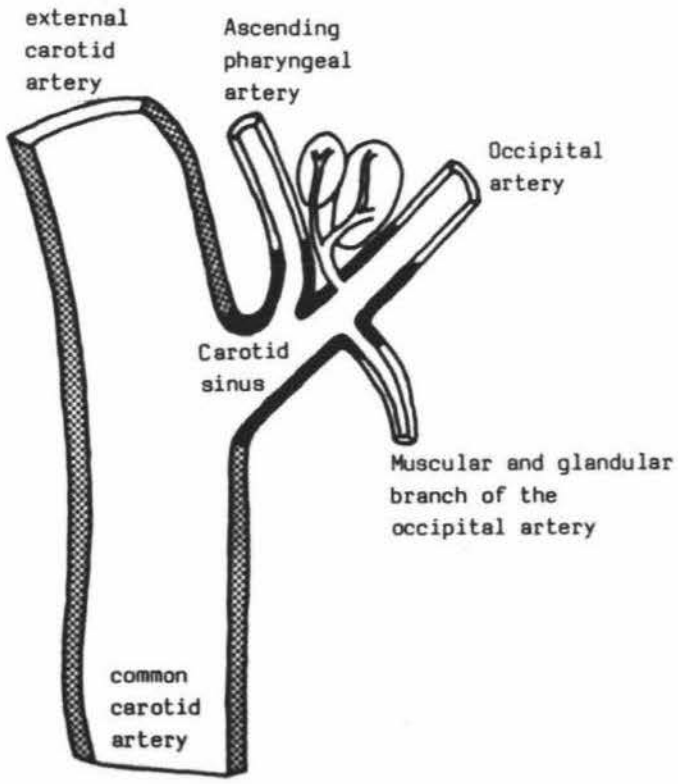
See Figure 4.1.

Although in the human and other mammals the carotid sinus wall has been described by a number of authors as reduced in total thickness compared with the adjoining vascular structures (Binswanger, 1879; Boyd, 1937; Sunder-Plassman, 1930; Ábrahám, 1969), others, including most of the recent workers, disagree (Stahel, 1886; Rees, 1966, 1967a; Rees and Jepson 1970; Bagshaw and Fischer, 1971).

The carotid sinus tunica media is thinner than that of the adjoining vascular structures (de Castro, 1928; Sunder-Plassman, 1930; Addison, 1939, 1944, 1945; Ábrahám, 1964). This is especially so ventromedially, at the point of greatest dilatation of the sinus wall (de Castro, 1928; Sunder-Plassman, 1930; Addison, 1944, 1945; Muratori, 1963, 1967). Conversely, the carotid sinus tunica adventitia is increased in thickness (de Castro, 1928; Sunder-Plassman, 1930; Adams, 1955; Bagshaw and Fischer, 1971).



The carotid bifurcation in the human. Adapted from Muratori (1967).



The carotid bifurcation in the sheep.

Figure 4.1 Schematic illustration of the carotid bifurcation in the human and sheep. In these illustrations the white areas indicate portions of the arteries with muscular structure; the black areas indicate portions with elastic structure and the stippled areas indicate portions with mixed structure.

Boyd (1937) stated that the carotid sinus dilatation is an integral part of the baroreceptor mechanism and not merely a passive non-adaptive pathological result of the thinning of the tunica media. He suggested that the presence of a dilatation causes more change in the tension of the vessel than will occur in a narrower vessel and that the thinning of the media allows any change in the blood pressure to be registered more readily by the nerve endings hence increasing the efficiency of the carotid sinus mechanism. Muratori (1959, 1963, 1967) described the carotid bifurcation as an area of structural transition between the segment with elastic structure and the segment of muscular structure. Rees (1967a), however, like Boyd, did not accept that the carotid bifurcation was merely an area of structural transition; he questioned whether the high elastin and low muscle content and the especially rich nerve supply of the carotid bifurcation were not special adaptations to baroreceptor function. The relative proportions of different tissues in the carotid sinus tunica media, particularly the thinning of the media-intima layer and the high ratio of internal radius to media-intima thickness, possibly influence the magnitude or rate of stretch of the media-intima layer. The thicker tunica adventitia probably bears more of the pressure within the vessel than is usual in arteries since the media is thinner at this site. This specialisation of the carotid sinus tunica media and tunica adventitia appears to ensure that the nerve endings in the region are readily stimulated by pressure changes.

4.2.1.2 Structure of the Walls of the Carotid Bifurcation in the Sheep

The composition of the tunica media of the vessels forming the carotid bifurcation of the sheep appears to follow the general mammalian pattern reported by Rees (1966, 1967a), Rees and Jepson (1970) and Bagshaw and Fischer (1971).

Sha-Ban (1974) described the tunica media of the vessels forming the carotid bifurcation of the sheep as predominantly elastic in the carotid sinus, muscular in the occipital artery, and musculo-elastic in the common carotid and external carotid arteries. The extent of the 'elastic segment' of Rees (1966, 1967a) is variable according to the position of the carotid body. Whether the carotid body is located close to the origin of the occipital and ascending pharyngeal arteries, or distal to this point, the occipital arterial elastic segment extends beyond the level of the carotid body. The structural transition from the carotid sinus to the adjoining occipital and ascending pharyngeal arteries is usually abrupt as reported in other species by Rees (1966, 1967d).

See Figure 4.1.

In the sheep, unlike other species studied by many of the recent workers, the carotid sinus wall has been described as thinner than the wall of the adjoining vascular structures (May, 1965; Ábrahám, 1969; Sha-Ban, 1974).

The tunica intima of the carotid sinus is thinner than the intima of the occipital artery and, like that of the common carotid and occipital arteries, consists mainly of endothelium and a thin layer of subendothelial connective tissue. The external border of the tunica intima is marked by a single internal elastic lamina (similar to the lamina of the tunica media) which differs from the common carotid, external carotid and occipital arteries, where a double internal elastic lamina separates the intima from the media.

The tunica media is also thinner than the media of the adjoining vascular structures (May, 1965; Sha-Ban, 1974). The media consists mainly of 12 or more layers of fenestrated elastic laminae arranged concentrically at the origin and distal portion, and longitudinally in the middle portion of the carotid sinus (Ábrahám, 1969; Sha-Ban, 1974). In the interstices between laminae are relatively few smooth muscle cells (Ábrahám, 1969), fine elastic and collagenic fibers, and a considerable amount of amorphous intercellular substance in which the cells of the tunica media are embedded. The outermost limit of the media is marked by the external elastic lamina.

The tunica adventitia is slightly thicker at the origin of the carotid sinus than at the level of the carotid body (Ábrahám, 1969; Sha-Ban, 1974) and it consists mainly of irregularly arranged connective tissue containing collagen fibers. There are a few elastic fibers in the deeper adventitial layer. Elastic fibers are present in the superficial tunica adventitial layer at the origin and distal portion of the carotid sinus, but not in its middle (Sha-Ban, 1974). The adventitia is rich in small blood vessels, lymphatics and nerve fibers.

4.2.2 Innervation of the Carotid Sinus

De Castro (1926, 1928) appears to have been the first to report the extraordinary richness of the innervation of the carotid sinus. In mammals, the carotid sinus receives its nerve supply from four sources: the carotid sinus nerve which arises from the glossopharyngeal nerve, the external carotid nerve which arises from the cranial cervical ganglion, the vagus nerve, and the

hypoglossal nerve (Code and Dingle, 1935; Mitchell, 1953, 1956; Adams, 1958; Ábrahám, 1967, 1969).

Three weeks after transection of the carotid sinus nerve, a few major nerve bundles of degenerating appearance were observed in the tunica adventitia of the carotid sinus and only the sparse adrenergic nerves remained in the deeper parts of the adventitia. Three weeks after combined carotid sinus nerve section and superior cervical ganglionectomy, very few nerves of normal appearance were observed within the carotid sinus wall (Rees, 1967a). The results of these denervation experiments suggest that the contribution from nerves other than the carotid sinus and external carotid nerves is unimportant in the carotid bifurcation region, though there is variation between species in the extent of innervation by the vagus and hypoglossal nerves (Adams, 1958).

4.2.2.1 The Carotid Sinus Nerve

The carotid sinus nerve is a route for afferent as well as some efferent fibers. Thus, sympathetic (de Castro, 1926; Eyzaguirre and Uchizono, 1961; Mishra and Hess, 1978) and parasympathetic (de Castro, 1926, 1928, 1940, 1951; de Kock, 1954; McDonald and Mitchell, 1975, 1981) fibers destined to end in the carotid sinus tunica media and tunica adventitia and on ganglion cells, arteries and arterioles of the carotid body run with the carotid sinus nerve. According to most investigators, the carotid sinus nerve usually divides, at the upper pole of the carotid body, into two or more filaments which supply the carotid sinus and carotid body (Hering, 1924; de Castro, 1926, 1928; Eyzaguirre and Uchizono, 1961; Kondo, 1971). In the sheep, the carotid sinus nerve divides into three to five filaments (Sha-Ban, 1974).

Early studies employing the light microscope suggested that in the cat the carotid sinus nerve contains approximately 650 to 700 fibers of which some 68%, according to the classification of Erlanger and Gasser (1937), are fast conducting myelinated A fibers of 1.0 to 9.0 μm diameter and fewer are slow conducting non-myelinated C fibers of 0.1 to 3.0 μm diameter (Gerard and Billingsley, 1923; de Castro, 1940, 1951; Douglas and Schaumann, 1956; Ask-Upmark and Hillarp, 1961). This numerical ratio is debated however - more modern techniques using phase contrast and electron microscopy (Eyzaguirre and Uchizono, 1961) have revealed a larger proportion of non-myelinated fibers and similar findings in a range of species are reported by Rees (1967a) and McDonald (1983a,b). This difference in findings may be related to the large proportion of non-myelinated nerve fibers in the carotid sinus nerve which are

less than 1.0 µm in diameter and close to the optical resolving power of the light microscope (0.2 µm).

Of the A fiber population supplying the sinus region, approximately 33% innervate baroreceptors and 67% chemoreceptors (de Castro, 1951), whereas of the C fiber population 29% supply baroreceptors, 17% chemoreceptors, and the remaining 34% are sympathetic and other types of fibers (Eyzaguirre and Uchizono, 1961; Eyzaguirre and Lewin, 1961; Laurent and Barrés, 1964; Fidone and Sato, 1969).

4.2.2.1.1 Depth of the Terminal Nerve Fibers

Light microscopic studies of the carotid sinus have failed to resolve with certainty the ultimate depth of the fine sensory nerve ramifications.

Terminal nerve fibers have been reported in the tunica intima of the carotid sinus wall by Tschernjachiwsky (1928), Ochoterena (1936), and Meijling (1938), but their claims have not been substantiated by others (Ábrahám, 1969; Aumonier, 1972). On the basis of histological evidence, a penetration of terminal nerve fibers into the tunica media of the carotid sinus wall has been both confirmed (Rjinders, 1933; Palme, 1934; Ochoterena, 1936; Meijling, 1938; de Castro, 1940, 1951; Jabonero, 1951; Stöhr, 1951; Boss and Green, 1956; Willis and Tange, 1959; Eyzaguirre and Uchizono, 1961; Rees, 1966, 1968; Reis and Fuxe, 1968; Sha-Ban, 1974; Knoche and Addicks, 1976), and denied (Riisager and Weddell, 1962; Knoche and Schmidt, 1964; Rees, 1967a; Aumonier, 1972). Of those who favour an innervation of the carotid sinus tunica media, Rjinders (1933) claims that the medial nerves are sensory baroreceptor fibers and terminate in the tunica media upon smooth muscle cells. On the other hand, most investigators propose that nerve fibers in the carotid sinus tunica media are sympathetic and motor to the smooth muscle cells (Ochoterena, 1936; Meijling, 1938; de Castro, 1940; Stöhr, 1951; Jabonero, 1951). Tunica adventitia terminal nerve fibers were described in the deeper parts of the tunica by de Castro (1926, 1928, 1940), Sunder-Plassman (1930, 1933), Ábrahám (1941, 1949, 1953, 1958, 1964, 1967, 1969), Knoche and Schmidt (1964), Dropmann (1965), Rees (1966, 1967a,b, 1968), and Reis and Fux (1968). Sensory endings have been reported at all levels in the tunica adventitia by Riisager and Weddell (1962), some fibers lying deeply between the adventitia and media and others situated at a more superficial level.

The divergent reports on the relationship between nerve terminals and the layers of the arterial wall may be explained by species differences, the staining techniques employed, or inadequate definition by authors of the three histological layers of the vessel wall. The latter explanation is probably the main cause of this variation. The internal and external elastic laminae are defined as the innermost and outermost of the elastic sheets, respectively (Rhodin, 1980), and in all regions of the carotid tree, except the sinus, can be identified without difficulty bordering the inner and outer aspects of the tunica media, respectively. In the carotid sinus wall, comparable laminae bordering the media are not always readily identifiable owing to the sparse and irregular muscle content of the wall. Thus, confusion is created by failure to distinguish clearly between tunica adventitia and tunica media, when a sharp boundary of separation is lacking. De Castro (1928), for example, interprets the amuscular stratum of elastic laminae in which he located the receptor terminals as the inner layer of the tunica media to the border of the smooth muscle coat, whereas Willis and Tange (1959) follow the definition given by standard textbooks of histology (Ham and Cormack, 1979) and take the tunica media as the portion of arterial wall lying between the internal and external elastic laminae. According to this definition, the layer described by de Castro as the inner stratum of the tunica adventitia belongs to the tunica media. Clearly, terminal baroreceptor fibers described as adventitial by one author might belong to the media according to another.

An attempt to clarify the controversy that exists over the depth at which sensory terminals are located will be made by reference to a detailed description of the sensory innervation of the rabbit carotid sinus by Rees (1966). The rabbit, which has been extensively studied, appears to have sensory nerves penetrating only to the medio-adventitial border and the greater volume of literature suggests this is also the case in other species.

4.2.2.1.2 Innervation of the Carotid Sinus

In the rabbit, those branches of the carotid sinus nerve which skirt outside the carotid body capsule pass into the wall of the carotid sinus. Less frequently, nerve bundles first traverse the substance of the carotid body. The second- and third-order branches lie at first in the superficial parts of the tunica adventitia as several large, smooth, undulating, independent nerve bundles enclosed in a perineural sheath. These branches measure upwards of

10 µm in diameter, and contain thick medullated fibers and numbers of nonmyelinated fibers of much smaller diameter (Rees, 1966). Eyzaguirre and Uchizono (1961) and Rees (1967a) state that fibers without myelin sheaths outnumber myelinated fibers in the proximal portion of the carotid sinus nerve as well as in the carotid sinus. Before passing more deeply into the carotid sinus wall, the thicker fibers lose their myelin sheaths. Fibers in the deeper tunica adventitial layers occur singly, or in small groups, and vary widely in diameter (0.2 to 4.5 µm). More deeply still, thick and fine smooth fibers both pursue an undulating course to the innermost stratum of the tunica adventitia and closely approach the smooth muscle of the tunica media. Fibers penetrate the wall of the carotid sinus no further than the medio-adventitial junctional region.

Superficial to the medio-adventitial border in the deep layers of the tunica adventitia are further tertiary or quaternary arborisations which might be interpreted as sensory (baroreceptor) terminals. The fiber terminals are intimately related over wide areas to elastin at the medio-adventitial border, to collagen in the inner one-half of the tunica adventitia, and to the surfaces of isolated smooth muscle cells in the adventitia.

In sensory recordings from the carotid sinus nerve, von Euler, Liljestrand and Zotterman (1941) and Heymans and Neil (1958) reported the presence of large and many small action potentials. If the height of an action potential can be accepted as an index of fiber size, these results indicate that sensory impulses are conveyed from the carotid sinus by large and small diameter nerve fibers. On the basis of spike height variation in carotid sinus nerve action potentials, Landgren (1952) postulated a dual sensory innervation to the walls of the carotid sinus. He suggested that the receptors of one type are in series and the other in parallel with the muscular elements. Those in series have the terminal fibers related to tunica adventitial collagen and muscle cells, while those in parallel have the terminal nerves related to elastin at the medio-adventitial border. There is no histological confirmation of this hypothesis.

4.2.2.1.3 Morphology of the Baroreceptor Terminals

The histological features of the carotid sinus baroreceptor terminals have been described in a wide variety of mammals - mouse, rabbit, cat, dog, ox, monkey, and human. A number of detailed papers on the light and electron microscopic appearance of baroreceptors of the carotid sinus have been

provided by a number of workers including de Castro, 1928; Riisager and Weddell, 1962; Ábrahám, 1969, 1981; and Knoche, Addicks and Schmidt, 1975.

From conventional light microscopic observations of silver impregnated nerves, Willis and Tange (1959) described an intimate entwining of the elastic fibers by the nerve terminals in the amuscular outer zone of the tunica media. According to de Castro (1926, 1928, 1940), gold impregnated nerve terminals in the inner border of the tunica adventitia lie parallel to the long axis of the vessel where they are situated between lamellae of collagen fibers and also between the elastic lamellae of this layer.

De Castro (1928) identified two types of sensory nerve endings in the inner border of the tunica adventitia. Sixty to seventy percent of the terminations formed large, loose plexuses of diffuse arborisations of 'tortuous' 'varicose' fibers with 'fig leaf or barley-berry formations', derived from a few thinly medullated parent nerve fibers which ran for a long distance. These terminations were classified as type I endings (see Figure 4.2). The remainder constituted the type II endings (see Figure 4.3). Type II endings were distributed to a smaller area of vascular wall, forming an extremely rich arborisation with 'bush-like neurofibrillar networks' with 'ivy-leaf-shaped or spine-like enlargements', derived from a single heavily medullated parent nerve fiber that was identifiable for some distance. This three-dimensional structure of the baroreceptor terminals enables their consideration as distortion receptors, which will respond to deformation of the vessel wall in any direction (Heymans and Neil, 1958; Paintal, 1972). Similar forms of nerve fibers have been identified by others in the carotid sinus (Sunder-Plassman, 1930; Ábrahám, 1949, 1953, 1958, 1964, 1967; Adams, 1955, 1957; Willis and Tange, 1959) and also in the common carotid artery (Nonidez, 1935, 1937, 1941; Boss and Green, 1956), aortic arch and innominate arterial bifurcation (Nonidez, 1935, 1941), pulmonary arteries (Coleridge, Kidd and Sharp, 1961; Knoche and Blümche, 1964) and ductus arteriosus (Muratori, 1937; Boyd, 1941).

A further classification of baroreceptor terminals was introduced by Willis and Tange (1959), who divided them into two categories, uniaxonic terminations which are glomerular in shape and derived from a single parent axon, and multiaxonic terminations which are diffusely branched and derived from two or more parent axons. Another view was taken by Ábrahám (1953) who regarded the nerve terminations in the carotid sinus as of such variable form

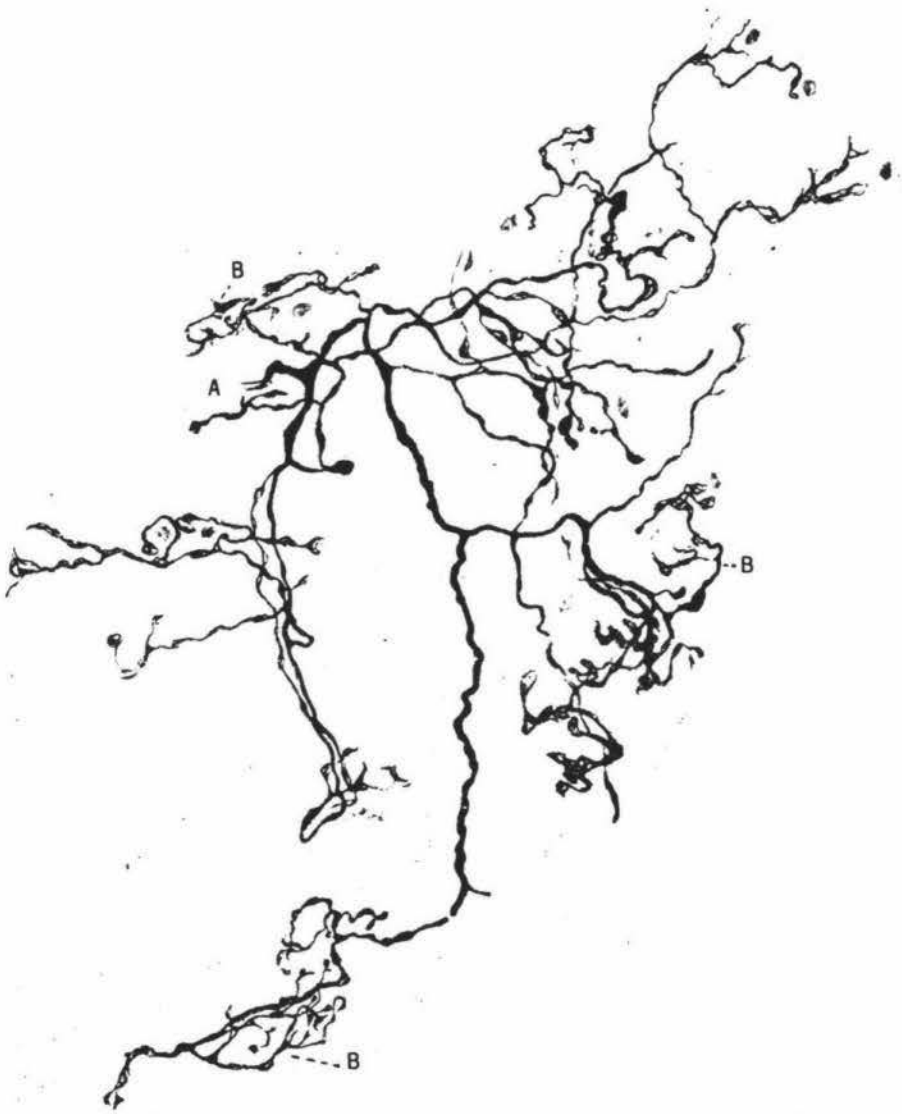


Figure 4.2 Type I baroreceptor from the wall of the carotid sinus of an adult man, tangential section. Magnification: 400.
Adapted from de Castro (1928).
A, large myelinated nerve fiber; B, terminal nerve endings.

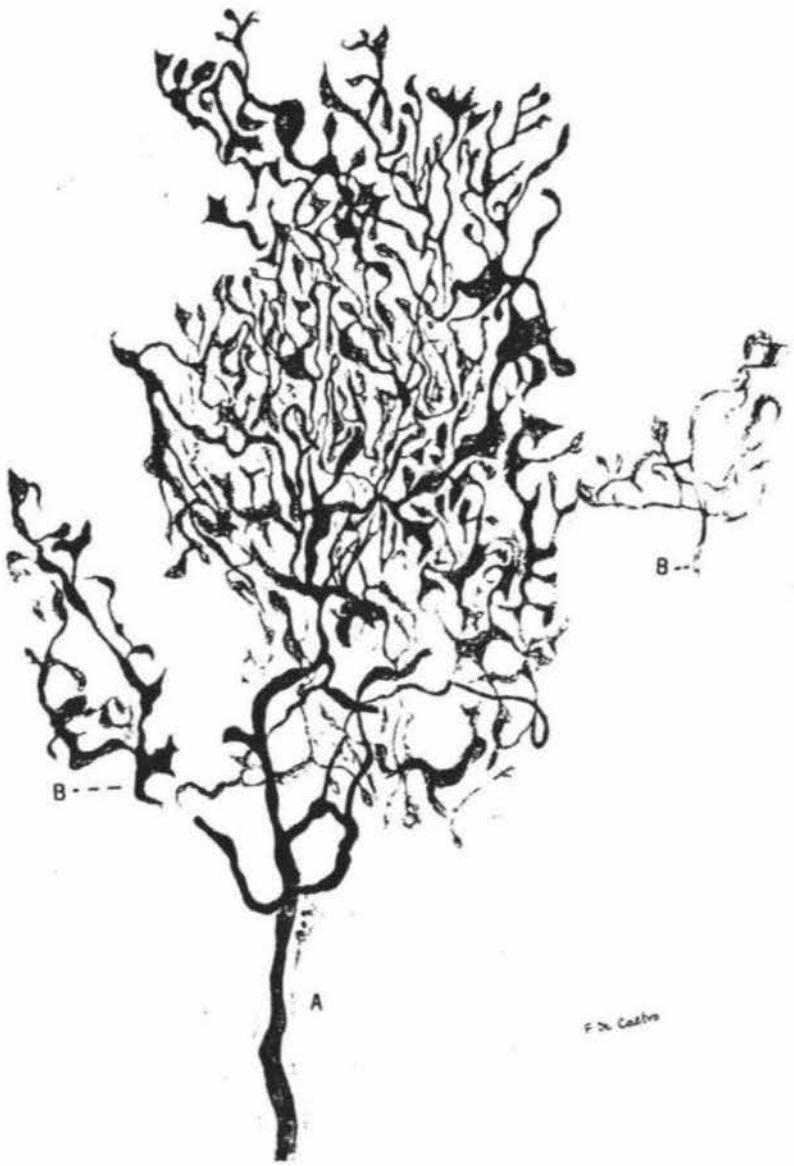


Figure 4.3 Type II baroreceptor from the wall of the carotid sinus of an adult man, tangential section. Magnification: 1050.
Adapted from de Castro (1928).
A, large myelinated nerve fiber; B, terminal nerve endings.

that any classification would prove difficult. Riisager and Weddell (1962) have also criticised the rigorous classification of baroreceptor endings into morphological types, and postulate that in the carotid sinus there is a rapid 'turnover' of nerve fibers and endings in response to normal mechanical wear, comparable to that which takes place in the conjunctiva and the skin. They regard the de Castro type I and II endings as being at opposite poles respectively in a cycle of degenerative and regenerative change. Accordingly, the type I ending is representative of either a stable terminal or a newly formed, recently regenerated nerve ending and the type II ending represents a terminal undergoing degeneration. Many of the bizarre appearances described by de Castro were interpreted by Riisager and Weddell as manifestations of regenerative or degenerative processes. Both Rees (1966) and Aumonier (1972), however, identified only a small portion of the nerve terminals exhibiting morphological features similar to those which were interpreted by Riisager and Weddell (1962) as indicating nervous degeneration or regeneration. It may be relevant that the mammalian material Rees used was obtained from young animals, since Riisager and Weddell inferred that the process of 'turnover' of nerve fibers in the carotid sinus wall might be less rapid, and morphological changes in the nerves less evident, in young subjects (Knoche and Addicks, 1976).

4.2.2.1.4 Innervation of the Carotid Sinus in the Sheep

De Castro (1951), Eyzguirre and Uchizono (1961) and Sha-Ban (1974) described undulating myelinated sensory nerve fibers and many non-myelinated nerve fibers that could be traced to the deeper tunica adventitia, medio-adventitial border and superficial tunica media in the sheep carotid sinus. The larger (2.5 to 5.0 µm diameter) myelinated nerve fibers in the superficial tunica adventitia exhibited regular beading along their course (Ábrahám, 1969; Sha-Ban, 1974). The fine (1 µm diameter) myelinated nerve fibers branched in the superficial tunica adventitia, or before reaching the medio-adventitial border, and entered the deeper adventitia to the medio-adventitial border or the superficial tunica media (Sha-Ban, 1974).

4.2.2.1.5 Morphology of the Baroreceptor Terminals in the Sheep

In the lamb and sheep, the terminal fibers of about 0.5 µm diameter end in relation to the smooth muscle fibers (Sha-Ban, 1974) as diffuse endings bearing no specific receptor apparatus. However, Ábrahám (1958, 1969) stated that in the carotid sinus of the sheep, at the end of both larger and

smaller smooth branches of nerves, are either single, or more usually double, end coils whose smoothly descending fibers end in delicate fibrillar end plates attached flatly to the tunica adventitial portion facing the media. These are unique among the known receptors of the sinus region and appear sufficiently specific to the sheep that the picture of such a single nerve end system would leave no doubt as to its origin.

4.2.2.2 The External Carotid Nerve

The vasomotor contribution to the carotid sinus from the external carotid nerve is of minor importance (Adams, 1958).

The identity of vasomotor external carotid nerve fibers arising from the superior cervical ganglion is lost in the regional nerve plexus. In the rabbit, cat and dog (Knoche and Addicks, 1976; Knoche and Kienecker, 1977) two or more post-ganglionic filaments from the superior cervical ganglion enter the area of the carotid bifurcation, whereas in the sheep, the external carotid nerve divides into three to five filaments (Sha-Ban, 1974). The dorsal filaments enter the carotid body while the caudal filaments enter the bifurcation and disappear in the carotid sinus periarterial tissue.

In the outer-half of the rabbit carotid sinus tunica adventitia, non-myelinated nerve bundles are occasionally distributed along the course of the vasa vasorum, but whether these fibers ultimately terminate in relation to these vessels and whether they are vasomotor has not been determined (Rees, 1966, 1967a,b; Reis and Fluxe, 1968). Catecholamine fluorescence studies show only a discontinuous fluorescent network in the inner-half of the carotid sinus wall tunica adventitia close to the sensory receptors. This sparse vasomotor innervation consists of thin (0.4 to 1.1 μm diameter) smooth fibers which are varicose according to Knoche and Kienecker (1977). These fibers are preferentially associated with the isolated circumferentially and longitudinally arranged smooth muscle cells that are set back 13 to 20 μm from the elastic membranes of the medio-adventitial border.

No histological studies seem to have been reported on the vasomotor innervation of the carotid sinus in the sheep.

4.2.3 Extent of the Carotid Baroreceptor Zone

The extent of the carotid baroreceptor zone has been determined using histological methods.

Addison (1944, 1945) postulated that the special distribution of elastic tissue at the carotid bifurcation indicates the extent of vessel wall involved in the carotid sensory zone. Thus, the receptor area in the guinea-pig and cat occupies the carotid dilatation and root of the occipital and ascending pharyngeal arteries; in the rabbit and dog it occupies the dorsal wall of the common carotid artery (immediately below the bifurcation) and the first part of the internal carotid artery; and in the human it occupies the caudal part of the carotid sinus.

In 1940 de Castro determined the extent of the carotid baroreceptor zone in the dog by mapping the portions which evoked a reflex hypotension upon electrical stimulation of the carotid bifurcation arterial wall. The dilatated origin of the internal carotid artery and root of the occipital artery received the densest innervation. In the cat and ruminant, where the internal carotid artery is vestigial, the pressure sensitive portion of the carotid bifurcation included the proximal segment of the occipital artery (de Castro, 1928).

Of the mammals possessing a persistent internal carotid artery, only in the hedgehog, where the occipital and ascending pharyngeal arteries arise by a common trunk from the dilatated portion of the internal carotid artery, i.e., from the carotid sinus itself, is there histological evidence which indicates participation of the occipital artery in the baroreceptor reflex. The dense sensory innervation in the hedgehog incorporates the origin of the occipital and ascending pharyngeal arteries and to some extent the wall of the internal carotid artery, the wall of which is thicker in the carotid sinus region than above and below (Adams, 1957).

4.2.3.1 Baroreceptor Innervation of the Common Carotid Artery

That the carotid baroreceptor zone might be more extensive than had been previously supposed is suggested by observations made, in the cat, by Green (1953, 1954a,b, 1967) and Boss and Green (1954a,b, 1956) who located in the cat a number of supplementary baroreceptor areas in the common carotid artery where baroreceptor activity was similar to that in the carotid sinus. Five such areas were described for the right common carotid artery, distributed at

intervals along the length of the vessel between the level of the cranial thyroid artery and the subclavian bifurcation. Area 1 was situated at the origin of the right subclavian artery, area 1a lay about 10 mm distal to this point, area 2 was about 40 mm below the origin of the cranial thyroid artery, area 3 was approximately 30 mm below the origin of that vessel and area 4 was situated at the origin of the cranial thyroid artery and dorsal muscular branch.

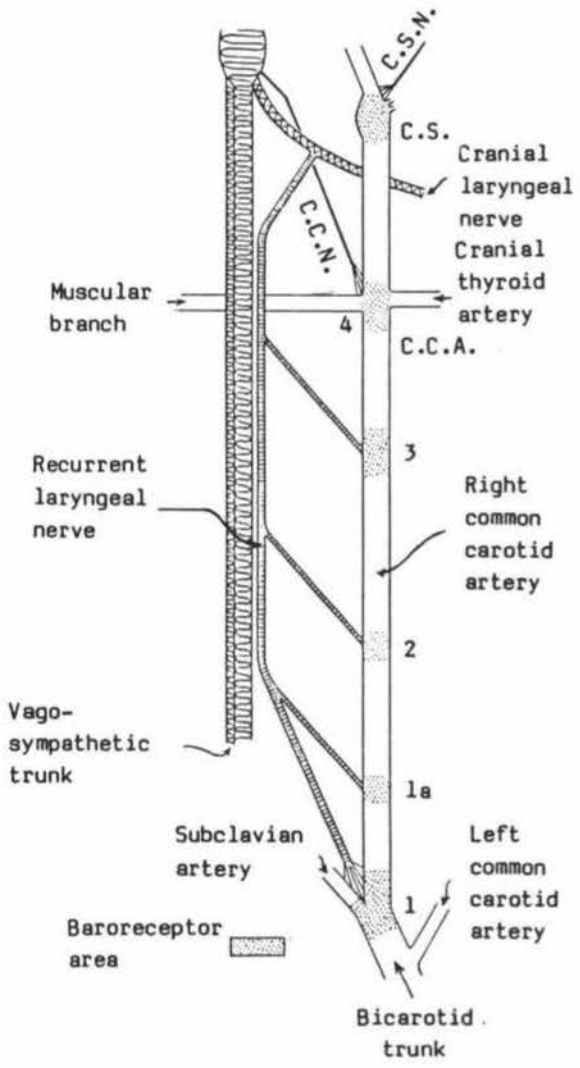
The right baroreceptor area 4, which Green (1953) named the 'common carotid area', is supplied by a right vagal branch, named the 'common carotid nerve', arising at the level of the right nodose ganglion; the remaining areas each receive fibers from the right recurrent laryngeal nerve originating from the vagus at the junction of the common carotid and subclavian arteries. Similar areas exist on the left side of the neck in the cat and these are supplied by the left recurrent laryngeal nerve, which separates from the vagus at the aortic arch.

See Figure 4.4.

Boss and Green (1956) described the histological features of the common carotid arterial wall principally in baroreceptor areas 1a, 2 and 3 from which no arterial branches arise : thus the arterial structure associated with baroreceptor innervation could be distinguished from the modification of the vessel wall at the origin of a branch. The characteristics reported were:

1. thinning of the tunica media and a reduction in the muscularity,
2. sometimes fewer elastic laminae in the tunica media, but occasionally elastic laminae of unchanged number and increased thickness,
3. less corrugated elastic laminae,
4. adventitial collagen in finer bundles which were intricately interwoven.

Within the baroreceptor areas small nerve trunks, usually single, but occasionally multiple at the level of the cranial thyroid artery, passed myelinated nerve fibers to the same side of the arterial wall. The fibers ran longitudinally in the tunica adventitia for distances up to 0.3 mm and then turned towards the tunica media, branching into many fine fibers in the innermost adventitia. The myelin sheath was retained up to, or a little beyond, the site of branching of the axis. The innermost nervous structures were situated immediately next to the outermost part of the tunica media on the side corresponding to the entry of the nerve fibers and such a mass extended



	Rabbit	Cat	Dog
C.S.	+	+	+
4	+	+	+
3	+	+	-
2	+	+	-
1a	+	+	-
1	+	+	+

Figure 4.4 The distribution of baroreceptors in the right common carotid artery of the rabbit, cat, and dog. A similar distribution exists on the left common carotid artery. Adapted from Boss and Green (1956).
C.C.A., common carotid area; C.C.N., common carotid nerve; C.S., carotid sinus; C.S.N., carotid sinus nerve.

longitudinally 1.0 to 8.0 mm, and circumferentially for almost one-third of the distance about the circumference. The myelin sheaths of adjacent fibers were reported to fuse. Fibers thickened and irregular in outline, running in and near the arterial wall, often divided or fused at some distance from the site of terminal ramification so that a series of varicosities formed. It was not possible to distinguish one baroreceptor area from another by the form of the nervous structures present (Boss and Green, 1956).

These nervous structures are similar to those reported by de Castro for the carotid sinus (1928) and Nonidez (1935, 1937, 1941) for the common carotid artery in the kitten and puppy.

Aumonier (1972) confirmed the findings of Green (1953, 1954a,b, 1967) and Boss and Green (1954a,b, 1956) and further studied baroreceptor areas in the common carotid artery of the rabbit and dog. It may be noted in Figure 4.4 that the rabbit conforms to Green and Boss and Green's findings for the cat, but the dog lacks area 1a, 2 and 3 on both sides.

4.3 MATERIALS AND METHODS

4.3.1 Animal Dissection

Adult sheep were anaesthetised with sodium pentobarbitone (Anathal,V.R. Laboratories Pty Ltd, Australia, 30 mg/kg body weight in a 6% solution) injected into an external jugular vein before dissection to obtain tissue samples. For the sucrose-potassium-phosphate glyoxylic acid fluorescence, the sheep were injected intravenously with 15 mg noradrenaline (Levophed, Winthrop Laboratories, Australia) 5 minutes before the arteries were taken (Keatinge, 1966). Immediately prior to taking samples, the animals were euthanased with 30 ml saturated magnesium sulphate injected intravenously and then the entire length of the left and right common carotid arteries was removed for histological examination.

4.3.2 Section Fixation, Processing and Cutting Procedure

The solutions used below are described in Appendix I.

4.3.2.1 Paraffin Wax Embedded Sections

The arterial specimens were rinsed in physiological saline to remove blood and placed in fixative (Bouin's fluid, solution III) for 24 hours. To prevent the loss of water-soluble picrates from the tissue, the specimens were then transferred into 70% alcohol.

Following fixation, the arterial specimens were sketched, transected every 5 mm and labelled. The tissue blocks were loaded into an automatic tissue processor (Shandon Elliot Scientific Co. Ltd, England); see Table 4.1 for processing schedule.

The tissue blocks were next embedded in 56°C melting point paraffin wax with a Tissue Tek Tissue II Embedding Centre (Miles Laboratories, U.S.A.) and sections were cut at 10 or 20 µm thickness using a base sledge microtome (Leitz Wetzlar, Germany) or at 40 µm thickness using a sliding microtome (Reichert, Germany). Sections were floated on warm (46°C) water, picked up onto 3 x 1 inch glass microscope slides which were either lightly albuminised (solution IV) or (for immunocytochemistry) coated with poly-L-lysine (solution V). The slides were then air-dried overnight at 37°C.

TABLE 4.1 PROCESSING SCHEDULE FOR THE SHANDON, ELLIOT AUTOMATIC TISSUE PROCESSOR

Process	Reagent	Time
Dehydration	70% ethyl alcohol	1 hour
	95% ethyl alcohol	1 hour
	100% ethyl alcohol I	1 hour
	100% ethyl alcohol II	1 hour
	100% ethyl alcohol III	1 hour
	100% ethyl alcohol IV	1 hour
Clearing	Chloroform	1 hour
	Xylene I	1 hour
	Xylene II	1 hour
Impregnation	Paraffin wax 56°C MP I	2 hours
	Paraffin wax 56°C MP II	2 hours

4.3.2.2 Cryostat Sections

The arterial specimens were rinsed in physiological saline to remove blood, the carotid sinus region was excised and quenched in isopentane cooled in liquid nitrogen. After mounting on a pre-cooled chuck with a synthetic mounting medium (Tissue Tek O.C.T., Miles Laboratories, U.S.A.), the specimens were wrapped in aluminium foil and their temperature allowed to equilibrate to that of the cryostat chamber (Lipshaw MFG Co., Michigan, -20 to -30°C) over 90 minutes.

The sections were cut at 30 µm thickness using a rotary microtome (Lipshaw MFG Co., Michigan). The sections were mounted for fluorescence by touching a room temperature untreated glass microscope slide against the dry section. Dry sections were mounted for immunocytochemistry on a room temperature poly-L-lysine (solution V) coated slide. The mounted sections were stored in a refrigerator at 4°C.

For fluorescence, the sections were placed in fixative (acetone) for 5 seconds. For immunocytochemistry, the sections were placed in fixative (Bouin's fluid, solution III) for 10 minutes, then transferred into PBS (solution VI).

4.3.3 Staining, Fluorescent and Immunocytochemical Procedures

4.3.3.1 Toluidine Blue Stain

For paraffin wax embedded sections:

1. Dewax in xylene I (5 minutes) and xylene II (5 minutes); bring sections through absolute alcohol and 70% alcohol to tapwater.

For both paraffin wax embedded and frozen sections:

2. Stain in 1.0% toluidine blue for 2 minutes.
3. Wash quickly in tapwater.
4. Rapidly dehydrate in 70% alcohol, absolute alcohol I and absolute alcohol II; clear in xylene I and xylene II and mount sections in DPX mountant (B.D.H. Chemicals Ltd, England).

4.3.3.2 Verhoeff's Haematoxylin Stain

1. Dewax in xylene I (5 minutes) and xylene II (5 minutes); bring sections through absolute alcohol and 70% alcohol to tapwater.
2. Mordant in Lugol's iodine (solution VII) for 5 minutes.
3. Rinse in tapwater.

4. Immerse in 5% sodium triphosphate for 5 minutes.
5. Rinse well in tapwater.
6. Stain in Verhoeff's haematoxylin (solution VIII) until sections are jet black (15-30 minutes).
7. Rinse in tapwater.
8. Differentiate in 2% ferric chloride until collagen is almost colourless but elastin remains black.
9 Rinse in running tapwater for 5 minutes.
10. Counterstain in Van Giesen (Solution IX) for 7 minutes.
11. Rinse in tapwater.
12. Dehydrate and differentiate in 70% alcohol, absolute alcohol I and absolute alcohol II; clear in xylene I and xylene II and mount sections in DPX mountant.

4.3.3.3 Sucrose-Potassium-Phosphate Glyoxylic Acid Fluorescence

(de la Torre and Surgeon, 1976)

1. Quickly dip frozen section in room temperature SPG (solution XII) three times (1 dip/second).
2. Air dry slides with a hair dryer for 3-5 minutes and place in a 80 ± 1°C oven for 5 minutes.
3. Mount the section in DPX mountant.
4. Place the coverslipped slides on a 80°C (exactly) hotplate for 90 seconds to remove autofluorescent air bubbles.

4.3.3.4 Anti-Neuron Specific Enolase Antibody Immunocytochemistry

See Figure 4.5

For paraffin wax embedded sections:

1. Dewax in xylene I (5 minutes) and xylene II (5 minutes); bring sections through absolute alcohol and 70% alcohol to tap water.
2. Equilibrate in PBS (solution VI).

For both paraffin wax embedded and frozen sections:

3. Inscribe a circle around the section with a diamond pencil.
4. Dry slides with absorbent paper outside the circle.
5. Pretreat control and treatment sections in a moist chamber for 5 minutes with 2-4 drops of 1% BSA (solution XI), see Figure 4.5a.
6. Drain off the 1% BSA and dry slides with absorbent paper as above.
7. Incubate control sections with 2-4 drops of 1% BSA (solution XI and

Figure 4.5 Anti-Neuron Specific Enolase Immunocytochemical Method.

Key

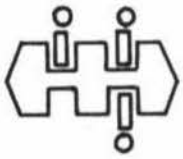
NSE antigen

Electrostatic site

BSA

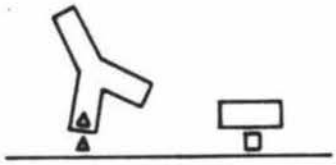
Specific primary anti-NSE antibody

Specific secondary biotin-labelled anti-rabbit immunoglobulin G antibody

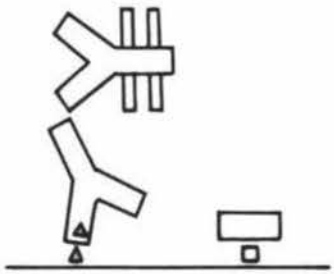


Streptavidin biotinylated horseradish peroxidase complex - avidin has four binding sites/molecule for biotin which is coupled to peroxidase

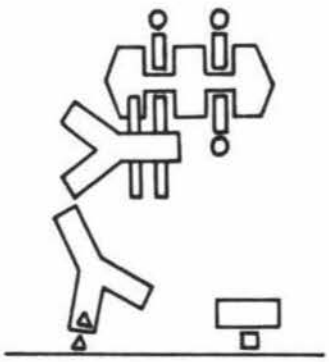
a. Tissue non-specific electrostatic binding sites blocked by BSA



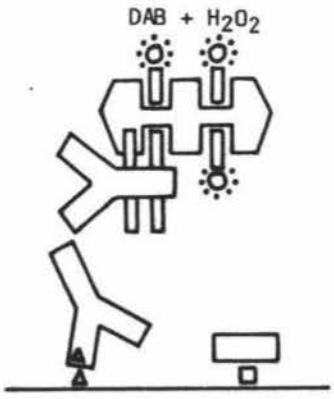
b. Specific primary anti-NSE antibody reacts with NSE antigen



c. Specific secondary biotin-labelled anti-rabbit immunoglobulin G antibody reacts with primary antibody



d. Streptavidin biotinylated horseradish peroxidase complex reacts with secondary antibody



e. Peroxidase developed by the DAB technique

treatment sections with 2-4 drops of anti-NSE antibody from rabbit (Dakopatt, Medic DDS, N.Z., diluted 1/1000 with 1% BSA in PBS) in a moist chamber for 60 minutes or overnight in a refrigerated room at about 4°C, see Figure 4.5b.

8. Drain off the 1% BSA and anti-NSE antibody and rinse slides in three changes of PBS (Solution VI) for 1 minute each.
9. Dry slides with absorbent paper as previously.
10. Incubate control and treatment sections in a moist chamber for 30 minutes with 2-3 drops of anti-rabbit biotinylated immunoglobulin species specific whole antibody from donkey (Amersham International pic, U.K., diluted 1/200 with 1% BSA in PBS), see Fig. 4.5c.
11. Drain off the anti-rabbit immunoglobulin and rinse slides in three changes of PBS (solution VI) for 1 minute each.
12. Again dry slides with absorbent paper.
13. Incubate control and treatment sections in a moist chamber for 20 minutes with 2-3 drops of streptavidin-biotinylated horseradish peroxidase complex (Amersham International pic, U.K., diluted 1/200 with 1% BSA in PBS), see Figure 4.5d.
14. Drain off streptavidin complex and rinse slides in two changes of PBS (solution VI) for 1 minute each.
15. Develop the control and treatment section peroxidase on a slide rack over the sink with 5-10 drops of DAB (solution XII) for 3-4 minutes (control the stain intensity by frequently checking a treatment section with a microscope during this period), see Figure 4.5e.
16. Rinse in tapwater.
17. Counterstain in Mayer's haemalum (solution XIII) for 1 minute.
18. Rinse in tapwater.
19. Blue in Scott's tapwater (solution XV) for 1 minute.
20. Rinse in tapwater.
21. Dehydrate and differentiate 70% alcohol, absolute alcohol I and absolute alcohol II; clear in xylene I and xylene II, and mount sections in DPX mountant.

4.3.4 Microscope and Photographic Equipment

The slides were examined with a Leitz Ortholux microscope (Leitz Wetzlar, Germany). For the fluorescence technique, both the primary lamp filter Schott BG12 and the secondary barrier filter Leitz K530 were required. Photomicrographs were taken on Kodak Ektachrome 50 ASA film (Eastman Kodak,

U.S.A.) using a Leica 35 mm camera (Leitz Wetzlar, Germany). The exposure times were measured and calibrated with a Micro-Six L exposure meter (Gossen, Germany). The colour prints used in this thesis were reproduced from 35 mm transparencies by Kodak New Zealand Ltd.

4.3.5 Measurement of the Dimensions of the Common Carotid Artery

In each of the eighteen sections representative of the length of the left common carotid artery cranial to the thoracic inlet of sheep number 6 of experimental series 2 in chapter 3, the tunica intima, tunica media, tunica adventitia and total vessel wall thickness was measured with a micrometer, at six sites:

1. adjacent to the large nerve trunk,
2. opposite to the large nerve trunk,
3. 60° clockwise from site 1,
4. 60° clockwise from site 2,
5. 60° anticlockwise from site 1,
6. 60° anticlockwise from site 2.

The data was divided into two groups, one of areas A, B and C and another of the intervening areas. Paired *t*-tests were then undertaken of the measurement sites both within and between these two groups.

4.4 RESULTS

This study was undertaken in sheep to investigate:

1. the structure of the carotid sinus and common carotid arterial wall as demonstrated by Verhoeff's haematoxylin stain.
2. the distribution of sensory and vasomotor nerve fibers in the carotid sinus and common carotid arterial wall using anti-neuron specific enolase antibody immunohistochemistry and the sucrose-potassium-phosphate glyoxylic acid fluorescence technique of de la Torre and Surgeon (1976).

4.4.1 Structure of the Wall of the Carotid Sinus

Wax embedded sections of three carotid sinuses were stained with Verhoeff's haematoxylin. With this stain, which distinguishes elastic tissue from collagen, elastic tissue and nuclei are coloured black, collagen red, muscle yellow, red blood cells bright yellow and general cytoplasm shades of green-brown.

It was not possible to compare the thickness of the carotid sinus wall with that of the adjoining vascular structures.

The tunica intima endothelium was a simple squamous type bounding the lumen, and resting upon a thin basal lamina. The underlying subendothelium was thin and composed of delicate fibro-elastic tissue and some longitudinal smooth muscle. The internal elastic lamina was the outermost component of the tunica intima and consisted of a single fenestrated membrane.

In some areas the tunica media was thinner than that of the adjoining vascular structures. In these regions the primary constituent was fenestrated elastic laminae arranged concentrically in 8 to 20 layers. Neighbouring laminae were frequently connected by slanting elastic fibers. In the interstices between laminae were a few longitudinal smooth muscle cells, fine elastic and collagen fibers. Elsewhere, the structurally unmodified tunica media of the carotid sinus was composed of circular smooth muscle in which 4 to 6 concentric layers of fenestrated elastic laminae alternated with smooth muscle in a regularly layered fashion. Collagenous bundles also occurred in the ground substance. The outermost component of the tunica media, the external elastic membrane, was not always readily identifiable, especially at the origin of the occipital artery.

In the areas of tunica medial thinning the tunica adventitia was thicker than the adventitia of the adjoining vascular structures. The tunica adventitia consisted of irregularly arranged connective tissue containing longitudinal collagen bundles. There were a few interspersed circular elastic fibers and smooth muscle cells in the deeper adventitia. The tunica adventitia graded off into the supportive areolar tissue nearby.

See Plates 4.1 and 4.2.

4.4.2. Structure of the Wall of the Common Carotid Artery

Seven wax embedded sections taken at 5 mm intervals along the length of the left common carotid artery cranial to the thoracic inlet were stained with Verhoeff's haematoxylin.

The majority of the endothelial cells lining the vascular wall were simple squamous cells resting upon a thin basal lamina. The underlying fibroelastic subendothelium formed the greatest part of this tunic. The external tunica intimal layer, the internal elastic lamina, was a circular, fenestrated double membrane.

The tunica media consisted of 5 to 6 concentrically arranged equidistantly spaced elastic laminae. A network of delicate elastic fibers interconnected the elastic lamina. These layers divided the helically arranged smooth muscle cells into layers 2 to 5 cells wide. Circumferential collagen bundles embedded in ground substance held the muscle cells and elastic components together; some elastic fibers were scattered amongst the individual muscle cells. The circular external elastic lamina was the outermost component of the tunica media.

The innermost part of the tunica adventitia was an almost continuous network of up to 8 layers of concentric elastic laminae. External to this membrane, interwoven collagen bundles formed a fibrous tissue sleeve around the tunica media. There were a few smooth muscle cells and fibroblasts in the deeper tunica adventitia. The adventitia graded off into the supportive areolar tissue nearby.

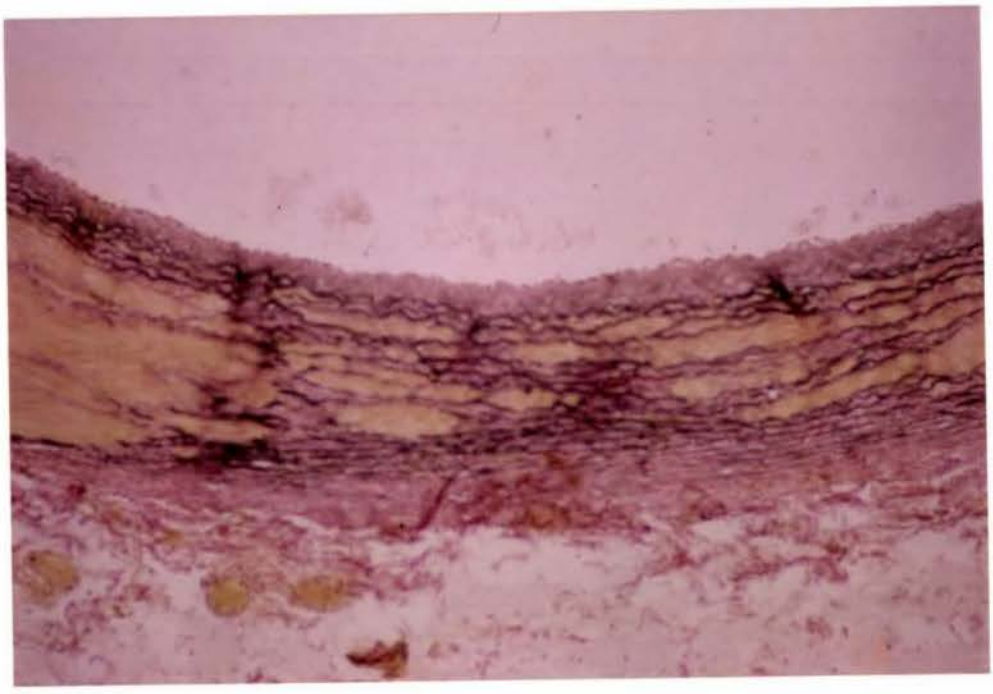
See Plates 4.3 and 4.4.

Plate 4.1 Transverse section of the left common carotid artery at the level of the origin of the occipital artery demonstrating the structural modification of the left carotid sinus

Magnification: 100. Stain: Verhoeff's haematoxylin.

Plate 4.2 Transverse section of the right common carotid artery at the level of the origin of the occipital artery demonstrating the structural modification of the right carotid sinus

Magnification: 90. Stain: Verhoeff's haematoxylin.



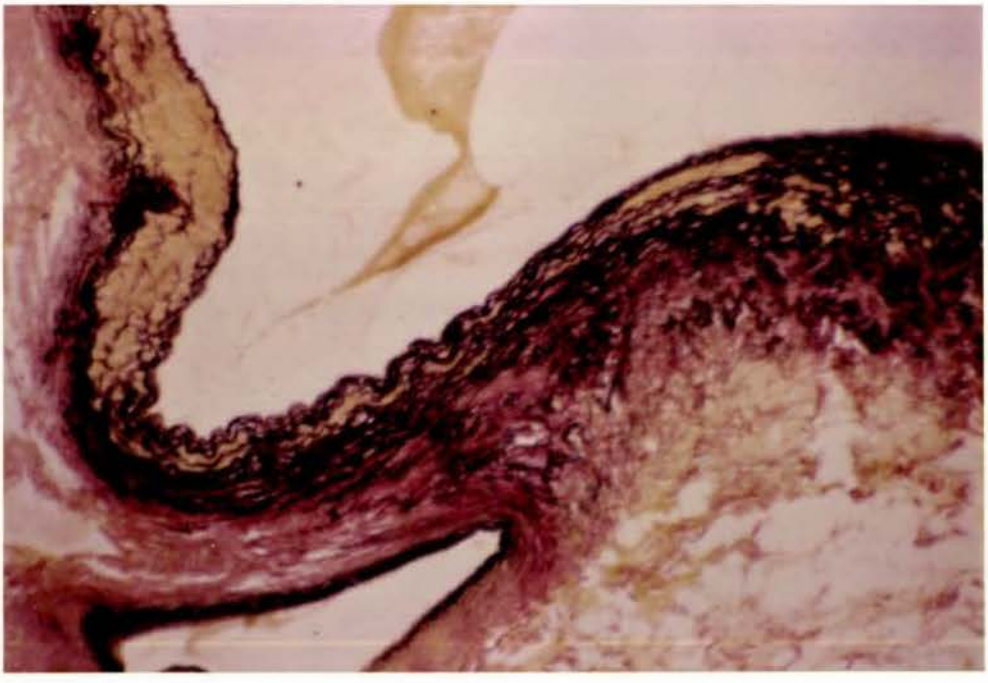
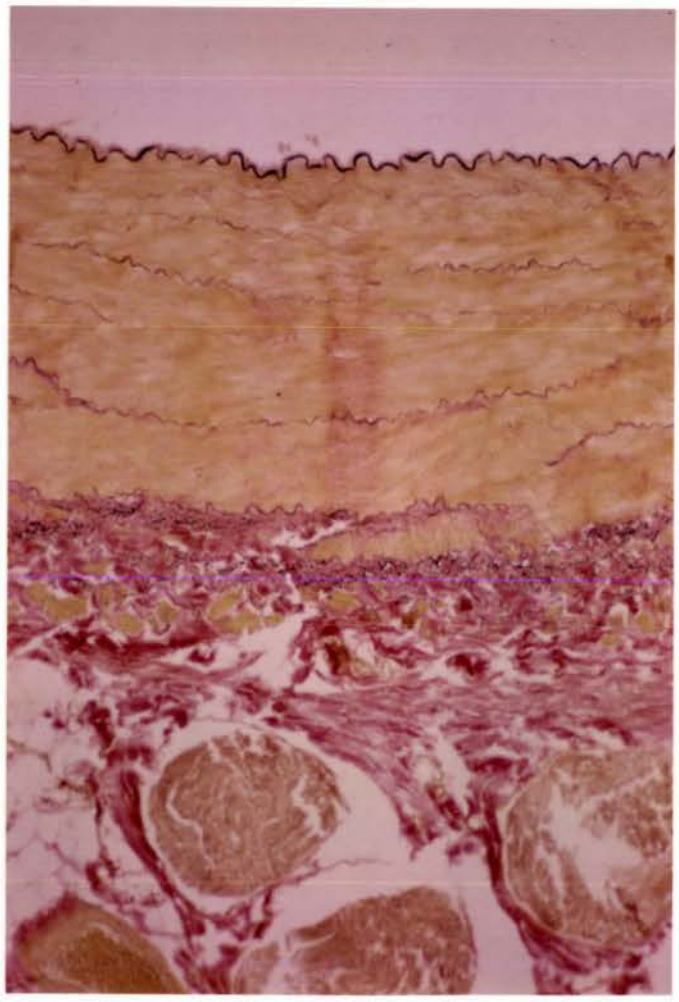


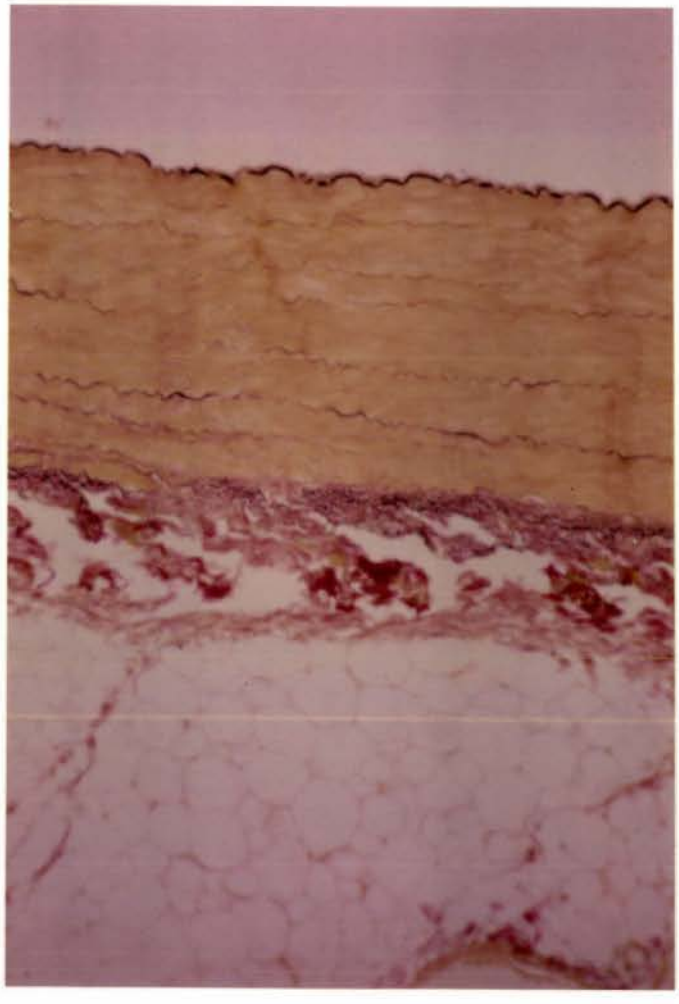
Plate 4.3 Transverse section of the left common carotid artery 35 mm from the origin of the occipital artery demonstrating the structure of nerve fiber area A.

Magnification: 100. Stain: Verhoeff's haematoxylin.

Plate 4.4 Transverse section of the left common carotid artery 35 mm from the origin of the occipital artery demonstrating the structure adjacent to nerve fiber area A.

Magnification: 100. Stain: Verhoeff's haematoxylin.





The thickness of the tunica intima, tunica media and tunica adventitia and hence the total thickness of the vessel wall varied at particular sites, but overall was almost uniform down the entire length of the common carotid artery studied (see Section 4.4.4.3).

4.4.3 Innervation of the Carotid Sinus

4.4.3.1 Identification of the carotid sinus

To ensure that the wax embedded and cryostat sections prepared for anti-NSE antibody immunocytochemistry were of the carotid sinus itself, they were quickly stained with toluidine blue which clearly distinguished the thinning of the tunica media and the metachromasia of the tunical collagen of the carotid sinus.

4.4.3.2 Sensory and Vasomotor Innervation of the Carotid Sinus

Wax embedded and cryostat sections of seven carotid sinuses were reacted with the anti-NSE antibody. The enzyme NSE is involved in the neuronal glycolytic pathway and this immunocytochemical technique clearly distinguishes nervous fibers from the supportive tissue - nervous and muscular tissue are coloured orange-brown. See Plate 4.5.

At the origin of the occipital artery, large nerve bundles were evident in the superficial tunica adventitia. Fibers in the deeper adventitia occurred singly or in small groups and pursued a tortuous course to the medio-adventitial border where arborisation occurred. See Figure 4.6 and Plates 4.6 and 4.7.

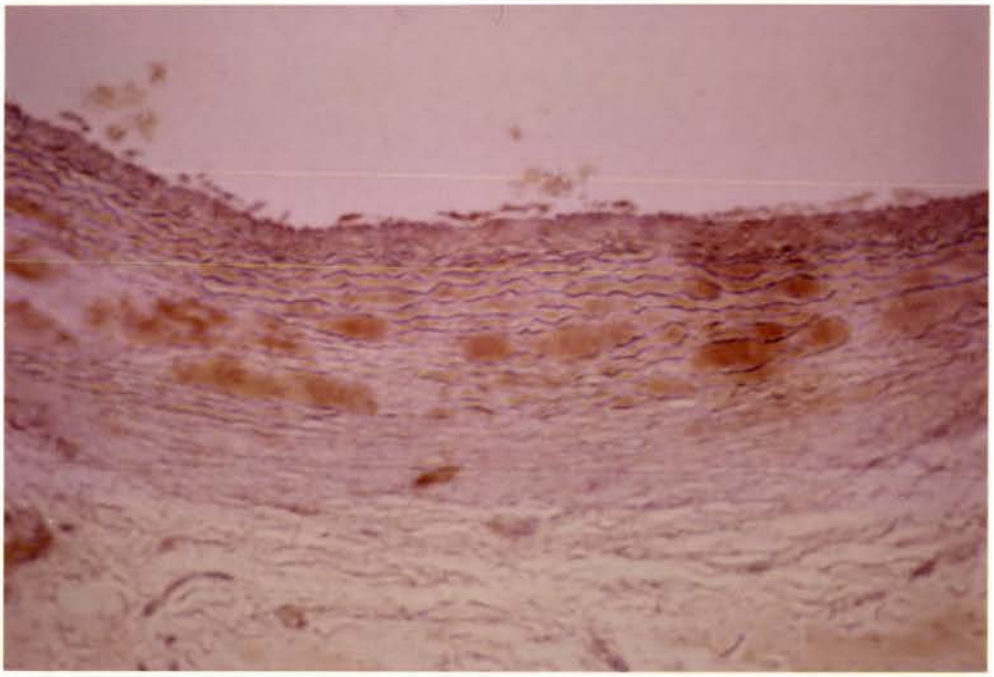
4.4.3.3 Vasomotor Innervation of the Carotid Sinus

Two cryostat sections of the carotid sinus were reacted with sucrose-potassium-phosphate glyoxylic acid. This reaction distinguishes adrenergic vasomotor fibers from the supportive tissue - adrenergic fibers fluoresce brilliantly, elastin and collagen autofluoresce.

The vasomotor innervation of the carotid sinus was extremely sparse, only a few circumferentially and longitudinally running fibers occurred within the tunica adventitia and outer half of the tunica media. See Plates 4.8 and 4.9.

Plate 4.5 Transverse section of the left common carotid artery of the level of the origin of the occipital artery demonstrating the appearance of vascular smooth muscle.

Magnification: 100. Stain: Anti-NSE antibody immunocytochemistry.



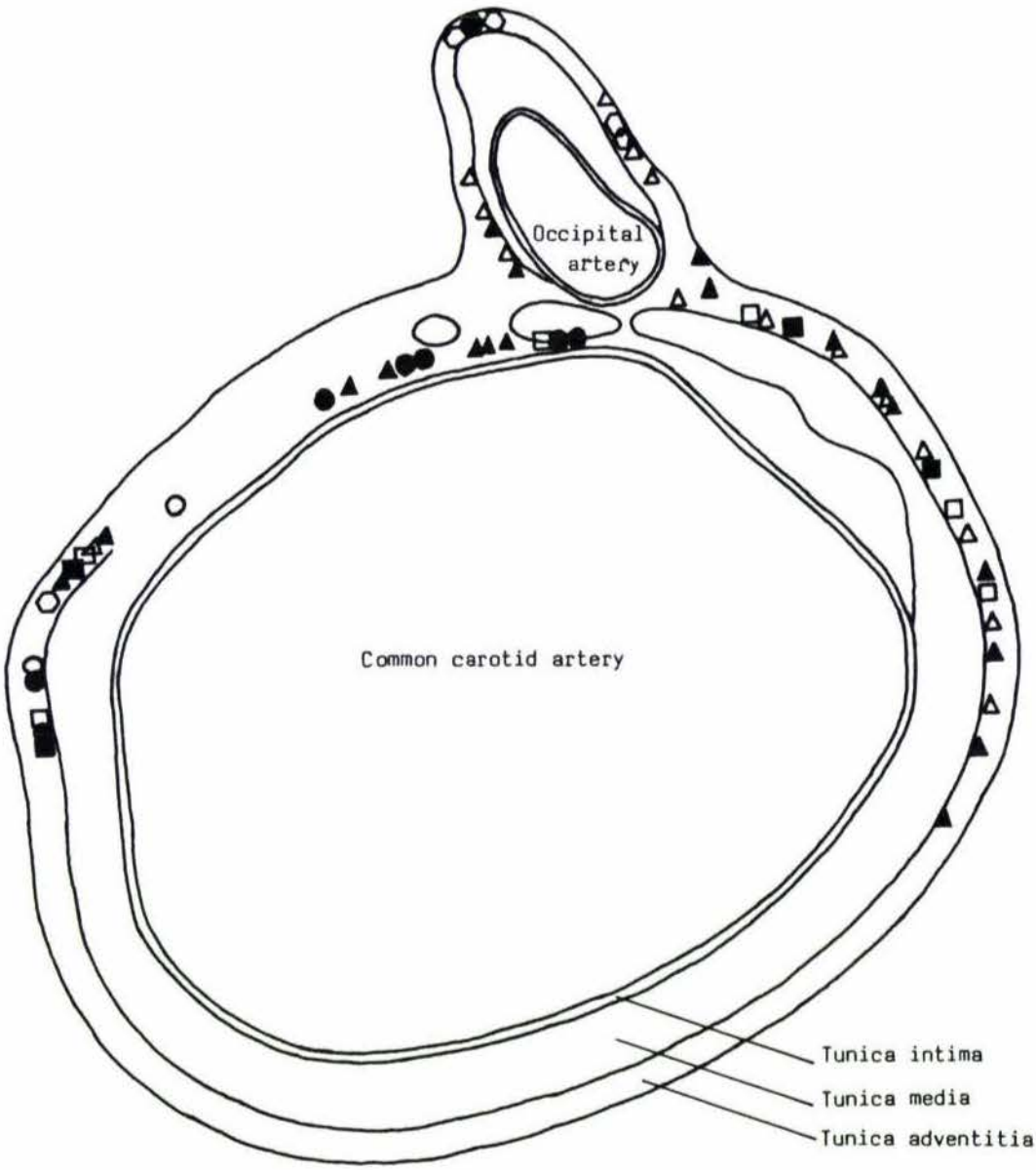


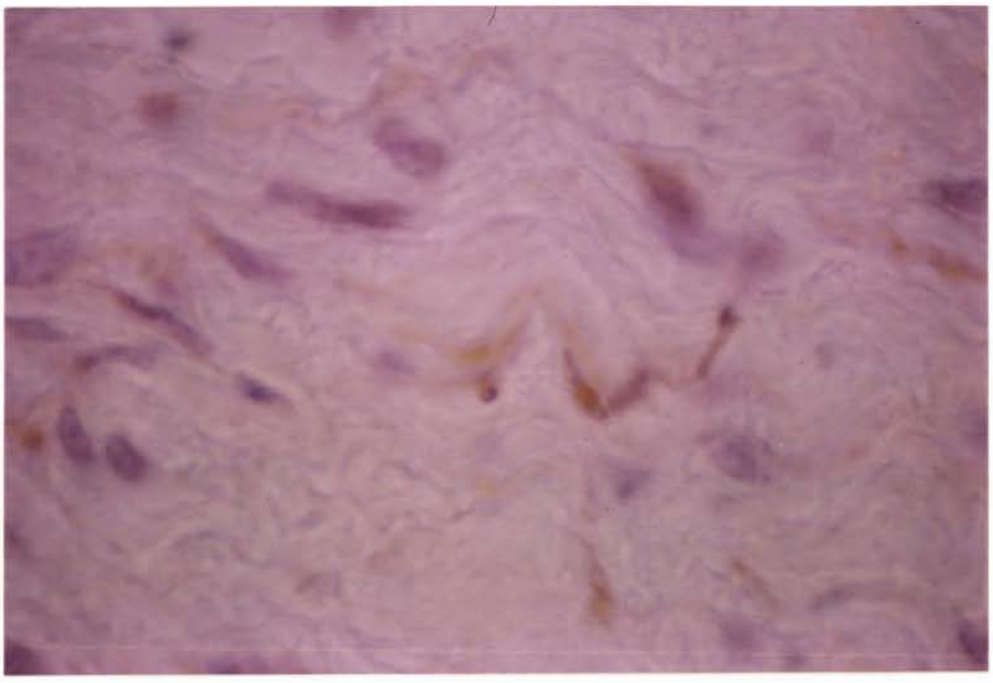
Figure 4.6 A composite diagram of the nerve axon location in seven carotid sinuses at the level of the origin of the occipital artery from the common carotid artery. Each carotid sinus is represented by a different symbol

Plate 4.6 Transverse section of the left common carotid artery at the level of the origin of the occipital artery demonstrating the appearance of the left carotid sinus terminal nerve fibers.

Magnification: 1660. Stain: Anti-NSE antibody immunocytochemistry.

Plate 4.7 Transverse section of the right common carotid artery at the level of the origin of the occipital artery demonstrating the appearance of the right carotid sinus terminal nerve fibers.

Magnification: 1660. Stain: Anti-NSE antibody immunocytochemistry.



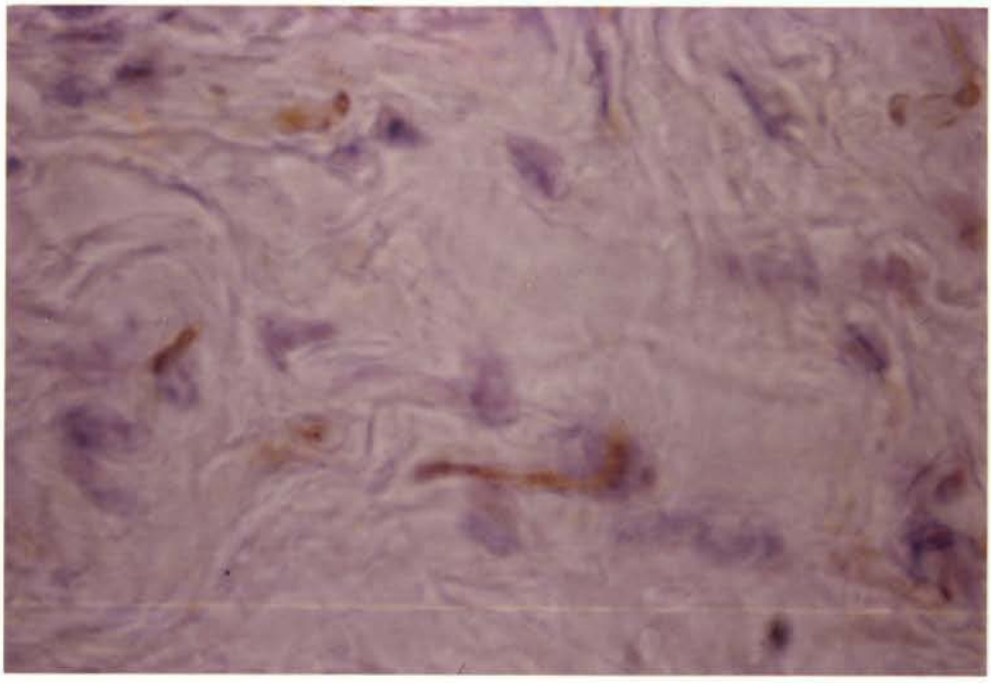


Plate 4.8 Transverse section of the left parotid salivary gland demonstrating the adrenergic innervation of a capillary. This was the control section for the SPG fluorescence method used to identify the adrenergic innervation of the carotid sinus and common carotid artery.

Magnification: 100. Stain: SPG fluorescence.

Plate 4.9 Transverse section of the left common carotid artery at the level of the origin of the occipital artery demonstrating the sparse adrenergic innervation of the left carotid sinus.

Magnification: 100. Stain: SPG fluorescence.

4.4.4. Innervation of the Common Carotid Artery

4.4.4.1 Sensory and Vasomotor Innervation of the Common Carotid Artery

Eighteen wax-embedded sections representative of the length of the left common carotid artery cranial to the thoracic inlet were reacted with the anti-NSE antibody.

Three fusiform areas, labelled A, B and C, with local concentrations of nerve fibers were distributed along the length of the artery. The large cranial nerve fiber area, labelled A, arose at the origin of the occipital artery from the common carotid artery and extended longitudinally 53 mm to a level beyond the origin of the cranial thyroid artery. The cranial and caudal poles of this area encompassed 25 to 30% of the common carotid artery circumference and the midpoint between these poles encompassed 70%. Area B was the middle and smaller nerve fiber area of the common carotid artery. It arose 157 mm from the origin of the occipital artery and extended longitudinally 40 mm. 20 to 35% of the common carotid artery circumference was covered by the cranial and caudal poles of this area, while 30 to 40% was covered midway between these poles. The caudal nerve fiber area, labelled C, arose 223 mm from the origin of the occipital artery from the common carotid artery. This area was not traced beyond the level of the thoracic inlet so that only the cranial pole circumferential extension could be measured. This pole encompassed 25% of the common carotid artery circumference.

See Table 4.2 and Figure 4.7.

Within these fusiform-shaped areas, small nerve trunks occurred medially in the superficial tunica adventitia adjacent to a large nerve trunk. These trunks branched and passed many fine fibers to the medio-adventitial border on the side corresponding to the entry of the nerve trunks. The form and density of this innervation did not vary within, or between, nerve fiber areas A, B and C.

See Plates 4.10 and 4.11.

4.4.4.2 Vasomotor Innervation of the Common Carotid Artery

To demonstrate the adrenergic vasomotor innervation of the common carotid artery, two cryostat sections from nerve fiber area A were reacted with sucrose-potassium-phosphate glyoxylic acid.

TABLE 4.2 CHARACTERISTICS OF THE LEFT COMMON CAROTID ARTERIAL NERVE FIBER AREAS A, B AND C OF SHEEP NUMBER 6 IN EXPERIMENTAL SERIES 2

Section Number	Nerve Fiber Area	Circumferential Extension %	Longitudinal Extension (mm)	
			Upon Fixation†	In situ
Origin of occipital artery				
1		30	0	0
2		60	2	7
3	A	70	5	20
4		50	10	35
Origin of cranial thyroid artery				
5		25	14	53
6			19	69
7			22	82
8			26	95
9			29	106
10			32	117
11			35	130
12			39	144
13		20	43	157
14	B	40	46	170
15		30	50	183
16		35	53	197
17			56	208
18 Level of thoracic inlet (cervical vertebra 7)	C	25	61	223

† These figures are corrected to give the distances in the living sheep; retraction on dissection and shrinkage in preparation caused a 3.7-fold reduction in length of the artery.

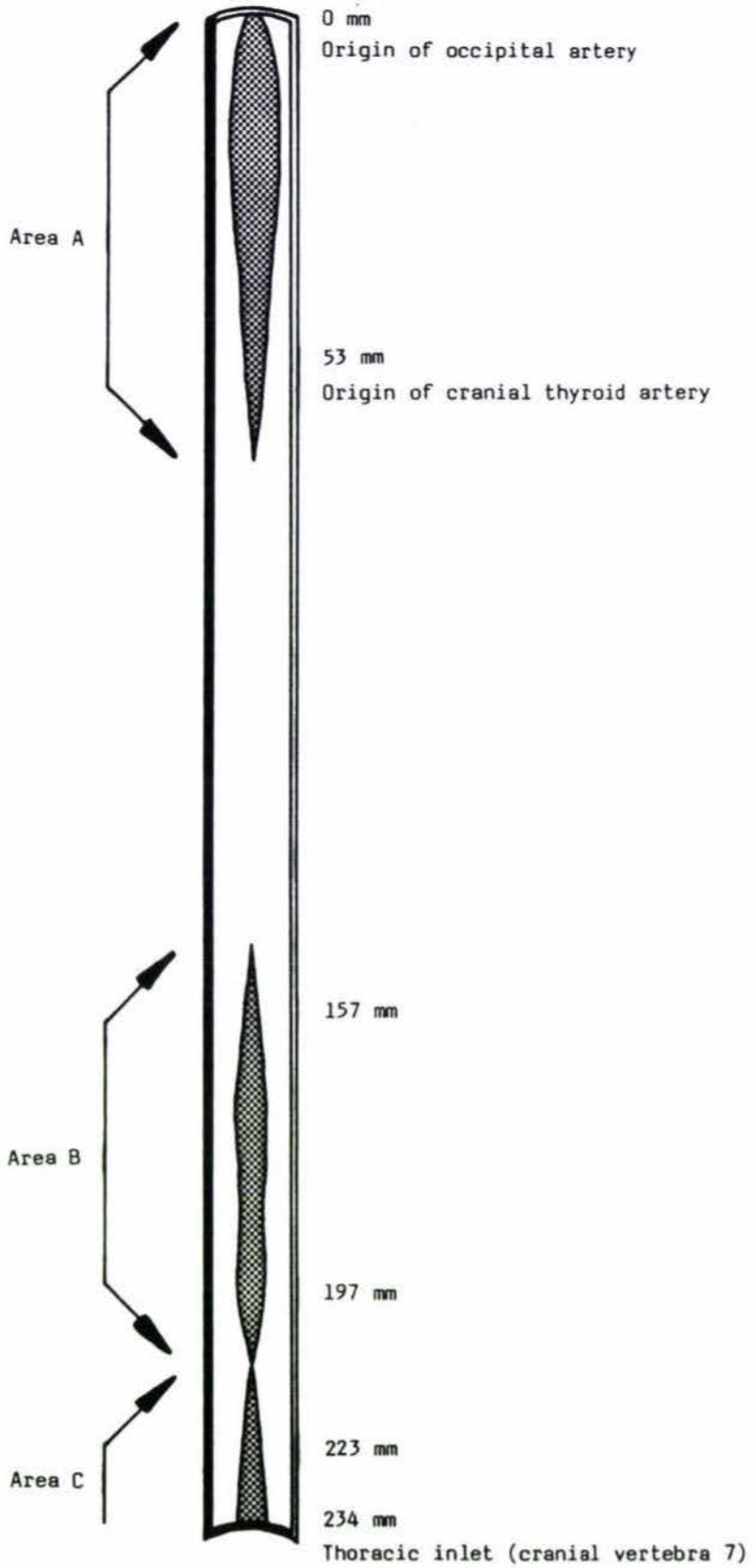


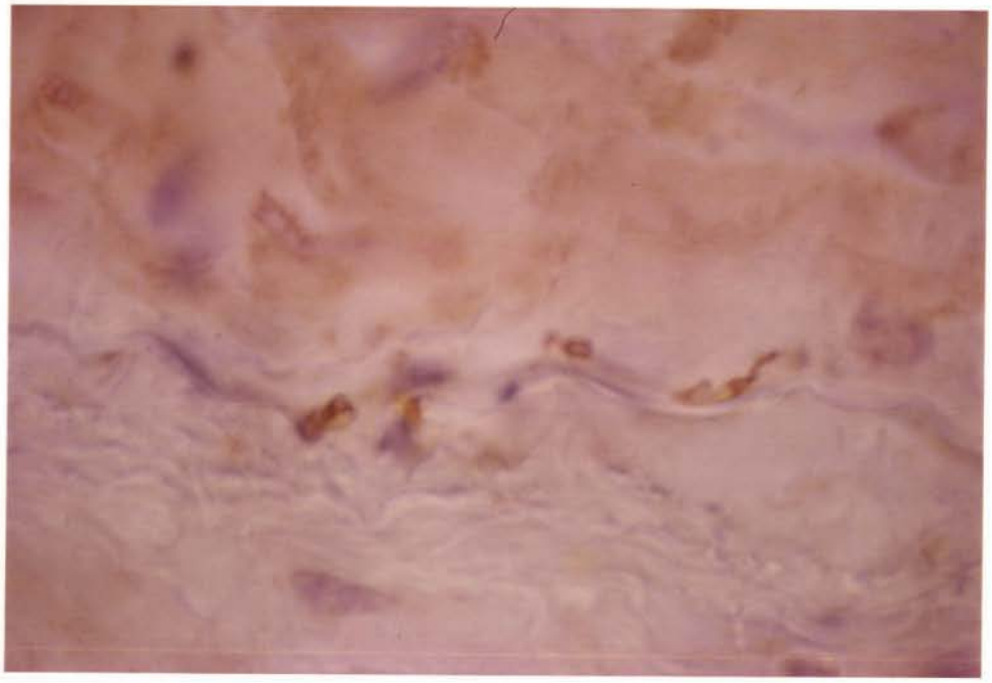
Figure 4.7 The distribution of baroreceptors along the left common carotid artery in sheep number 6 of experimental series 2. The extent of the nerve fiber area is indicated by stippling.

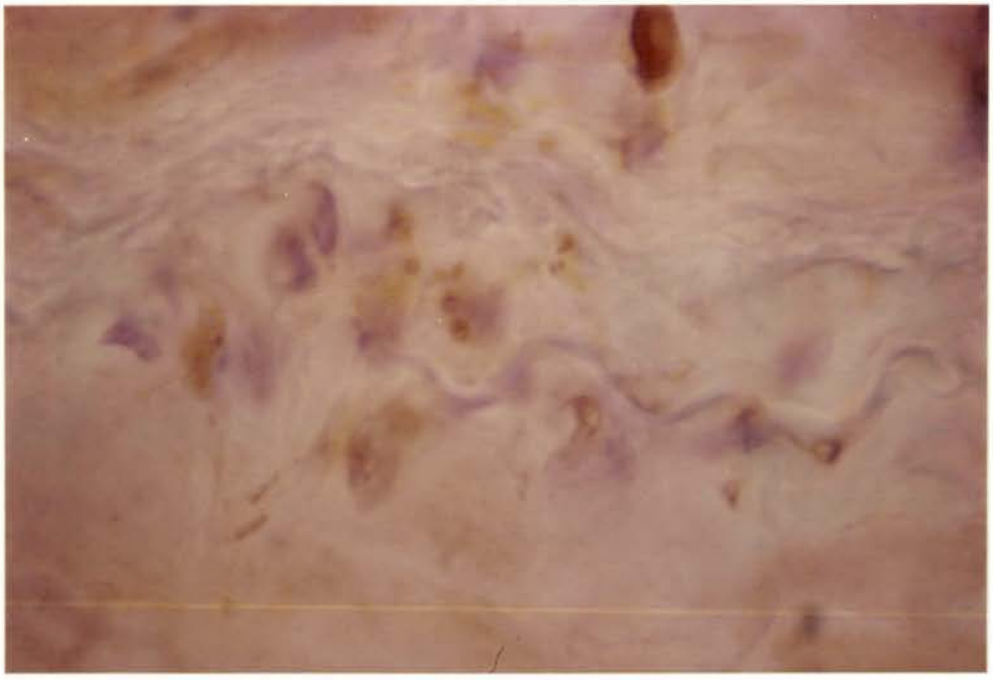
Plate 4.10 Transverse section of the medio-adventitial border of the left common carotid artery demonstrating the terminal nerve fibers of area A.

Magnification: 1660. Stain: Anti-NSE antibody immunocytochemistry.

Plate 4.11 Transverse section of the medio-adventitial border of the left common carotid artery demonstrating the terminal nerve fibers of area A.

Magnification: 1660. Stain: Anti-NSE antibody immunocytochemistry.





An extremely sparse vasomotor innervation of the common carotid artery was demonstrated within the tunica media. These undulating fibers ran both longitudinally and circumferentially and penetrated to the outer half of the tunica media only.

4.4.4.3 Thickness of the Wall in Nerve and Non-nerve Fiber Areas of the Common Carotid Artery

Paired t-tests of the tunical and total wall thickness at six measurement sites (for raw data see Appendix 3, Table 5) were undertaken within and between areas A, B and C and the intervening areas (see Figure 4.8). This statistical analysis revealed that of the 48 comparisons undertaken, only 11 were significant.

Of the latter comparisons, within areas A, B and C the tunica media of site 3, situated on one extreme of the nerve fiber area, was thicker than in the corresponding site on the opposite side of the artery where there were no nerve fibers. The tunica media and tunica adventitia of the intervening areas were thicker, whereas the tunica intima was thinner at site 1, adjacent to the large medial nerve trunk, than in the corresponding site on the opposite side of the vessel. Further, at site 5, situated on one extreme of the nerve trunk, the tunica adventitia and total wall were thicker than in the opposite arterial wall. Comparisons of areas A, B and C with the intervening areas demonstrated that the tunica intima and tunica media of site 1, adjacent to the large medial nerve trunk in areas A, B and C, were thicker than in the intervening areas. Similarly, at site 2, a non-nerve fiber area opposite to the nerve trunk, the tunica adventitia and total wall were thicker than in the intervening areas.

It, therefore, appears that in the nerve fiber areas of A, B and C, neither the tunica medial nor tunica adventitial thickness differed significantly from the non-nerve fiber areas or the intervening areas. Overall, given the variable nature of the differing depths, the thickness of the tunica intima, tunica media and tunica adventitia and hence the total wall thickness of the common carotid artery was little modified down the entire length of the left vessel studied.

See Table 4.3.

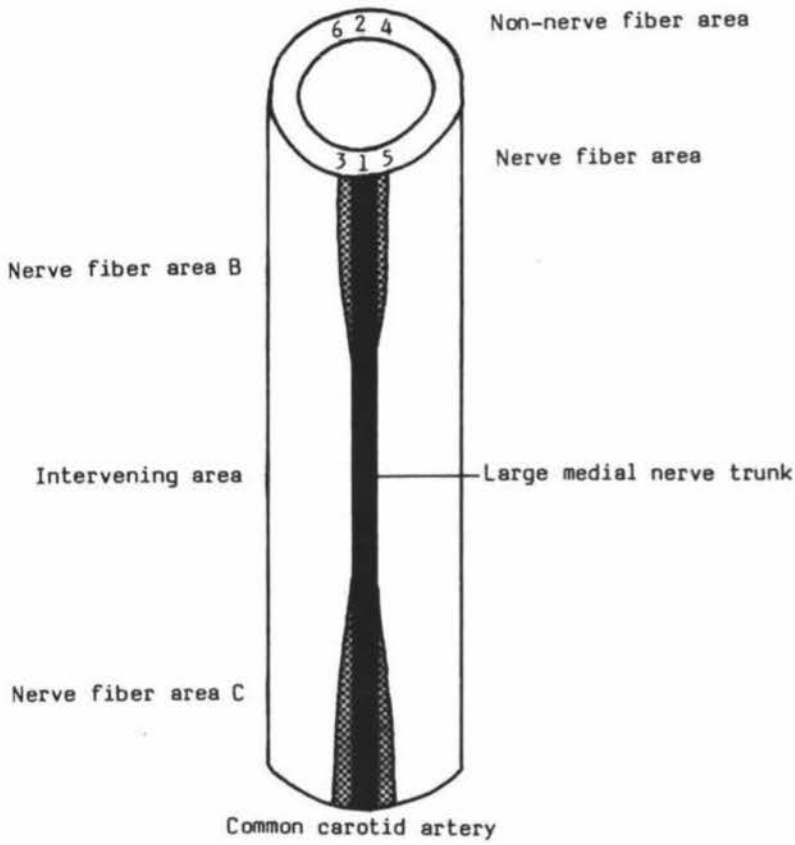


Figure 4.8 Measurement sites of the wall of the left common carotid artery

TABLE 4.3 ARTERIAL WALL THICKNESS (MEAN ± SEM, μm) IN NERVE FIBER AREAS A, B AND C AND NON-NERVE FIBER AREAS OF THE LEFT COMMON CAROTID ARTERY OF SHEEP NUMBER 6 IN EXPERIMENTAL SERIES 2 AND RESULTS OF t-TEST ANALYSES

Location in Common Carotid Arterial Wall	No. Sections per Area	Site Number					
		NFA 1	NNFA 2	NFA 3	NNFA 4	NFA 5	NNFA 6
Tunica intima: Areas A, B and C	10	9 ± 0.9	9 ± 1.1	7 ± 0.8	7 ± 0.5	7 ± 0.6	8 ± 0.8
Intervening areas	8	6 ± 0.4	7 ± 0.9	6 ± 0.5	7 ± 0.7	6 ± 0.8	6 ± 0.9
Tunica media: Areas A, B and C	10	409 ± 13.8	366 ± 15.9	387 ± 17.2	339 ± 11.3	367 ± 11.5	371 ± 23.5
Intervening areas	8	364 ± 12.4	318 ± 16.8	339 ± 18.7	333 ± 18.0	346 ± 7.3	324 ± 16.9
Tunica adventitia: Areas A, B and C	10	139 ± 16.7	145 ± 15.8	121 ± 11.1	137 ± 26.1	123 ± 26.0	119 ± 11.7
Intervening areas	8	161 ± 11.3	93 ± 5.9	122 ± 14.3	91 ± 6.7	148 ± 11.5	110 ± 6.2
Total vessel wall: Areas A, B and C	10	565 ± 14.5	526 ± 29.0	518 ± 25.3	483 ± 34.1	503 ± 19.8	506 ± 26.2
Intervening areas	8	539 ± 16.1	416 ± 20.2	473 ± 29.4	430 ± 20.5	519 ± 20.6	438 ± 19.8

Contrast Number	Source of Variation	Site Number	Degrees of Freedom	t
	Tunica intima: Areas A, B and C			
1	Intervening areas	1 versus 2	14	2.401*
2	Areas A. B and C versus intervening areas	1	16	2.533*
3	Tunica media: Areas A, B and C	3 versus 4	18	2.339*
4	Intervening areas	1 versus 2	14	2.218*
5	Areas A, B and C versus intervening areas	1	16	2.381*
	Tunica adventitia: Areas A, B and C			
6	Intervening areas	1 versus 2	14	5.261***
7		5 versus 6	14	2.893*
8	Areas A, B and C versus intervening areas	2	16	2.764*
	Total vessel wall: Areas A, B and C			
9	Intervening areas	1 versus 2	14	4.748***
10		5 versus 6	14	2.784*
11	Areas A, B and C versus intervening areas	2	16	2.953**

4.5 DISCUSSION

4.5.1 The Carotid Sinus

Sheep have not featured conspicuously in studies of the carotid sinus region but, as is evident from the preceding chapter, they show variations in the baroreceptor reflex responses characteristic in other species. It was in an effort to learn whether these reflex differences were supported by structural modifications that this histological study was undertaken.

4.5.1.1 Structure of the Wall of the Carotid Sinus

In this work the tunica media of the carotid sinus predominantly contained elastic laminae with a few smooth muscle cells between each succeeding elastic membrane. In the sheep, therefore, the carotid sinus tunica media was classified as of the elastic type according to the three vessel medial types of Arey (1957). This finding is consistent with those of Sha-Ban (1974) in the sheep and Rees (1966, 1967a), Rees and Jepson (1970) and Bagshaw and Fischer (1971) in most mammalian species except the hedgehog (Adams, 1957).

The thickness of the carotid sinus tunica intima, tunica media, tunica adventitia, and total vessel wall relative to that of the adjoining vascular structures, was difficult to determine in these specimens. The reasons for this problem was that, in the sheep, the carotid sinus is located at the origin of the occipital artery. The retraction of this artery upon removal of the common carotid artery from the animal and further shrinkage during preparation made location of the occipital artery difficult following fixation. The carotid sinus could, therefore, only be found by cutting serial transverse sections of the cranial common carotid artery. In view of this, sections of the carotid sinus were often cut obliquely making accurate measurement of the tunical layers difficult. A thinning of the tunica media in association with an increased tunica adventitia thickness was, however, noted in many areas.

May (1965), Ábrahám (1969) and Sha-ban (1974) reported that in the sheep the wall of the carotid sinus was reduced in total thickness compared with the adjoining vascular structures - this is contrary to the view held by most of the recent workers in other mammals (Rees, 1966, 1967a; Rees and Jepson, 1970; Bagshaw and Fischer, 1971). This thinning of the media and thickening of the adventitia is in agreement with the findings of May, Ábrahám and Sha-Ban in the sheep and of work in other mammals (de Castro, 1928; Sunder-Plassman, 1930; Addison, 1944, 1945) except the hedgehog (Adams, 1957).

4.5.1.2 Innervation of the Carotid Sinus

4.5.1.2.1 Sensory Innervation

In this study, the pattern of innervation of the carotid sinus was essentially confined to the structurally modified vessel wall, i.e., thinned, elastic tunica media and thickened tunica adventitia. In modified areas of the vessel wall where the external elastic lamina was clearly visible, the terminal arborisations did not pass beyond the medio-adventitial border. This is contrary to the work of Sha-Ban (1974) who traced fiber branches to the superficial media in the sheep, but similar to that of de Castro (1951), Ábrahám (1958, 1969) and Eyzaguirre and Uchizono (1961) in the sheep, and many other workers in other species (including de Castro, 1926, 1928, 1940; Sunder-Plassman, 1930, 1933; Ábrahám, 1941, 1949, 1953, 1958, 1964, 1967, 1969; Rees, 1966, 1967a,b, 1968). These terminal ramifications appear to be sufficiently characteristic in appearance to constitute presumptive evidence for baroreceptor terminals.

4.5.1.2.2 Vasomotor Innervation

In these sheep the vasomotor innervation of the carotid sinus was so sparse that the aforementioned innervation may be regarded as sensory. No other histological studies appear to have been reported on the vasomotor innervation of the carotid sinus in the sheep.

4.5.2 The Common Carotid Artery

That the carotid arterial baroreceptor zone might be more extensive than had been previously supposed (Bazett and Bard, 1956) was suggested by Nonidez (1935, 1937, 1941), Green (1953, 1954a,b, 1967), Boss and Green (1954a,b, 1956) and Aumonier (1972) who located a number of supplementary baroreceptor areas in the common carotid artery of the rabbit, cat and dog. Until this present study, no work appears to have been conducted on the sensory innervation of the common carotid artery of the sheep.

4.5.2.1 Structure of the Wall of the Common Carotid Artery

In the single vessel examined, the tunica media of the common carotid artery contained many elastic laminae and thick smooth muscle bands between each succeeding elastic membrane. Therefore, in the sheep the common carotid arterial tunica media was classified as of the musculoelastic type according to

the three vessel medial types of Arey (1957). This finding is similar to those of Sha-Ban (1974) in the sheep, and Rees (1966, 1967a), Rees and Jepson (1970) and Bagshaw and Fischer (1971) in various mammalian species.

The uniformity of the tunica intima, tunica media and tunica adventitia thickness and, therefore, total wall thickness down the entire length of the common carotid artery in this study corresponds to the findings of May (1965) in the sheep. In this work the structure of the common carotid arterial wall did not differ significantly between areas with concentrations of nerve fibers and regions with none, though occasionally the tunica media was thickened in the area of nerve fibers. These findings differ from those in the cat where a thinning and reduction in muscularity of the tunica media has been described in all areas of nerve fibers (Boss and Green, 1954a,b, 1956). These authors felt able, therefore, to distinguish the arterial composition associated with the origin of a branch from the modifications associated with baroreceptor innervation.

Few studies have been made on the composition of branches and most of these have been directed at the so-called medial defects (composed of collagen and elastin fibrils) associated with the development of saccular aneurysms. Branches are regions where vessel diameter and, hence intramural tension, changes rapidly and therefore the composition of the vessel wall might be expected to be modified. Berry (1973) found two basic variations of composition at branches:

1. where the wall of the branch formed an angle of less than 100° with the parent vessel - the number of elastic laminae was reduced in the wall of the smaller branch,
2. where the wall of the branch formed an angle of greater than 100° with the parent vessel - the number of elastic laminae was progressively and gradually reduced by fusion of one with another. Stehbens (1957) stated that medial defects occurred principally at this type of branch.

Clark and Glagov (1985) reported that the organisational and functional structural units of the tunica media and the musculo-elastic fascicle was smallest, least uniform and most numerous in regions of branching or curvature. The musculo-elastic fascicle is composed of the elastic lamina, together with smooth muscle and the scleroprotein between it and the next lamina. These two patterns of composition are probably different responses to changing wall tensions in these areas. Most investigators have suggested that tunica medial defects could not be linked to the development of weak arterial

walls; they occur without obvious detriment and are merely a biologically disadvantageous aspect of normal development (Stehbens, 1957, 1963; Crawford, 1959; Hassler, 1961).

No histological studies appear to have been conducted on the common carotid artery of the rabbit and dog to measure the thickness of the tunica media and tunica adventitia and, therefore, total wall thickness in areas with and without baroreceptor innervation.

From research in the rat, guinea-pig, rabbit, cat, dog and human, Boyd (1937) and later Rees (1967a) proposed that the specialisation of the carotid sinus tunica media and tunica adventitia ensured that the baroreceptors in the region were readily stimulated by pressure changes. The histological arrangement in the hedgehog reported by Adams (1957) seems particularly relevant to the controversy of whether or not a thinning, decreased muscularity and increased elasticity of the tunica media and thickening of the tunica adventitia is necessary for baroreceptor function. Although the hedgehog has a large carotid sinus, this does not show the same modification of its wall as characterises the carotid sinus of other mammals. The tunica media was not reduced at all in thickness or muscularity, and further the wall of the sinus was considerably thicker than that of either the internal carotid artery above the carotid sinus or the common carotid artery below it even though there was no comparable increase in elasticity. By contrast, the origin of both the occipital and ascending pharyngeal arteries and the short common trunk from which they arise had very thin fibrous walls. Furthermore, there was a very substantial baroreceptor innervation of the carotid sinus and specialised wall at the origin of the occipital and ascending pharyngeal arteries, although the occipital and ascending pharyngeal arteries appeared to dominate the baroreceptor function of these zones. The fact that this innervation was just as dense in the thick walled carotid sinus as it was around the adjacent thin-walled occipito-ascending pharyngeal trunk discounts the consistent structural differences of the kind described by Boss and Green (1954a, 1956).

The lack of structural specialisation in areas of baroreceptor innervation in the common carotid artery of the sheep in this study and the carotid sinus of the hedgehog (Adams, 1957) suggests that these modifications are not an essential adaptation for baroreceptor function.

4.5.2.2 Innervation of the Common Carotid Artery

4.5.2.2.1 Sensory Innervation

In the common carotid artery of this research, three areas of nerve fibers designated A, B and C were found distributed along the length of the left common carotid artery between the level of the occipital artery and the thoracic inlet. These fusiform areas were situated on the medial side of the vessel adjacent to a large nerve trunk. The terminal ramifications demonstrated in these areas were similar to those found in the carotid sinus and were presumed to be baroreceptor terminals. No other histological studies appear to have been reported on the sensory innervation of the common carotid artery in the sheep.

Ábrahám (1969), however, found that in cattle and humans there were many sensory nerve bundles in the common carotid artery immediately caudal to the sinus. These consisted of two to three, and occasionally more, thick myelinated fibers which usually branched after a short path, the rami gradually became thinner and formed plexuses with many lamellar thickenings before the end fibers terminated in all kinds of end formations. These terminations were lesser in number and smaller than those of the carotid sinus and did not show the typical ivy-leaf shape. The terminal relationship between nerve and muscle occurred across the medio-adventitial border opposite to deficiencies in the external elastic lamina (Rees, 1967a). In view of the differences in end formation number and structure in cattle and humans, the fibers passing in the wall of the common carotid artery seemed to distribute from the vagus nerve, although these structures are by no means identical with the vagally supplied baroreceptors described by Ábrahám (1969) in the aortic arch of many species.

The sensory baroreceptor innervation of the feline right and left common carotid arteries has been described in detail by Green (1953, 1954a,b, 1967) and Boss and Green (1954a, 1956) who located five areas of nerve fibers designated 1, 1a, 2, 3 and 4.

Assuming that the length of the ovine common carotid artery was approximately twice (actual figure 1.744) that of the vessel in the cat, areas A, B and C in the sheep, therefore, corresponded to areas 4, 2 and 1 together with 1a, respectively. The sheep appeared to lack area 3 of the cat. Although the ovine longitudinal (40-53 mm in the sheep, 1-8 mm in the cat) and

circumferential extension (20-70% in the sheep, 35% in the cat) of these areas was relatively greater than that in the cat, the form of the nervous structures were similar.

Aumonier (1972) confirmed the findings of Green (1953, 1954a,b, 1967) and Boss and Green (1954a, 1956) and further studied the baroreceptor areas in the common carotid arteries of the rabbit and dog. The rabbit conformed to the findings for the cat, but the dog lacked areas 1a, 2 and 3. It thus seems that of the rabbit, cat, dog and sheep studied, the sheep has the most extensive sensory innervation of the common carotid artery. This is because even though the sheep lacks area 3 of the cat, the greater longitudinal and circumferential extensions of the ovine regions ensures a larger total area of baroreceptor innervation in the sheep.

In the cat, the right nerve fiber area 4 was innervated by a right vagal branch arising at the level of the nodose ganglion; the remaining areas on the right side of the neck each received fibers from the right recurrent laryngeal nerve originating from the vagus at the origin of the subclavian artery from the common carotid artery. On the left side of the neck all the nerve fiber areas were supplied by the left recurrent laryngeal nerve which separates from the vagus at the aortic arch.

The origin of the recurrent laryngeal nerve in the sheep is similar to that in the cat; it passes around the caudal face of the arch and then runs along the left ventral surface of the trachea to the thoracic inlet. In the cervical region the nerve follows the ventrolateral surface of the trachea, inclining more dorsally towards the cranial end of the trachea, to pass across the dorsal surface of the thyroid gland and disappear beneath the cricopharyngeal muscles on the caudo-dorsal surface of the larynx. In view of the fact that the baroreceptor areas A, B and C of this study straddle a large nerve trunk of the medial surface of the left common carotid artery, the recurrent laryngeal nerve of the sheep follows the ventrolateral surface of the trachea which is medial to the common carotid artery and the majority of baroreceptor areas in the feline common carotid artery are supplied by the recurrent laryngeal nerve, it is proposed that the baroreceptor areas in the left common carotid artery of the sheep may be innervated by the left recurrent laryngeal nerve. It is equally possible, however, that baroreceptor areas A, B and C are innervated by the left vagus nerve which, in the sheep, descends the neck related to the dorso-lateral or dorso-medial surface of the common carotid artery in the common fascial sheath.

4.5.2.2.2 Vasomotor Innervation

Large musculoelastic vessels such as the common carotid artery are not well innervated by vasomotor nerves (Burnstock, 1975). In this work the adrenergic vasomotor innervation of the common carotid arterial wall was extremely sparse, with only a few circumferential and longitudinal fibers passing in the tunica adventitia and outer tunica media. The vast majority of axons in densely innervated areas of the ovine common carotid artery may, therefore, be regarded as sensory.

These findings agree with those of Keatinge (1966) who found adrenergic nerve fibers to penetrate the outer half to three-quarters of the tunica media smooth muscle, with none in the inner quarter to one-half of the media of the sheep. Most of these fibers ran circumferentially giving off branches to the thick circular bands of collagen and elastin, and the irregular collagen strands between the smooth muscle cells and in the deeper parts of the tunica media. A few fibers were described as running longitudinally in the tunica adventitia and in the thick collagen bands that sometimes penetrated the outer portion of the tunica media. Seven to fourteen days after superior cervical ganglionectomy, all these adrenergic nerve fibers disappeared (Keatinge, 1966).

In the rabbit, however, Rees (1966, 1967b) stated that the adrenergic fibers were confined to the medio-adventitial border. There is some evidence to suggest that the degree of adrenergic nerve penetration into the arterial wall is largely related to wall thickness (Ehinger, Falck and Sporrong, 1967; Dolezel, 1972; Bevan and Purdy, 1973). Thus in large animals such as the dog, sheep, pig, cow and human, nerves commonly penetrated the tunica media of large elastic, musculoelastic and muscular arteries, whereas even the media of the largest vessels in the mouse, rat, guinea-pig and rabbit was rarely penetrated.

The sparsely innervated tunica media such as that found in both the carotid sinus and common carotid artery in this study is evidently very sensitive to circulating adrenal medullary catecholamines, the absence of nerves in the tunica media leaves the muscle devoid of neural terminal sites for noradrenalin inactivation, thus facilitating the diffusion of the catecholamine from the adrenals to the vascular muscle (Furness and Burnstock, 1975; Nilsson, Goldstein and Nilsson, 1986). Burnstock (1975) and Nilsson, Goldstein and Nilsson (1986) have argued that the response to

nerve stimulation in such vessels requires a higher frequency of stimulation, is slow in onset and weaker compared to that of smaller arteries. Under physiological conditions large blood vessels, such as the carotid sinus and common carotid artery, appear to be mainly under hormonal control by circulating catecholamines - any adrenergic nerve control is weak and sluggish. The relative importance of circulating catecholamines is poorly understood. It may be that circulating catecholamines have little effect on the activity of most vessels in inactive animals, but that during such situations as fright or heavy exercise, the resulting high levels of circulating catecholamines have profound effects on vessel tone, although there are differential effects on different types of vessel and in different species (Burnstock, 1975).

CHAPTER 5

DISCUSSION

The carotid sinus baroreceptor reflex system has been intensively studied since its discovery, perhaps largely because of the relative ease with which these structures can be approached experimentally. The latter consideration is fortunate because the carotid sinus reflex is probably the most important arterial reflex for circulatory homeostasis under normal physiological conditions.

The carotid sinus is a dilatation at the origin of the internal carotid artery in many species, including the rat, rabbit, dog and human. In animals such as the sheep, in which the extracranial part of the internal carotid artery is absent, the carotid sinus is located at the undilated origin of the occipital artery. The aim of this project was to improve the knowledge of the carotid sinus baroreceptor control mechanism in the sheep and compare it with that described in other species with a true carotid sinus. The role of carotid arterial baroreceptors was tested by the simple technique of common carotid arterial clamping alone and in combination with other cervical vessels.

Unilateral clamping of the common carotid artery immediately reduced the mean blood pressure and pulse pressure in the ipsilateral carotid sinus to a stable pressure that was probably below the baroreceptor threshold. The fall in cephalic pressure which occurs upon carotid arterial occlusion induces an immediate compensatory increase in blood flow in the contralateral common carotid artery, the vertebral arteries reacting to a lesser extent. This collateral flow pattern is a reflection of the clearly defined area supplied by these vessels. In the sheep, the entire brain is supplied from the common carotid arteries, whereas vertebral blood supplies only the cervical spinal cord and, in some individuals, the medulla oblongata. The large and sustained fall in carotid sinus pressure induced by clamping suggests that the many arterial anastomoses provide only minimal blood flow into the common carotid artery, so that the baroreceptor reflex is activated.

Bilateral clamping of the common carotid arteries immediately produced a lower stable mean blood pressure and pulse pressure within both carotid sinuses than occurred during unilateral carotid arterial clamping. The large fall in cephalic pressure which follows bilateral common carotid arterial occlusion induces an immediate compensatory increase in flow in the vertebral arteries that is sufficient to maintain cortical

activity (Linzell and Waites, 1957; Baldwin and Bell, 1963b, 1963d). The resultant reflex rise in peripheral mean blood pressure and pulse pressure was significantly greater than when one common carotid artery was clamped. This is a reflection of a larger population of baroreceptors detecting the low carotid sinus pressures during bilateral occlusion, compared with unilateral clamping.

In one-third of the sheep in this study, clamping the left common carotid artery caused a greater reflex rise in peripheral mean blood pressure than did occlusion of the right carotid artery. This difference in response may be due to the pattern of baroreceptor distribution along the common carotid artery. To date, only the sensory innervation of the left common carotid artery of one sheep, in which clamping the left or right carotid artery caused reflex responses of similar magnitude, has been investigated. In this vessel, three areas of nerve fibers, designated A, B and C, were found distributed along the length of the common carotid artery. The terminal nerve ramifications demonstrated in these areas were similar to those found in the carotid sinus and were presumed, in view of the extremely sparse vasomotor innervation, to connect with baroreceptors. It is assumed that the baroreceptor distribution along the right common carotid artery is similar to the left in this animal. However, this may not be in the case in the sheep in which the response to left common carotid arterial clamping was greater than the contralateral right artery, the baroreceptor innervation could have been extremely sparse in the right vessel.

Further histological studies of the ovine common carotid arterial baroreceptor innervation are necessary before the reflex response to left and right carotid arterial clamping can be correlated to the baroreceptor distribution. It would be most desirable to determine initially the physiological nature of the response to both unilateral left and right common carotid arterial clamping prior to, and following, vagotomy in each sheep, and group the animals into two sets - those in which the peripheral mean blood pressure response is greater upon left than right carotid arterial occlusion, and those in which the response to left and right occlusion is similar. The histological examination of the baroreceptor distribution and associated structure of the wall in the left and right common carotid artery could then be undertaken in individuals from each of the two sets.

On the other hand, the difference in left and right common carotid arterial reflex responses could be due to the sensitivity of the baroreceptors: the receptors in the left carotid artery being more sensitive than those in the contralateral right artery. That the baroreceptors within the ovine common carotid artery may be less sensitive than those in the carotid sinus has already been suggested by the low elastin content and

lack of tunica medial thinning associated at the areas of dense innervation. In fact, in the one common carotid artery studied the tunica media appeared thicker in regions of baroreceptor innervation. A similar lack of structural modification is reported in the aortic arch, the baroreceptors of which appear to be less sensitive to normal mean blood pressures than are the carotid sinus receptors (Edis, 1971; Donald and Edis, 1971; Pelletier, Clement and Shepherd, 1972). In the dog, maximal electrical stimulation of the central end of the carotid sinus nerve produced a reflex blood pressure and heart rate response that did not differ quantitatively from that seen upon electrical stimulation of the aortic arch recurrent laryngeal nerve (Cyon and Ludwig, 1866; Hering, 1924, 1927; Kendrick and Matson, 1973). There are, however, important differences in the level of baroreceptor excitation achieved by a given pressure stimulus (Edis, 1971). The stimulus-frequency experiments of Kendrick and Matson (1973) suggest that increasing the level of baroreceptor discharge is of less importance than baroreceptor recruitment in response to raising the pressure in the carotid sinus and the rate of baroreceptor discharge is of greater importance than recruitment of the aortic arch. Pelletier, Clement and Shepherd (1972) found that in the dog the threshold pressure sufficient to elicit a change in afferent impulse activity in the carotid sinus nerve was 62 mmHg, whereas that of the recurrent laryngeal nerve was much higher, averaging 95 mmHg. Moreover, the curve relating blood pressure of the integrated activity of the recurrent laryngeal nerve is substantially displaced to the right, except at the lowest and highest pressures, indicating that over a broad range the functionally significant aortic arch baroreceptors have a relatively high pressure threshold and are less sensitive to normal blood pressures (Donald and Edis, 1971; Pelletier, Clement and Shepherd, 1972). The aortic arch baroreceptors, therefore, only exert a significant buffering action at higher blood pressures and are virtually ineffective at blood pressures below normal levels, acting predominantly as an antihypertensive mechanism.

Further studies in which the left and right common carotid arteries are isolated would enable the variation of intraluminal pressure over a wide range, encompassing the linear portion of the baroreceptor reflex where reflex gain is at a maximum. Common carotid arterial pulse pressure may be held relatively constant and, provided the vagus nerves are cut, minimal buffering by the aortic arch and cardiopulmonary baroreceptors of peripheral pressure changes resulting from intraluminal pressure variation would occur. As the common carotid arterial blood pressure can be changed independently of peripheral pressure, the sensitivity of the carotid arterial baroreceptor population may be computed.

It is, of course, possible that both the distribution and sensitivity of baroreceptors vary between the left and right common carotid arteries. Thus, a large number of baroreceptors or more sensitive receptors in the left common carotid artery would detect a decreased intraluminal pressure and induce a peripheral mean blood pressure rise that is greater than from the right vessel.

In two sheep of this study, section of the right vagus nerve totally abolished the reflex rise in peripheral mean blood pressure and pulse pressure to occluding the right common carotid artery. In these cases, neither the size of the baroreceptor population nor its sensitivity appeared to be the cause of this effect. Rather the nature of the innervation appeared to be critical. In most mammals, the carotid sinus receives its nerve supply from the carotid sinus and external carotid nerves, the extent of innervation by the vagus and hypoglossal nerves being minimal (Adams, 1958). It is possible that in these two animals the baroreceptors of both the right carotid sinus and common carotid artery were innervated by the right recurrent laryngeal or vagus nerves, so that section of the latter nerve completely denervated these structures and nullified the reflex response.

There was a tendency for caudal clamping of the common carotid artery to induce a greater peripheral mean blood pressure response than cranial carotid arterial clamping. This observation may be explained by reference to the presence of baroreceptors down the length of the left common carotid artery of the sheep. Occlusion of the common carotid artery at a caudal position reduces the mean blood pressure and pulse pressure both within the carotid sinus and along the length of the carotid artery distal to the clamp. A relatively larger population of baroreceptors may detect these low pressures whereas fewer baroreceptors monitor the normotensive or hypertensive systemic pressures. A peripheral mean blood pressure response is, therefore, induced on caudal clamping that is greater than the reflex response upon cranial clamping of the common carotid artery where the hypotensive baroreceptor population essentially includes only those receptors within the carotid sinus and the baroreceptors down almost the entire length of the common carotid artery are distal to the clamp and detect the normotensive or hypertensive peripheral mean blood pressure, therefore, buffering any rise.

The magnitude of reflex responses to clamping different levels of the common carotid artery is a subject that deserves further study in a larger population of sheep.

Common carotid arterial clamping is one of several methods of assessing the carotid arterial baroreceptor reflex. Several problems are inherent in the method of carotid arterial clamping when utilised to demonstrate the baroreceptor reflex. These include:

1. possible changes in cerebral perfusion pressure during clamping (Cox and Bagshaw, 1979),
2. during clamping carotid sinus and common carotid arterial mean blood pressure is reduced from the basal peripheral mean blood pressure by an amount dependent upon the magnitude of the preocclusion pressure, the degree of clamping and the state of the vascular anastomoses between the vertebral and carotid systems (Whisnant, Millikan and Wakim, 1958),
3. as carotid sinus and common carotid arterial pressure is only reduced during clamping the stimulus to the baroreceptors is unidirectional, that is, there is an unloading of the receptors (Bagshaw and Cox, 1977),
4. in addition to changes in mean blood pressure, clamping also induces a decrease in carotid sinus and common carotid arterial pulse pressure which increases the reflex gain (Cox and Bagshaw, 1980a).

In view of these constraints, it may be advisable to study the common carotid arterial baroreceptor reflex by a variant of the Moissejoff (1927) technique in which pressure is varied within the vascularly isolated common carotid artery. It may even be better to use a conscious animal that does not require general anaesthesia which alters the characteristics of the baroreceptor reflex and modifies its interactions with neural inputs that originate from, or have synaptic relays in supramedullary brain centers (Korner, 1971; Kircheim, 1976). An indirect method used in investigating the baroreceptor reflex in the conscious state has been to alter blood pressure by inflating cuffs placed around the common carotid artery or by injecting pressor or depressor drugs which are believed to have no direct chronotropic action (Korner and Shaw, 1971; Pickering, Gribbon and Sleight, 1972; Korner, West, Shaw and Uther, 1974; Farris, Iannos, Jamieson and Ludbrook, 1980).

In ten of the fourteen sheep in this study, unilateral or bilateral section of the vagi caused a rapid 12 mmHg fall in the basal peripheral mean blood pressure. This effect may have resulted from the loss of peripheral chemoreceptor vagal afferents that reflexly maintain a degree of vasoconstriction due to the hypoxic, hypercapnic and acidaemic conditions caused by inadequate ventilation.

Overall, bilateral vagotomy appeared to enhance the peripheral mean blood pressure and pulse pressure response to clamping the cervical blood vessels; heart rate, on the other hand, was not significantly affected. Vagotomy removes the cardiac

parasympathetic components of the carotid sinus, common carotid arterial and aortic arch baroreceptor reflexes and deletes the vascular influence due to interruption of vagally mediated reflexes originating in the aortic arch and cardiopulmonary regions. Therefore, prior to vagotomy, the peripheral mean blood pressure and pulse pressure response to common carotid arterial clamping is moderate because the aortic and cardiopulmonary baroreceptors buffer the rise. Interruption of these afferents by sectioning the vagi eliminates any buffering action so that the full extent of the pressor response is observed. The enhanced occlusion response following vagotomy is similar to that reported in other species (Sagawa and Watanabe, 1965; Stinnett, Peterson and Bishop, 1979; Stephenson and Donald, 1980; Stinnett, Sepe and Manguson, 1981).

The work of this study has provided possible explanations for the three questions posed by the student demonstration of the carotid sinus baroreceptor reflex in the sheep: namely, what caused the fall in basal blood pressure upon section of both the left and right vagus nerves; why was the blood pressure and heart rate rise upon bilateral common carotid arterial clamping so poor; and why did bilateral vagotomy fail to enhance these responses to clamping?

In dorsally recumbant sheep, peripheral chemoreceptor vagal afferents may maintain a degree of reflex vasoconstriction due to the hypoxic, hypercapnic and acidaemic conditions caused by inadequate ventilation. Bilateral vagotomy will, therefore, interrupt this pressor reflex and induce a fall in basal blood pressure. The demonstration of the presence of extensive baroreceptor innervation down the length of the ovine common carotid artery means that the physiology student may, during occlusion of the artery, clamp over an area of baroreceptors. This action will stimulate the receptors beneath the clamp, therefore increasing the size of the baroreceptor population that buffers the systemic occlusion response and inducing a poor blood pressure and heart rate rise. Combined effects of vagal innervation of the carotid sinus or common carotid arterial baroreceptors may result in the failure, in some animals, of bilateral vagotomy to enhance the reflex response to clamping. Section of the vagus nerve in these individuals would, therefore, completely denervate these receptors and depress, rather than enhance, the reflex rise in blood pressure and heart rate.

APPENDIX 1

Solutions

I - Kaiserling's fixing fluid

Formalin	400 ml
Potassium acetate	60 g
Potassium nitrate	30 g
Tapwater	2 l

II - Solution F (Sha-Ban, 1974) volume %

Glycerine	10%
Formaldehyde	3%
Ethyl alcohol	3%
Glacial acetic acid	1%
Saturated aqueous picric acid	0.1-1.0%

III - Bouin's Fluid (Culling, 1974)

Picric acid, saturated aqueous solution	75 ml
Formalin (40% formaldehyde)	25 ml
Glacial acetic acid	5 ml

IV - Albumin Solution

White of egg
Glycerin
Distilled water
Thymol

Mix equal parts of egg white, glycerin and distilled water. Filter through coarse filter paper. Add a thymol crystal.

V - Poly-L-Lysine Solution

Poly-L-lysine hydrobromide (MW > 150 000, Sigma Chemical Co., USA)	10 mg
Distilled water	10 ml

Store frozen

VI - Phosphate Buffered Saline, pH 7.2

Sodium chloride	36 g
Disodium hydrogen phosphate (anhydrous)	4.54 g
Sodium dihydrogen phosphate ($2H_2O$)	1.09 g
Distilled water	to 4 litres

VII - Lugol's Iodine

Potassium iodide	10 g
Distilled water	25 ml
Iodine	5 g
Distilled water	to 500 ml

Dissolve potassium iodide in distilled water. Add iodine. Make up final volume to 500 ml with distilled water.

VIII - Verhoeff's Haematoxylin

5% Alcoholic haematoxylin	20 ml
10% Ferric chloride	8 ml
Verhoeff's iodine	8 ml

Prepare immediately before use.

IX - Van Giesen

1% Aqueous acid fuchsin	10 ml
Saturated aqueous picric acid	100 ml

X - Sucrose-Potassium-Phosphate Glyoxylic Acid Solution, pH 7.4

Sucrose	10.2 g
Potassium dihydrogen phosphate	4.8 g
Distilled water	100 ml
Glyoxylic acid	1.5 g
IN NaOH	
Distilled water	to 150 ml

Dissolve sucrose and potassium dihydrogen phosphate in water using a magnetic stirrer. Add glyoxylic acid and stir until the solution is clear. Titrate solution to pH 7.4 with IN NaOH. Make up final volume to 150 ml with distilled water.

XI - 1% Bovine Serum Albumin

Bovine serum albumin	0.5 g
Phosphate buffered saline (solution IV)	50 ml

XII - Diaminobenzidine Solution

3,3'diaminobenzidine tetrachloride	5 mg
Tris buffer (solution XII)	10 ml
1% hydrogen peroxide	1.2 ml

As this solution is unstable, use immediately. **Because Benzidine can be carcinogenic prevent undue exposure and contamination** by keeping one area of laboratory for the DAB development; wear gloves when handling solutions of DAB, and treat the solution with sodium hypochlorite to oxidise the DAB after it is finished with. Treat glassware, instruments and spills in a similar manner.

XIII - Tris Buffer, pH 7.6

Tris (hydroxymethyl methylamine)	3.05 g
1 M hydrochloric acid	18.5 ml
Distilled water	to 500 ml

XIV - Mayer's Haemalum

Haematoxylin	1 g
Distilled water	1 litre
Ammonium or potassium alum	50 g
Sodium iodate	0.2 g
Citric acid	1 g
Chloral hydrate	50 g

Add haematoxylin to water, heat gently to dissolve. Add alum, shake or heat gently to dissolve. Add sodium iodate followed by citric acid and chloral hydrate.

XV - Scott's Tapwater

Magnesium sulphate	20 g
Sodium bicarbonate	3.5 g
Distilled water	1 litre

APPENDIX 2

Experimental Clamping Protocols

Series 1 - Bilateral Common Carotid Arterial Clamping Before and After Vagotomy

Clamp L and R Cd CCA simultaneously, release (when blood pressure trace is stable)

Clamp L and R Cd CCA simultaneously, release

Cut L and R Vn and repeat above clamping regimen

Series 2 - Common Carotid Arterial Clamping Before and After Vagotomy

Clamp L Cd CCA, release (when blood pressure trace is stable)

Clamp R Cd CCA, release

Clamp R Cd CCA, release

Clamp L Cd CCA, release

Clamp L Cd CCA, release

Clamp R Cd CCA, release

Clamp L and R Cd CCA simultaneously, release

Clamp L and R Cd CCA simultaneously, release

Cut L (or R) Vn and repeat above clamping regimen

Cut remaining intact Vn and again repeat above clamping regimen.

Series 3 - Common Carotid Arterial Tying at Three Positions Before and After Vagotomy

Tie L (or R) Cd CCA, release (when blood pressure trace is stable)

Tie L (or R) Md CCA, release

Tie L (or R) Cn CCA, release

Tie L (or R) Cd CCA, release

Tie L (or R) Md CCA, release

Tie L (or R) Cn CCA, release

Tie L and R Cd CCA simultaneously, release

Tie L and R Cd CCA simultaneously, release

Cut L (or R) Vn and repeat above tying regimen

Cut remaining intact Vn and again repeat above clamping regimen.

Series 4 - Combined Common Carotid Arterial, Occipital Group and External Carotid Arterial Clamping Before and After Vagotomy

Clamp L Cd CCA, release (when blood pressure trace is stable)

Clamp R Cd CCA, release

Clamp R and L Cd CCA simultaneously, release

Clamp L Cn CCA, release

Clamp R Cn CCA, release

Clamp R and L Cn CCA simultaneously, release

Clamp L Cd CCA, followed by L OG, then L ECA; release in reverse order of clamping

Clamp R Cd CCA, followed by R OG, then R ECA; release in reverse order of clamping

Clamp L Cd CCA, followed by R OG, then L ECA; release in reverse order of clamping

Clamp R Cd CCA, followed by L OG, then R ECA; release in reverse order of clamping

Clamp L Cd CCA, followed by L OG, then R ECA; release in reverse order of clamping

Clamp R Cd CCA, followed by R OG, then L ECA; release in reverse order of clamping

Clamp L Cd CCA, followed by R OG, then R ECA; release in reverse order of clamping

Clamp R Cd CCA, followed by L OG, then L ECA; release in reverse order of clamping

Clamp L Cd CCA, L OG and L ECA, followed by R Cd CCA, R OG and R ECA; release in reverse order of clamping

Clamp R Cd CCA, R OG and R ECA, followed by L Cd CCA, L OG and L ECA; release in reverse order of clamping

Clamp L Cd then R Cd CCA, L then R OG, and L then R ECA; release in reverse order of clamping

Clamp R Cd then L Cd CCA, R then L OG, and R then L ECA; release in reverse order of clamping

Cut L and R Vn and repeat above clamping regimen.

APPENDIX 3

Raw Data

Table 1 Raw Data of Experimental Series 1

Sheep No.	Clamping Position	Peripheral Mean Blood Pressure, mmHg			
		Basal Value		Clamped Value	
		Int Vn	Cut LR Vn	Int Vn	Cut LR Vn
1	Cd LR CCA	77	75	82	97
	Cd LR CCA	90	92	107	111
2	Cd LR CCA	96	108	120	128
	Cd LR CCA	96	105	113	123

TABLE 2 RAW DATA OF EXPERIMENTAL SERIES 2

Sheep No.	Clamping Position	BASAL VALUES												CLAMPED VALUES											
		Peripheral Mean Blood Pressure mmHg			Peripheral Pulse Pressure mmHg			Heart Rate Beats/min			Respiratory Rate Breaths/min			Peripheral Mean Blood Pressure mmHg			Peripheral Pulse Pressure mmHg			Heart Rate Beats/min			Respiratory Rate Breaths/min		
		Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn
1	Cd L CCA	124	98	101	27	32	28	144	186	156	22	18	15	131	125	108	27	27	31	150	186	192	21	19	14
	Cd R CCA	122	105	106	27	31	26	162	216	174	22	19	14	134	118	114	27	27	26	162	204	174	21	19	15
	Cd R CCA	122	110	109	24	31	26	162	186	174	22	19	14	130	120	117	24	27	24	162	186	174	22	18	14
	Cd L CCA	120	114	110	24	27	27	180	186	174	21	19	14	128	135	120	24	27	24	192	186	180	21	19	14
	Cd L CCA	112	117	112	24	27	24	186	192	180	21	18	14	128	134	120	24	27	26	198	216	180	21	19	14
	Cd R CCA	114	116	111	27	27	27	204	198	168	21	19	14	121	121	120	27	28	27	204	192	168	21	18	15
	Cd LR CCA	111	116	111	29	27	27	210	192	156	21	18	15	186	200	180	47	56	45	204	180	204	21	19	16
	Cd LR CCA	107	113	106	32	24	27	204	180	126	21	18	15	188	183	180	45	44	48	198	198	210	21	18	14
2	Cd L CCA	115	129	141	38	37	44	126	138	138	19	18	14	131	142	145	43	43	42	126	144	144	19	18	15
	Cd R CCA	116	124	132	35	34	41	126	144	138	19	18	15	121	128	142	35	35	44	126	138	144	21	18	15
	Cd R CCA	120	121	142	33	32	46	126	144	144	20	18	15	123	144	147	39	37	49	126	144	150	20	18	15
	Cd L CCA	123	130	145	39	36	46	126	138	150	20	18	15	139	142	163	44	43	50	132	150	162	21	18	17
	Cd L CCA	122	123	133	36	34	35	132	144	150	20	18	17	140	147	161	44	45	49	138	144	162	21	18	17
	Cd R CCA	128	135	136	35	40	32	132	144	156	20	18	17	131	142	136	39	43	37	132	150	150	19	19	16
	Cd LR CCA	125	146	143	37	45	38	132	156	144	19	19	16	148	168	164	46	46	43	138	162	168	20	19	17
	Cd LR CCA	130	150	156	38	45	39	138	162	156	19	19	17	147	167	162	45	47	39	138	156	162	20	19	16
3	Cd L CCA	108	100	95	34	30	31	144	132	138	26	21	17	118	118	109	36	34	34	138	138	138	26	21	17
	Cd R CCA	108	100	95	35	29	29	138	132	138	26	22	17	122	116	110	34	33	33	138	144	138	26	21	17
	Cd R CCA	107	103	98	34	26	31	138	138	138	25	21	18	120	118	122	36	33	35	138	138	138	25	22	18
	Cd L CCA	108	103	100	32	28	31	132	132	132	25	21	18	117	120	117	36	33	38	138	144	138	25	21	18
	Cd L CCA	108	104	102	33	29	32	138	138	144	25	21	18	118	120	121	36	35	37	138	144	132	24	21	17
	Cd R CCA	108	105	106	32	31	33	132	138	138	24	21	17	120	121	115	38	36	38	138	144	138	25	21	18
	Cd LR CCA	108	103	106	32	30	33	132	138	138	24	21	17	147	169	169	45	50	54	144	162	156	23	21	19
	Cd LR CCA	108	104	105	32	29	31	138	144	138	23	20	18	147	167	167	45	50	53	144	162	156	23	21	19

Sheep No.	Clamping Position	BASAL VALUES												CLAMPED VALUES											
		Peripheral Mean Blood Pressure mmHg			Peripheral Pulse Pressure mmHg			Heart Rate Beats/min			Respiratory Rate Breaths/min			Peripheral Mean Blood Pressure mmHg			Peripheral Pulse Pressure mmHg			Heart Rate Beats/min			Respiratory Rate Breaths/min		
		Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn
4	Cd L CCA	122	113	80	33	22	24	150	174	174	22	21	21	134	136	104	37	22	20	156	186	180	22	21	21
	Cd R CCA	122	111	89	34	21	22	156	174	168	23	19	21	136	109	90	41	21	21	168	186	168	23	26	21
	Cd R CCA	123	109	92	34	21	21	162	180	174	24	21	21	135	110	91	40	21	21	174	174	174	24	21	21
	Cd L CCA	122	110	93	33	21	21	162	180	174	24	21	21	137	129	110	39	23	17	174	192	180	25	21	23
	Cd L CCA	120	109	93	34	22	21	168	180	192	25	21	21	134	132	112	39	23	16	168	192	180	24	21	21
	Cd R CCA	117	109	95	34	23	20	168	186	180	24	21	21	131	108	95	37	23	20	180	186	162	24	22	21
	Cd LR CCA	120	106	95	34	23	20	174	192	180	24	22	21	183	130	113	73	24	16	198	192	180	25	21	21
	Cd LR CCA	117	107	93	32	24	18	174	180	174	25	21	21	169	130	115	54	24	15	198	186	174	25	22	21
5	Cd L CCA	109	93	98	34	35	35	108	114	126	29	25	25	116	101	109	34	37	35	114	120	132	30	26	27
	Cd R CCA	106	91	96	33	34	34	114	120	132	29	27	26	113	103	107	35	35	34	114	120	138	27	27	27
	Cd R CCA	106	95	97	33	35	34	114	120	132	30	26	27	113	105	108	35	35	35	120	126	138	30	27	27
	Cd L CCA	105	94	97	34	35	35	120	120	138	30	27	26	113	102	109	35	37	35	120	126	126	29	26	27
	Cd L CCA	105	94	95	33	35	35	126	120	120	30	26	27	112	102	108	35	38	35	120	126	120	29	27	27
	Cd R CCA	105	98	95	33	35	35	126	120	126	30	29	27	109	106	107	35	35	35	120	126	120	29	27	26
	Cd LR CCA	104	98	98	34	35	35	126	132	120	30	29	26	136	125	164	39	37	53	126	132	138	33	26	29
	Cd LR CCA	97	96	100	34	33	29	120	132	120	29	26	26	127	132	169	37	39	51	150	144	144	30	26	27
6	Cd L CCA	91	79	70	32	27	28	102	126	126	19	15	16	97	94	81	36	27	28	108	132	132	18	15	16
	Cd R CCA	92	85	77	30	26	28	102	132	138	18	15	16	95	89	84	31	27	29	108	132	144	17	15	16
	Cd R CCA	91	87	80	29	26	28	108	132	144	18	15	15	94	91	83	30	27	29	108	132	138	17	15	16
	CD L CCA	92	86	81	27	27	28	108	132	138	17	15	16	98	93	87	31	28	29	114	126	144	16	15	16
	Cd L CCA	92	83	81	27	27	28	120	126	144	16	15	16	97	94	93	29	28	31	114	132	144	16	16	16
	Cd R CCA	87	83	84	26	28	28	120	132	150	15	15	16	94	87	93	28	27	30	120	132	150	15	15	17
	Cd LR CCA	91	82	86	27	28	30	120	132	150	16	16	16	121	104	137	36	31	43	126	138	174	17	16	18
	Cd LR CCA	94	84	89	27	27	31	126	132	156	17	16	16	104	103	143	32	30	45	126	138	180	15	16	17

TABLE 3. RAW DATA OF EXPERIMENTAL SERIES 3

Sheep No.	Tying Position	BASAL VALUES												TIED VALUES											
		Peripheral Mean Blood Pressure mmHg			Peripheral Pulse Pressure mmHg			Heart Rate Beats/min			Respiratory Rate Breaths/min			Peripheral Mean Blood Pressure mmHg			Peripheral Pulse Pressure mmHg			Heart Rate Beats/min			Respiratory Rate Breaths/min		
		Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn	Int. Vn	Cut L Vn	Cut LR Vn
1	Cd L CCA	104	88	82	34	34	29	120	120	120	19	17	20	119	93	95	40	33	32	126	120	120	18	18	19
	Md L CCA	111	90	86	37	34	32	114	120	120	18	18	19	123	99	92	43	34	34	126	114	120	18	17	20
	Cn L CCA	111	94	85	36	33	32	126	114	120	17	17	19	121	101	92	42	43	35	132	126	120	17	18	20
	Cd L CCA	112	96	84	35	32	32	126	120	120	18	17	19	121	104	93	41	34	36	132	126	120	18	18	19
	Md L CCA	111	97	86	35	31	33	132	126	120	17	18	20	123	103	93	39	34	36	138	120	120	18	17	19
	Cn L CCA	109	97	87	34	31	34	132	120	120	17	18	19	121	104	93	39	34	36	138	126	120	17	18	19
	Cd LR CCA	106	95	88	34	30	35	126	120	120	18	17	19	145	120	106	41	40	41	132	126	120	19	17	19
	Cd LR CCA	107	97	87	34	29	33	126	120	120	18	17	20	141	116	105	56	38	40	138	126	120	19	18	19
2	Cd R CCA	130	117	112	39	36	32	126	126	120	18	16	17	139	123	118	45	37	30	132	132	126	19	17	15
	Md R CCA	130	118	114	39	36	32	132	126	126	19	16	16	139	125	118	43	36	34	126	126	126	19	17	15
	Cn R CCA	132	120	115	37	36	33	126	126	126	18	20	15	137	126	118	38	37	34	114	132	126	19	17	16
	Cd R CCA	125	113	113	40	37	35	132	132	126	17	17	15	136	122	120	43	39	35	126	138	132	18	18	16
	Md R CCA	127	118	114	39	37	35	132	138	132	17	18	15	134	122	120	41	37	37	138	138	132	18	17	15
	Cn R CCA	127	114	115	39	37	38	132	132	138	17	17	15	133	119	122	40	36	39	120	126	138	18	18	15
	Cd LR CCA	127	114	116	39	34	39	132	120	138	18	17	15	164	166	177	49	59	59	144	132	162	19	17	16
	Cd LR CCA	126	121	121	39	32	32	144	132	138	17	18	15	162	165	175	49	55	59	150	114	150	18	17	16

Sheep No.	Tying Position	BASAL VALUES												TIED VALUES											
		Peripheral Mean Blood Pressure mmHg			Peripheral Pulse Pressure mmHg			Heart Rate Beats/min			Respiratory Rate Breaths/min			Peripheral Mean Blood Pressure mmHg			Peripheral Pulse Pressure mmHg			Heart Rate Beats/min			Respiratory Rate Breaths/min		
		Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn	Int. Vn	Cut R Vn	Cut LR Vn
3	Cd L CCA	109	92	89	33	33	35	114	132	144	18	19	20	120	101	92	47	34	36	114	132	150	20	19	19
	Md L CCA	104	95	82	43	33	34	108	138	156	18	19	20	118	107	91	51	36	35	108	144	150	17	19	19
	Cn L CCA	102	93	81	43	34	35	108	150	150	18	20	20	109	103	92	47	35	34	114	144	144	18	19	19
	Cd L CCA	97	90	78	35	34	32	120	132	144	18	20	20	111	103	91	47	35	34	120	144	150	18	19	20
	Md L CCA	98	92	81	37	32	33	126	114	144	18	19	20	112	101	93	45	35	33	126	144	150	17	19	20
	Cn L CCA	96	89	83	36	36	33	126	132	150	18	20	21	105	97	91	40	35	33	120	126	144	14	20	19
	Cd LR CCA	93	82	83	36	35	32	126	138	150	18	20	21	142	108	120	63	39	41	138	138	150	18	19	20
	Cd LR CCA	91	82	84	31	33	32	132	144	150	19	19	21	137	112	123	55	39	44	138	150	150	18	19	21
4	Cd R CCA	97	94	99	30	27	32	138	150	162	16	18	19	105	99	101	33	30	32	144	150	156	17	19	19
	Md R CCA	99	93	95	30	28	30	144	150	156	16	19	19	104	102	103	34	31	33	144	150	156	17	19	19
	Cn R CCA	96	95	95	29	29	31	144	150	162	17	20	18	104	104	102	32	32	33	150	156	156	17	19	19
	Cd R CCA	97	95	96	29	29	30	144	150	156	17	20	18	103	103	103	32	33	33	150	156	162	17	20	19
	Md R CCA	94	97	95	29	30	33	150	156	156	17	19	19	100	106	100	30	33	34	150	156	162	18	19	19
	Cn R CCA	91	96	95	27	31	31	150	150	162	17	19	19	97	103	100	28	33	34	150	156	156	18	19	19
	Cd LR CCA	91	97	96	27	31	31	144	156	156	17	19	18	111	128	132	36	45	45	150	156	156	18	19	19
	Cd LR CCA	93	103	101	27	33	31	150	150	162	18	19	18	112	135	132	35	46	45	150	156	156	18	19	19

TABLE 4 RAW DATA OF EXPERIMENTAL SERIES 4

Sheep No.	Clamping Position	BASAL: Peripheral Recordings: Mean Blood Pressure, mmHg: Intact Vn	Cut LR Vn	Pulse Pressure, mmHg: Intact Vn	Cut LR Vn	Heart Rate Beats/min: Intact Vn	Cut LR Vn	Respirtn. Rate Breaths/min: Intact Vn	Cut LR Vn	BASAL: Left Carotid Sinus Recordings: Mean Blood Pressure, mmHg: Intact Vn	Cut LR Vn	Pulse Pressure, mmHg: Intact Vn	Cut LR Vn	BASAL: Right Carotid Sinus Recordings: Mean Blood Pressure, mmHg: Intact Vn	Cut LR Vn	Pulse Pressure, mmHg: Intact Vn	Cut LR Vn
1	Cd L CCA	100	72	30	32	180	180	24	18	106	100	27	36	103	72	14	25
	Cd R CCA	97	69	30	33	186	180	24	17	104	96	29	38	96	69	24	23
	Cd LR CCA	93	70	30	32	180	186	24	18	102	99	29	37	94	73	24	27
	Cn L CCA	87	72	30	33	180	186	23	18	94	99	29	38	69	78	24	24
	Cn R CCA	90	70	30	33	186	168	23	18	96	100	29	38	91	75	24	29
	Cn LR CCA	83	68	30	32	186	180	23	18	95	96	30	38	89	70	24	33
	Cd L CCA	78	72	33	33	180	180	22	18	85	80	33	31	79	75	21	30
	Cd L CCA, L OG																
	Cd L CCA, L OG, L ECA																
	Cd L CCA, L OG																
	Cd L CCA																
	Cd R CCA	67	72	30	33	168	186	21	18	74	80	33	31	69	79	19	29
	Cd R CCA, R OG																
	Cd R CCA, R OG, R ECA																
	Cd R CCA, R OG																
	Cd R CCA																
	Cd L CCA	73	72	30	33	180	180	22	18	70	79	26	33	70	74	16	29
	Cd L CCA, R OG																
	Cd L CCA, R OG, L ECA																
	Cd L CCA, R OG																
	Cd L CCA																
	Cd R CCA	78	72	30	33	180	180	21	18	68	81	27	30	74	75	23	29
	Cd R CCA, L OG																
	Cd R CCA, L OG, R ECA																
	Cd R CCA, L OG																
	Cd R CCA																
	Cd L CCA	69	74	37	33	162	180	22	18	82	85	29	31	75	76	16	26
	Cd L CCA, L OG																
	Cd L CCA, L OG, R ECA																
	Cd L CCA, L OG																
	Cd L CCA																
	Cd R CCA	68	76	31	32	162	180	22	19	77	86	29	25	63	73	14	23
	Cd R CCA, R OG																
	Cd R CCA, R OG, L ECA																
	Cd R CCA, R OG																
	Cd R CCA																
	Cd L CCA	66	74	28	33	174	174	23	19	64	83	24	29	68	73	19	23
	Cd L CCA, R OG																
	Cd L CCA, R OG, R ECA																
	Cd L CCA, R OG																
	Cd L CCA																
	Cd R CCA	67	72	30	32	168	186	22	19	64	83	26	27	68	74	16	23
	Cd R CCA, L OG																
	Cd R CCA, L OG, L ECA																
	Cd R CCA, L OG																
	Cd R CCA																
	Cd L CCA	73	83	30	30	180	180	22	22	82	88	30	27	75	73	17	16
	Cd L CCA, L OG																
	Cd L CCA, L OG, L ECA																
	Cd L CCA, L OG, L ECA, Cd R CCA																
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG																
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG, R ECA																
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG																
	CD L CCA, L OG, L ECA, Cd R CCA																
	Cd L CCA, L OG, L ECA																
	Cd L CCA, L OG																
	Cd L CCA																
	Cd R CCA	83	87	28	30	180	174	23	20	67	92	27	26	80	76	21	19
	Cd R CCA, R OG																
	Cd R CCA, R OG, R ECA																
	Cd R CCA, R OG, R ECA, Cd L CCA																
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG																
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG, L ECA																
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG																
	Cd R CCA, R OG, R ECA, Cd L CCA																
	Cd R CCA, R OG, R ECA																
	Cd R CCA, R OG																
	Cd R CCA																

Sheep No.	Clamping Position	CLAMPED: Peripheral Recordings: Mean Blood Pressure, mmHg: Intact Vn	Cut LR Vn	Pulse Pressure, mmHg: Intact Vn	Cut LR Vn	Heart Rate Beats/min: Intact Vn	Cut LR Vn	Respirtn. Rate Breaths/min: Intact Vn	Cut LR Vn	CLAMPED: Left Carotid Sinus Recordings: Mean Blood Pressure, mmHg: Intact Vn	Cut LR Vn	Pulse Pressure, mmHg: Intact Vn	Cut LR Vn	CLAMPED: Right Carotid Sinus Recordings: Mean Blood Pressure, mmHg: Intact Vn	Cut LR Vn	Pulse Pressure, mmHg: Intact Vn	Cut LR Vn
1	Cd L CCA	107	79	30	32	180	174	24	17	59	55	6	5	108	75	14	21
	Cd R CCA	100	72	30	32	180	180	23	18	103	98	31	35	54	41	5	5
	Cd LR CCA	113	93	30	30	180	186	23	19	31	24	2	2	32	15	2	2
	Cn L CCA	97	77	30	33	180	180	23	18	54	57	6	5	94	81	24	26
	Cn R CCA	90	76	30	32	180	186	22	18	96	104	29	35	49	43	5	5
	Cn LR CCA	103	93	30	30	186	186	23	19	30	23	2	2	2	15	33	2
	Cd L CCA	83	77	30	35	180	186	23	18	38	39	6	4	83	78	19	29
	Cd L CCA, L OG	77	74	30	31	180	180	23	18	0	37	0	4	75	73	16	28
	Cd L CCA, L OG, L ECA	74	74	33	33	174	186	23	18	54	28	5	3	77	77	16	27
	Cd L CCA, L OG	77	75	33	32	174	174	23	18	43	39	4	4	80	76	16	26
	Cd L CCA	77	76	33	33	180	180	22	20	47	45	4	4	82	79	16	26
	Cd R CCA	73	75	30	32	174	186	22	18	81	83	31	28	48	39	3	5
	Cd R CCA, R OG	75	69	30	33	174	180	22	18	83	78	31	29	49	34	0	5
	Cd R CCA, R OG, R ECA	75	75	30	32	180	186	22	18	83	81	31	29	45	36	3	2
	Cd R CCA, R OG	77	73	30	30	180	192	22	17	83	79	31	30	14	39	3	5
	Cd R CCA	77	72	30	33	186	192	23	17	83	81	31	29	46	41	3	5
	Cd L CCA	77	79	30	32	180	192	22	18	11	47	3	5	77	76	14	28
	Cd L CCA, R OG	73	87	30	30	174	192	22	18	11	61	3	5	70	58	14	26
	Cd L CCA, R OG, L ECA	80	84	30	33	180	180	22	18	53	61	6	6	76	86	14	26
	Cd L CCA, R OG	77	82	30	33	174	198	21	18	37	51	3	5	75	82	14	27
	Cd L CCA	78	82	30	33	186	180	23	17	38	50	4	6	76	83	14	26
	Cd R CCA	70	71	30	32	180	186	22	19	68	80	27	27	36	41	3	5
	Cd R CCA, L OG	67	76	30	32	168	186	21	18	64	84	26	28	36	43	3	5
	Cd R CCA, L OG, R ECA	73	76	30	33	174	180	22	19	69	85	26	29	50	46	0	5
	Cd R CCA, L OG	70	76	30	33	180	180	23	18	69	86	26	29	40	44	2	5
	Cd R CCA	70	76	30	32	180	168	23	17	68	88	26	28	41	43	2	5
	Cd L CCA	73	88	30	30	174	180	24	19	37	43	3	4	71	81	16	19
	Cd L CCA, L OG	72	79	30	33	162	210	22	17	36	41	3	4	70	77	16	22
	Cd L CCA, L OG, R ECA	67	92	27	32	180	186	21	20	14	11	2	1	73	97	23	28
	Cd L CCA, L OG	76	77	30	30	168	186	20	20	26	26	3	2	69	68	14	19
	Cd L CCA	72	71	28	33	168	198	24	20	36	32	4	4	68	66	14	20
	Cd R CCA	70	77	30	33	162	192	22	17	75	84	28	24	41	39	2	5
	Cd R CCA, R OG	67	83	30	30	156	180	21	17	75	95	30	30	38	19	2	0
	Cd R CCA, R OG, L ECA	72	77	30	30	156	180	23	19	82	85	31	33	29	13	0	2
	Cd R CCA, R OG	69	69	30	30	156	204	24	20	76	74	25	23	35	27	0	2
	Cd R CCA	67	71	30	33	168	180	24	20	73	79	28	25	38	29	2	5
	Cd L CCA	72	87	30	32	174	180	22	19	34	47	2	4	71	82	15	19
	Cd L CCA, R OG	70	89	27	32	168	180	24	20	35	47	2	4	70	82	15	20
	Cd L CCA, R OG, R ECA	81	95	28	30	168	186	23	21	17	20	1	2	85	97	28	28
	Cd L CCA, R OG	70	84	30	32	174	186	22	20	30	37	2	4	71	76	16	19
	Cd L CCA	72	81	28	31	180	198	24	20	34	41	2	4	72	76	16	21
	Cd R CCA	67	76	28	30	174	186	22	18	64	83	24	29	43	41	2	5
	Cd R CCA, L OG	70	76	27	30	174	192	23	20	63	83	24	29	42	41	2	5
	Cd R CCA, L OG, L ECA	75	80	27	29	174	186	23	21	70	91	26	31	34	14	0	2
	Cd R CCA, L OG	63	73	27	30	168	192	24	20	60	82	23	23	40	32	2	5
	Cd R CCA	65	76	27	31	168	192	24	20	61	83	24	26	41	35	2	5
	Cd L CCA	80	94	31	32	180	186	22	23	45	36	4	3	79	75	15	14
	Cd L CCA, L OG	78	94	30	29	186	186	22	22	39	24	4	0	79	74	14	13
	Cd L CCA, L OG, L ECA	77	91	29	30	180	180	24	22	34	32	3	3	76	73	14	13
	Cd L CCA, L OG, L ECA, Cd R CCA	93	104	27	28	180	186	23	22	23	22	1	3	23	9	1	2
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG	96	108	29	30	192	180	24	23	23	22	1	3	23	13	0	0
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG, R ECA	96	121	33	36	192	186	20	20	24	24	1	5	27	52	1	6
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG	103	103	27	30	192	174	16	18	24	22	1	2	27	1	1	2
	CD L CCA, L OG, L ECA, Cd R CCA	102	107	27	30	192	180	15	17	25	23	1	2	27	13	0	2
	Cd L CCA, L OG, L ECA	82	94	27	29	192	180	13	17	33	31	0	0	43	68	6	12
	Cd L CCA, L OG	78	93	28	30	180	180	17	17	32	33	2	5	41	74	7	16
	Cd L CCA	75	92	30	33	180	174	20	20	37	36	4	4	41	74	8	15
	Cd R CCA	84	89	30	29	186	174	22	18	93	94	27	26	87	39	4	3
	Cd R CCA, R OG	81	89	29	28	192	180	22	20	90	94	26	24	19	43	0	3
	Cd R CCA, R OG, R ECA	81	88	29	28	180	174	24	20	89	91	25	25	41	47	3	5
	Cd R CCA, R OG, R ECA, Cd L CCA	97	104	30	31	192	174	22	18	15	13	0	0	17	46	3	6
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG	93	102	27	30	180	180	24	24	15	13	0	0	34	46	3	6
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG, L ECA	85	116	27	33	192	174	24	18	22	22	2	2	33	49	3	6
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG	98	113	23	30	192	180	22	17	11	10	1	0	35	50	5	6
	Cd R CCA, R OG, R ECA, Cd L CCA	107	107	27	32	180	174	20	17	18	16	2	2	38	52	5	6
	Cd R CCA, R OG, R ECA	87	86	27	25	180	180	17	15	21	84	21	19	41	48	5	5
	Cd R CCA, R OG	77	77	30	33	180	168	20	17	83	80	27	23	33	29	3	3
	Cd R CCA	76	87	30	32	180	156	20	22	82	88	28	21	34	33	5	5

Cont.....

Sheep No.	Clamping Position	BASAL														CLAMPED													
		Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings				Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings			
		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg	
		Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn
	Cd L CCA	68	77	28	30	174	186	24	20	80	86	29	26	70	75	12	19	71	81	28	32	186	186	24	20	43	45	4	4	70	74	12	17
	Cd L CCA, Cd R CCA																	80	96	30	30	168	180	24	20	27	24	0	0	31	20	0	2
	Cd L CCA, Cd R CCA, L OG																	79	97	27	30	180	180	24	18	17	15	0	1	27	13	0	2
	Cd L CCA, Cd R CCA, L OG R OG,																	77	99	27	29	174	192	23	24	10	15	0	1	23	8	0	2
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA																	83	100	25	30	180	192	22	22	15	16	1	6	23	5	0	2
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA, R ECA																	95	95	27	27	192	174	18	18	19	19	0	6	23	22	0	2
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA																	100	92	20	25	210	180	12	17	19	18	0	6	23	5	0	0
	Cd L CCA, Cd R CCA, L OG, R OG																	103	80	20	29	192	180	0	18	12	10	0	0	23	5	0	2
	Cd L CCA, CD R CCA, L OG																	105	80	20	25	240	186	0	20	13	10	0	0	23	9	0	0
	Cd L CCA, Cd R CCA																	107	80	20	23	192	192	0	15	19	14	0	0	23	9	0	0
	Cd L CCA																	92	78	27	23	216	186	20	0	30	24	0	0	62	54	11	9
	Cd R CCA	72	71	30	33	186	168	23	19	81	78	31	31	72	65	21	20	75	75	30	31	180	180	22	18	83	82	30	29	42	35	2	0
	Cd R CCA, Cd L CCA																	88	97	28	27	180	174	24	18	21	19	2	2	23	14	0	0
	Cd R CCA, Cd L CCA, R OG																	89	99	28	30	180	144	23	20	13	15	2	0	23	14	0	0
	Cd R CCA, Cd L CCA, R OG, L OG																	96	97	28	31	174	180	25	18	11	12	1	2	23	37	0	0
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA																	96	100	28	30	168	180	22	20	12	12	0	0	25	43	0	5
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA, L ECA																	98	97	23	28	192	174	0	17	24	25	1	2	26	47	0	5
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA																	108	99	22	27	240	162	0	17	12	12	0	1	26	48	0	5
	Cd R CCA, Cd L CCA, R OG, L OG																	115	98	24	30	240	180	0	17	13	12	0	1	23	11	0	0
	Cd R CCA, Cd L CCA, R OG																	122	99	24	27	240	180	0	17	21	17	0	1	23	14	0	1
	Cd R CCA, Cd L CCA																	132	94	27	28	240	174	0	20	23	17	0	1	23	14	0	0
	Cd R CCA																	115	75	23	27	180	180	10	18	102	81	17	22	23	27	0	2
2	Cd L CCA	108	96	32	33	138	120	32	19	82	84	20	32	107	79	24	29	114	101	32	31	138	120	30	19	63	65	1	7	11	85	20	21
	Cd R CCA	111	97	29	31	138	120	32	19	85	87	13	28	106	83	23	27	114	100	32	33	138	120	30	19	86	90	14	27	85	91	9	7
	Cd LR CCA	112	98	31	31	138	120	32	16	85	94	15	26	104	86	22	27	128	115	36	36	138	126	30	15	46	38	1	2	63	35	2	2
	Cn L CCA	111	104	29	36	138	126	30	18	84	96	15	27	108	90 -	21	29	119	113	29	33	138	126	30	19	70	52	2	10	114	102	21	26
	Cn R CCA	110	108	31	36	138	126	29	17	107	99	17	29	108	95	21	29	115	109	32	36	132	126	32	18	89	98	11	28	89	66	13	10
	Cn LR CCA	107	101	31	36	138	120	32	16	85	94	12	29	100	90	22	29	126	121	36	38	138	120	32	17	50	47	1	4	60	43	2	5
	Cd L CCA	108	93	32	41	138	120	32	14	83	67	8	27	98	83	24	32	113	101	33	42	138	120	30	15	72	44	1	6	102	87	22	27
	Cd L CCA, L OG																	114	88	34	35	132	120	30	14	69	36	1	6	102	87	22	27
	Cd L CCA, L OG, L ECA																	114	101	34	41	132	126	32	16	69	65	1	17	101	89	23	23
	Cd L CCA, L OG																	113	99	32	44	132	120	27	13	62	54	1	6	100	86	21	29
	Cd L CCA																	113	103	33	44	144	132	27	15	62	57	1	6	102	90	22	29
	Cd R CCA	105	98	34	41	138	120	30	14	86	74	6	23	98	89	27	32	112	106	34	41	138	120	32	16	89	76	5	21	79	66	10	10
	Cd R CCA, R OG																	97	101	32	38	132	120	30	16	76	73	5	20	68	62	10	10
	Cd R CCA, R OG, R ECA																	103	98	35	38	138	120	30	16	77	69	5	22	86	13	21	0
	Cd R CCA, R OG																	98	105	34	33	132	120	30	15	78	75	4	17	76	83	10	9
	Cd R CCA																	102	101	32	41	132	126	30	14	79	71	4	22	73	65	10	12
	Cd L CCA	104	77	36	38	132	120	33	14	79	70	19	24	96	82	27	28	111	99	41	40	132	126	32	10	67	51	6	4	104	88	24	24
	Cd L CCA, R OG																	74	103	33	38	132	132	32	13	50	45	6	6	84	79	24	27
	Cd L CCA, R OG, L ECA																	103	91	36	38	126	120	32	13	70	55	10	10	93	75	24	28
	Cd L CCA, R OG																	107	91	32	40	132	126	34	15	62	46	5	6	96	78	24	29
	Cd L CCA																	104	90	36	41	132	132	30	15	39	46	6	6	94	75	23	29
	Cd R CCA	103	87	33	41	126	120	30	13	77	68	19	21	94	81	24	29	107	95	36	38	126	126	32	15	82	64	19	23	69	53	10	10
	Cd R CCA, L OG																	108	91	36	38	126	120	30	14	80	64	19	21	76	52	10	10
	Cd R CCA, L OG, R ECA																	113	90	33	38	126	120	33	13	83	61	19	23	94	68	21	24
	Cd R CCA, L OG																	109	90	36	38	132	120	30	13	81	60	24	23	82	50	12	12
	Cd R CCA																	107	85	36	41	120	120	35	14	79	59	19	23	78	52	12	12
	Cd L CCA	107	86	33	40	126	126	33	13	80	63	24	25	98	76	23	32	118	94	38	40	126	120	33	15	63	44	6	6	101	80	23	28
	Cd L CCA, L OG																	110	89	33	41	126	120	33	12	60	37	6	4	97	70	22	27
	Cd L CCA, L OG, R ECA																	117	102	38	38	126	120	33	8	46	27	2	1	106	94	24	20
	Cd L CCA, L OG																	108	96	38	41	120	120	33	11	63	44	6	6	98	79	23	30
	Cd L CCA																	112	96	35	41	126	120	32	14	60	44	6	6	99	79	23	31
	Cd R CCA	107	96	36	41	126	132	33	18	83	64	17	26	98	82	24	34	109	98	36	41	126	126	33	13	82	67	17	22	78	48	10	9
	Cd R CCA, R OG																	101	90	32	39	120	126	32	12	73	57	17	21	69	38	10	9
	Cd R CCA, R OG, L ECA																	103	128	36	31	126	138	32	0	74	80	27	25	48	34	5	2
	Cd R CCA, R OG																	101	101	33	36	126	144	32	0	72	70	19	19	70	56	10	6
	Cd R CCA																	106	102	36	38	126	144	33	17	79	71	17	19	76	57	12	6
	Cd L CCA	105	89	37	38	126	126	33	15	79	60	21	27	96	74	27	34	113	101	35	38	126	126	32	13	65	47	7	6	101	82	24	31
	Cd L CCA, R OG																	103	94	35	38	126	126	30	16	55	42	8	6	87	72	24	29
	Cd L CCA, R OG, R ECA																	87	99	35	37	126	120	32	14	47	28	3	4	101	83	23	31
	Cd L CCA, R OG																	108	88	38	37	126	126	32	13	65	42	6	6	96	77	23	27
	Cd L CCA																	113	93	36	37	132	120	30	15	105	44	6	6	64	76	22	28
	Cd R CCA	104	92	36	36	126	120	32	12	78	65	21	19	95	80	27	30	110	89	35	39	126	132	32	15	82	65	17	17	67	52	11	11
	Cd R CCA, L OG																	106	91	35	36	126	120	33	11	73	50	17	19	71	32	10	11
	Cd R CCA, L OG, L ECA																	111	94	35	36	126	120	30	11	83	70	23	21	56	33	6	6
	Cd R CCA, L OG																	110	92	35	33	126	120	30	7	82	62	19	15	80	53	11	12
	Cd R CCA																	109	94	36	31	132	132	30	11	82	61	19	17	82	54	11	12
	Cd L CCA	109	91	35	35	126	120	29	10	82	83	20	17	99	76	27	34	113	123	35	36	132	126	30	13	61	52	7	6	102	82	22	28

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Sheep No.	Clamping Position	BASAL														CLAMPED													
		Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings				Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings			
		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg	
		Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn
	Cd L CCA, L OG															115	91	35	36	126	132	32	12	62	51	6	5	99	80	22	27
	Cd L CCA, L OG, L ECA															112	88	35	35	132	132	30	9	77	58	13	7	95	73	27	26
	Cd L CCA, L OG, L ECA, Cd R CCA															121	106	35	35	132	132	30	14	68	54	8	6	53	30	5	2
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG															114	100	37	35	126	120	30	13	71	55	10	8	20	16	2	0
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG, R ECA															144	135	38	33	138	126	25	0	92	72	8	4	65	98	0	5
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG															174	147	41	37	156	156	18	0	93	72	9	4	17	24	0	0
	Cd L CCA, L OG, L ECA, Cd R CCA															131	150	40	37	156	156	20	0	68	67	6	4	39	32	2	2
	Cd L CCA, L OG, L ECA															117	120	40	36	132	144	22	6	75	70	14	10	103	103	24	21
	Cd L CCA, L OG															103	101	39	46	132	156	30	13	51	47	6	6	90	84	26	34
	Cd L CCA															110	103	37	42	132	144	30	15	58	50	4	4	100	84	8	15
	Cd R CCA	105	88	37	36	132	126	32	11	78	64	22	17	97	83	27	34	109	96	36	38	126	126	32	14	81	65	20	16	78	54	12	11
	Cd R CCA, R OG																	101	93	37	35	126	120	30	14	74	60	20	20	53	46	5	6
	Cd R CCA, R OG, R ECA																	99	89	37	36	132	132	30	15	74	61	21	16	66	66	5	12
	Cd R CCA, R OG, R ECA, Cd L CCA																	109	106	35	29	126	132	30	18	28	36	3	0	43	55	2	10
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG																	101	101	35	33	126	126	32	17	29	31	0	0	50	60	2	10
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG, L ECA																	144	127	38	27	138	132	27	0	93	70	11	5	79	82	2	4
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG																	147	148	41	38	144	156	22	0	34	34	1	4	78	80	5	6
	Cd R CCA, R OG, R ECA, Cd L CCA																	122	145	38	36	132	144	20	0	35	38	1	2	76	75	5	5
	Cd R CCA, R OG, R ECA																	106	125	36	32	132	144	24	0	77	68	17	8	64	84	7	6
	Cd R CCA, R OG																	100	114	36	31	126	114	30	0	71	65	19	12	38	43	5	2
	Cd R CCA																	95	108	36	33	132	126	30	13	69	62	20	13	58	53	7	5
	Cd L CCA	106	125	36	28	126	174	30	10	80	112	19	19	102	108	24	27	112	135	36	28	132	168	30	13	66	77	6	5	99	107	22	24
	Cd L CCA, Cd R CCA																	120	159	38	36	126	168	30	8	46	63	2	2	58	45	5	2
	Cd L CCA, Cd R CCA, L OG																	19	163	38	38	132	168	30	9	45	63	2	2	56	43	5	2
	Cd L CCA, Cd R CCA, L OG, R OG																	88	145	36	31	132	168	27	9	44	67	2	5	53	40	5	2
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA																	114	140	35	28	126	162	30	0	70	108	7	7	48	38	5	2
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA, R ECA																	172	152	41	33	138	168	26	0	97	124	8	9	118	124	12	11
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA																	145	150	37	28	168	204	17	0	76	105	4	6	41	29	2	0
	Cd L CCA, Cd R CCA, L OG, R OG																	146	152	44	28	168	220	17	0	31	59	0	0	39	29	2	0
	Cd L CCA, Cd R CCA, L OG																	120	122	41	27	132	216	0	0	31	59	1	0	39	29	2	0
	Cd L CCA, Cd R CCA																	117	112	40	28	132	234	0	0	32	56	1	0	39	24	2	0
	Cd L CCA																	106	92	38	31	132	240	20	0	44	62	3	0	93	73	27	20
	Cd R CCA	106	113	35	38	132	180	29	10	80	107	21	19	98	92	24	32	106	118	36	36	138	192	34	7	78	107	18	17	76	57	11	16
	Cd R CCA, Cd L CCA																	123	144	36	31	132	168	30	9	48	63	3	2	59	39	2	0
	Cd R CCA, Cd L CCA, R OG																	114	142	35	31	132	192	30	5	38	62	4	2	26	34	1	0
	Cd R CCA, Cd L CCA, R OG, L OG																	102	128	38	31	132	180	27	5	35	59	2	2	24	29	0	0
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA																	112	125	35	32	132	180	32	5	35	53	2	2	71	88	7	10
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA, L ECA																	146	121	41	31	138	216	29	0	97	106	8	5	74	114	7	6
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA																	149	139	44	31	156	240	22	0	34	53	2	2	77	84	6	5
	Cd R CCA, Cd L CCA, R OG, L OG																	137	128	41	32	144	240	0	0	34	50	2	2	23	22	1	0
	Cd R CCA, Cd L CCA, R OG																	124	104	38	27	132	240	24	0	34	49	2	2	22	18	0	0
	Cd R CCA, Cd L CCA																	119	91	37	18	138	216	24	0	34	49	2	2	37	16	2	0
	Cd R CCA																	110	82	37	17	132	240	24	0	68	70	21	13	62	26	7	2
3	Cd L CCA	93	86	31	33	120	144	17	11	72	67	22	22	78	68	23	16	102	105	30	34	144	150	17	11	39	37	3	2	92	85	22	16
	Cd R CCA	92	88	31	34	138	144	17	10	74	72	18	22	84	73	22	16	96	101	29	34	144	144	17	11	77	73	17	20	44	29	4	3
	Cd L R CCA	91	92	30	34	144	144	17	11	76	69	20	22	80	72	22	18	120	123	29	37	144	144	17	11	24	22	2	2	33	21	2	2
	Cn L CCA	92	88	38	34	156	144	17	11	77	70	17	21	80	71	24	16	105	110	33	34	156	144	17	11	39	38	2	2	91	86	21	16
	Cn R CCA	93	92	31	34	156	144	16	11	78	77	23	18	82	71	21	16	99	93	31	34	156	144	17	10	83	76	20	16	48	28	4	2
	Cn L R CCA	89	92	28	33	150	144	17	10	74	75	21	18	80	71	21	16	121	128	30	36	156	150	17	11	24	27	2	0	32	23	2	2
	Cd L CCA	94	92	31	34	156	144	17	11	79	74	2	22	83	70	21	17	107	105	29	33	150	144	18	10	44	36	2	2	91	83	21	13
	Cd L CCA, L OG																	64	111	30	35	144	144	17	11	44	26	2	0	80	86	21	16
	Cd L CCA, L OG, L ECA																	69	103	30	34	156	150	17	11	48	53	2	6	88	80	18	16
	Cd L CCA, L OG																	105	100	30	34	156	144	16	11	47	36	2	2	75	77	18	16
	Cd L CCA																	73	106	30	34	156	156	16	15	49	36	2	2	91	80	18	16
	Cd R CCA	91	93	30	34	156	150	16	11	76	68	21	13	78	71	21	16	88	98	30	34	156	144	16	11	76	63	2	12	31	26	3	4
	Cd R CCA, R OG																	85	90	28	34	144	138	16	11	71	64	2	12	21	22	2	0
	Cd R CCA, R OG, R ECA																	85	93	29	34	150	144	15	11	76	67	2	13	42	16	2	1
	Cd R CCA, R OG																	92	90	25	34	150	144	15	11	76	69	2	13	33	32	2	2
	Cd R CCA																	92	90	30	34	144	156	17	11	76	71	2	13	46	32	3	2
	Cd L CCA	88	87	30	33	156	144	16	11	74	73	22	20	73	71	16	16	99	111	31	31	144	144	16	11	36	36	2	2	73	84	14	13

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Sheep No.	Clamping Position	BASAL														CLAMPED													
		Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings				Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings			
		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg	
		Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn
	Cd L CCA, R OG															99	102	32	33	144	144	17	11	36	43	2	1	73	81	12	13
	Cd L CCA, R OG, L ECA															103	101	30	33	150	144	16	10	63	76	7	0	74	79	12	13
	Cd L CCA, R OG															108	116	31	34	150	150	17	11	19	40	1	1	79	84	13	16
	Cd L CCA															105	117	30	36	156	156	15	11	19	40	1	2	77	91	13	16
	Cd R CCA	94	91	28	34	150	144	16	11	78	78	16	16	73	68	16	16	96	86	28	33	144	144	17	11	76	76	6	14	45	37	3	4
	Cd R CCA, L OG																	95	92	27	33	144	144	16	11	80	80	1	13	45	22	3	4
	Cd R CCA, L OG, R ECA																	99	91	30	35	150	150	16	11	81	82	7	9	49	21	5	2
	Cd R CCA, L OG																	95	96	30	34	144	156	16	11	83	79	1	11	46	37	5	3
	Cd R CCA																	77	96	30	34	156	144	17	11	80	82	1	7	46	42	5	4
	Cd L CCA	92	92	34	33	150	144	16	10	77	76	22	22	75	56	17	8	110	116	33	31	150	156	16	11	38	33	3	2	85	74	14	8
	Cd L CCA, L OG																	110	124	34	33	156	156	17	12	39	28	3	2	84	14	16	0
	Cd L CCA, L OG, R ECA																	136	122	34	32	150	150	17	11	31	29	1	2	21	12	0	0
	Cd L CCA, L OG																	117	116	35	29	150	156	16	12	43	36	3	2	92	74	13	8
	Cd L CCA																	118	119	34	33	144	156	16	12	46	37	4	2	97	80	16	8
	Cd R CCA	94	97	32	34	162	156	17	12	73	79	17	26	79	71	16	13	102	99	31	32	144	150	17	11	76	80	18	21	33	31	2	4
	Cd R CCA, R OG																	100	107	27	31	150	144	17	11	74	79	18	21	16	31	0	4
	Cd R CCA, R OG, L ECA																	101	100	22	30	144	150	17	12	91	92	29	28	16	29	0	4
	Cd R CCA, R OG																	103	96	20	32	144	144	16	11	73	79	14	13	32	38	2	5
	Cd R CCA																	96	92	24	34	150	150	17	11	75	76	17	16	44	37	3	5
	Cd L CCA	90	89	22	35	144	144	16	11	76	75	20	22	75	72	16	14	112	113	18	34	156	156	17	11	40	37	2	2	84	82	13	12
	Cd L CCA, R OG																	121	125	20	33	150	156	16	12	30	37	1	2	110	83	13	12
	Cd L CCA, R OG, R ECA																	127	133	17	33	156	150	17	12	21	31	1	2	29	125	2	25
	Cd L CCA, R OG																	113	122	16	32	156	156	17	12	43	42	2	2	96	97	16	14
	Cd L CCA																	114	124	16	33	162	156	17	11	44	44	2	2	96	100	16	13
	Cd R CCA	78	99	17	30	144	150	17	10	94	80	18	22	79	79	14	17	99	103	16	30	150	156	16	11	76	82	16	17	42	38	2	3
	Cd R CCA, L OG																	114	113	11	28	156	150	17	12	80	78	14	22	32	36	2	3
	Cd R CCA, L OG, L ECA																	100	105	12	27	150	144	17	12	82	93	19	14	29	27	2	2
	Cd R CCA, L OG																	97	93	11	26	150	156	16	12	78	76	9	1	42	37	2	2
	Cd R CCA																	98	99	13	28	156	156	17	12	82	80	11	1	42	39	2	2
	Cd L CCA	93	78	38	31	144	150	17	12	77	88	18	22	79	76	18	13	106	112	34	31	150	144	16	11	40	36	2	1	89	83	18	14
	Cd L CCA, L OG																	109	115	34	33	156	144	16	10	40	36	2	1	88	86	18	16
	Cd L CCA, L OG, L ECA																	85	95	34	27	156	144	16	11	22	50	1	7	83	71	17	13
	Cd L CCA, L OG, L ECA, Cd R CCA																	113	112	34	32	156	144	16	10	10	29	1	3	17	19	0	0
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG																	112	119	34	28	162	138	17	11	11	51	1	1	11	12	0	0
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG, R ECA																	114	121	34	30	156	144	16	11	11	59	1	2	58	65	0	3
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG																	113	122	34	31	156	144	16	11	12	58	1	2	16	18	0	0
	Cd L CCA, L OG, L ECA, Cd R CCA																	109	121	34	31	144	144	17	11	13	53	0	2	21	36	0	2
	Cd L CCA, L OG, L ECA																	101	111	33	31	156	156	17	11	18	84	0	2	79	92	13	18
	Cd L CCA, L OG																	100	106	34	31	156	144	15	12	34	58	0	2	79	86	16	18
	Cd L CCA																	105	100	34	33	156	156	17	7	37	58	0	2	86	89	13	18
	Cd R CCA	97	92	38	32	156	144	17	10	79	77	21	20	78	74	21	18	91	95	35	30	150	144	17	10	72	78	19	20	32	31	2	3
	Cd R CCA, R OG																	85	94	34	31	144	144	17	11	69	78	19	20	30	32	0	2
	Cd R CCA, R OG, R ECA																	86	94	34	31	144	150	17	10	68	78	19	20	58	21	2	0
	Cd R CCA, R OG, R ECA, Cd L CCA																	108	119	30	31	150	144	16	11	23	27	1	1	58	21	2	0
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG																	109	118	33	30	144	144	17	11	13	11	1	0	64	29	2	0
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG, L ECA																	109	115	33	33	144	144	18	11	78	79	4	13	68	53	2	4
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG																	112	119	33	33	144	144	17	12	22	26	0	1	58	46	2	1
	Cd R CCA, R OG, R ECA, Cd L CCA																	114	122	34	33	156	144	17	10	22	27	1	1	61	46	2	1
	Cd R CCA, R OG, R ECA																	106	99	34	33	156	144	15	10	62	81	4	1	70	41	5	1
	Cd R CCA, R OG																	96	102	34	23	144	144	17	12	63	77	6	6	32	34	2	1
	Cd R CCA																	93	98	34	26	144	144	17	11	64	77	7	9	32	42	2	3
	Cd L CCA	110	92	37	34	156	144	17	11	77	76	18	22	85	66	18	12	128	100	38	29	156	144	17	11	40	34	2	2	89	66	18	8
	Cd L CCA, Cd R CCA																	129	122	37	28	150	156	17	13	27	25	1	2	32	24	2	0
	Cd L CCA, Cd R CCA, L OG																	134	128	39	33	156	150	16	10	27	25	1	2	30	16	2	1
	Cd L CCA, Cd R CCA, L OG, R OG																	133	105	36	30	156	144	18	11	27	25	1	2	17	13	1	1
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA																	117	102	36	33	156	156	18	14	84	73	6	6	16	11	2	0
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA, R ECA																	119	116	34	31	150	144	18	12	85	79	6	9	69	64	4	4
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA																	136	115	34	30	156	156	18	12	81	74	6	9	16	15	0	0
	Cd L CCA, Cd R CCA, L OG, R OG																	125	115	34	30	162	156	17	12	27	24	1	1	21	13	1	1
	Cd L CCA, Cd R CCA, L OG																	131	115	38	30	156	144	17	13	27	25	1	1	25	26	1	1
	Cd L CCA, Cd R CCA																	126	120	37	31	168	156	17	12	27	27	1	1	25	27	1	3
	Cd L CCA																	113	112	35	31	156	156	17	11	43	34	2	1	93	77	18	11
	Cd R CCA	96	108	38	32	156	144	17	10	77	78	18	19	82	73	21	16	98	95	38	30	156	144	16	10	52	74	4	19	47	36	11	1
	Cd R CCA, Cd L CCA																	101	113	38	27	150	144	17	11	26	27	2	1	22	18	2	1
	Cd R CCA, Cd L CCA, R OG																	101	115	37	30	144	144	17	11	26	27	3	1	29	18	2	1

Cont.....

Sheep No.	Clamping Position	BASAL														CLAMPED													
		Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings				Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings			
		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg	
		Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn
	Cd R CCA, Cd L CCA, R OG, L OG															106	118	38	30	144	156	16	11	32	27	3	1	27	9	9	0
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA															98	116	37	30	144	144	17	11	27	27	2	1	21	11	3	0
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA, L ECA															108	116	37	30	156	144	17	12	91	83	6	5	122	11	1	1
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA															104	116	38	29	156	156	16	13	27	32	3	1	23	11	1	1
	Cd R CCA, Cd L CCA, R OG, L OG															112	119	39	31	150	156	15	11	31	31	4	1	27	20	7	1
	Cd R CCA, Cd L CCA, R OG															105	120	40	31	156	144	17	12	28	27	4	1	24	21	4	1
	Cd R CCA, Cd L CCA															99	118	40	33	144	150	17	12	31	27	3	1	32	28	1	1
	Cd R CCA															104	106	31	30	144	156	17	12	44	36	4	1	54	41	10	2
4	Cd L CCA	80	58	27	30	126	126	24	17	83	56	26	20	77	52	28	25	85	59	27	27	126	126	24	17	44	29	4	3	79	53	25	23
	Cd R CCA	82	59	27	28	132	126	24	17	79	56	21	18	77	52	28	25	85	63	27	27	126	126	24	17	82	56	21	16	42	25	5	3
	Cd L R CCA	82	61	27	28	126	126	24	17	81	58	25	19	75	55	23	23	91	69	27	22	126	120	25	18	29	18	2	1	27	15	3	2
	Cn L CCA	77	59	27	27	126	126	24	16	77	53	27	16	72	53	24	23	86	58	27	27	126	120	24	17	47	29	5	3	77	51	23	23
	Cn R CCA	81	60	27	28	126	126	24	17	80	55	24	16	76	52	25	25	84	64	27	27	126	126	24	17	82	56	23	15	47	26	5	4
	Cn L R CCA	83	65	27	28	132	126	23	17	80	57	26	20	75	52	25	24	89	69	27	23	126	120	23	17	27	18	3	2	27	15	3	2
	Cd L CCA	81	57	27	31	132	120	23	17	79	55	25	19	76	51	25	23	85	63	27	28	132	120	23	17	46	27	4	3	77	51	24	21
	Cd L CCA, L OG															84	54	27	26	132	120	22	16	46	27	4	3	71	44	25	21
	Cd L CCA, L OG, L ECA															84	61	27	26	132	114	23	16	78	53	13	10	76	51	24	21
	Cd L CCA, L OG															85	61	27	26	132	120	27	16	47	29	5	3	77	52	25	21
	Cd L CCA															82	61	27	26	132	126	22	17	47	29	5	3	77	52	24	21
	Cd R CCA	79	58	28	30	132	120	23	17	83	57	26	19	74	51	28	23	81	64	27	26	126	120	23	16	78	56	23	18	42	24	6	3
	Cd R CCA, R OG															81	61	28	26	126	126	23	16	78	54	24	18	42	24	6	3
	Cd R CCA, R OG, R ECA															81	63	28	27	132	114	23	16	78	56	23	18	71	50	14	11
	Cd R CCA, R OG															81	63	28	26	132	120	24	16	77	55	24	18	44	26	6	4
	Cd R CCA															82	66	28	26	132	120	24	16	79	56	23	18	44	26	6	4
	Cd L CCA	79	61	28	30	132	114	23	17	82	60	26	20	73	57	26	20	83	66	28	28	132	120	24	16	44	29	3	3	77	57	23	21
	Cd L CCA, R OG															74	65	26	26	126	120	23	16	44	29	3	3	77	56	23	23
	Cd L CCA, R OG, L ECA															77	58	27	26	126	114	22	17	69	52	13	8	71	50	23	20
	Cd L CCA, R OG															74	61	30	26	126	114	22	16	41	29	4	3	69	52	23	21
	Cd L CCA															77	63	30	26	126	120	22	16	41	30	4	3	69	62	24	20
	Cd R CCA	78	61	31	29	126	114	23	16	79	57	28	18	72	54	28	23	81	69	30	31	132	114	22	16	74	58	24	14	42	25	5	3
	Cd R CCA, L OG															76	62	31	26	132	120	23	17	74	54	23	14	42	25	5	3
	Cd R CCA, L OG, R ECA															78	68	31	26	132	120	23	17	74	57	24	15	67	50	13	11
	Cd R CCA, L OG															78	68	31	26	120	114	22	16	74	58	24	15	42	27	6	4
	Cd R CCA															78	66	31	26	132	120	23	16	74	55	24	15	42	27	6	4
	Cd L CCA	79	63	31	30	126	120	22	17	80	60	28	20	70	55	25	25	82	67	30	27	132	114	23	16	40	29	3	3	71	58	20	22
	Cd L CCA, L OG															86	74	28	22	138	114	23	16	39	29	3	3	67	58	20	22
	Cd L CCA, L OG, R ECA															88	74	27	18	132	120	23	0	25	18	1	2	82	70	35	30
	Cd L CCA, L OG															77	55	30	26	126	120	24	0	37	25	4	2	65	45	20	16
	Cd L CCA															78	47	30	31	126	120	24	13	39	22	4	3	67	46	20	23
	Cd R CCA	79	56	31	34	132	120	23	16	81	52	25	19	71	49	21	25	80	62	30	31	126	114	23	17	77	51	23	18	42	22	5	4
	Cd R CCA, R OG															84	63	28	30	132	114	22	17	77	51	23	18	42	22	5	4
	Cd R CCA, R OG, L ECA															83	62	28	26	132	126	23	16	86	64	36	33	25	13	3	2
	Cd R CCA, R OG															80	53	30	28	126	114	24	14	74	46	24	15	42	19	6	4
	Cd R CCA															80	57	31	27	132	114	22	15	77	50	24	15	42	19	6	4
	Cd L CCA	79	59	31	32	132	126	23	17	82	58	28	20	71	51	25	25	82	69	31	28	126	120	22	16	40	29	4	2	72	58	23	23
	Cd L CCA, R OG															86	77	28	21	132	126	22	17	40	29	4	2	72	58	23	23
	Cd L CCA, R OG, R ECA															88	78	29	23	132	114	23	17	26	18	3	1	84	72	36	32
	Cd L CCA, R OG															81	63	30	27	132	114	24	15	40	25	4	3	72	53	24	20
	Cd L CCA															81	63	29	26	144	114	24	15	40	25	4	3	71	53	24	20
	Cd R CCA	80	62	31	31	132	120	23	16	82	60	28	18	72	54	28	25	83	72	31	27	132	114	23	16	79	85	25	15	42	24	5	3
	Cd R CCA, L OG															86	76	31	26	126	114	22	15	79	85	25	15	42	24	5	3
	Cd R CCA, L OG, L ECA															86	71	28	23	132	114	22	17	88	74	36	28	29	15	3	2
	Cd R CCA, L OG															82	60	32	27	138	120	22	16	79	53	25	13	44	20	6	3
	Cd R CCA															82	66	32	27	132	114	22	16	79	85	25	15	44	22	6	4
	Cd L CCA	81	76	34	31	132	120	22	16	78	58	30	20	73	56	28	25	85	72	31	28	132	120	22	16	37	31	4	2	74	60	23	24
	Cd L CCA, L OG															85	72	31	27	138	114	22	15	42	31	4	2	74	62	23	23
	Cd L CCA, L OG, L ECA															76	66	31	28	132	120	22	15	68	57	12	7	68	56	23	23
	Cd L CCA, L OG, L ECA, Cd R CCA															87	68	30	25	132	120	22	15	68	49	10	7	25	13	2	2
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG															88	62	31	24	138	96	22	17	76	47	10	7	25	17	2	2
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG, R ECA															132	63	26	18	144	108	0	0	90	51	9	5	88	42	10	7
	Cd L CCA, L OG, L ECA, Cd R CCA, R OG															100	90	28	19	144	120	0	0	75	49	8	5	28	11	2	2
	Cd L CCA, L OG, L ECA, Cd R CCA															93	71	31	20	144	120	0	0	69	49	8	5	25	13	2	2
	Cd L CCA, L OG, L ECA															74	55	36	27	144	120	0	0	63	49	10	8	63	45	24	20
	Cd L CCA, L OG															69	49	36	27	132	120	0	11	29	20	3	2	60	40	28	20
	Cd L CCA															69	46	34	28	132	108	0	13	32	20	3	2	63	38	28	23
	Cd R CCA	79	58	32	32	138	108	23	15	79	48	23	17	77	47	30	24	85	61	30	30	132	114	23	16	81	50	20	15	45	20	3	3
	Cd R CCA, R OG															82	60	30	30	132	114	23	16	78	50	20	15	45	19	3	3
	Cd R CCA, R OG, R ECA															83	59	31	30	132	108	24	16	78	48	20	15	69	42	13	13

Cont.....

Sheep No.	Clamping Position	BASAL														CLAMPED													
		Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings				Peripheral Recordings								Left Carotid Sinus Recordings				Right Carotid Sinus Recordings			
		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Heart Rate Beats/min		Respirtn. Rate Breaths/min		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg		Mean Blood Pressure, mmHg		Pulse Pressure, mmHg	
		Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn	Intact Vn	Cut LR Vn
	Cd R CCA, R OG, R ECA, Cd L CCA															92	77	28	25	132	114	23	15	25	15	0	2	74	51	8	10
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG															92	67	28	19	132	108	22	16	25	20	0	2	76	26	9	8
	Cd R CCA, R OG, R ECA, Cd L CCA, L OG, L ECA															89	63	26	18	132	102	23	0	78	52	10	5	72	45	6	8
	Cd R CCA, R OG, R ECA Cd L CCA, L OG															91	61	25	21	144	114	18	0	23	13	1	0	66	39	5	6
	Cd R CCA, R OG, R ECA Cd L CCA															88	62	27	23	144	114	13	0	23	13	1	0	64	39	3	6
	Cd R CCA, R OG, R ECA															79	52	28	30	132	114	17	0	67	38	15	8	62	36	3	7
	Cd R CCA, R OG															87	47	28	31	126	114	21	0	75	33	18	10	44	13	3	3
	Cd R CCA															89	40	30	32	132	114	22	0	78	31	18	10	44	10	3	3
	Cd L CCA	85	75	30	28	132	114	22	15	80	66	22	25	79	66	28	20	90	79	28	28	144	108	22	15	44	36	4	3	82	66	25	25
	Cd L CCA, Cd R CCA																	96	97	28	26	144	120	22	15	30	23	2	1	30	20	3	1
	Cd L CCA, Cd R CCA, L OG																	93	104	28	28	144	114	22	15	28	22	2	1	30	19	1	1
	Cd L CCA, Cd R CCA, L OG, R OG																	106	97	26	27	132	108	21	14	28	22	2	1	26	17	1	1
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA																	87	72	27	28	132	108	22	15	64	63	5	11	5	5	1	1
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA, R ECA																	98	83	28	18	138	102	0	0	72	68	5	8	79	61	11	10
	Cd L CCA, Cd R CCA, L OG, R OG, L ECA																	95	81	23	18	144	114	0	0	63	58	5	6	24	13	3	3
	Cd L CCA, Cd R CCA, L OG, R OG																	92	79	26	18	132	120	15	0	25	17	1	2	24	14	3	2
	Cd L CCA, Cd R CCA, L OG																	89	78	27	18	132	114	17	0	26	17	1	2	25	13	3	2
	Cd L CCA, Cd R CCA																	91	74	28	22	144	108	20	0	28	16	1	2	28	13	3	2
	Cd L CCA																	89	63	26	26	132	120	20	0	40	24	1	2	76	49	24	18
	Cd R CCA	86	67	30	29	132	114	21	15	84	56	25	18	90	56	31	23	89	73	30	27	132	114	17	15	83	57	23	14	49	24	6	3
	Cd R CCA, Cd L CCA																	96	95	28	25	138	114	22	15	27	20	3	0	29	15	4	2
	Cd R CCA, Cd L CCA, R OG																	93	92	28	23	138	114	21	15	27	18	3	2	28	15	4	2
	Cd R CCA, Cd L CCA, R OG, L OG																	93	90	28	23	144	108	22	13	25	18	1	2	29	15	4	2
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA																	93	86	27	26	132	108	24	16	25	17	1	2	58	62	10	12
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA, L ECA																	101	86	26	18	138	114	21	0	77	67	6	6	68	60	10	9
	Cd R CCA, Cd L CCA, R OG, L OG, R ECA																	99	81	27	18	138	114	20	0	25	15	1	1	75	53	11	9
	Cd R CCA, Cd L CCA, R OG, L OG																	99	77	28	19	132	120	20	0	30	15	1	1	29	13	3	2
	Cd R CCA, Cd L CCA, R OG																	99	68	28	21	132	108	22	0	30	15	1	1	31	10	3	2
	Cd R CCA, Cd L CCA																	99	58	28	24	132	108	20	0	30	13	1	1	31	10	3	2
	Cd R CCA																	90	48	28	26	132	120	20	0	76	29	15	5	43	10	6	3

TABLE 5 RAW DATA OF ARTERIAL WALL THICKNESS (μm) OF THE LEFT COMMON CAROTID ARTERY OF SHEEP 6 IN EXPERIMENTAL SERIES 2

Section Number	Area	Tunica Intima						Tunica Media						Tunica Adventitia						Total Vessel Wall					
		1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6
Origin of occipital artery																									
1		13	15	5	5	8	13	340	450	270	400	320	350	188	205	75	283	335	150	540	670	350	680	660	510
2		10	10	5	8	10	10	400	340	410	300	390	390	138	180	113	45	150	135	550	530	530	350	550	530
3	A	10	13	10	8	8	8	430	290	420	290	360	300	138	100	83	63	93	123	560	420	530	380	450	430
4		13	10	10	8	8	8	400	330	370	340	370	310	143	75	125	50	75	85	570	410	500	410	470	410
Origin of cranial thyroid artery																									
5		8	8	8	10	8	8	450	320	390	290	390	310	63	100	155	95	80	58	540	430	550	380	490	390
6		5	5	8	8	5	8	350	240	330	290	330	290	163	100	158	90	100	145	530	330	500	390	440	440
7		5	8	8	5	8	5	340	280	350	270	360	310	200	88	125	80	153	103	550	350	500	340	520	420
8		5	10	5	5	5	10	330	290	270	290	330	280	100	103	43	100	123	95	450	420	320	400	460	390
9		5	8	5	5	5	5	420	320	370	390	340	300	138	80	133	113	188	100	580	420	500	490	350	410
10		5	8	5	8	8	8	380	340	310	310	350	320	150	63	150	100	185	108	550	420	450	420	560	420
11		8	10	8	10	10	5	370	320	370	340	330	310	188	98	160	50	133	118	560	410	550	410	480	410
12		8	8	8	8	5	5	320	360	280	360	360	350	163	118	83	100	175	90	500	490	390	480	540	440
13		8	5	5	8	5	5	370	370	320	360	350	270	125	175	83	205	143	163	520	560	410	590	500	440
14	B	5	5	5	8	8	8	350	340	430	340	300	400	175	125	123	188	125	170	550	490	560	540	440	590
15		10	10	10	5	10	5	450	400	410	350	410	460	63	150	133	75	50	80	540	580	550	450	490	560
16		5	5	5	5	5	8	450	420	450	360	410	490	235	225	138	150	58	105	680	650	600	490	490	620
17		5	5	5	5	5	8	400	390	430	410	390	430	185	100	125	93	125	120	590	490	570	510	620	570
18 Level of thoracic inlet (cervical vertebra 7)	C	5	8	5	5	5	5	450	400	400	360	370	430	125	113	188	213	120	125	600	520	600	560	490	580

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