ANALYSIS OF THE PHYSICAL AND PHYSIOLOGICAL EVENTS RESULTING FROM CALORIC IRRIGATION OF THE HUMAN TEMPORAL BONE

by

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This is to certify that neither this thesis, nor any part of it has been presented, or is being currently submitted in candidature for any degree at any other university. Further, except where specific reference is made, the work described in this thesis is the result of the investigation of the candidate.

G. O'Neill

Candidate

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ABSTRACT

O'NEILL, G. (1985) 'Analysis of the Physical and Physiological Events Resulting from Caloric Irrigation of The Human Temporal Bone' Ph.D. Thesis, C.N.A.A. (London).

Analysis of results obtained from caloric tests showed that, on average, a significant sequential response decline was present for the four caloric responses. The effect of this decline was to produce an 'apparent' canal paresis of 4% of the second ear to be irrigated. There was no significant effect upon the calculation of directional preponderance. Also, differences in both maximum slow phase velocity and the latency of this maximum were found to exist between the warm and cold caloric responses. Although the difference of nystagmus intensities may be explained by the difference in the magnitude of the respective water temperatures, there remained a possible influence of a stimulus-related adaptation effect upon the response latencies.

Regarding pathways and mechanisms of heat transfer during caloric stimulation of the labyrinth, a study of horizontal serial sections of human temporal bones showed that the most direct anatomical route from the external auditory meatus to the lateral semicircular canal is through the air of the middle ear cleft. The bony posterior-inferior extension of the external meatus, which has been generally accepted as the main route for caloric stimulation, was found to be a highly cellular structure and was not seen in serial section until a level was reached which was well below that of the lateral limb of the semicircular canal. Additionally, temperature measurement in isolated temporal bones showed that convection within the middle ear cleft was a significant heat transfer mechanism in caloric stimulation. The mathematical model incorporating temperature profiles based on those from cadaveric temporal bones and which also included a term describing adaptation gave good prediction of caloric primary nystagmus. The true mechanism of vestibular adaptation was however considered to be stimulus related and would therefore be more accurately modelled by a non-linear term.

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INTRODUCTION

Various lesions in the vestibular system are known to produce quite marked effects on the maintenance of equilibrium. The sudden, severe and long lasting vertigo of Ménière's disease (or more precisely 'endolymphatic hydrops') is a typical example. Other examples include benign paroxysmal positional vertigo, the single severe vertiginous attack in vestibular neuronitis and the constant unsteadiness often found in patients having had long periods of treatment with specific aminoglycosides (streptomycin and gentamycin).

As is the case with other medical conditions, correct diagnosis of the cause of either true vertigo or unsteadiness is important with regard to the treatment precribed for the patient e.g. the ability to detect the presence of an acoustic neuroma is of particular importance since this tumour, if not removed, gradually invades into the brainstem causing various neurological problems including blindness. Coma and death eventually follow. Early detection when the neuroma is usually confined to the internal auditory meatus is also important. When the tumour is large and has encompassed major brainstem structures surgical removal is very difficult, sometimes resulting in unavoidable loss of ipsilateral function of the facial nerve.

Although the clinical interview provides much information, the use of modern tests including radiology

allows for a more objective means of diagnosis. It is in this area that the caloric test has become much used in E.N.T. clinics internationally. The results of the test, taken in conjunction with audiological findings, help to ascertain not only if there is vestibular dysfunction present but also if this is due to a peripheral (end-organ) or central lesion.

The usefulness of any diagnostic test is clearly dependant upon its ability to differentiate between normal systems and abnormal ones. This depends upon the number, magnitude and the type of errors inherent in the test procedure, including errors produced from the source (patient). Usually a 95% confidence interval ($\pm$ 2 SD) is used to determine if results are significant or not. Because, for caloric tests in normals, this 'normal range' is relatively large, there is inevitably a significant number of results which are false negatives i.e. patients who have vestibular dysfunction but fall within the range of normals. In order to reduce this problem a greater knowledge of the errors inherent in caloric testing is necessary. Much of the work presented in this thesis has been undertaken with this in view. Further, analysis of the system response to caloric testing can give important information of a fundamental nature of the function of both peripheral and central vestibular mechanisms. Such an analysis involving the use of a mathematical model has been carried out and is also reported.

Following an outline of the anatomy and physiology of the vestibular system in Chapter 1, Chapter 2 deals

with a detailed description of the caloric test and the various factors which influence the response. In Chapter 3 is presented a study which was designed to examine the possibility of the presence of a systematic error in the form of a sequential decline in the four caloric responses. Chapter 4 examines differences in the responses from the warm and cold stimuli.

Since the mechanism of heat transfer in the temporal bone is fundamental to thermal stimulation of the vestibular end-organ, an experimental analysis was carried out to ascertain the magnitude of temperature changes in various parts of the temporal bone and also the effect of anatomical variation upon these changes. This work is presented in Chapter 5. Chapter 6 deals with a mathematical model of temperature generation and nystagmus response from a standard caloric irrigation. The model predicts temperature changes in various parts of the temporal bone and with the additional use of equations describing the hydrodynamics of the canal system, predicts the intensity of nystagmus activity with respect to time. The model includes the use of an adaptive term, the effect and implications of which are fully discussed. Finally, Chapter 7 presents conclusions covering the major topics in the thesis and also suggestions for further study.

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CHAPTER 1

ANATOMY AND PHYSIOLOGY OF THE VESTIBULAR SYSTEM

1.1 Anatomy

i) Temporal Bone - Gross Features.

The human temporal bone can be considered for simplicity to be divided into four main portions, namely squamous, mastoid, tympanic and petrous (Figs 1.1 - 1.3). The squamous portion is a vertical plate of bone superior to the external auditory meatus. Temporal muscle is attached to the lateral surface and the medial surface embraces the cerebral hemisphere. The mastoid portion is a thick projection posterior to the external auditory meatus. One of the more important structures of this is the group of mastoid air cavities which is continuous with the posterior borders of the middle ear. The tympanic portion of the temporal bone is a roughly quadrilateral, curved plate of bone which forms the anterior and inferior walls, and part of the posterior wall of the external auditory meatus. The petrous portion, in which is located the vestibular end-organ, can be considered as a three sided pyramid with its base in the vertical plane and attached to the medial side of the squamous, mastoid and tympanic portions. The three sides comprise an anterior, posterior and inferior surface. The superior semicircular canal can be located as the 'arcuate eminence' found near the middle of the anterior surface. Anterio-laterally

to this eminence is a smooth area of bone which forms the roof of the middle ear cavity. Near the middle of the posterior surface can be found the internal auditory meatus. On the inferior surface which lies in a horizontal plane can be located, among other structures, the jugular bulb and external carotid foramen.

ii) External Auditory Meatus

This canal which is roughly eliptical in cross section extends from the pinna inwards towards the tympanic membrane (Figs 1.1 and 1.4). Since the tympanic membrane is at an oblique plane to the vertical, the auditory meatus varies in depth from about 25 mm to 31 mm [Anson and Donaldson (1967; p18)]. The whole canal is lined with skin. The lateral portion is made up of fibrocartilage whereas the medial portion is bone. Fine hairs and sebaceous glands are to be found in the former portion only. Cerumen secreating glands occur mostly in the cartilaginous portion.

iii) Tympanic Membrane

Situated at the medial end of the external auditory meatus, this membrane divides the meatus from the middle ear cavity (Fig 1.4). It is set obliquely forming an angle of approximately 140^{o} with the superior wall of the meatus. Its long axis measures approximately 9-10 mm while the short axis is approximately 8-9 mm [Anson and Donaldson (1967; p20)]. However, these figures for obliquety and size vary considerably. The membrane is about 0.1 mm in thickness and is made up of three laminations. The most lateral of these is a cutaneous layer, a continuation of

the skin which lines the external meatus. Next is a layer made up of a network of radial and circular fibres. Finally and most medially situated is the mucous layer which is part of the mucous membrane of the middle ear cavity.

iv) Tympanic Cavity

Located between the outer and inner ear, this cavity is lined with mucous membrane and of roughly 2 cc volume (Fig 1.4). It can be best described by consideration of its six boundary walls namely a) lateral boundary (membranous wall), comprising mainly the tympanic membrane. b) medial boundary (labyrinthine wall), comprising the promontory of the cochlea, prominence of the facial canal and prominence of the lateral semicircular canal. c) anterior boundary (carotid wall). Here is located the eustachian tube orifice, wall of the carotid canal and channel of the tensor tympani muscle. d) posterior boundary (mastoid wall). This area contains many air cells. e) roof (tegmental wall) comprising a thin sheet of bone, the tegmen tympani which separates the middle ear space from the cranial cavity. f) floor (jugular wall), an irregular surface of air cells and closely related to the fossa for the internal jugular vein.

Within the tympanic cavity can be found three small bones, the malleus, incus and stapes. The malleus is attached to the tympanic membrane and also to the incus. This latter bone is attached to the stapes which is connected to the oval window on the labyrinthine wall of the tympanic cavity. These bones, acting as a lever

system, transmit vibrations of the tympanic membrane through to the cochlea fluid.

v) Mastoid Cavity

This cavity, lying behind the tympanic cavity can be divided into three areas namely a) mastoid antrum - a large superior space communicating with the tympanic cavity via the aditus. b) central mastoid tract - extending inferiorly from the mastoid antrum (Fig 1.4). This tract may consist of a single air space or of several air cells. c) peripheral mastoid area - consisting of small air cells situated around the central mastoid tract.

Flisberg and Zsigmond (1965) report the size of the mastoid air cell system in normals to be $12.22 \pm 2.61 cm^3$.

vi) Inner Ear

a) Bony labyrinth: Medial to the tympanic cavity and contained within the petrous portion of the temporal bone is the bony labyrinth of the inner ear (Figs 1.4 and 1.5). Posteriorly, this labyrinth comprises the three semicircular canals which are arranged at roughly right angles to one another. Each have a cross sectional diameter of about 1 mm [Schuknecht (1974; p.40)], and form two-thirds of a circle of diameter approximately 6.5 mm [Igarashi (1967)]. The horizontal or 'lateral' semicircular canal is most laterally situated and can be located as a prominence on the medial wall of the tympanic cavity. The plane of this canal subtends an angle of approximately 25^{o} with the Reid horizontal plane. The angles which the superior and posterior canals make with the Reid frontal plane are

approximately 49° and 40° respectively [Blanks et al. (1975)]. The ends of the canals open into the vestibule. However, one limb of the posterior canal unites with one limb of the superior to form the 'common crus'.

The vestibule, situated centrally between the semicircular canals and the cochlea, is a chamber of roughly 4 mm diameter. There are two well defined recesses in the vestibule, the elliptical recess which houses the utricle, and the spherical recess for the saccule. Anteriorly, the vestibule is continuous with the scala vestibuli of the cochlea. The bony cochlea is a snail-shaped structure of two and one half turns with an axial length from base to apex of approximately 5 mm [Schuknecht (1974; p41)].

b) Membranous labyrinth: Enclosed within the bony labyrinth is the membranous labyrinth which contains endolymphatic fluid. This is surrounded by perilymphatic fluid and is separated from the bony labyrinth by a supportive network of connective tissue and blood vessels. The main regions of the membranous labyrinth, all of which are interconnected by the endolymphatic fluid are cochlea duct, vestibular end-organs and endolymphatic duct and sac.

The cochlea duct begins in a recess of the vestibule. It is roughly triangular in cross section and extends within the osseous spiral canal through basal, middle and apical coils ending in the cupular cecuum. The cochlea duct contains the spiral organ of Corti - a structure in which can be found the terminations of the cochlea nerve.

The vestibular end-organs comprise the utricle,

saccule and the three semicircular canals. The utricle is an oval shaped tube which lies in the elliptical recess of the vestibule. The saccule is a flattened, irregularly shaped sac which lies in the spherical recess of the vestibule. Both utricle and saccule contain a sensory area termed the macule. The macule of the utricle lies predominently in a horizontal plane whereas that of the saccule is in a mainly vertical plane. The surface of both maculae are covered by the otolithic membrane, a structure consisting of an acid-mucopolysaccharide gel and containing crystals of calcium carbonate - the otoconia [Lim (1973)]. These crystals range from 0.5 to 30 microns in diameter and have a density of more than twice that of water [De Vries (1950)]. The stereocilia of the macular hair cells protrude into this otolithic membrane. A curved central zone called the striola divides each macule into two areas. The kinocilia of the hair cells on one side of the striola are oriented in the opposite direction to those on the other side. In the utricle, the kinocilia face the striola whereas in the saccule, they face away from it. Since the striola is curved, hair cells are oriented at different angles, thus making the macule a multi-dimensional sensor.

The three membranous semicircular canals contained in the bony labyrinth each have a cross-sectional diameter of about 0.3 mm [Igarashi (1967)]. The superior and posterior canals join at their non-ampullated ends to form the 'common crus' before entry into the utricle. At the ampullated end of each canal near the utricle can be found

the crista, a crest-like septum which crosses the ampulla perpendicular to the long axis of the canal (Fig 1.6). Upon this crista lies a gelatinous mass - the cupula which extends to the opposite wall of the ampulla. Contrary to popular belief, it seems that the hair cells which are located on the surface of the crista, within the sub-cupula space, do not penetrate into the cupula [Friedmann (1974 p.315), Dohlman (1980)]. The kinocilium of the hair cells of each crista are all orientated in the same direction. However, whereas in the vertical canals the kinocilia are directed towards the canal side of the ampulla, in the horizontal canal this direction is reversed.

vii) Blood Supply

Blood is supplied to the inner ear via the labyrinthine artery which originates from either the basilar or anterior-inferior cerebellar artery. The labyrinthine artery sub-divides into three branches namely a) the vestibular artery supplying parts of the saccule, utricle and semicircular canals, b) the cochlea artery supplying the apical two turns of the cochlea and c) the vestibulocochlea artery supplying two thirds of the basal turn of the cochlea, the greater part of the saccule, the body of the utricle, the posterior semicircular canal and parts of the lateral and superior semicircular canal.

Venous drainage of the labyrinth is via a) the vein of the cochlea aqueduct from the base of the cochlea, the saccule and part of the utricle, b) the vein of the vestibular aqueduct from the semicircular ducts and the

remainder of the utricle and c) the internal auditory vein from the apical and middle cochlea turns.

viii) Afferent and Efferent Vestibular Pathways

The cristae and maculae of the vestibular end-organ are innervated by bipolar ganglion cells (ganglion of Scarpa) which form the superior and inferior divisions of the vestibular portion of the VIIIth cranial nerve. The superior division supplies the cristae of the lateral and superior semicircular canals, the utricula macula and the anterosuperior part of the macula of the saccule. The inferior division supplies the crista of the posterior canal and the main portion of the macula of the saccule. The vestibular nerve contains in the region of 18,000 fibres [Schuknecht (1974; p.73)]. After passage through the internal auditory meatus fibres pass on to the four vestibular brainstem nuclei situated on the floor of the fourth ventricle. Projections from these nuclei extend to the cerebellum, extra-ocular nuclei and spinal cord thus forming the vestibulo-cerebellar, vestibulo-ocular and vestibulo-spinal tracts respectively.

Although the main route for vestibulo-ocular connections is through the medial longitudinal fasciculus, other routes are known to exist e.g. nystagmus produced from labyrinthine stimulation is not abolished by section of the M.L.F. [Carpenter and Sutin (1983; p.384)].

Experiments involving the measurement of eye muscle contraction and relaxation from stimulation of specific vestibular end-organ receptors has given important information on vestibulo-ocular tracts. Also, by

recording in different vestibular and oculomotor nuclei after selective stimulation of each semicircular canal, precise pathways have been formulated. In the case of horizontally induced eye movements, the two vestibular nuclei of interest are the medial in which lie excitatory neurons, and the superior which contains inhibitory neurons. Excitatory connections with the ipsilateral medial rectus are made through the ipsilateral M.L.F. and inhibitory connections with the contralateral medial rectus run in the reticular substance beneath the M.L.F. Input to the lateral rectus muscle (excitatory and inhibitory) runs directly to the contralateral and ipsilateral abducens nuclei respectively [Ito (1975)]. A diagramatic representation of these pathways is shown in Fig 1.7.

The otolith-ocular connections are less well understood than those of the semicircular canals. Stimulation of all macular fibres results in irregular eye movements. Stimulation of discrete parts of the utricle and saccule results in mostly vertical and vertical-rotatory eye movements [Suzuki et al. (1969), Fluur and Mellström (1971)].

The presence of an efferent vestibular system has been found in cat [Gacek and Lyon (1974), Warr (1975)] and monkey [Goldberg and Fernández (1977)]. Areas responsible for efferent activity have been located bilaterally in the brainstem, inferior to the medial vestibular nucleus, medial to the ventral portion of the lateral vestibular nucleus and lateral to the abducens

nucleus. The action of this system on afferent activity would seem to be different in different animal species, e.g. Dieringer et al. (1977) found that in cat, stimulation of the efferent system produced supression of afferent activity in only four out of forty-one afferent units. In monkey, Goldberg and Fernández (1977) found that excitation of central pathways resulted in an increase in afferent activity. From consideration of these and other studies, Wilson and Melvill Jones (1979; p123) indicate the possibility of species differences related to ascent in the phylogenetic scale.

1.2 Physiology

i) End-Organ and Nerve

The theory of action of the vestibular end-organ is that of a mass exerting a force (inertia or gravity) on a deformable group of sensory hair cells. In the semicircular canals the force is generated by the inertia of the contained endolymph. Thus during angular movement, as the skull accelerates in one direction, an inertia force on the cupulae is produced in the opposite direction. In the utricle and saccule, whereas a force is generated during linear acceleration by the inertia of the otolithic membrane, during static body tilt, a force is exerted on the underlying sensory hairs by the action of gravity on this membrane. The deflection of sensory hairs causes a modulation in the discharge rate of the primary afferent neurons and this then becomes the neural

input to the central vestibular system.

Ewald (1892) opened the membranous labyrinth in pigeons and generated ampullopetal and ampullofugal flows of the contained fluid. He noticed that this produced movements of the eyes and head in the plane of the stimulated semicircular canal and in the direction of fluid flow. Steinhausen (1931) and Dohlman (1938) both showed that in fish, the cupula provides an apparently watertight seal in the ampulla and that it moves with fluid movement in the canal.

Lowenstein and Sand (1940) working with elasmobranches reported that there existed in the crista two distinct neural response units, one with, and one without spontaneous activity at rest. Also, that ampullopetal stimulation of the horizontal canal crista increased the activity of the spontaneously firing units and activated an additional population of previously silent ones. Ampullofugal stimulation however decreased the spontaneous activity without any effect on the silent population.

Fernández and Goldberg (1971) and Goldberg and Fernández (1971a,b) recorded the activity of peripheral neurons innervating the semicircular canal of the squirrel monkey in response to constant angular accelerations and also sinusoidal stimulation. Among some of the important findings from this work are a) All neurons exhibited increases and decreases in their resting discharge depending on the direction of stimulation,

b) For the horizontal canal, deflection of the cupula toward the utricle produced an excitatory response (increase in discharge). For the vertical canals this was reversed, c) Inhibitory responses were usually smaller than the excitatory responses for the same magnitude of stimulation. A large asymmetry at large stimulus magnitudes could be accounted for by the fact that although it was possible to silence a unit's discharge by a large inhibitory stimulus, it was not possible to saturate a unit's response to an excitatory stimulus. d) Although the torsion-pendulum model of the end-organ probably adequately represents the motion of the cupula and endolymph, it cannot account for the response dynamics of the first order afferents innervating the semicircular canals. Two other factors to be taken into account in this respect are low frequency adaptation and high frequency phase lead.

Again in the squirrel monkey, Fernández and Goldberg (1976a,b,c) studying the otolith organs found that a) The saccus functions mainly (if not solely) as an equilibrium organ. b) Polarization vectors for the utricular and saccular units are at approximately right angles to one another. c) In response to static tilts and force trapezoids, excitatory responses are slightly larger than inhibitory responses. d) Adaptation was more marked in so-called 'irregular' units i.e. neurons whose discharge rate was irregular.

ii) Nystagmus

As indicated earlier, stimulation of the vestibular end-organs by, for example, rotation about a vertical axis, sets up rhythmic movements of the eyes termed 'nystagmus'. Vestibular-induced nystagmus is characterised by two phases, the slow and the fast. It is presently accepted that these two phases are quite separate phenomena. Under certain circumstances such as brain lesions and sleep, a slow phase can be generated without a fast phase [Holmes (1938), Nathanson and Bergmann (1958)]. Also, many drugs have differential effects on fast and slow phases [Melvill Jones and Sugie (1972)].

Regarding the generation of the fast phase, the idea that there exists a feedback system incorporating ocular muscle stretch receptors whereby a fast phase is generated when the eyes have reached a specific position in the orbit during the slow phase, is contrary to experimental findings. It has been shown that complete removal of the eye and its muscles has little effect on the discharge from oculomotor neurons [McIntyre (1939)]. The precise mechanism responsible for fast phase generation is unfortunately not known. It has been suggested that neurons in the parapontine reticular formation monitor vestibulo-ocular signals and play an important role in the production of fast phases of nystagmus [Baloh and Honrubia (1979; p62)].

Since upon stimulation the slow phase reflects the

activity of the vestibular end-organ, a measure of this has proved to be useful as a clinical aid in the diagnosis of vestibular disorders.

iii) Habituation and Adaptation

Habituation is the decrease in vestibulo-ocular response from repeated stimulation. Adaptation is a decrease in response during sustained stimulation.

Hood (1973) showed the existence of adaptation in the response from the caloric test. After the initial response had subsided, a resurgence of nystagmus activity could be observed when the subject was moved into a different position. This indicated that although there still remained a small stimulus at the end-organ, adaptation had effectively reduced the response to zero.

Two important findings indicate that habituation and adaptation are indeed separate effects, a) that simultaneous bilateral irrigations of equal temperature do not cause habituation [Collins (1965a)], b) unilateral caloric irrigation results in habituation of nystagmus in one direction regardless of the ear stimulated or the temperature of the stimulus [Proctor and Fernández (1963)]. Neither of these findings can be explained by adaptation of primary afferent neurons.

iv) Suppression of Nystagmus

Any clue which will give the subject information to establish a frame of reference will normally result in suppression of an induced nystagmus. This includes visual, tactile, auditory and proprioceptive inputs.

Visual fixation can result in significant inhibition of nystagmus but in the clinical situation this is overcome by either the use of Frenzel glasses or recording in darkness.

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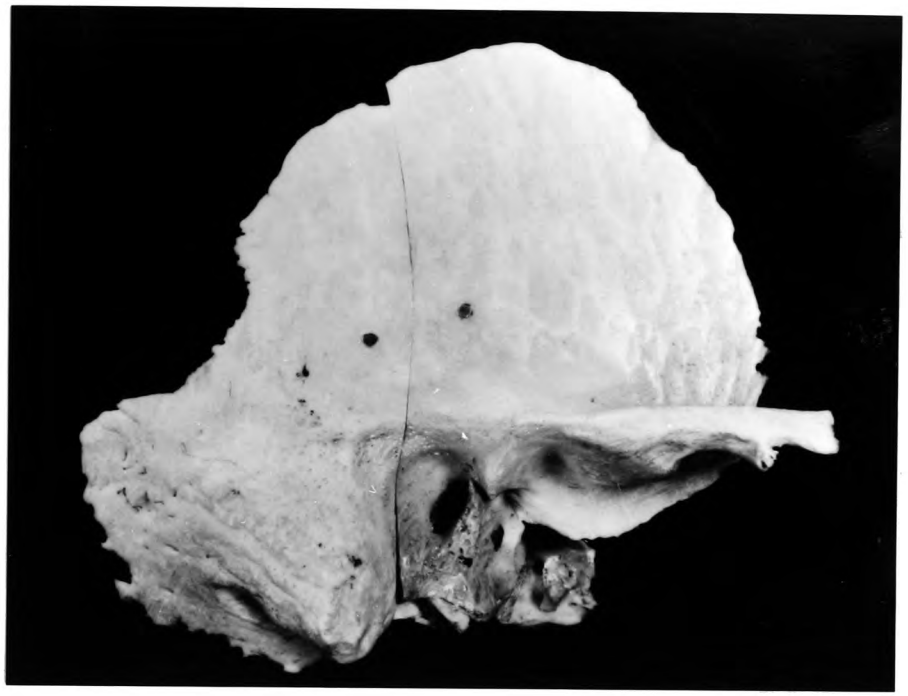


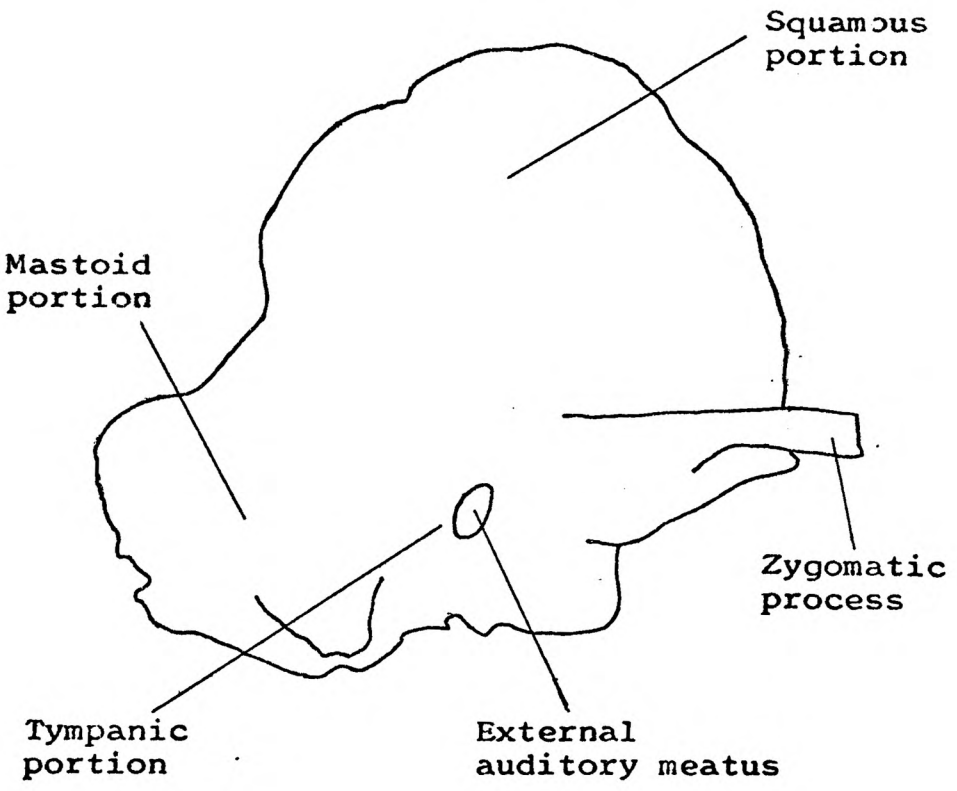
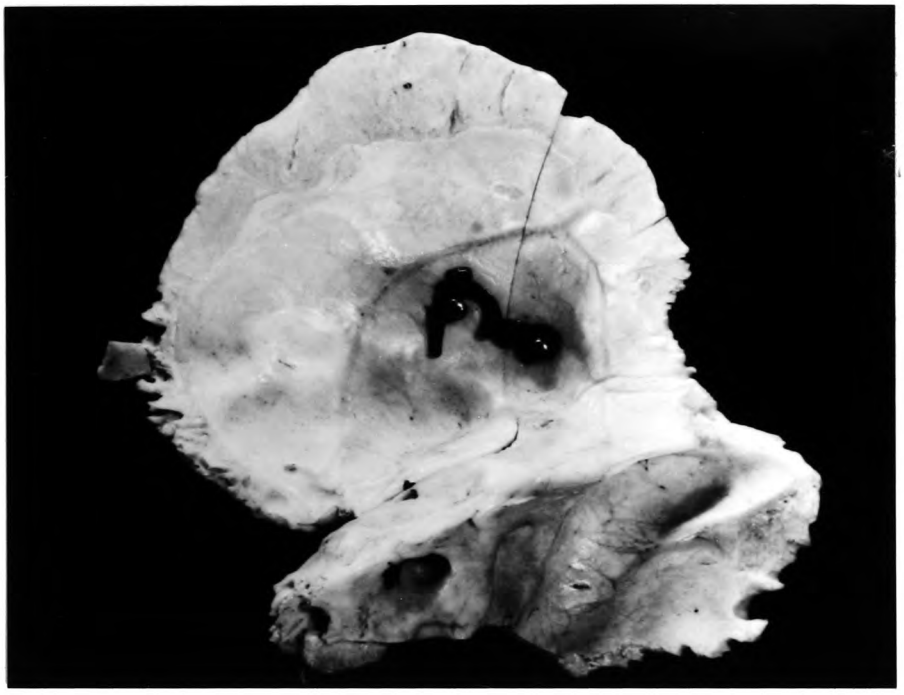


Fig 1.1 Lateral view of the right temporal bone.



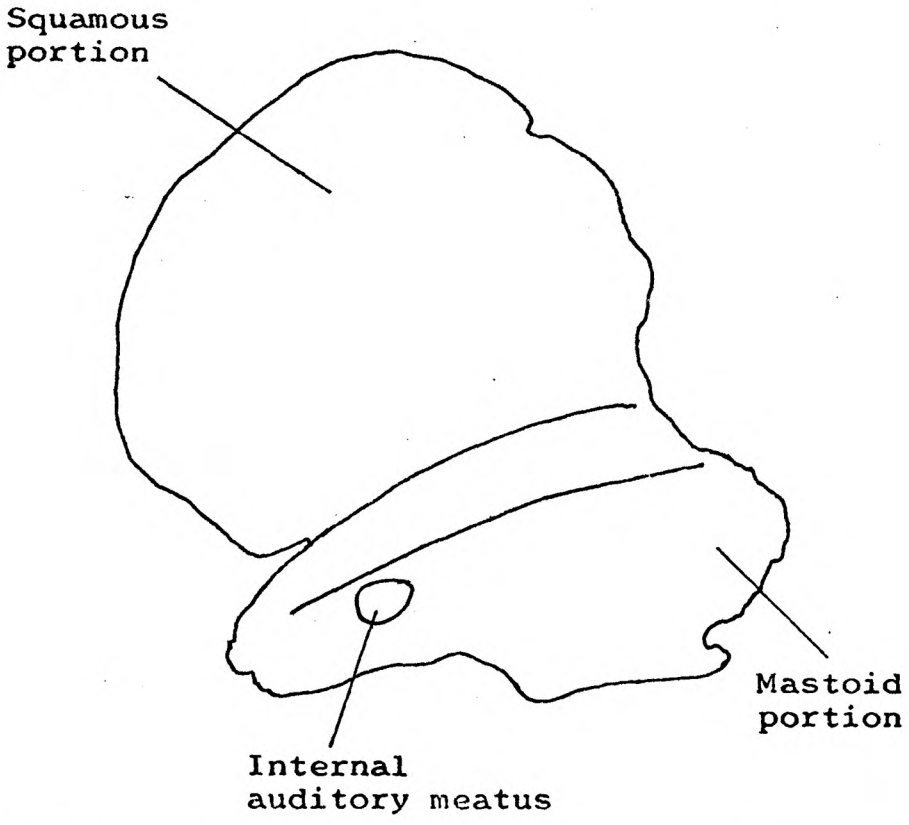


Fig.1.2 Medial view of the right temporal bone.

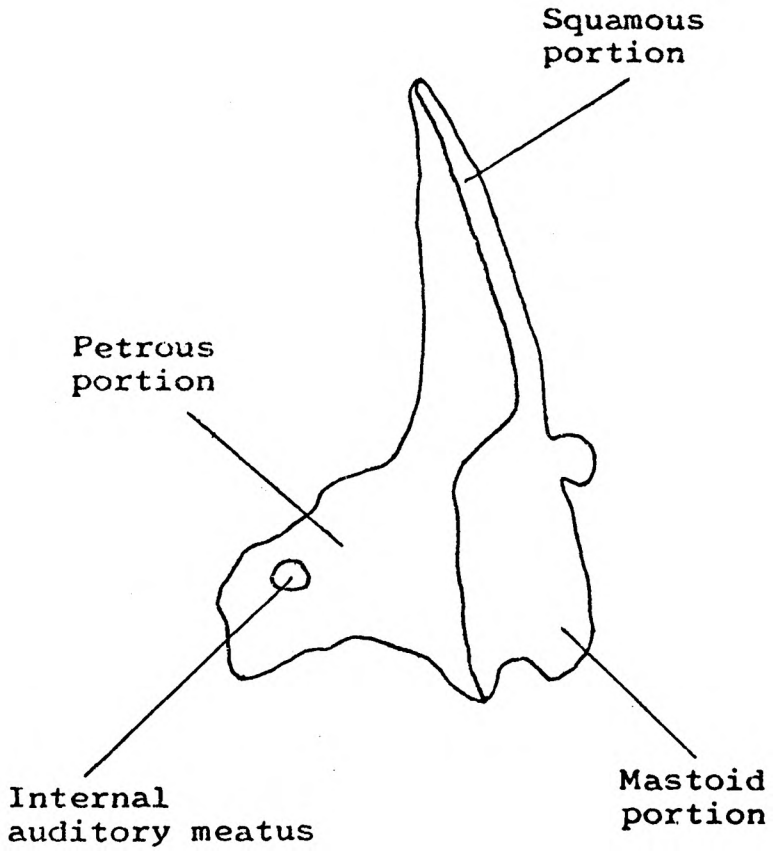


Fig 1.3 Posterior view of the right temporal bone.

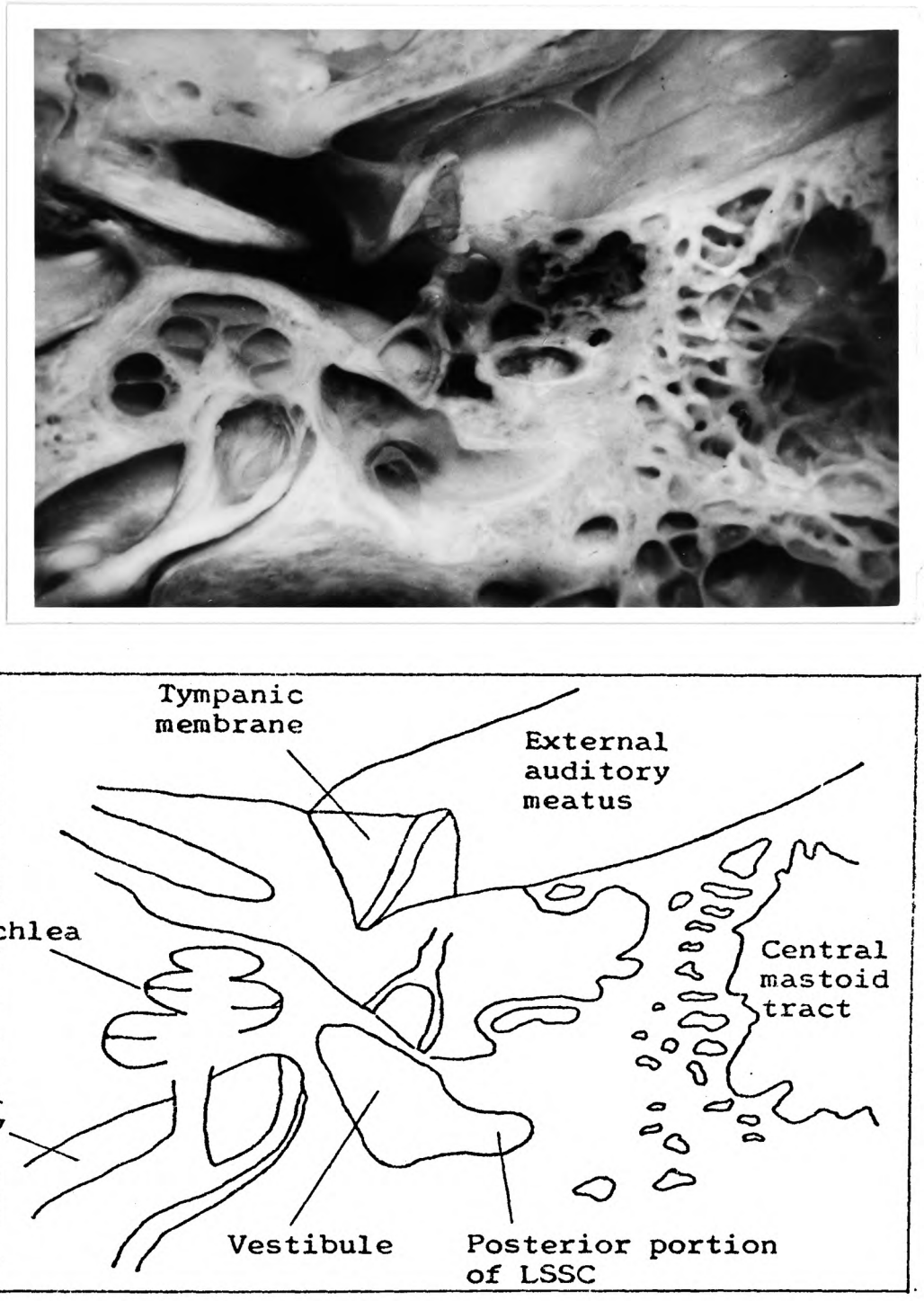


Fig 1.4 Horizontal section of the right human temporal bone.

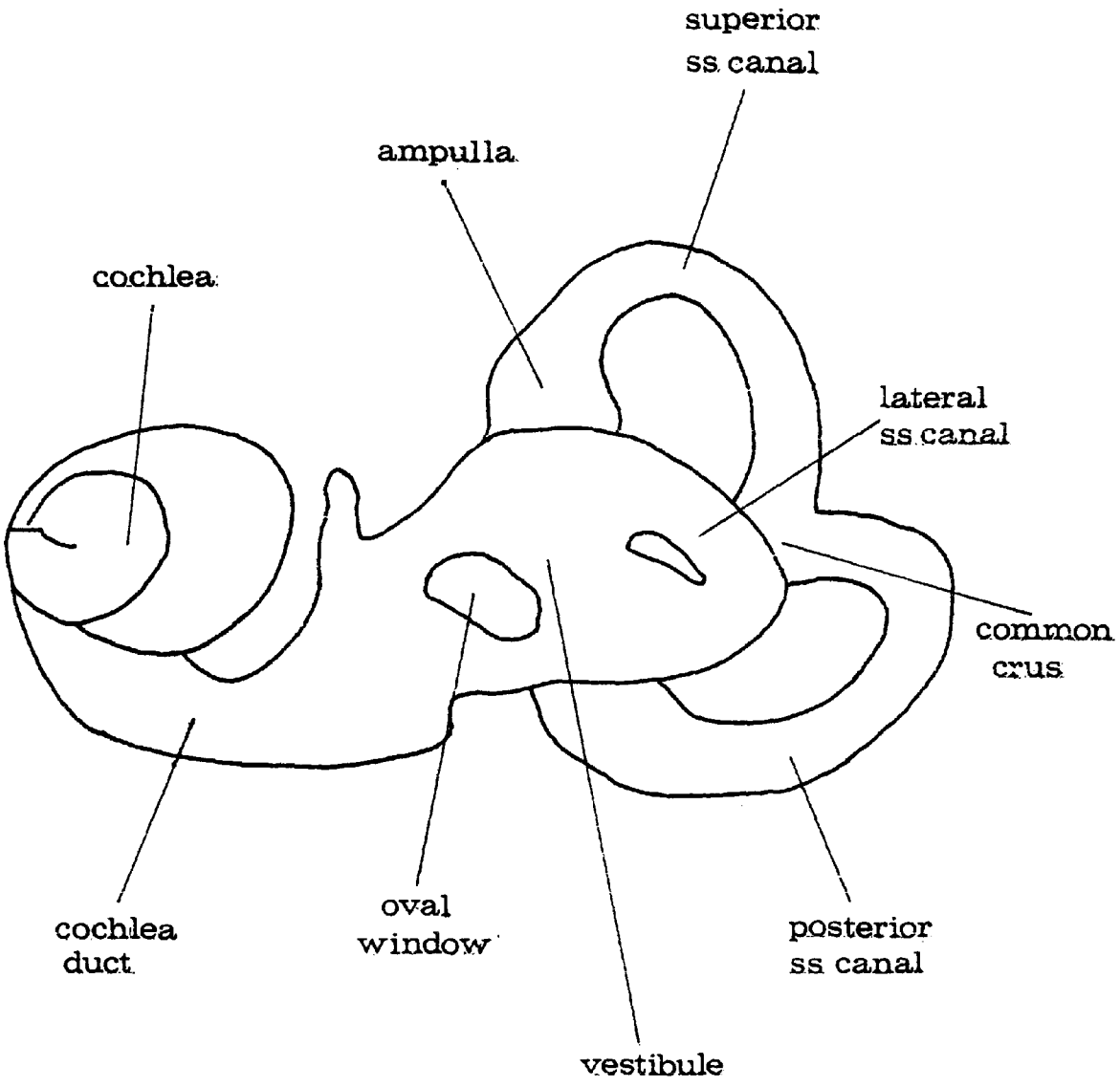


Fig 1.5 Outline of the Bony Labyrinth.

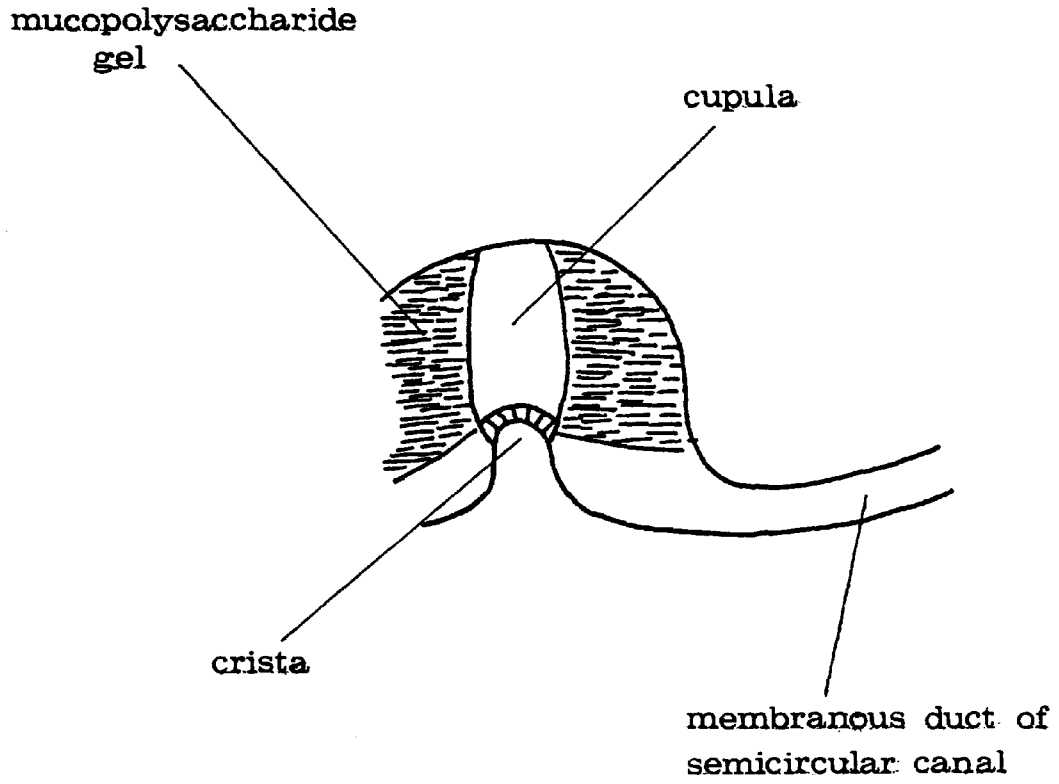
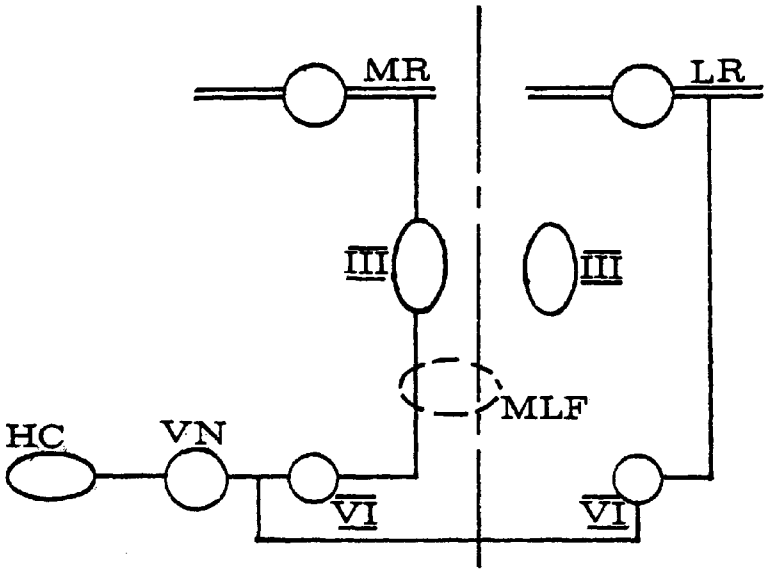
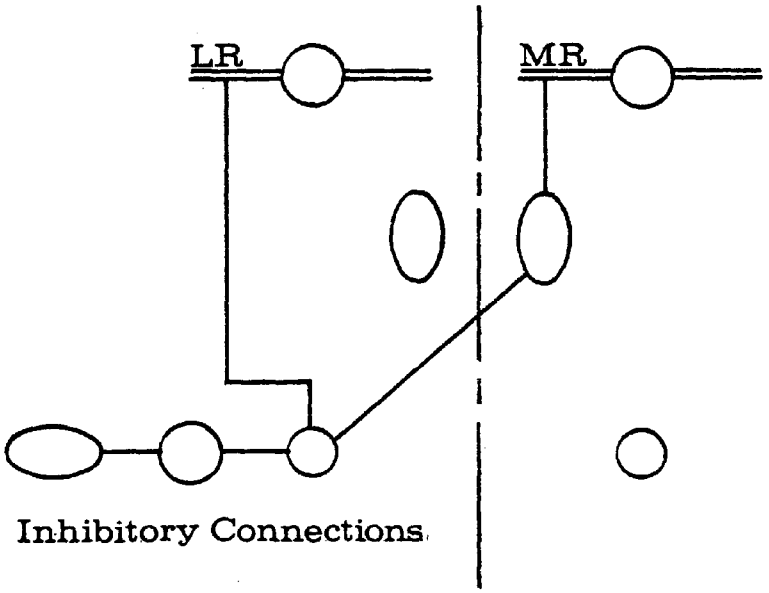


Fig 1.6 Schematic diagram of ampullary contents [After Dohlman (1980)].



Excitatory Connections



Inhibitory Connections

Fig 1.7 Horizontal semicircular canal system - vestibulo-ocular pathways.

MR - medial rectus; LR - lateral rectus
HC - horizontal semicircular canal
VN - vestibular nucleus; VI - abducens nucleus
III - oculomotor nucleus.

CHAPTER 2

THE CALORIC TEST

2.1 Introduction

A variety of tests have been devised over the years to test vestibular function. Stimulation techniques include rotational acceleration [Wilmot (1965), Mathog (1972), Baloh et al. (1979)], pendulum swings [Jongkees and Philipszoon (1964)], electrical field generation [Jongkees and Philipszoon (1964), Breson et al. (1971)], positioning tests [Aschan et al. (1957), Cawthorne and Hallpike (1957)] and the generation of thermal gradients in the inner ear [Jongkees (1948b), Henriksson (1956), Sills et al. (1977)]. Measurement of the response of the vestibular system to such stimuli has included analysis of past-pointing reactions, body sway and eye movements. The following paragraphs will be limited to a discussion of thermal stimulation via the external auditory meatus using measurements of eye movements to quantify the response.

The principle underlying the caloric test is that a temperature gradient generated in the inner ear will cause density changes in the contained fluid of the lateral semicircular canal. The resulting out-of-balance hydrostatic force produces a pressure difference across the cupula and deflection of this membrane.

This in turn leads to a modulation of the discharge rate of the primary afferent neurons. Nystagmus is produced through the connections of the vestibulo-ocular tract.

Although Bárány as early as 1906 had postulated such a theory, various other views were later put forward as alternatives to this. These included direct thermal stimulation of the vestibular nerve [Bartels (1911)], vascular reactions [Kobrak (1918)], otolithic stimulation [Borries (1925)] and a central mechanism [Brunner (1921)]. Bárány's theory however has now gained widespread acceptance. It explains the relationship between the stimulus temperature and direction of the resulting nystagmus, the reversal of nystagmus when the subject is tested in the prone position instead of the supine and furthermore, the occurrence of a mainly horizontal nystagmus suggests selective stimulation of the lateral semicircular canal.

2.2. Basic Technique

In practice, use is made of the technique developed by Fitzgerald and Hallpike (1942). This has been modified somewhat in recent years to incorporate the use of electronystagmographical analysis. The patient lays supine with neck flexed at 30^{o} to the horizontal plane. In this position the lateral semicircular canal is roughly in the vertical plane (ampulla uppermost) and best suited for stimulation

by hydrostatic buoyancy forces in the endolymph. Cooling the temporal bone by irrigating the external meatus with water at 30°C results in endolymph movement which deflects the cupula away from the utricle and an associated nystagmus with the fast phase directed away from the irrigated ear. Similarly, heating the temporal bone with water at 44°C results in cupula deflection towards the utricle and nystagmus directed towards the irrigated ear. The amount of water used for each irrigation is between 250-500 cm^3 over an irrigation period of either 30 or 40 seconds.

The nystagmus which results from this stimulation gradually increases in intensity, reaches a maximum at about forty seconds after the cessation of irrigation and then slowly decreases. A secondary nystagmus of low intensity can sometimes be observed after the primary response, this being attributed to the mechanism of adaptation [Malcolm and Melvill Jones (1970), Barnes and Benson (1978)]. Since it has been shown that a temperature gradient can exist at the end organ for over ten minutes, a reasonable period of time (at least five minutes) is allowed before the start of a subsequent irrigation into the opposite ear.

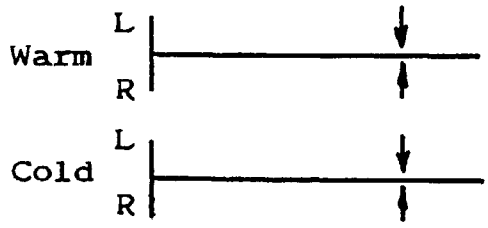
Eye movements are recorded by placing a surface electrode close and lateral to each eye. Use is made of the potential difference which exists between the cornea and retina where movements of the eyes in their orbits results in a changing field potential at the surrounding

skin surface [Miskolczy-Fodor and Arnold (1959)]. A recording of this potential difference gives a good measure of eye position [Geddes et al. (1973)]. Before commencement of each irrigation, a calibration is undertaken so that a 10^{o} arc of eye movement corresponds to a 10 mm pen deflection on the recorder. The subject is instructed that immediately following the caloric irrigation he/she is to look straight ahead and concentrate on a counting sequence for the period of recording.

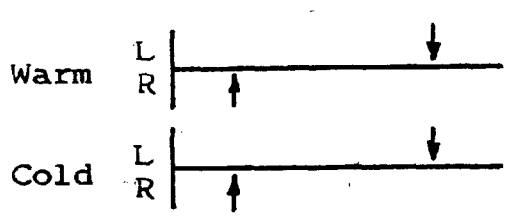
Recording nystagmus can be carried out by using either AC or DC amplifiers. DC amplifiers will record true eye position but they cannot compensate for base line drift. AC amplifiers, although unable to record a maintained eye position can record transient changes such as a series of nystagmus beats, and without the problem of drift. AC amplification with a time constant of 3-10 seconds is the preferred means of measurement in the clinical situation.

At the end of the test the examiner is left with four response traces, two for the warm stimulus in both ears and two for the cold. Measurements can be made of nystagmus duration, frequency, amplitude and slow phase velocity [Miskolczy-Fodor (1961), Sills et al. (1977)]. Unfortunately, in a normal population each of these parameters shows a large degree of variance. For this reason pathology is detected in an individual by comparing the response of one labyrinth with that of the other rather than using an absolute intensity scale such as that used for the measurement of hearing loss.

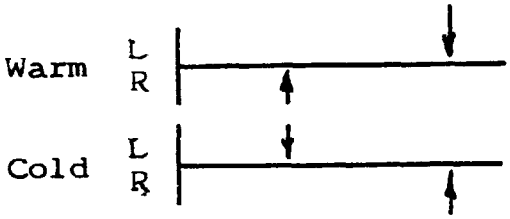
A typical normal response pattern is shown below where the responses are active and well balanced.



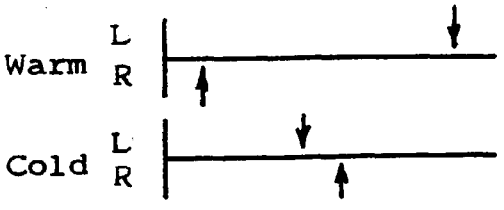
Asymmetry of this pattern is used as an indication of vestibular pathology in the end organ and/or the neural pathways. Asymmetry is expressed as percentage canal paresis and percentage directional preponderance. Simply, canal paresis is a reduction of response to the warm and cold stimuli in one ear. Directional preponderance occurs when the stimuli which produce a nystagmus in one direction result in greater responses than those producing a nystagmus in the opposite direction. In a clinical population however it is not uncommon for a mixed pattern to occur e.g. a left directional preponderance with a right canal paresis. The following diagrams illustrate the various patterns.



a) Right CP



b) Left DP



c) Left DP + Right CP

2.3 Response Measures

Henriksson (1956) showed the poor correlation between duration of the caloric nystagmus and its slow phase speed. In three subjects, all having unilateral sensorineural deafness and one complaining of severe dizziness, caloric testing showed that all three subjects had normal reactions when duration was considered. However, all had grossly abnormal reactions lateralizing to the affected ear when slow phase velocity was used as the quantifying parameter. Henriksson also investigated patients who had a unilateral radical mastoidectomy where a caloric stimulus would be much larger at the lateral semicircular canal on the operated side than on the healthy side. In these cases a measure of duration yielded roughly equal responses from the two sides whereas maximum slow phase velocity showed much larger responses from the affected ear.

In support of the above findings, Jongkees and Philipszoon (1964) found that in a group of 255 patients complaining of vertigo, 11 had a significant canal paresis with regard to duration, 19 with regard to duration taken in conjunction with maximum slow phase velocity, and 38 with regard only to maximum slow phase velocity. Also Baloh et al. (1977a) found that in 35 patients suspected of having unilateral peripheral vestibular lesions, analysis of maximum slow phase velocity identified nearly three times as many abnormalities as did duration of the response.

In the light of these reports it seems probable that nystagmus duration, rather than being an accurate measure of vestibular sensitivity is more a reflection of the duration of the physical stimulus at the lateral semicircular canal coupled with the effects of adaptation.

Attempts to extract more information from the caloric response have led several workers to implement a computer analysis of nystagmus recordings. Herberts et al. (1968) developed a system whereby ENG signals were fed directly onto magnetic tape and from there analysed by a digital computer. Voots (1969) used electronic integration techniques to produce an analogue output of eye velocity. His system also included a numerical print-out of slow phase velocity every ten seconds during the recording.

Although these early attempts at signal analysis gave good results when applied to nystagmus of relatively large amplitude, it was soon realised that for clinical use in pathological cases where the signal is often small and irregular, some means of manual decision-making must be incorporated into the system. With this in mind, Anzaldi and Mira (1975) developed a digital system which allowed the operator to scan the nystagmus record and amend certain parts of the recording which the computer programme could not deal with effectively. A further interactive technique has been reported by Huygen (1979) where regression analysis is used on the signal.

The need for detailed analysis of caloric responses similar to the above techniques is highlighted by the

findings of Zangemeister and Bock (1979) who showed a connection between anatomical variation in temporal bones and the caloric response with respect to both intensity and latency of the nystagmus. Since hand calculations are totally unfeasible for such an analysis, it is likely that computer systems will become more commonplace in ENT clinics in the future.

It is worthy of note that Hamid and Hinchcliffe (1980) have suggested an alternative index of vestibular sensitivity called 'interbeat interval', defined as the time difference between two successive nystagmus beats. This apparently has a small variance in a normal population and is easily measured from the ENG trace. With this measure, Hamid and Hinchcliffe claim to be able to detect a significantly higher percentage of vestibular abnormalities than is possible by means of the slow phase velocity. Until more work on this is carried out at other centres, the slow phase velocity will undoubtedly continue to be of primary use.

2.4 Normal Values

Table 2.1 shows the range of normal values of maximum slow phase velocity obtained by several investigators from a standard caloric test. It is evident that for any one particular stimulus there is a large variance of response in a normal population. Table 2.2 shows the range of normal values for canal paresis and directional preponderance again based on a

standard caloric test. Percentage values were calculated from the formula of Jongkees and Philipszoon (1964) where

$$\% \text{ Canal Paresis} = \left\{\frac{(RC + RW) - (LC + LW)}{RC + RW + LC + LW}\right\} \times 100$$

$$\% \text{ Directional Preponderance} = \left\{\frac{(RC + LW) - (LC + RW)}{RC + RW + LC + LW}\right\} \times 100$$

where RC = response to cold irrigation of the right ear
RW = " " warm " " " " "
LC = " " cold " " " left "
LW = " " warm " " " " "

If the results of table 2.2 are averaged, values are

$-0.37 \pm 10.52\%$ for canal paresis

$+1.07 \pm 10.97\%$ for directional preponderance

2.5 Sources of Error

Error, unfortunately is present in all measurements. In the caloric test consideration can be given to three main areas in which errors are generated.

a) Stimulation

i) Fluctuation in fluid temperature: Water bath temperatures are controllable to within $\pm$ 0.2°C. In addition to this, a heat loss is present along the length of the delivery tube [O'Neill (1978)]. It seems unlikely however that this heat loss would fluctuate enough to have a significant effect on the fluid irrigation temperature.

ii) Poor irrigation: The effectiveness of heat

transfer in forced convection is not only a function of the temperature of the fluid but also of the heat transfer coefficient at the fluid-solid boundary. This coefficient is highly dependant upon the pattern of fluid flow [Rogers and Mayhew (1969)]. Theoretically, a poor irrigation of the external meatus would lower the temperature generated in the temporal bone by a reduction in this heat transfer coefficient.

iii) Residual temperature gradient: Although a caloric nystagmus will have ceased within ten minutes of the cessation of irrigation, there may still be a residual temperature gradient present within the inner ear [Hood (1973)]. The effect of this upon subsequent heating or cooling of the temporal bone is minimised by alternating the ear to be tested and also allowing at least a five minute period between each irrigation.

b) Patient-Recording

i) Changes in corneo-retinal potential: It has been shown that in humans, the corneo-retinal potential varies with respect to time and is particularly influenced by changes in ambient levels of illumination [Francois et al. (1955), Hart (1967), Aantaa (1970)]. These problems can, to a certain degree, be overcome by calibration before each irrigation and testing in one setting of illumination.

ii) Alertness: The degree of subject alertness can significantly alter the intensity of a caloric

nystagmus [Lidvall (1962)]. In an attempt to maintain a constant level of arousal, the patient is instructed to perform mental arithmetic during the period of recording of the response.

iii) Fixation: The ability of a subject to visually fixate on a stationary image can markedly diminish the intensity of induced caloric nystagmus [Levy et al. (1977)]. Baloh et al. (1977b) found in normals that whereas the condition of eyes open in darkness gave the largest response, the use of Frenzel glasses in a dimly lit room gave the least amount of response asymmetry.

iv) Adaptation: Secondary nystagmus is sometimes generated in the caloric response as a result of the process of adaptation [Milojevic and Allen (1967), Barnes and Benson (1978)]. The effect which adaptation has upon successive caloric responses is, at present, not clear.

v) Habituation: A response decline is known to occur upon repeated stimulation of the vestibular end-organ. A process termed 'habituation' is considered to be responsible for this phenomenon [Forssman et al. (1963), Proctor and Fernandez (1963)]. This subject will be dealt with in more detail in chapter 3 of this thesis.

vi) Anatomical asymmetry: Zangemeister and Bock (1979) have demonstrated a relationship between mastoid pneumatisation and caloric response. They have also

shown that significant differences between left and right sided responses occur in normal subjects who have asymmetrical mastoid pneumatisation. This subject will be discussed further in chapter 5 of this thesis in which is presented an analysis of heat transfer pathways in the temporal bone.

vii) Existing spontaneous nystagmus: A spontaneous nystagmus which is present with the subject in the caloric position will influence the responses of the caloric test, e.g. a right beating spontaneous nystagmus will enhance the responses to warm irrigation of the right ear and cold irrigation of the left ear. It will also inhibit responses from the remaining stimuli. This problem can be overcome, to some degree by first measuring the intensity of the spontaneous nystagmus and thereafter adding to and subtracting from the relevant caloric responses.

viii) Position of the eyes: An induced caloric nystagmus can be seen to be enhanced when the subject's eyes deviate in the direction of the fast phase. It is therefore important that during recording, the subject's gaze is in the straight ahead direction.

ix) Skin-electrode impedance: The interelectrode impedance must be low (preferably less than 5KΩ) in order to reduce unwanted noise. Although disposable surface electrodes can be used, cleaner and more stable signals are produced from re-usable silver/silver chloride surface electrodes. With such electrodes, the skin

surface is abraded by the use of a special syringe which is also used to apply the electrode gel.

x) Amplifier time constant: The characteristics of the AC amplifier, being determined by the value of its time constant, can distort the signal from low intensity slow phase eye movements of about $1\text{-}3^{o}/s$. This does not usually cause serious problems since if any or all responses are of such low intensity, the overall pattern in terms of directional preponderance, unilateral or bilateral canal paresis is usually strongly evident.

c) Analysis

i) Marking errors: Errors in quantifying the response can be minimised by having a standardised marking technique, taking as many data points as is necessary for an accurate assessment, and for marking to be carried out by one individual.

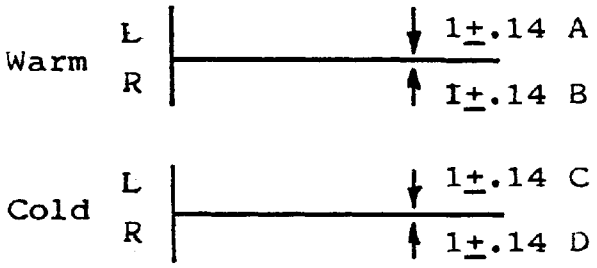
2.6 Random Errors

Considering 'n' independent sources of random error, then if x_1, x_2 --- x_n are the respective standard deviations, the standard deviation of one caloric response will be:

$$\left\{ x_1^{\,2} + x_2^{\,2} + \text{---} \; x_n^{\,2} \right\}^{\frac{1}{2}}$$

For eight sources of random error, each having a SD of $\pm$ 5%, then the SD of the response will be $\pm$ 14%. If it

is next assumed that each of the four caloric responses are independent of each other and that each response, without error, is unity as shown below, then comparing responses A and B,



$$SD\ (A - B) = (.14^2 + .14^2)^{\frac{1}{2}} = \pm .20$$

Similarly $SD\ (C - D) = \pm .20$

For the formula for vestibular imbalance

$$\% CP = \left\{ \frac{(A - B) + (C - D)}{A + B + C + D} \right\} \times 100$$

where expected SD of denominator $\ll$ denominator, then

$$\text{expected SD of the formula} = \frac{(.20^2 + .20^2)^{\frac{1}{2}}}{4} \times 100$$

$$= \pm 7\%$$

The value compares reasonably well with the results of two separate experimental studies on the reproducibility of caloric responses. Henriksson (1956) performed two caloric tests on each of ten normal subjects. Calculations performed upon this data show that when differences

in response (% CP test 2 - % CP test 1) are evaluated for all subjects, a SD of ± 13% results. For % DP the SD is ± 15%. Hamid and Hinchcliffe (1980) performed ten consecutive caloric tests on one normal subject. Their SD of response was ± 7% for % CP and 6% for % DP. The results of these studies are shown in Tables 2.3 and 2.4 respectively.

It is thus evident that the large normal range for canal paresis and directional preponderance (approx. ± 20% based on 2SD) is to a significant degree attributable to the inherent problems involved with accurate measurement of vestibular function rather than actual vestibular imbalance in a normal population.

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Author	Procedure	No of Subjects	Cold Left	Cold Right	Warm Left	Warm Right
Henriksson (1956)	darkness with eyes open 250ml/40 sec.	25	30.4 ± 8.5	28.9 ± 9.9	28.8 ± 14.7	29.8 ± 14.2
Preber (1958)	eyes closed 200ml/40 sec.	50	20.9 ± 4.7	22.1 ± 5.2	23.5 ± 7.5	22.8 ± 6.4
Mehra (1964)	eyes closed 250ml/40 sec.	31	20.5 ± 9.4	21.5 ± 8.4	25.9 ± 12.2	26.2 ± 14.3
Sills et al. (1977)	semidarkness with eyes open and Frenzel glasses 250ml/40 sec.	43	15.3 ± 7.7	14.5 ± 6.7	21.3 ± 11.7	21.0 ± 12.0
Hamid and Hinchcliffe (1980)	semidarkness with eyes open and covered 30 sec. irrigation	10	16.0 ± 6.1	16.8 ± 5.4	21.1 ± 11.9	15.2 ± 7.8

Table 2.1 Normal values (± 1SD) of maximum slow phase velocity (^{o}/s) for each caloric stimulus obtained by several investigators from a standard caloric test.

Author	Procedure	No of Subjects	%age Canal Paresis	%age Directional Preponderance
Henriksson (1956)	darkness with eyes open 250ml/40 sec.	25	+ 0.16 ± 8.60	- 2.96 ± 11.02
Aschan et al. (1956)	100ml/30 sec.	25	+ 0.86 ± 8.56	- 1.37 ± 8.84
Preber (1958)	eyes closed 200ml/40 sec.	50	+ 0.56 ± 5.27	+ 2.13 ± 5.83
Jongkees and Philipszoon (1964)	eyes closed 250ml/30 sec.	47	- 0.80 ± 7.50	+ 1.10 ± 8.70
Coats (1966)	eyes closed 40 sec. irrigation	30	+ 0.84 ± 9.50	+ 6.12 ± 13.20
Sills et al. (1977)	semidarkness with eyes open and Frenzel glasses 250ml/40 sec.	43	+ 1.70 ± 11.70	- 2.70 ± 14.20
Vesterhauge and Kildegaard Larsen (1977)	eyes closed 190ml/30 sec.	49	- 0.20 ± 9.40	- 2.40 ± 12.00
Hamid and Hinchcliffe (1980)	semidarkness with eyes open and covered 30 sec. irrigation	10	- 6.10 ± 23.60	+ 8.60 ± 14.00

Table 2.2 Normal values (± 1SD) for percentage canal paresis and directional preponderance obtained by several investigators from a standard caloric test. [Positive signs are used for left canal paresis and left directional preponderance. Negative signs are used for right canal paresis and right directional preponderance].

Subject	%age Canal Paresis 1st test	2nd test	Difference	%age Directional Preponderance 1st test	2nd test	Difference
1	- 4	+28	+32	-36	+ 4	+40
2	+ 6	0	- 6	- 6	+ 5	+11
3	+10	+16	+ 6	+10	+ 1	- 9
4	+17	+13	- 4	- 1	- 3	- 2
5	- 4	0	+ 4	+11	0	-11
6	- 9	- 2	+ 7	+12	+21	+ 9
7	+ 1	-19	-20	+11	+ 2	- 9
8	0	0	0	0	0	0
9	- 3	+ 3	+ 6	+ 2	+ 8	+ 6
10	+17	+19	+ 2	-13	-15	- 2
		Mean	+ 3		Mean	+ 3
		SD	±13		SD	±15

Table 2.3 Reproducibility of caloric results - calculations upon data of Henriksson (1956). Two caloric tests performed on each of ten normal subjects. [Positive signs used for left canal paresis and left directional preponderance. Negative signs used for right canal paresis and right directional preponderance].

Test No.	% age Canal Paresis	% age Directional Preponderance
1	- 4	0
2	+20	+ 8
3	+ 7	+ 1
4	+14	- 1
5	+18	0
6	+13	0
7	+ 7	- 1
8	+ 6	- 7
9	+ 7	+14
10	+15	+11
Mean	+10	+ 3
SD	± 7	± 6

Table 2.4 Reproducibility of caloric results - data of Hamid and Hinchcliffe (1980) of repeat testing of one subject. [Positive signs used for left canal paresis and left directional preponderance. Negative signs used for right canal paresis and right directional preponderance].

CHAPTER 3

RESPONSE DECLINE IN THE CALORIC TEST

3.1 Introduction

A progressive decline in response to repeated unidirectional* vestibular stimulation has been known to occur in both animals and man. However, the different test conditions and reponse analysis employed has made close comparison of the results of different studies difficult. Early work [Griffith (1920), Dodge (1923), Lumpkin (1927)] involved rotational accelerations of particularly large magnitude, beyond that of the normal physiological range. Injury to the cupula from such stimuli has subsequently been considered a strong possibility. Later work [Hallpike and Hood (1953), Hood and Pfaltz (1954), Lidvall (1961), Fluur and Mendel (1962), Lidvall (1962), Capps and Collins (1965), Collins (1965b), Aschan (1967), Johnson and Torok (1970)] involved lower levels of rotational acceleration and also caloric stimulation. Among the various response parameters studied were number of nystagmus beats, duration, frequency, latency, cumulative eye speed, duration of vertigo and slow phase displacement.

*unidirectional is meant here to refer to the direction of endolymph movement i.e. either ampullopetal or ampullofugal.

There seems to be comparitively few studies on either animals or man in which response decline has been investigated for caloric stimulation using slow phase velocity as the response measure. Since this parameter is of particular importance in this thesis, the findings of some of these studies will be presented and discussed. Firstly, some description of the term 'response decline' is needed. The term was used by Hallpike and Hood (1953) in order to describe a response pattern where it was found that a progressive decline in response occurred to successive unidirectional stimuli. The use of the term avoided the problem of specifying what mechanism (or mechanisms) was responsible for the observed phenomenon. In this sense then, response decline merely indicated that a decline in response had occurred during the specified tests. It has since become apparent that two, quite separate physiological mechanisms namely adaptation and habituation can give rise to a reduction in response during certain types of vestibular stimulation. Adaptation being a transient effect influences the response output to sustained vestibular stimulation such that the level of response activity, after reaching a maximum, begins to decline [Brown and Wolfe (1969), Stockwell et al. (1973)]. Habituation however relates to the decrease of response activity to repeated stimulation where periods of up to weeks may intervene between successive tests [Henriksson et al. (1961), Forssman et al. (1963), Capps and Collins (1965)]. Although the terms 'response

decline' and 'habituation' are often used synonomously it is clear that response decline cannot always be solely attributable to habituation. For example, during caloric stimulation, the effect that a residual temperature gradient has upon subsequent heating or cooling of the temporal bone and hence end-organ stimulation cannot necessarily be considered insignificant, particularly when the irrigations are given at short intervals in the same ear. Similarly, short term effects of adaptation may also affect subsequent responses to stimuli presented at short intervals.

Henriksson et al. (1961) studied the responses to repetitive caloric stimulation in cats. The tests were performed on conscious animals in full light conditions. Response decline of slow phase velocity was clearly demonstrated when water at a constant temperature was irrigated into the same ear a number of times and the successive respones compared. Upon further experimentation the authors showed i) that a nystagmus induced in one direction by repetitive irrigations had little effect on a nystagmus induced in the opposite direction by a subsequent irrigation. ii) response decline also occurred even when irrigations were performed at a rate of only one a day. iii) habituation could be retained for long periods (weeks).

Proctor and Fernández (1963) in similar experiments on cats studied the influence of vision upon the

acquisition of habituation. In their study, visual fixation was eliminated in six cats by the use of a blindfold secured over the eyes with adhesive tape. The results showed a clear response decline of slow phase velocity upon repetitive unilateral caloric stimulation. Visual fixation was eliminated in one cat by performing the tests in darkness. The responses obtained were similar to those for the blindfolded cats. The conclusions arrived at by the authors, by making comparison with the previous findings of Henriksson et al. is that vision may have some influence in developing habituation but it is not a critical factor.

Forssman et al. (1963) investigated four response measures namely maximum eye velocity, nystagmus duration, maximum laterotorsion and maximum vertigo to repeated unilateral irrigations in humans. Each subject received twelve consecutive irrigations of the right ear with water at 30°C. The duration of each irrigation was forty seconds and the interstimulus interval was five minutes. Their results, when mean values are assessed, clearly show the establishment of a response decline for all four parameters with maximum vertigo and maximum slow phase velocity showing the largest rates of decline. However, the authors state that "the mode of response decline of each of the four qualities showed considerable individual differences".

Regarding a conventional bithermal bilateral caloric test, it is clear that visual fixation and

alertness have a significant effect upon the magnitude of the responses obtained. Other influences such as habituation, adaptation and stimulus interaction may also be present to a greater or lesser extent. Although several studies on normal subjects [Henriksson (1956), Preber (1958), Mehra (1964), Sills et al. (1977)] have indicated little difference in the average responses between ears for both the warm and cold stimulus, the findings of Milojevic and Allen (1967), Press et al. (1979) and Hamid and Hinchcliffe (1980) are remarkable in that they show a significant asymmetry between the first two reactions. In these studies the first reaction was, on average, of larger intensity than the second. This effect seems to be strongly related to the sequence of irrigations rather than to the ear irrigated or temperature of water used. The possibility of 'some form' of a sequential response decline occurring in the caloric test warranted the following investigation.

3.2 Materials and Method

One hundred and twenty subjects were each allocated at random to one of four different caloric test sequences. The subjects were patients who had been referred from the E.N.T. out-patient clinic for routine investigation of problems concerning hearing and/or balance. Caloric tests were performed with the patient lying supine at 30^{o} to the horizontal. A flow of water at the pre-set temperature was introduced into the ear for thirty

seconds whereupon the room lights were switched off and the nystagmus recorded using E.N.G. The patients were instructed that during the period in darkness they were to keep their eyes open and concentrate on a counting sequence (upwards from zero in steps of five). The test sequences employed, designated A, B, C and D are shown in Table 3.1.

Each patient was examined initially for spontaneous and positional nystagmus. Spontaneous nystagmus which was present in the caloric test position before the commencement of the first irrigation was noted and the subsequent caloric responses were adjusted accordingly by a simple process of addition and subtraction. Responses were quantified by measuring the maximum slow phase velocity. This was done by taking the average of approximately five measurements at the peak activity of the response. Several readings were taken of the warm and cold water temperature throughout the period of the study. The values for the mean and SD in the delivery nozzle were, for the warm water $43.3 \pm 0.2^{\circ}C$ and for the cold $29.3 \pm 0.3^{\circ}C$.

Regarding statistical analysis of the data, the rather complex repeated measures design was studied by analysis of variance. The mean values of response by group and period give rise to a 15df sum of squares that may be split up in a number of ways, permitting the testing of a number of different hypotheses for the observed pattern of response decline.

3.3. Results

Tables 3.2 to 3.5 show the caloric responses together with the calculated percentage canal paresis and directional preponderance for each subject in each of the sequence groups. Table 3.6 shows means and SDs by period again for the four sequence groups. Averaging appropriate values gives mean values for right and left ears of $19.70^{\circ}/s$ and $19.57^{\circ}/s$ respectively. Mean values for nystagmus to right and left are $20.26^{\circ}/s$ and $19.00^{\circ}/s$. The corresponding significances are shown in Table 3.7. For ear irrigated there is no significance. For direction of nystagmus $0.05 < p < 0.1$. It can also be seen from this table that there is an almost linear decline of response with period ($p < 0.01$). Table 3.8 shows that this decline is limited to the warm stimulus only. For the cold stimulus there is a decrease in response from period 1 to 2 and again a much smaller decline from period 3 to 4. However, the mean response for period 3 is larger than that for period 2.

Table 3.9 shows an analysis of the possibility of response decline being dependant upon repetition of either the direction of induced nystagmus or the ear irrigated. The corresponding partitioning of the between periods variation in Table 3.7 is shown in Table 3.10 and indicates that the period effect could be due to either of these possibilities.

Tables 3.11 and 3.12 show that the period effect is not specific to the temperature of the stimulus.

An alternative analysis of the results was undertaken which involved expressing the percentage contribution of each period value to the total for each patient in each of the sequence groups. These results are shown in Table 3.13 with the corresponding analysis of variance shown in Table 3.14. It can be seen that the effects of temperature and period are still highly significant but that the interaction between these (Table 3.15), and the effect of nystagmus direction (to the right 25.55, to the left 24.45) is not significant. Also the difference between right and left ear responses (24.59 v 25.41) is not significant. Moreover, when the data is treated in this way, the hypothesis of response decline being specific to temperature, (which was not significant previously in Tables 3.11 and 3.12), now becomes tenable (Tables 3.16 and 3.17).

If a model is to be fitted to the data, the best fit would be one in which there is a response decline from period 1 to period 2 and a similar decline from 3 to 4 with periods 2 and 3 being equal. The fitted mean values for this, as a percentage, are 26.93, 25.00, 25.00 and 23.07. The data can therefore be represented by a period effect thus; period 1: + 1.93%, period 4: - 1.93%. The temperature effect can likewise be represented as cold: + 3.08%, hot: - 3.08%. This leads to a table of fitted values - Table 3.18. For each group the expected directional preponderance is zero but the expected canal paresis will depend on the sequence group. This will be

a bias of 3.87% left canal paresis in groups B and D in which the right ear is irrigated first and 3.87% right canal paresis in groups A and C in which the left ear is first irrigated.

Table 3.19 shows a comparison between the percentage canal paresis which is predicted by the model and the mean percentage canal paresis in the sample for each sequence group. If 4% is taken as the bias value, the number of false positives and false negatives for each sequence group where the normal range was originally taken as 0 $\pm$ 20% can be determined. The results are shown in Table 3.20. It will be seen that out of 36 patients who were originally classified as outside the normal range with regards to canal paresis, 4 of these were false positives (11%). Of the remaining 84 patients originally classified as being within the normal range, 1 was a false negative (1%).

Table 3.21 shows the numbers of significant canal paresis and directional preponderance in the total patient sample (canal paresis being classified using the bias values found previously for each sequence group). It will be seen that of the 120 patients, 21 (18%) had significant canal paresis, 8 (7%) had significant directional preponderance and 12 (10%) had both significant canal paresis and directional preponderance.

Of the 8 patients who had significant directional preponderance only, one had a first degree spontaneous nystagmus in the direction of the preponderance and one

had a bilateral spontaneous nystagmus (first degree to left and first degree to right) together with a positionally induced fatiguable nystagmus in the opposite direction to the caloric directional preponderance. The remaining 6 patients had neither spontaneous nor positional nystagmus.

3.4 Discussion

The significant difference between caloric responses for the warm and cold stimuli is not surprising when the respective water temperatures are compared with the skull temperature. If the latter is taken as 37°C then the warm stimulus represents a mean temperature difference of 6.3°C and the cold, a mean difference of 7.7°C. Although it is not clear precisely what effect blood flow has on the heat transfer characteristics of the temporal bone during warm and cold caloric irrigations, it would seem reasonable to assume that the larger temperature difference of the cold stimulus would manifest itself as a similar increase in the temperature gradient generated across the lateral semicircular canal and hence a larger nystagmus response. However, the results of Chapter 4 in which the latency of nystagmus response was compared for the warm and cold stimuli show that the cold stimulus produces a significantly shorter latency response than does the warm. This finding adds to the problem of explaining the increased response of the cold stimulus as merely a larger temperature difference at the external auditory canal

since a shorter latency response would be indicative of more efficient heat transfer through the temporal bone leading to a larger temperature generation at the lateral semicircular canal and hence a larger nystagmus response.

Providing that the difference in magnitude between the warm and the cold stimulus is not excessively large, there should be little effect on the ability of the caloric test to indicate vestibular imbalance. For example, regarding the pattern of canal paresis, the affected side would show a hypoactive response when cold responses are compared between ears and also when warm responses are compared. In the case of directional preponderance, although the responses to the lesser of the two stimuli will be reduced in intensity in comparison to what they would be if the stimuli were of equal magnitude, a preponderance will still be evident in the overall pattern.

What is of particular importance regarding the effectiveness of the caloric test is the finding that a systematic decline in response occurs which manifests itself as a significant bias in the determination of percentage canal paresis. A bias is introduced no matter what temperature of water is used for the first irrigation or what ear is irrigated first. An explanation of the mechanism or mechanisms responsible for this phenomenon is difficult because of the several factors which may contribute to the observed overall pattern.

The possibility that response decline is solely dependant upon a repetition of the direction of induced

nystagmus would merely result in reduced responses from the last two irrigations without producing any bias in the overall response pattern. The theory that decline is purely dependant upon the number of irrigations would compare favourably with the observed data except for the second and third period responses which are, in practice, of equal magnitude.

Consideration of the effect that secondary nystagmus would have upon subsequent responses shows that this acting alone would have a quite different effect to that observed. For example, an initial cold irrigation of the left ear would, in a number of subjects, produce a secondary nystagmus beating to the left several minutes after the end of irrigation which, in theory, would increase the primary response to the cold irrigation of the right ear. This would result in a reversal of the observed pattern.

In this study, irrigations were alternated between left and right ears so that at least ten minutes elapsed between irrigations of the same ear. Although this would minimise the possibility of a residual temperature gradient affecting subsequent heating or cooling of the inner ear, if the effect was indeed present, it could not alone account for the observed decline of response from period 1 to period 2 which represent irrigations of different ears.

A further consideration is the alertness of the subjects which has been found to be an important factor

in retention of response activity during repetitive vestibular stimulation [Lidvall (1962), Collins (1965b)]. In this present study, an attempt to maintain alertness was made by instructing the subject to concentrate on a simple arithmetic task (counting upwards from zero in steps of five). The observed decline in caloric responses may possibly be attributable to this task being insufficient to retain alertness. However, during a caloric reaction, many subjects find difficulty in performing even the most simple arithmetic tasks.

A possible explanation for a retention of response activity for period 2 and 3 is that period 3 represents a change of stimulus temperature which may be a sufficient means of causing 'alertness' for a short period and hence a retention of response activity.

On the basis of this study, the practice of some centres of starting the irrigation sequence in the 'worse ear' or having a random sequence clearly reduces the ability of the test to show up vestibular imbalance. Strict adherance to a set irrigation sequence, taking into account the bias involved for that particular sequence would improve the effectiveness of the caloric test significantly. In this study, 11% of patients originally classified as outside normal limits with regards to canal paresis were subsequently found to be false positives. There is however likely to be a significant number of patients having vestibular pathology which remains undetected because of the wide normal range.

A significant canal paresis (without a significant directional preponderance) occurred approximately 2½ times more often than did a significant directional preponderance (without a significant canal paresis). A possible explanation for this is that a large proportion of the patients classified as outside normal limits had peripheral vestibular disease which is reflected more often by a 'canal paresis' pattern of response than by directional preponderance.

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Group	Period				Number of Subjects
	1	2	3	4	
A	CL	CR	WL	WR	30
B	CR	CL	WR	WL	30
C	WL	WR	CL	CR	30
D	WR	WL	CR	CL	30

Table 3.1 Caloric test sequences
CL = Cold Left; WL = Warm Left.
CR = Cold Right; WR = Warm Right.

Subject	Caloric responses (°/s) SPV				%age CP	%age DP
	Cold Left	Cold Right	Warm Left	Warm Right		
A1	26	18	21	13	20R	0
A2	27	18	24	12	26R	4L
A3	8	24	6	55	70L	36R
A4	18	43	14	38	43L	1L
A5	38	27	28	23	14R	5R
A6	17	18	16	9	10R	13L
A7	12	16	13	18	15L	2R
A8	15	14	12	9	8R	4L
A9	41	38	28	16	12R	7L
A10	40	52	38	53	15L	2R
A11	15	16	8	8	0	0
A12	20	17	12	12	5R	5R
A13	44	4	19	0	88R	31R
A14	12	13	13	15	6L	4R
A15	32	36	19	16	1L	7L
A16	33	24	22	14	18R	1R
A17	24	0	8	2	90R	53R
A18	22	16	25	17	18R	3L
A19	18	16	18	18	3R	3R
A20	5	21	8	19	51L	9L
A21	20	22	28	11	19R	23L
A22	13	18	10	13	15L	4L
A23	13	14	13	8	8R	13L
A24	31	21	7	10	10R	19R
A25	23	24	14	18	6L	4R
A26	12	8	17	13	16R	0
A27	24	33	15	34	26L	9R
A28	18	16	13	17	3L	9R
A29	32	23	33	13	29R	11L
A30	31	15	12	7	32R	17R
Mean	22.80	20.83	17.13	17.03	5.53R	3.37R
SD	10.28	10.90	8.09	12.64	32.35	15.38

Table 3.2 Caloric responses (°/s SPV) - Sequence A.

Subject	Caloric responses (°/s) SPV				%age CP	%age DP
	Cold Right	Cold Left	Warm Right	Warm Left		
B1	9	7	8	6	13L	0
B2	33	31	27	27	0	0
B3	39	38	19	18	2L	0
B4	17	12	12	10	14L	6L
B5	23	16	12	9	17L	7L
B6	24	19	14	18	1L	9L
B7	27	25	12	12	3L	3L
B8	18	22	23	25	9R	3R
B9	16	26	20	21	13R	11R
B10	30	27	34	24	11L	6R
B11	26	40	6	8	20R	15R
B12	26	40	17	8	6R	25R
B13	14	3	2	0	68L	47L
B14	22	14	10	8	19L	11L
B15	32	11	9	8	37L	33L
B16	11	17	12	11	10R	14R
B17	27	35	38	0	30L	46R
B18	26	15	20	11	28L	3L
B19	5	5	4	12	31R	44L
B20	18	18	18	16	3L	3R
B21	28	10	27	4	59L	7R
B22	42	42	32	40	5R	5L
B23	26	25	18	15	5L	2R
B24	18	21	8	10	9R	2R
B25	12	15	14	17	10R	0
B26	16	22	0	8	30R	4L
B27	0	8	5	4	41R	53R
B28	28	32	23	20	1R	7R
B29	6	5	6	6	4L	4L
B30	23	20	18	18	4L	4L
Mean	21.40	20.70	15.60	13.13	4.53L	0.47R
SD	9.80	11.20	9.57	8.66	23.72	20.22

Table 3.3 Caloric responses (°/s SPV) - Sequence B.

Subject	Caloric responses (°/s) SPV				%age CP	%age DP
	Warm Left	Warm Right	Cold Left	Cold Right		
C1	12	20	23	24	11L	9R
C2	25	23	43	38	5R	2R
C3	8	5	10	10	9R	9L
C4	33	21	22	22	12R	12L
C5	22	20	20	26	5L	9L
C6	12	12	15	13	4R	4R
C7	16	12	21	12	21R	8R
C8	15	16	25	25	0	0
C9	22	38	27	22	10L	19R
C10	23	16	33	22	19R	4R
C11	9	8	8	7	6R	0
C12	8	10	13	21	20L	12L
C13	38	52	22	33	17L	2R
C14	8	9	21	20	0	3R
C15	22	53	32	41	27L	15R
C16	13	33	38	32	12L	25R
C17	10	5	20	4	54R	28R
C18	12	9	19	14	15R	4R
C19	42	34	25	30	2R	10L
C20	27	17	26	24	13R	9L
C21	33	44	33	24	1L	15R
C22	43	36	50	25	21R	12R
C23	22	30	32	25	1L	14R
C24	11	0	5	0	100R	38L
C25	18	16	9	32	28L	33L
C26	12	10	18	11	18R	10R
C27	11	9	10	11	2R	7L
C28	7	16	23	7	13R	47R
C29	17	28	18	26	21L	3R
C30	20	13	22	22	9R	9L
Mean	19.03	20.50	22.77	20.77	5.73R	2.53R
SD	10.32	13.91	10.32	10.04	24.72	16.80

Table 3.4 Caloric responses (°/s SPV) - Sequence C.

Subject	Caloric responses (°/s) SPV				%age CP	%age DP
	Warm Right	Warm Left	Cold Right	Cold Left		
D1	6	20	10	26	48R	3R
D2	30	17	25	17	24L	6R
D3	12	12	34	22	15L	15L
D4	15	32	32	27	12R	21L
D5	12	7	23	17	19L	2L
D6	15	18	17	25	15R	7R
D7	12	14	18	12	7L	14L
D8	10	12	13	16	10R	2R
D9	61	46	36	48	2L	14R
D10	27	17	23	30	3L	17R
D11	32	18	22	28	8L	20R
D12	5	11	8	10	24R	12L
D13	17	18	17	28	15R	13R
D14	40	28	35	28	15L	4R
D15	16	29	21	26	20R	9L
D16	28	12	32	28	20L	12R
D17	8	23	22	26	24R	14L
D18	8	4	24	23	8L	5R
D19	11	11	12	15	6R	6R
D20	12	12	16	20	7R	7R
D21	18	6	27	3	67L	22L
D22	40	27	27	32	6L	14R
D23	11	12	14	26	21R	17R
D24	14	9	12	15	4L	16R
D25	27	10	13	30	0	43R
D26	23	28	35	18	12L	21L
D27	26	20	20	16	12L	2R
D28	40	33	28	36	1R	11R
D29	5	6	9	6	8L	15L
D30	20	38	17	26	27R	9L
Mean	20.03	18.33	21.40	22.67	0.20L	2.17R
SD	13.00	10.31	8.38	9.19	20.62	14.99

Table 3.5 Caloric responses (°/s SPV) - Sequence D.

Group	Period 1		Period 2		Period 3		Period 4	
	Stim-ulus	Mean ± SD	Stim-ulus	Mean ± SD	Stim-ulus	Mean ± SD	Stim-ulus	Mean ± SD
A	CL	22.80 ± 10.28	CR	20.83 ± 10.90	WL	17.13 ± 8.09	WR	17.03 ± 12.64
B	CR	21.40 ± 9.80	CL	20.70 ± 11.20	WR	15.60 ± 9.57	WL	13.13 ± 8.66
C	WL	19.03 ± 10.32	WR	20.50 ± 13.91	CL	22.77 ± 10.32	CR	20.77 ± 10.04
D	WR	20.03 ± 13.00	WL	18.33 ± 10.31	CR	21.40 ± 8.38	CL	22.67 ± 9.19

Table 3.6. Means and standard deviations (^{o}/s SPV) by stimulus, group and period.

Source of variation	df	SS	MS	F	
Periods - linear effect	1	395.3	395.3	7.60	$p < .01$
Periods - nonlinear effect	2	0.5	0.3	0.01	ns
Periods	3	395.8			
Interaction periods x temperatures	3	568.2	189.4	3.64	$p < .05$
Interaction periods x ears	3	132.0	44.0	0.85	ns
Interaction periods x directions	3	136.7	45.6	0.86	ns
Groups	3	716.9	239.0	0.83	ns
Interaction groups x temperatures	3	391.3	130.4	2.51	$.05 < p < .1$
Interaction groups x ears	3	108.9	36.3	0.70	ns
Interaction groups x directions	3	15.7	5.2	0.10	ns
	12	1232.8			
Temperature of stimulus	1	1984.5	1984.5	38.18	$p < .001$
Ear irrigated	1	1.9	1.9	0.04	ns
Direction of nystagmus	1	190.0	190.0	3.66	$.05 < p < .1$
Cells	15	3409.2			
Subjects within groups	116	33371.6	287.7	5.53	$p < .001$
Residual	348	18088.7	52.0		
Total	479	54869.5			

Table 3.7 Analysis of variance of caloric response (^{o}/s SPV) by group, period and stimulus.

Period	Stimulus		Mean
	Warm	Cold	
1	19.53	22.10	20.82
2	19.42	20.77	20.09
3	16.37	22.08	19.22
4	15.08	21.72	18.40
Mean	17.60	21.67	19.63

Table 3.8 Mean caloric responses (^{o}/s SPV) by period and stimulus.

Period	Effect of repetition of direction of induced nystagmus or the ear irrigated			
	Absent		Present	
	No of Subjects	Mean (%)	No of Subjects	Mean (%)
1	120	20.82	0	-
2	120	20.09	0	-
3	0	-	120	19.22
4	0	-	120	18.40

Table 3.9 Analysis of response decline occurring by habituation to repetition of either the direction of induced nystagmus or the ear irrigated.

Source of Variation	df	SS	MS	F
Habituation	1	323.4	323.4	6.22 $p < 0.05$
Rest of period effect	2	72.4	36.2	0.70 n.s.
Periods	**3**	**395.8**		

Table 3.10 Analysis of variance relating to data of Table 3.9.

Period	Habituation to Stimulus Temperature			
	Absent		Present	
	No of Subjects	Mean (%)	No of Subjects	Mean (%)
1	120	20.82	0	-
2	0	-	120	20.09
3	120	19.22	0	-
4	0	-	120	18.40

Table 3.11 Analysis of response decline occurring by habituation to stimulus temperature.

Source of Variation	df	SS	MS	F
Stimulus temperature habituation	1	72.0	72.0	1.39 n.s.
Rest of period effect	2	323.8	161.9	3.11 $p < 0.05$
Periods	3	395.8		

Table 3.12 Analysis of variance relating to data of Table 3.11.

Group	Period 1		Period 2		Period 3		Period 4	
	Stim-ulus	Mean ± SD	Stim-ulus	Mean ± SD	Stim-ulus	Mean ± SD	Stim-ulus	Mean ± SD
A	CL	30.47 ± 13.24	CR	25.97 ± 8.17	WL	22.30 ± 6.91	WR	21.27 ± 10.89
B	CR	30.77 ± 12.22	CL	28.87 ± 9.15	WR	21.50 ± 7.99	WL	18.87 ± 8.95
C	WL	24.13 ± 10.19	WR	22.47 ± 7.73	CL	28.73 ± 7.97	CR	24.67 ± 8.38
D	WR	23.00 ± 7.47	WL	21.80 ± 7.12	CR	27.10 ± 8.13	CL	28.10 ± 7.52

Table 3.13. Means and standard deviations of slow phase eye velocity, expressed as a percentage, by stimulus, group and period.

Source of variation	df	SS	MS	F	
Periods - linear effect	1	788.9	788.9	7.22	$p < .01$
Periods - nonlinear effect	2	121.3	121.3	1.11	ns
Periods	3	910.2			
Interaction periods x temperatures	2	48.2	24.1	0.22	ns
Interaction periods x ears	2	15.0	7.5	0.07	ns
Interaction periods x directions	2	226.0	113.0	1.03	ns
(Groups	0)				
Interaction groups x temperatures	3	620.4	206.8	1.89	ns
Interaction groups x ears	3	550.6	183.5	1.68	ns
Interaction groups x directions	3	28.5	9.5	0.09	ns
	9	1199.4			
Temperature of stimulus	1	4563.3	4563.3	41.74	$p < .001$
Ear irrigated	1	80.0	80.0	0.73	ns
Direction of nystagmus	1	145.2	145.2	1.33	ns
Cells	12	5987.9			
(Subjects within groups	0)				
Residual	348	38050.1	109.3		
Total	360	44038.0			

Table 3.14 Analysis of variance of caloric response for percentage based data of Table 3.13.

N.B. Because the percentage method is used, variation between subjects is automatically zero; labels corresponding to variation between groups and between subjects within groups are left in the table for comparability with table 3.7, but are assigned 0 df. For the same reason the total df's are not (120 x 4)-1 but 120 x (4-1).

Period	Stimulus		Mean
	Warm	Cold	
1	23.57	30.62	27.09
2	22.13	27.42	24.77
3	21.90	27.92	24.91
4	20.07	26.38	23.22
Mean	21.92	28.08	25.00

Table 3.15 Mean caloric responses, expressed as a percentage, by period and stimulus.

Period	Habituation to Stimulus Temperature			
	Absent		Present	
	No of Subjects	Mean (%)	No of Subjects	Mean (%)
1	120	27.10	0	-
2	0	-	120	24.77
3	120	24.91	0	-
4	0	-	120	23.22

Table 3.16 Analysis of response decline by habituation to stimulus temperature for percentage based data.

Source of Variation	df	SS	MS	F
Stimulus temperature habituation	1	480.0	480.0	4.39 $p < 0.05$
Rest of period effect	2	430.2	215.1	1.97 n.s.
Periods	3	910.2		

Table 3.17 Analysis of variance relating to data of Table 3.16.

Group	Period 1		Period 2		Period 3		Period 4	
	Stimulus	Mean	Stimulus	Mean	Stimulus	Mean	Stimulus	Mean
A	CL	30.02	CR	28.08	WL	21.92	WR	19.98
B	CR	30.02	CL	28.08	WR	21.92	WL	19.98
C	WL	23.85	WR	21.92	CL	28.08	CR	26.15
D	WR	23.85	WL	21.92	CR	28.08	CL	26.15
Average		26.93		25.00		25.00		23.07

Table 3.18 Table of fitted values, expressed as a percentage by stimulus, group and period, based on a model with temperature and period effects.

Group	Observed %age canal paresis (mean ± SD)	%age canal paresis fitted by model
A	5.53 R ± 32.35	3.87 R
B	4.53 L ± 23.72	3.87 L
C	5.73 R ± 24.72	3.87 R
D	0.20 L ± 20.62	3.87 L

Table 3.19 Comparison of the mean percentage canal paresis in each sequence group with that predicted by the model, using percentage based values of caloric responses.

Group	No. of subjects originally falling outside normal range (0 ± 20%)	No. of false positives according to re-classification	No. of false negatives according to re-classification
A	10	1	0
B	9	0	0
C	8	2	1
D	9	1	0
Total	36	4	1

Table 3.20 Number of false positives and false negatives in the original sample obtained by comparison with re-classification according to the bias value for each sequence group.

Group	Significant CP	Significant DP	Only significant CP	Only significant DP	Significant CP with significant DP
A	9	4	6	1	3
B	9	6	4	1	5
C	7	5	4	2	3
D	8	5	7	4	1
Total	33	20	21	8	12

Table 3.21 Numbers of significant canal paresis (CP) and directional preponderance (DP) in the total patient sample, (canal paresis classified using the bias value for each sequence group.

CHAPTER 4

DIFFERENCES BETWEEN THE WARM AND COLD CALORIC RESPONSES

4.1 Introduction

Several investigators have found that the nystagmus response from the cold caloric stimulus is, on average, of longer duration than that from the warm stimulus [Henriksson (1956), Hamersma (1957), Preber (1958), Mehra (1964), Sills et al.(1977)]. Since in all these studies the cold stimulus was administered first, the test sequence remains a possible influence upon the results obtained. With regard to maximum slow phase velocity however, these studies indicate a tendency for the response from the warm stimulus to be greater than that from the cold. Although it is clear that the caloric response is influenced by many factors, the precise reasons for the observations above are not known.

From the early work of Ewald (1892) on pigeons, it was thought that there was asymmetry in the sensitivity of the vestibular end-organ between ampullopetal and ampullofugal stimuli. This theory eventually became known as Ewald's 2nd Law. Although this lends support to the results of those studies in which the maximum slow phase velocity response for the warm stimulus was found to be greater than that for the cold, there is significant

evidence which indicates that within relatively large limits, the sensitivity of the end-organ is essentially symmetrical [Hallpike (1961), Mehra and Das Moudgil (1967)].

Regarding the influence of vasodilation on caloric response, Jongkees (1948a) found that the use of amyl nitrite reduced the duration of the response from the cold stimulus with no effect upon the response from the warm stimulus. It is difficult to know what effect there is upon maximum slow phase velocity since response duration is not closely correlated with eye velocity [Henriksson (1956)]. Also, the effect of habituation may have been an important influence in these experiments.

The following study was undertaken in order to examine possible differences in the response profiles between the two stimuli which were used for the practical content of this thesis.

4.2 Materials and Method

Forty subjects were allocated at random to one of four different caloric test sequences shown in Table 4.1. The subjects were patients who had been referred from the E.N.T. out-patients' clinic for routine investigation of problems concerning hearing and/or balance. Tests were carried out according to the procedure outlined in Chapter 3 (3.2) of this thesis. To avoid contamination of the response by previous irrigations, only the response of the first irrigation was used for analysis purposes. For each subject, the nystagmus recording was divided into intervals of five seconds and the average slow phase

velocity calculated for each interval. These values were then 'normalised' by dividing each by the maximum slow phase velocity.

4.3 Results

Tables 4.2 and 4.3 show, for each subject, the normalised slow phase velocity (SPV) values during the period 0 to 90 seconds after the cessation of irrigation. Two methods of analysis were employed to investigate possible differences in latency between the responses from the warm and cold stimuli.

The first method involved determination of the time of occurrence of the first maximum intensity value for each subject. The mean and SD for each group is shown in Table 4.4. A 't' test performed on this data shows no significant difference between the latencies of the warm and cold responses, ($t = 0.9$).

The second method of analysis involved calculation of the 'averaged peak latency' for each subject by taking the mean of the times of the three largest intensity values. [These values are shown 'ringed' in Tables 4.2 and 4.3] . The mean and SD for each group is shown in Table 4.5. With the data treated in this way, there is found to be a significant difference between the warm and cold response latencies, ($t = 2.9$; $p < 0.01$).

The mean values for intensity of nystagmus for each interval are shown graphically in Fig. 4.1. It is evident that the cold response reaches a maximum

earlier than does the warm response, but the rates of decline are approximately equal.

The mean and SD of maximum slow phase velocity for the two stimuli are shown in table 4.6. Although the mean cold response is larger than the warm, the difference does not reach significance.

4.4 Discussion

In this study it was found that the maximum intensity of the response from the cold caloric stimulus was, on average, of larger magnitude and of shorter latency than that from the warm stimulus. Although the difference for nystagmus intensity did not reach significance, the results of Chapter 3 where a much larger number of responses were analysed showed that a significant difference does indeed exist between the respective responses. Since the cold stimulus used in these studies, relative to skull temperature, is greater than the warm stimulus, then this alone could possibly account for the difference in nystagmus intensities.

It is of interest to compare the results of this present study with those of Baertschi et al.(1975) in which, using air, they found that the warm stimulus produced the higher intensity nystagmus and the shorter latency response. Thus in both studies, the higher intensity nystagmus is associated with a shorter latency response. To account for their findings, Baertschi et al. suggest that during the warm irrigation an increase

in thermal conductivity occurs from vasomoter changes in the skin and hence a greater heat transfer takes place to the inner ear. This theory, however, would not account for the results of this present study in which the cold response was the greater. It may be postulated that nystagmus latency is, to a degree, dependant upon the intensity of the stimulus rather than its character (warm or cold).

The precise mechanisms which are responsible for the latency changes are at present unknown. In the mathematical model of caloric nystagmus presented in Chapter 6 it is seen that alteration in the value of the adaptation time constant produces changes in the latency of the response. Since there is some experimental evidence which suggests that adaptation in vestibular stimulation is related to stimulus magnitude in a non-linear fashion [Brown and Wolfe (1969)], it may be that this is a significant influence upon caloric response latency.

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Group	Period				No. of Subjects
	1	2	3	4	
A	CL	CR	WL	WR	10
B	CR	CL	WR	WL	10
C	WL	WR	CL	CR	10
D	WR	WL	CR	CL	10

Table 4.1 Caloric test sequences.
CL, CR - Cold irrigation of Left/Right ear
WL, WR - Warm " " " "

Time post-irrigation (s)			0	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	Max SPV (°/s)
Subject	1	WR	.10	.42	.48	.70	.78	.87	(.93)	(1.00)	(1.00)	.87	(.93)	(.90)	.73	.70	.73	.70	.59	.54		11.5
	2	"	.39	.65	.75	.46	.61	.68	(.96)	(1.00)	.79	.79	.75	.74	.78	(.90)	.70	.54	.46	.41		14.8
	3	"	.24	.32	.52	.80	(1.00)	(.89)	(.89)	(.89)	(.84)	(.89)	.80	.80	.59	.52	.47	.41	.39	.29		71.2
	4	"	.33	.43	.51	.78	(.96)	(.92)	(1.00)	.81	(.96)	(.96)	.80	.70	.62	.52	.49	.43	.38	.32		20.5
	5	"	.15	.19	.31	.42	.45	.58	.76	(.90)	(1.00)	(1.00)	.88	(.95)	.86	.86	.71	.55	.38	.40		27.5
	6	"	.16	.17	.50	.57	.57	(.85)	.67	.71	.75	(.82)	(1.00)	.77	.74	.65	.72	.67	.64	.72		24.0
	7	"	.73	.59	.68	.73	.82	(.96)	(1.00)	(.94)	(1.00)	.85	.76	.76	.76	.59	.43	.45	.38	.35		19.8
	8	"	.08	.21	.26	(.86)	(1.00)	(.86)	(.52)	.48	.52	.45	.48	.40	.43	.41	.38	.36	.37	.23		43.3
	9	"	.20	.30	.38	.71	.70	.74	.79	(1.00)	(.91)	.83	(.86)	(.91)	.79	.85	.79	.74	.58	.42		24.8
	10	"	.16	.45	.60	.63	.89	(.90)	(1.00)	(.97)	(1.00)	(1.00)	(.90)	.74	.84	.83	.59	.44	.37	.26		11.9
	11	WL	.20	.39	.53	.53	.53	.33	.48	.54	.81	(1.00)	(.86)	(.86)	(.88)	.75	.63	.37	.36	.41		21.0
	12	"	.13	.21	.33	.48	.63	.70	(.97)	(1.00)	(.94)	.77	.77	.47	.59	.49	.39	.37	.33	.30		33.8
	13	"	.26	.30	.61	.59	.72	.91	.87	.87	.94	(.96)	(1.00)	.81	(.98)	.89	.70	.63	.53	.49		17.7
	14	"	.33	.44	.53	.76	.84	.81	(1.00)	(.90)	(.93)	.85	.84	.78	.60	.61	.57	.51	.45	.45		12.8
	15	"	.31	.32	.41	.61	.71	.76	(1.00)	(.89)	(.91)	.83	.73	.45	.61	.45	.47	.45	.45	.42		23.6
	16	"	.27	.26	.37	.48	.68	.75	(.94)	(1.00)	(.98)	(1.00)	(1.00)	(1.00)	(1.00)	(1.00)	.91	.84	.81	.64		17.0
	17	"	.18	.27	.43	.56	.69	(.93)	(1.00)	.77	(.84)	.73	.70	.64	.62	.53	.47	.43	.36	.24		28.0
	18	"	.30	.38	.60	(1.00)	(.92)	(.84)	(.84)	(.84)	(.84)	(.84)	.78	.75	.73	.62	.62	.53	.46	.40		51.4
	19	"	.15	.39	.67	.62	.78	.81	.83	(.84)	(1.00)	(.96)	.75	.72	.81	.65	.62	.36	.36	.37		18.0
	20	"	.21	.39	.45	.54	.55	.68	.63	.76	(1.00)	(.93)	(.90)	.78	.84	.68	.66	.61	.57	.39		11.9
Mean			.24	.35	.49	.64	.74	.79	.85	.86	.89	.87	.82	.75	.74	.68	.60	.52	.46	.40		25.23
SD			.14	.13	.13	.15	.16	.15	.16	.15	.12	.13	.12	.16	.14	.17	.14	.14	.12	.13		14.99

Table 4.2 Normalised slow phase velocities for the period 0-90 seconds post-irrigation.
WR = Warm irrigation of Right ear; WL = Warm irrigation of Left ear.
Three largest values for each subject are shown 'ringed'.

Time post-irrigation (s)			0	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	Max SPV (°/s)
Subject	1	CR	·15	·22	·47	·52	·75	(·82)	(·82)	(1.00)	(·86)	(·86)	·71	·68	·62	·59	·57	·58	·41	·43		27.5
	2	"	·51	·51	·88	·76	·87	(·96)	(1.00)	(·96)	(·92)	·90	·77	·65	·55	·37	·48	·34	·27	·26		19.6
	3	"	·28	·51	(·89)	·80	·80	·87	(1.00)	(·98)	(·89)	·87	·80	·87	·78	·75	·35	·67	·33	·39		18.4
	4	"	·64	·68	·79	·85	(1.00)	(1.00)	(·95)	(·88)	·71	·66	·72	·71	·68	·62	·54	·38	·33	·27		29.0
	5	"	·16	·27	·47	·65	·75	·84	(·92)	(·96)	(1.00)	·88	·90	·84	·67	·80	·74	·54	·46	·37		20.5
	6	"	·31	·41	·90	·79	·90	(1.00)	·88	·77	(·94)	(·96)	·80	·82	·79	·77	·70	·69	·63	·42		19.6
	7	"	·32	·40	·70	·77	·72	·72	(·86)	(1.00)	(·94)	(·94)	·80	·71	·70	·61	·57	·49	·29	·32		20.5
	8	"	·37	·53	·61	·67	·71	·80	(1.00)	(1.00)	(·93)	(1.00)	(·90)	·80	·71	·66	·73	·61	·52	·51		38.7
	9	"	·41	·49	·57	·68	·83	(·90)	(·90)	(·95)	(1.00)	(·95)	·85	·77	·81	·71	·68	·65	·66	·55		29.0
	10	"	·31	·40	·60	·76	·86	(·93)	(1.00)	(·96)	·81	·86	·81	·73	·71	·63	·63	·63	·54	·47		43.3
	11	CL	·32	·47	·64	·75	(·94)	(·88)	(·88)	·83	(·88)	(1.00)	·77	·79	·79	·79	·68	·66	·48	·42		34.9
	12	"	0.00	·22	·36	·44	·70	·84	(1.00)	·91	·93	(·98)	(·94)	·36	·69	·58	·63	·52	·44	·35		16.6
	13	"	·18	·39	·57	·70	·70	·68	(·87)	(·81)	·78	(1.00)	(·87)	·67	·64	·64	·63	·47	·39	·40		13.8
	14	"	·26	·33	·57	·70	·84	(·92)	(1.00)	(·87)	·78	·84	·75	·51	·40	·44	·35	·34	·41	·26		17.0
	15	"	·15	·32	·51	·69	(·83)	(1.00)	(·86)	·81	·81	·76	·76	·56	·52	·53	·36	·40	·40	·37		43.3
	16	"	·39	·53	·63	(·94)	(·97)	(1.00)	(·97)	(1.00)	(·97)	·88	(·94)	·77	·77	·63	·58	·54	·42	·32		32.7
	17	"	·63	·80	·72	·82	(1.00)	(1.00)	(·94)	(·91)	·89	(·91)	·72	·80	·70	·69	·60	·63	·58	·55		32.7
	18	"	·75	·68	·81	(·94)	(·88)	(·94)	(1.00)	·72	·80	·67	·64	·54	·44	·46	·44	·35	·24	·23		20.5
	19	"	·33	·42	·68	·75	·85	·90	(·96)	(1.00)	(·93)	·86	·78	·78	·72	·79	·91	·70	·64	·65		14.8
	20	"	·24	·45	·85	·89	·89	(·94)	(1.00)	(·97)	·89	·89	·89	·80	·89	·75	·64	·61	·67	·53		30.8
Mean			·33	·45	·66	·74	·84	·89	·94	·91	·88	·88	·81	·71	·68	·64	·59	·54	·46	·40		26.16
SD			·18	·15	·15	·12	·09	·09	·06	·09	·08	·09	·08	·13	·12	·12	·14	·12	·13	·11		9.31

Table 4.3 Normalised slow phase velocities for the period 0-90 seconds post-irrigation.
CR = Cold irrigation of Right ear; CL = Cold irrigation of Left ear.
Three largest values for each subject are shown 'ringed'.

	Stimulus	
	Warm	Cold
Mean (s)	36.25	34.00
SD	9.16	7.09

Table 4.4 Latency of caloric response. First method of analysis - Time for first peak (seconds, post-irrigation) ['t' statistic = 0.9 (n.s.)].

	Stimulus	
	Warm	Cold
Mean (s)	41.23	35.30
SD	7.71	5.04

Table 4.5 Latency of caloric response. Second method of analysis - 'Averaged peak latency' by taking mean latency for three highest intensity values (seconds, post-irrigation) ['t' statistic = 2.9; $p < 0.01$].

	Stimulus	
	Warm	Cold
Mean (°/s)	25.23	26.16
SD	14.99	9.31

Table 4.6 Mean and SD of nystagmus maximum slow phase velocity (°/s) for the warm and cold caloric stimulus (n = 20 for each group).

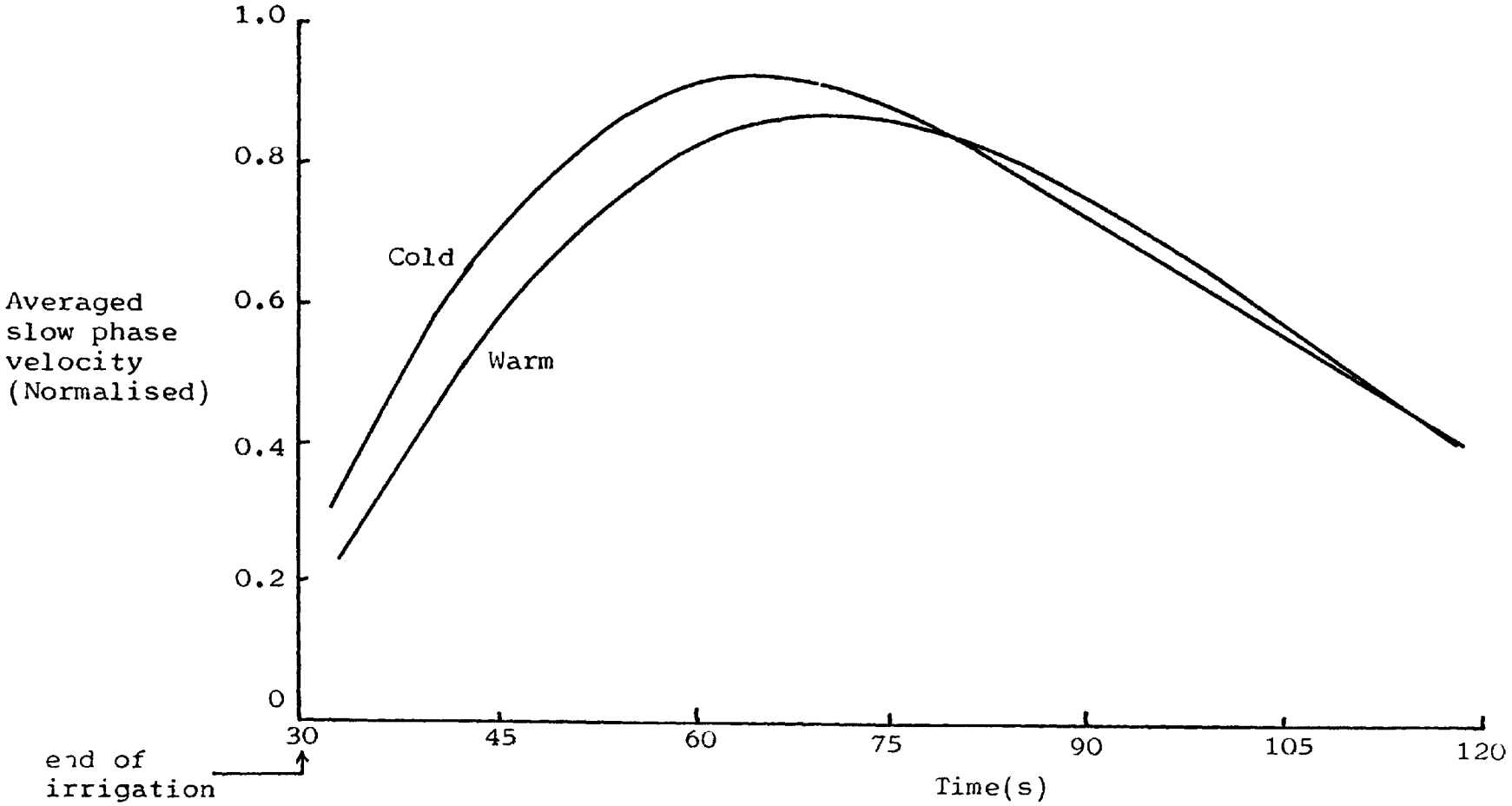

Fig. 4.1 Mean values of nystagmus intensity (^{o}/s - normalised) for the warm and cold caloric stimuli.

CHAPTER 5

TEMPERATURE GENERATION WITHIN THE TEMPORAL BONE

5.1 Introduction

Since Bárány (1906) published his hypothesis on the production of nystagmus resulting from caloric irrigation of the external auditory meatus, there have been several attempts to elucidate the physics and physiology relating to the phenomenon. Regarding heat transfer in the temporal bone, Meurman (1924) used a Cu/Const. thermocouple to measure the temperature generated in the ampulla of the lateral semicircular canal when water was irrigated into the external meatus of human cadaveric heads. Compared to the quantity of water now used in clinical testing, Meurman's was relatively low, namely 2.5, 5 and 10 cm^3 delivered via a syringe. Water temperatures varied between 9 and 14 ^{o}C below head temperature. The measured temperature changes were of the order of 0.03 to 0.15 ^{o}C. Dohlman (1925) using a stimulus more comparable with that now used clinically recorded temperature differences across the lateral semicircular canal in cadavers of approximately 0.75 ^{o}C.

A 'probable' pathway through which the heat energy in the irrigating medium reaches the inner ear was proposed by Schmaltz (1932). He showed the existence of a bony connection between the posterior-inferior wall of

the external meatus and the lateral semicircular canal. This he takes as the main route of heat transfer. Using equations for unsteady one-dimensional heat conduction, Schmaltz calculated the velocity and displacement of endolymph in the lateral semicircular canal.

Cawthorne and Cobb (1954) reported the results of experiments in which they measured the temperature at several locations in the ears of humans during and immediately after caloric irrigation. These investigations were performed on patients during surgery for destruction of the labyrinth. No attempt was made to correlate the results with the nystagmus which would be induced in a conscious patient and no remarks are made regarding the pathway of heat transfer to the inner ear.

A study was undertaken by Harrington (1969) in an attempt to clarify the problem of what is the main heat transfer pathway involved in caloric stimulation. Thermistors were placed in several positions in the ears of human cadaveric temporal bones and of anaesthetized cats. For the human temporal bones the stimulus was 100 cm^3 of water for 20 seconds and for cats, 10 cm^3 for 20 seconds. The conclusions which are drawn from the results are i) the temperature in the vestibule, although not as great as that in the lateral semicircular canal began to increase sooner than that in the latter. ii) removal of the 'bony-bar' did not significantly alter the generated temperatures in the inner ear. From these findings, Harrington states "the bony connection from the posterior ear canal wall to the horizontal semicirc-

ular canal is not as important in the transfer of caloric stimulation as previously supposed".

Young (1972) placed thermistors in the ears of human half-skulls and irrigated with a sinusoidal air stimulus of ± 6 °C re. bone temperature. By comparison of the results with a one-dimensional mathematical model of heat transfer he concludes that the bony-bar is the main route of heat transfer. He does however concede that significant temperatures are generated in the middle ear air space.

Since the conclusions from the work of Harrington (1969) and Young (1972) are conflicting, the question of heat transfer pathways during caloric stimulation still remains unanswered. The work reported in the following pages of this chapter was carried out in an attempt to clarify the situation.

5.2 Anatomy of the Temporal Bone in Relation to Possible Routes of Heat Transfer During a Caloric Test.

A sectional view of the human temporal bone shows the vestibular labyrinth to be well insulated from fluctuations of air temperature outside the skull. As indicated previously, even 'mass syringing' of the external meatus with water at ± 7 °C re. body temperature produces relatively small temperature changes within the inner ear.

The following sketches, illustrating the anatomy of the human temporal bone, were made by the author from a selection of the temporal bone collection of Professor

H.F. Schuknecht, Head of the Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, U.S.A. The sketches are of horizontal sections of the temporal bone in which the plane of cutting is parallel to the axis of the modiolus of the cochlea. Progressively lower levels of section are shown.

Fig. 5.1 shows part of the superior portion of the external meatus, the middle ear cleft including the malleus and incus, and the inner ear including the two vertical limbs of the superior semicircular canal and the beginning of the lateral limb of the lateral semicircular canal.

Fig. 5.2 shows the same structures, in particular the extension of the lateral semicircular canal into the middle ear cleft (prominence of the lat. ssc.), and the well pneumatised mastoid cavity posteriorly.

In Fig. 5.3 is shown the beginning of the bony ridge which extends from the posterior wall of the external meatus to the inner ear. Again, the well pneumatised mastoid cavity can be seen posteriorly.

Fig. 5.4 clearly shows the external meatus and tympanic membrane, part of the medial portion of the lateral semicircular canal and a larger area of bony ridge.

Fig. 5.5, at the level of the oval window, shows the medial portion of the lateral semicircular canal where it joins with the vestibule.

At a level below the lateral semicircular canal, Fig. 5.6 shows the middle ear cleft, bony ridge and mastoid cavity.

A similar series of horizontal sections are shown in Figs. 5.7 - 5.12 except that in this case there is fibro-osseous sclerosis of the mastoid.

Some points of note regarding possible pathways of heat transfer are:

1. In its most lateral position, the lateral semicircular canal forms a prominence on the medial wall of the middle ear cleft. The air within the cleft separates this prominence from the laterally situated tympanic membrane and external meatus.
2. The bony ridge extending from the posterior-inferior portion of the external meatus to the inner ear forms neither a sizable nor direct route for heat transfer between the two regions. The ridge is not encountered in the horizontal section until the lateral canal is well formed posterio-medially.
3. The pneumatisation of the mastoid cavity can vary from a honeycomb of many cells to a very dense structure devoid of air cells. The effect of such variation on heat transfer within the temporal bone may well be significant.

5.3 Temperature Measurement - Materials and Method

Isolated human cadaveric temporal bones were used for this study. Thermocouples made of Chromel/Constantan and of 0.5 mm diameter were placed in several positions within each bone and temperature changes recorded during and subsequent to caloric irrigation of the external meatus with water at a flowrate of 500 ml/min

for 30 seconds. Details of the thermocouples are given in the Appendix at the end of the thesis.

The thermocouple locations were as follows:

1. A differential arrangement of exposed junctions with one end in the delivery nozzle and the other under the skin of the external meatus in a position near to the posterior-inferior area of the tympanic membrane. This allowed measurement of the stimulus temperature relative to the bone and also the rate at which the temperature of the external meatus returned to its pre-stimulus level.
2. A differential arrangement of insulated junctions with one end in the lateral limb of the lateral semicircular canal and the other in the medial limb. The placement of these thermocouples was made via the internal auditory meatus. Firstly, tissue and nerves in the meatus were removed and then the meatus was widened slightly at its medial end by drilling, leaving the falciform crest intact. Removal of a very small amount of bone in the lateral end of the superior vestibular area allowed access to the lateral limb of the lateral semicircular canal. Using a 2 mm diameter drill, a hole was made beginning at a point on the posterior wall of the internal meatus, medial to the falciform crest, and from there directed posteriorly towards the medial limb of the lateral semicircular canal. Drilling was continued until the medial limb was encountered. After initial experience had been gained of this method of access, the procedure became relatively straight forward with the medial limb being

located at the first attempt of drilling.

To ensure that the procedure above did, in fact, locate the thermocouples correctly, the following work was undertaken. In two bones, a wire thread was manoeuvred completely around the lateral canal, being viewed through the internal meatus. In another bone (not used for temperature measurement), extensive drilling, which included removal of the tegmen, a portion of the medial wall of the middle ear cleft and superior surface of the internal meatus, revealed that previous placement of the thermocouples had been accurate.

This arrangement of thermocouples allowed direct measurement of the temperature difference across the lateral semicircular canal.

3. A single insulated thermocouple in the medial limb of the lateral semicircular canal via the internal meatus. This thermocouple was located in a position similar to that of the medial limb thermocouple of the differential arrangement described previously.

The positions so far described constituted the thermocouple arrangement for caloric irrigations on what will be referred to as the 'intact bone'. Further tests were carried out with additional thermocouples in the following positions:

4. A single exposed thermocouple in the middle ear air space in a position approximately midway between the tympanic membrane and prominence of the lateral semi-circular canal. Placement of this thermocouple was

achieved by first drilling away a portion of the tegmen and finally re-sealing the cleft using plastic insulation material. It will later be shown that placement of the thermocouple in this way does not significantly alter the maximum temperature change generated across the lateral semicircular canal.

5. A single insulated thermocouple at the mid-point of the 'bony-bar', positioned by access via the tegmen as described in 4. For subsequent tests, this access allowed removal of the bony-bar by drilling.

The cold junctions of the thermocouples which were not used differentially were placed in a vacuum flask containing paper insulation at room temperature. The thermocouples were connected to DC amplifiers, the outputs of which were connected to a multichannel UV recorder. Details of the equipment and the data for the calibration and stability of the system can be found in the Appendix.

After placement of the thermocouples the temporal bone was placed in a transparent plastic box containing polystyrene insulating material. The external meatus was aligned with a hole in the front wall of the box allowing irrigation to be carried out. The use of ear-mould material enabled sealing of gaps between the external meatus and the container. The supply of water for irrigation was provided by a thermostatically controlled water bath and pump, details of which are in the Appendix. A diagram of the complete experimental set-up is shown in Fig. 5.13.

When the system had stabilised, irrigation of the external meatus was undertaken and the temperature changes recorded. In a large number of tests, the irrigation was carried out at least twice in order to determine the degree of repeatability which might be expected under the experimental conditions. At least twenty minutes intervened between successive tests.

After temperature measurement in the 'intact bone', an area of tegmen was removed and thermocouples placed in the middle ear air space and on the bony-bar as described previously. Caloric irrigations were again carried out and temperature changes recorded. Next, the bony-bar was completely removed by drilling and the test repeated. Finally, temperature changes were measured with insulation material completely filling the middle ear cleft.

It was found upon repeated testing that perforation of the tympanic membrane developed in a number of bones. This reduced the amount of data available, particularly for the condition where packing was present in the middle ear cleft. Table 5.1 shows the number of experiments undertaken for each of the eight temporal bones. Bone number 2 developed a perforation upon the first irrigation but is included in the table in order to avoid problems with renumbering the test results.

5.4 Results

In order to tabulate the data from each trace, measurements were taken for each thermocouple position at suitable time intervals along the trace - a procedure

which involved a large amount of hand measurement and calculation. Also, since the temperature change at the external meatus could not in practice be precisely controlled to 7 ^{o}C for each irrigation, it was necessary to correct values for the temperature changes in the various locations to correspond to this temperature change.

Tables 5.2 - 5.8 give the test results for each of the temporal bones in which temperature changes were recorded. Shown for each thermocouple position is i) the actual maximum temperature change (M), ii) the corrected temperature change based on a 7 ^{o}C change at the external meatus (MN), and iii) the latency of the maximum change (L) measured from the beginning of irrigation.

Since the temperature change at the medial limb of the lateral semicircular canal in the majority of bones increased throughout the period of recording, a latency value is not applicable. Similarly, in the majority of bones, the temperature change at the external meatus immediately began to decrease upon cessation of irrigation and again, a latency value is not applicable.

It can be seen that in most cases, at least two irrigations were undertaken for each condition of the temporal bones, which allowed an evaluation of the repeatability of the measurements. Table 5.9 shows the values of the maximum temperature change across the lateral semicircular canal and also the latency of this maximum for tests 1 and 2 in each of the 'intact' temporal bones. For the seven bones, the mean difference for the magnitude of the temperature change between

successive irrigations is - 0.01 ^{o}C with a SD of 0.04 ^{o}C. For the latency difference, the values are + 1 second and 10 seconds respectively. These values indicate that no appreciable systematic error was introduced into the experiment as a result of successive irrigations of the temporal bones.

Table 5.10 shows the values for the averaged maximum temperature change produced across the lateral semicircular canal and the averaged latency of this maximum for each condition of the temporal bones. Although the amount of data is lacking for statistical analysis, some observations upon the results may be made, namely:

i) Removal of an area of the tegmen had little influence upon the maximum temperature change. Compared to the intact bone, there was, on average, an increase of 10% with removal of the tegmen.

ii) Removal of the bony-bar resulted in a decrease of 11% in the maximum temperature change when compared to the condition in which an area of tegmen was removed.

iii) Packing the middle ear cleft in three bones resulted in a decrease of temperature change in two bones and no change in the remaining bone. On average, this decrease amounted to 38% when compared to the average temperature change for the previous condition of the bones.

iv) There was little change in the latency of maximum temperature change for all the conditions of the temporal bones.

Figs. 5.14 - 5.19 show the time course of the mean

temperature change (± 1 SD) for each thermocouple location. Although there was no thermocouple to measure the absolute temperature change at the lateral limb, results for this location were deduced from the measurements obtained at the medial limb and across the lateral semicircular canal. For the external meatus, the medial limb and across the lateral semicircular canal, results are from 'intact' bones. For the middle ear cleft and bony-bar, results are from temporal bones in which an area of tegmen had been removed for placement of the thermocouples but where the bony-bar remained unaltered.

Fig. 5.14 shows that the temperature change at the external meatus rises quickly to reach a plateau at the end of irrigation, after which it immediately begins to decline slowly towards its original pre-irrigation value. The temperature profiles for the middle ear cleft and bony-bar, shown in Figs. 5.15 and 5.16, are very similar with maximum temperature changes of approximately 1.5 ^{o}C occurring about 75 seconds after the start of irrigation.

The temperature changes at the lateral and medial limbs of the semicircular canal are shown in Figs. 5.17 and 5.18 respectively. As might be expected, the change at the lateral limb is greater and occurs more quickly than that at the medial limb. The temperature change at both these locations is significant even after six minutes, being 0.76 ^{o}C at the lateral limb and 0.60 ^{o}C at the medial limb. Whereas the temperature change at the lateral limb starts to decline very slowly after

approximately 150 seconds, the change at the medial limb is maintained over the entire recording period of six minutes.

As shown in Fig. 5.19 the temperature difference across the lateral semicircular canal changes relatively slowly to reach a maximum of 0.47 ^{o}C at 74 seconds after the start of irrigation. Its rate of decline is relatively slow in comparison to its rate of increase with a temperature difference of approximately 0.15 ^{o}C still present after six minutes.

5.5 Discussion

Regarding the study of the structure of the temporal bone, it is clear that there is no direct route for conduction heat transfer to take place between the external meatus and inner ear. The only route through bone of any significant size is that of the posterior-inferior extension of the external meatus termed the 'bony-bar'. However, it has been shown that this, if it is indeed a route, is a very indirect one, being seen in serial section at a level well below that of the lateral semicircular canal. Additionally, in the majority of temporal bones, this bony-bar consists of numerous air cells which would in theory make it a highly insulating medium. In cases where there is sclerosis of bone in this area, it may be postulated that the bar would then constitute a relatively good conduction pathway. In this respect, the findings of Zangemeister and Bock (1979) are of interest since they show a large intensity of nystagmus response of short

latency in ears where there is sclerosis of the mastoid process.

The most direct route anatomically is that from the tympanic membrane through the middle ear cleft (air) to the prominence of the lateral semicircular canal. Heat transfer by this route would necessitate natural convection between the tympanic membrane and middle ear air, and again, natural convection between middle ear air and the medial wall of the cleft. Transfer from the lateral limb to the medial limb of the semicircular canal would occur by conduction through bone. Since the rate of heat transfer by natural convection in most physical processes is relatively low in comparison to conduction, it may be argued that convection is an unlikely mechanism in caloric stimulation of the labyrinth. However, temperature changes in the inner ear occur slowly, indicating a poor heat transfer medium and therefore the middle ear air space cannot be ruled out as an insignificant pathway. Furthermore, the temperature change which takes place in the middle ear air can only occur by convection. The magnitude and latency of this change as shown in Fig. 5.15 indicates that significant heat transfer does indeed occur by this mechanism. This, coupled with the observation that the lateral limb of the semicircular canal forms a bony prominence on the medial wall of the middle ear cleft makes a strong case for the argument that caloric stimulation is by convection heat transfer across the middle ear cleft. It is remarkable that complete removal of the bony-bar, on average, has a relatively

small effect on the temperature difference generated across the lateral semicircular canal. By comparison, a significant effect is produced by packing the middle ear cleft with insulating material.

Although in practice, heat transfer must take place through both the middle ear cleft and bony-bar, there are two main problems in identifying the precise contribution of each pathway. Firstly, neglecting capacitive effects, the two pathways may be likened to the electrical analogy of current flow through two parallel resistors R1 and R2 where the total resistance is R1R2/(R1+R2). For this network, a change in one resistor will not affect the overall resistance in direct proportion to its value, e.g. if the two resistors are initially equal, a doubling in value of one will result in only a 32% increase in total resistance. Secondly, heat transfer in the temporal bone takes place through a highly insulating medium which is evident from the observations of the slowly changing temperatures within the bone. In such a case, it is difficult to isolate one pathway by placing insulation material into the bone since the thermal characteristics of the insulator are likely to be not too different from those of the temporal bone itself. The amount of experimental data required to perform useful statistical analysis in such a case would be substantial and beyond the scope of the present investigation. The results presented here, however, taken in conjunction with those of Harrington (1969) support the view that the air within the middle ear cleft is an important medium for heat

transfer in the caloric test.

It is not difficult to understand why only small temperature changes occur in the inner ear from such a comparatively large temperature change at the external meatus. The reasons for this are i) the poor thermal conduction characteristics of the temporal bone ii) the transient nature of the stimulus, and iii) three-dimensional diffusion of heat energy through the temporal bone. Regarding the temperature difference generated across the lateral semicircular canal, the orientation of the plane of the canal to the direction of heat transfer, the conductivity of bone between the lateral and medial limbs and the dimensions of the canal, are of additional importance.

In view of the findings of this study, it is doubtful that one-dimensional conduction in a homogeneous medium can be considered a valid simplification for a theoretical model of heat transfer in the temporal bone. A model based on combined transient convective and conductive mechanisms in three-dimensions in a non-isotropic medium presents a difficult problem which still awaits formulation. There is, however, no reason to doubt that in the cadaveric temporal bone at least, the relatively small temperature changes involved in caloric stimulation can be adequately represented by a linear model. In the following chapter, temperature generation in the cadaveric temporal bone will be modelled by the use of a series of first order lag terms. This will be done to provide a caloric temperature input

to the hydrodynamic model of the canal system which will in turn be used to provide a modelled output of nystagmus slow phase velocity. The result will then be compared to caloric nystagmus as recorded in humans in order to indicate to what degree temperature differences in the cadaveric temporal bone reflect those occurring 'in-vivo'.

If results in the isolated temporal bone can be taken as an approximation to those which occur in humans, then it is clear that the thermal stimulus affects the whole labyrinth and not only the lateral semicircular canal. At present, the modifying influence which thermal effects in the utricle and semicircular canal neural fibres have on the response from endolymph movement in the canal is not clear. There is evidence which suggests a direct thermal effect upon semicircular canal neuroepithelium which produces an increase in neural discharge with heating and a decrease of discharge with cooling [Coats and Smith (1967)]. In the normal caloric position, nystagmus produced by this additional effect would complement that produced by endolymph movement. Also, experiments performed on Spacelab have shown the production of nystagmus by caloric irrigation of subjects in a microgravity environment [Benson (1984)]. The theory of Bárány (1906) which is currently accepted as a true explanation of caloric nystagmus, would not allow for nystagmus generation in such a situation. This finding has created a renewed interest in the basic mechanisms involved in caloric nystagmus.

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Bone No.	Condition of Bone			
	Intact bone	Tegmen removed	Bony-bar removed	Packing in middle ear cleft
1	✓	✓	✓	—
2	Perforation			
3	✓	✓	✓	✓
4	✓	✓	✓	✓
5	✓	—	—	—
6	✓	✓	✓	—
7	✓	✓	✓	✓
8	✓	✓	✓	—

Table 5.1 Tests carried out on the temporal bones.

Bone 1		External Meatus		Across LSSC			Medial limb LSSC		Middle Ear Cleft			Bony-Bar		
Test No.	Condition	M	MN	M	MN	L	M	MN	M	MN	L	M	MN	L
1	INTACT	7.4	7	.21	.20	50	.41	.39	—	—	—	—	—	—
2	BONE	7.0	7	.22	.22	65	.42	.42	—	—	—	—	—	—
3	PORTION OF TEGMEN REMOVED (ROOF COVERED)	8.9	7	.25	.20	55	.48	.38	.80	.63	98	.96	.76	75
4	BONY - BAR	9.6	7	.45	.33	54	.90	.66	1.25	.91	60	—	—	—
5	OUT	7.9	7	.40	.35	60	.92	.82	1.30	1.15	105	—	—	—
6	(ROOF COVERED)	5.0	7	.32	.45	75	.60	.84	1.07	1.50	105	—	—	—

Table 5.2 Caloric irrigation of Bone 1 - results of temperature measurement. M - actual maximum temperature change (^{o}C); MN - corrected temperature change based on a $7^{o}C$ change at the external meatus (^{o}C); L - latency of maximum temperature change measured from the beginning of irrigation.

Bone 3		External Meatus		Across LSSC			Medial limb LSSC		Middle Ear Cleft			Bony-Bar		
Test No.	Condition	M	MN	M	MN	L	M	MN	M	MN	L	M	MN	L
1	INTACT	7.2	7	.40	.39	90	.58	.56	—	—	—	—	—	—
2	BONE	10.6	7	.50	.33	90	.87	.58	—	—	—	—	—	—
3	PORTION OF	5.6	7	.31	.39	75	.21	.26	—	—	—	—	—	—
4	TEGMEN	6.8	7	.38	.39	90	.32	.33	—	—	—	—	—	—
5	REMOVED,	6.4	7	.33	.36	75	.25	.27	1.30	1.42	50	2.30	2.52	70
6	ROOF COVERED	7.9	7	.44	.39	72	.30	.27	1.80	1.59	40	2.80	2.48	70
7	BONY - BAR OUT	7.4	7	.49	.46	66	.30	.28	1.45	1.37	60	—	—	—
8	(ROOF COVERED)	7.8	7	.49	.46	66	.30	.28	1.47	1.37	63	—	—	—
9	"	8.8	7	.42	.33	70	—	—	3.35	2.66	45	—	—	—
12	"	7.4	7	.23	.22	60	—	—	1.63	1.54	40	—	—	—
13	"	8.0	7	.27	.24	65	—	—	1.63	1.43	45	—	—	—
10	BONY - BAR OUT	9.6	7	.28	.20	70	—	—	1.66	1.21	55	—	—	—
11	PACKING IN	7.4	7	.26	.25	75	—	—	1.48	1.40	60	—	—	—
14	M.E. CLEFT	8.6	7	.18	.15	75	—	—	1.45	1.18	50	—	—	—

Table 5.3 Caloric irrigation of Bone 3 - results of temperature measurement. M - actual maximum temperature change (^{o}C); MN - corrected temperature change based on a 7^{o}C change at the external meatus (^{o}C); L - latency of maximum temperature change measured from the beginning of irrigation.

Bone 4		External Meatus		Across LSSC			Medial limb LSSC		Middle Ear Cleft			Bony-Bar		
Test No.	Condition	M	MN	M	MN	L	M	MN	M	MN	L	M	MN	L
1	INTACT	8.2	7	.30	.26	60	1.08	.92	—	—	—	—	—	—
2	BONE	6.8	7	.29	.30	60	.76	.78	—	—	—	—	—	—
3	PORTION OF	7.5	7	.23	.21	54	.41	.38	1.60	1.49	60	—	—	—
4	TEGMEN	8.8	7	.29	.23	57	.51	.41	2.00	1.59	60	—	—	—
5	REMOVED	8.2	7	.25	.21	66	.45	.38	1.77	1.51	63	—	—	—
6	ROOF COVERED	7.6	7	.24	.22	63	.42	.39	1.70	1.57	63	2.10	1.93	57
7	BONY - BAR	9.4	7	.21	.16	57	.58	.43	4.50	3.35	50	—	—	—
8	OUT	8.6	7	.20	.16	57	.44	.36	3.70	3.01	48	—	—	—
12	(ROOF COVERED)	8.8	7	.19	.15	50	.40	.32	3.30	2.63	40	—	—	—
13	"	7.9	7	.18	.16	50	.37	.33	2.93	2.60	42	—	—	—
9	BONY - BAR OUT	7.0	7	.15	.15	69	.24	.24	1.55	1.55	55	—	—	—
10	PACKING IN	6.4	7	.14	.15	69	.40	.44	1.13	1.24	70	—	—	—
11	M.E. CLEFT	9.2	7	.22	.17	66	.42	.32	1.60	1.22	75	—	—	—

Table 5.4 Caloric irrigation of Bone 4 - results of temperature measurement. M - actual maximum temperature change (^{o}C); MN - corrected temperature change based on a 7^{o}C change at the external meatus (^{o}C); L - latency of maximum temperature change measured from the beginning of irrigation.

Bone 5		External Meatus		Across LSSC			Medial limb LSSC		Middle Ear Cleft			Bony-Bar		
Test No.	Condition	M	MN	M	MN	L	M	MN	M	MN	L	M	MN	L
1	INTACT	8.7	7	.39	.31	70	.48	.39	—	—	—	—	—	—
2	BONE	8.0	7	.38	.33	70	.46	.40	—	—	—	—	—	—

Table 5.5 Caloric irrigation of Bone 5 - results of temperature measurement. M - actual maximum temperature change (^{o}C); MN - corrected temperature change based on a 7^{o}C change at the external meatus (^{o}C); L - latency of maximum temperature change measured from the beginning of irrigation.

Bone 6		External Meatus		Across LSSC			Medial limb LSSC		Middle Ear Cleft			Bony-Bar		
Test No.	Condition	M	MN	M	MN	L	M	MN	M	MN	L	M	MN	L
1	INTACT	9.3	7	1.04	.78	75	1.10	.83	—	—	—	—	—	—
2	BONE	9.4	7	.99	.74	60	1.20	.89	—	—	—	—	—	—
3	PORTION OF TEGMEN	8.3	7	.96	.81	100	.67	.57	2.05	1.73	100	2.25	1.90	90
4	REMOVED, (ROOF COVERED)	9.5	7	.99	.73	80	.70	.52	2.12	1.56	90	2.47	1.82	75
5	BONY-BAR OUT	10.8	7	.95	.62	100	.84	.54	2.81	1.82	100	—	—	—
6	(ROOF COVERED)	9.5	7	.85	.63	85	.94	.69	2.46	1.81	100	—	—	—

Table 5.6 Caloric irrigation of Bone 6 - results of temperature measurement. M - actual maximum temperature change (^{o}C); MN - corrected temperature change based on a 7^{o}C change at the external meatus (^{o}C); L - latency of maximum temperature change measured from the beginning of irrigation.

Bone 7		External Meatus		Across LSSC			Medial limb LSSC		Middle Ear Cleft			Bony-Bar		
Test No.	Condition	M	MN	M	MN	L	M	MN	M	MN	L	M	MN	L
1	INTACT	5.5	7	.56	.71	100	.75	.95	—	—	—	—	—	—
2	BONE	7.3	7	.73	.70	95	.79	.76	—	—	—	—	—	—
3	PORTION OF TEGMEN	6.3	7	.93	1.03	95	.62	.69	1.73	1.92	110	1.01	1.12	210
4	REMOVED (ROOF COVERED)	5.7	7	.84	1.03	90	.51	.63	1.59	1.95	110	.92	1.13	180
5	BONY-BAR OUT	4.2	7	.59	.98	105	.50	.83	.99	1.65	180	—	—	—
6	(ROOF COVERED)	6.7	7	.83	.87	100	.66	.69	1.37	1.43	150	—	—	—
7	BONY-BAR OUT	5.6	7	.41	.51	80	.29	.36	.55	.69	135	—	—	—
8	PACKING IN M.E. CLEFT	6.6	7	.54	.57	105	.45	.48	.87	.92	195	—	—	—

Table 5.7 Caloric irrigation of Bone 7 - results of temperature measurement. M - actual maximum temperature change (^{o}C); MN - corrected temperature change based on a 7^{o}C change at the external meatus (^{o}C); L - latency of maximum temperature change measured from the beginning of irrigation.

Bone 8		External Meatus		Across LSSC			Medial limb LSSC		Middle Ear Cleft			Bony-Bar		
Test No.	Condition	M	MN	M	MN	L	M	MN	M	MN	L	M	MN	L
1	INTACT	3.6	7	.35	.68	70	.22	.43	—	—	—	—	—	—
2	BONE	7.7	7	.68	.62	80	.31	.28	—	—	—	—	—	—
3	PORTION OF TEGMEN	5.7	7	.57	.70	80	.15	.18	1.98	2.43	35	1.36	1.67	55
4	REMOVED (ROOF COVERED)	7.5	7	.70	.65	85	.32	.30	2.36	2.20	40	1.61	1.50	65
5	BONY-BAR OUT	8.4	7	.58	.48	85	.41	.34	1.61	1.34	85	—	—	—
6	(ROOF COVERED)	8.1	7	.52	.45	85	.29	.25	1.45	1.25	75	—	—	—

Table 5.8 Caloric irrigation of Bone 8 - results of temperature measurement. M - actual maximum temperature change (^{o}C); MN - corrected temperature change based on 7^{o}C change at the external meatus (^{o}C); L - latency of maximum temperature change measured from the beginning of irrigation.

Bone No.	Temp. change - MN(^{o}C)			Latency (s)		
	Test 1	Test 2	Diff	Test 1	Test 2	Diff
1	0.20	0.22	+ 0.02	50	65	+ 15
3	0.39	0.33	- 0.06	90	90	0
4	0.26	0.30	+ 0.04	60	60	0
5	0.31	0.33	+ 0.02	70	70	0
6	0.78	0.74	- 0.04	75	60	- 15
7	0.71	0.70	- 0.01	100	95	- 5
8	0.68	0.62	- 0.06	70	80	+ 10
		Mean	- 0.01		Mean	+ 1
		SD	0.04		SD	10

Table 5.9 Repeatability of results (Intact bone) - Comparison of Test 1 and Test 2 results for maximum temperature change produced across the lateral semicircular canal and the latency of this maximum(normalised values - MN re 7^{o}C temperature change at external meatus).

Bone No.	Intact bone		Tegmen removed		Bony-bar removed		Packing in m.e. cleft	
	MN(^{o}C)	L(s)	MN(^{o}C)	L(s)	MN(^{o}C)	L(s)	MN(^{o}C)	L(s)
1	0.21	58	0.20	55	0.38	63	-	-
3	0.36	90	0.38	78	0.34	65	0.20	73
4	0.28	60	0.22	60	0.16	54	0.16	68
5	0.32	70	-	-	-	-	-	-
6	0.76	68	0.77	90	0.63	93	-	-
7	0.71	98	1.03	93	0.93	103	0.54	93
8	0.65	75	0.68	83	0.47	85	-	-
Mean	0.47	74	0.55	77	0.49	77	0.30	78
SD	0.23	15	0.33	16	0.27	19	0.21	13

Table 5.10 Maximum temperature changes across lateral semicircular canal (normalised values - MN) and latency (L) for different anatomical conditions in seven temporal bones.

Fig. 5.1 Horizontal section of the human temporal bone (H.B.) showing part of the superior portion of the external meatus (EAC), the middle ear cleft including the malleus (M) and incus (I), and the inner ear including the two vertical limbs of the superior semicircular canal (SSC) and the beginning of the lateral limb of the lateral semicircular canal (LSSC).

Fig. 5.2 Horizontal section of the human temporal bone (H.B.) at a level of 1.2mm inferior to previous figure. The prominence of the lateral semicircular canal is particularly noticeable as is the well pneumatised mastoid cavity posteriorly.

Fig. 5.3 Horizontal section of the human temporal bone (H.B.) at a level of 0.8mm inferior to previous figure showing the beginning of the bony ridge which extends from the posterior wall of the external meatus to the inner ear.

Fig. 5.4 Horizontal section of the human temporal bone (H.B.) at a level of 0.8mm inferior to previous figure showing larger area of bony ridge and part of the medial portion of the lateral semicircular canal.

Fig. 5.5 Horizontal section of the human temporal bone (H.B.) at a level of 0.8mm inferior to previous figure showing medial portion of the lateral semicircular canal where it joins with the vestibule. [S-stapes footplate; FN-facial nerve.]

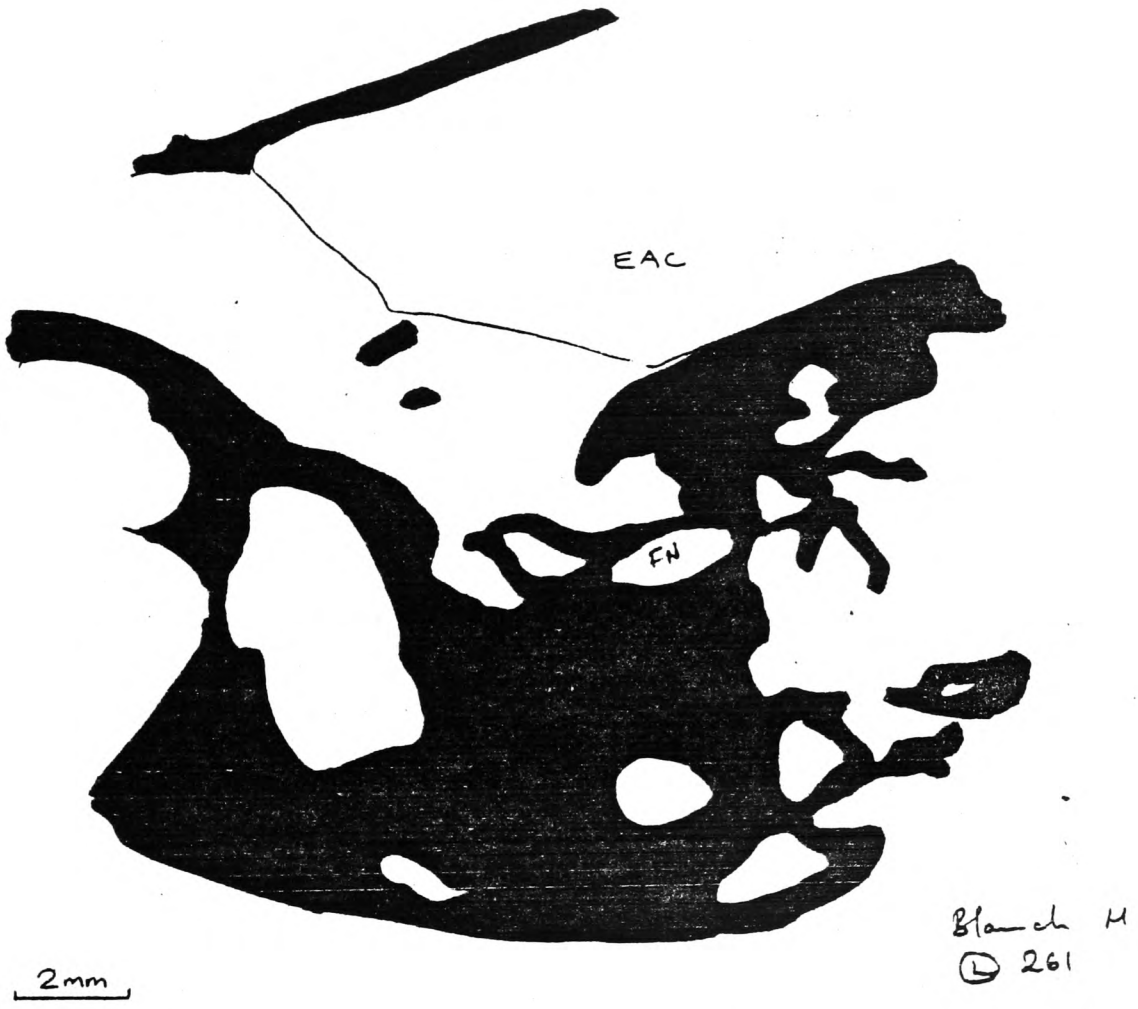


Fig. 5.6 Horizontal section of the human temporal bone (H.B.) at a level of 1.2mm inferior to previous figure showing middle ear cleft, bony ridge and mastoid cavity.

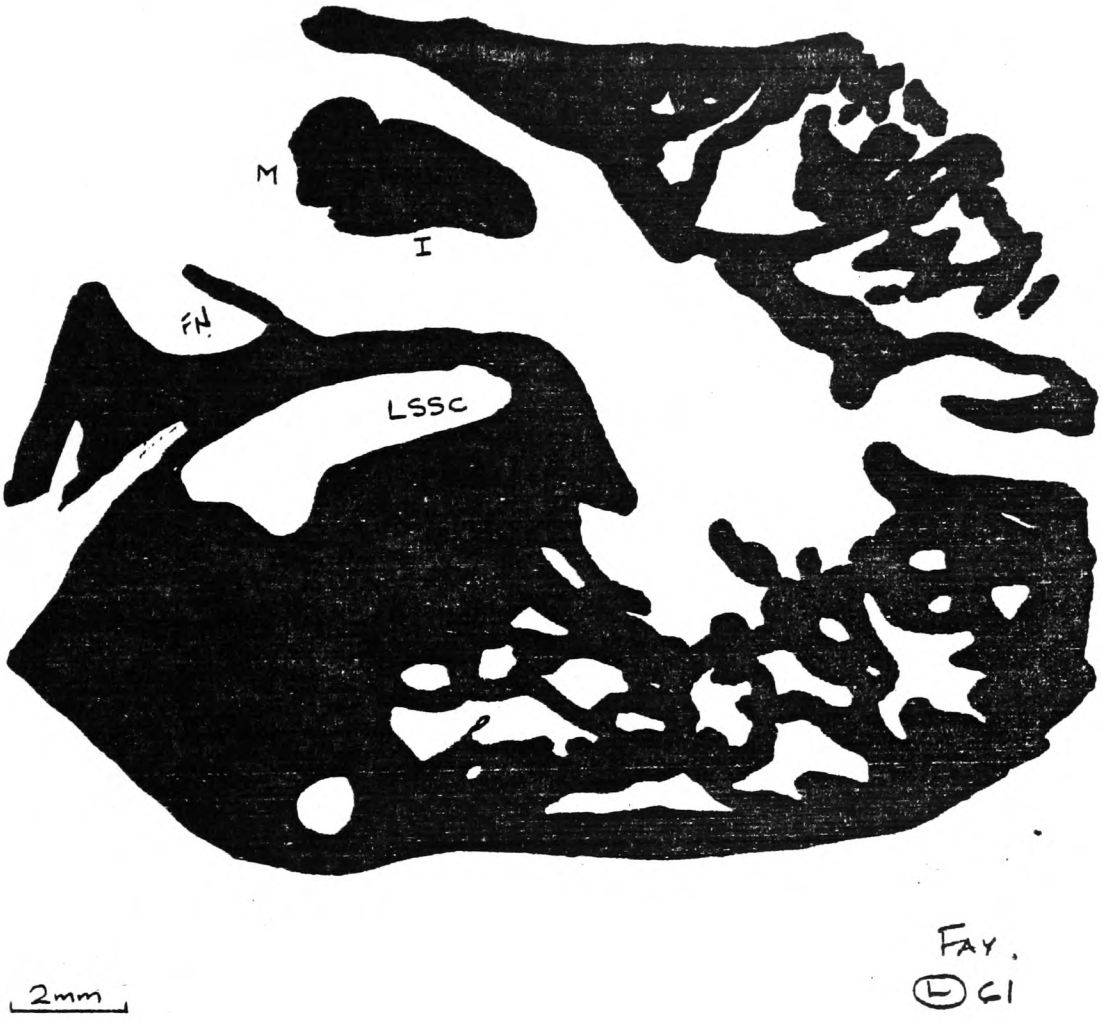


Fig. 5.7 Horizontal section of the human temporal bone (C.M.F.) showing the malleus (M), incus (I), the beginning of the lateral limb of the lateral semicircular canal (LSSC) and fibro-osseous sclerosis of the mastoid process posteriorly.

Fig. 5.8 Horizontal section of the human temporal bone (C.M.F.) at a level of 1.2mm inferior to previous figure.

Fig. 5.9 Horizontal section of the human temporal bone (C.M.F.) at a level of 0.6mm inferior to previous figure showing the beginning of the bony ridge which extends from the posterior wall of the external meatus to the inner ear.

Fig. 5.10 Horizontal section of the human temporal bone (C.M.F.) at a level of 0.6mm inferior to previous figure. [S-stapes footplate].

Fig. 5.11 Horizontal section of the human temporal bone (C.M.F.) at a level of 1.0mm inferior to previous figure. Of particular note is the bony-ridge, the sclerotic mastoid and the medial limb of the lateral semicircular canal.

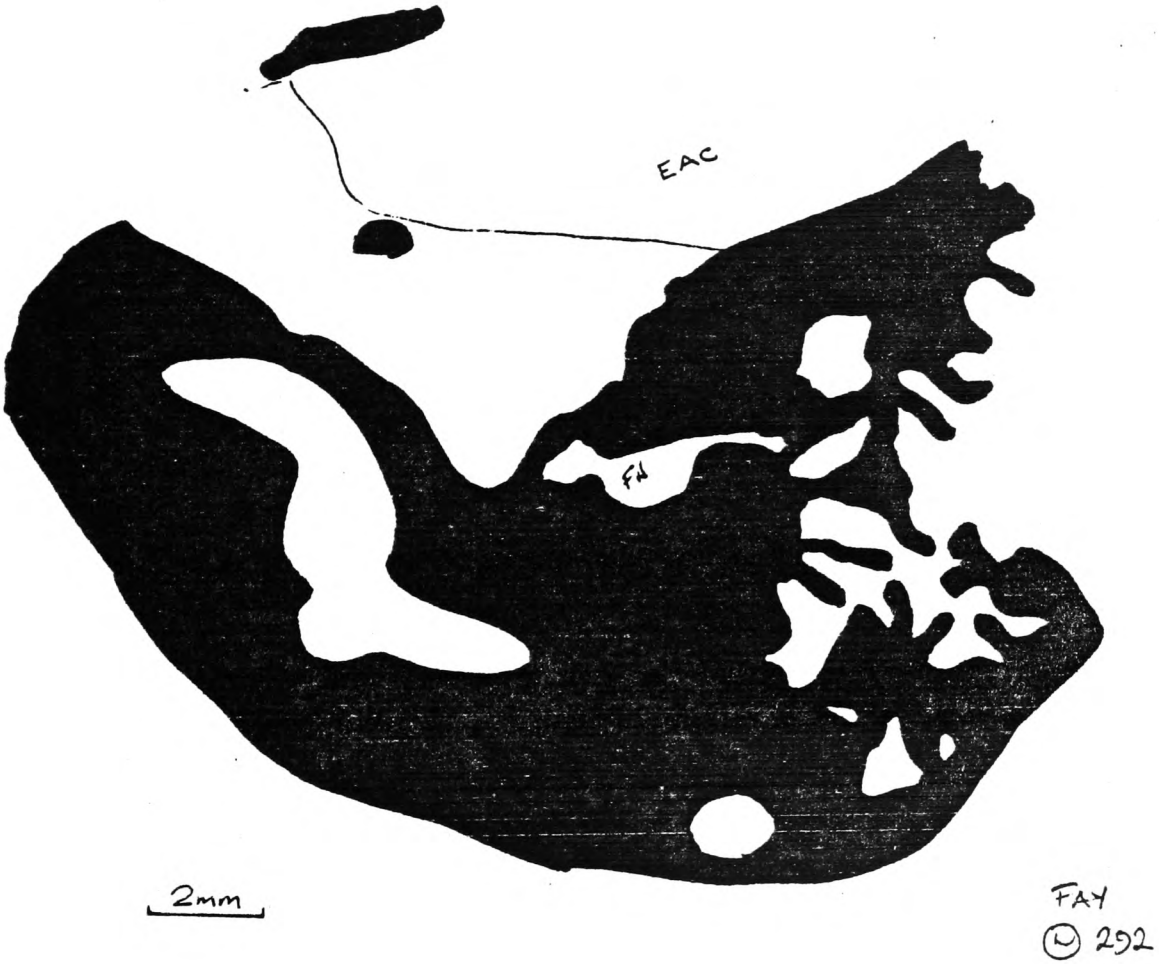


Fig. 5.12 Horizontal section of the human temporal bone (C.M.F.) at a level of 1.2mm inferior to previous figure. [FN-facial nerve].

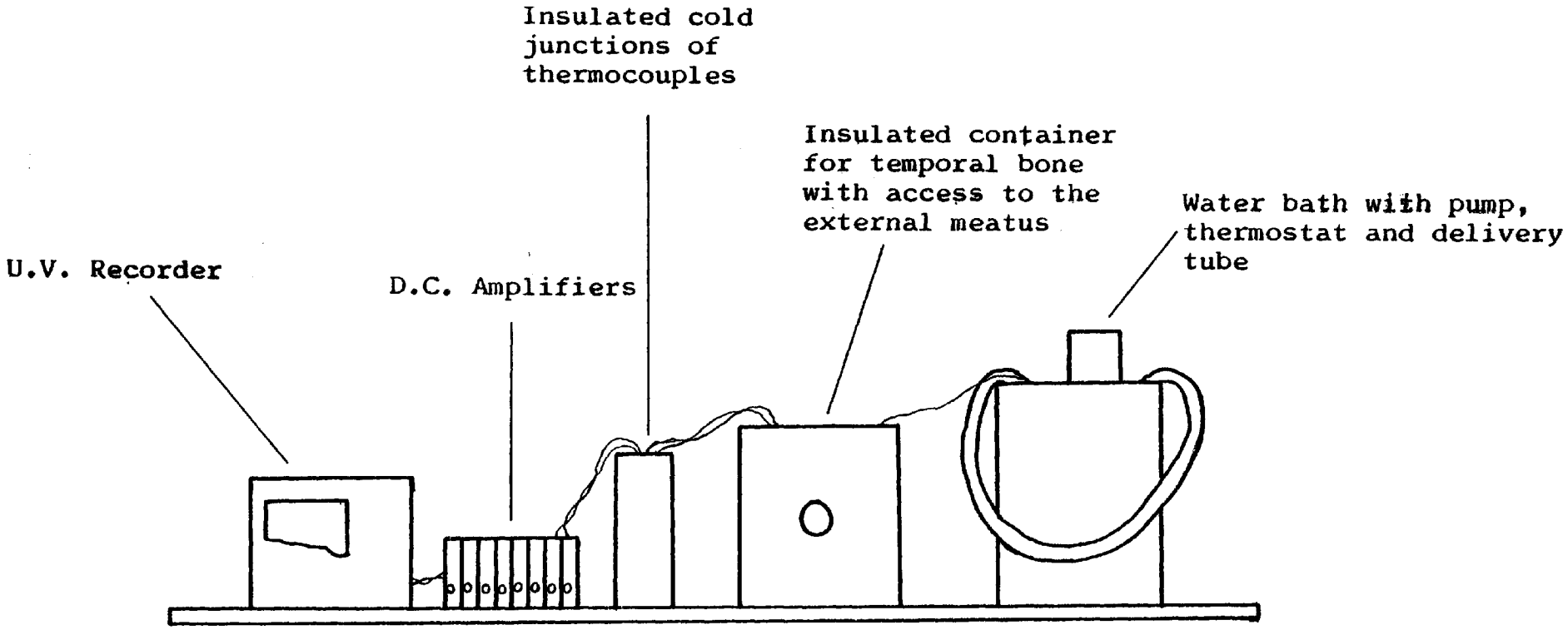


Fig. 5.13 Experimental set-up for stimulus generation and temperature measurement in human cadaveric temporal bones.

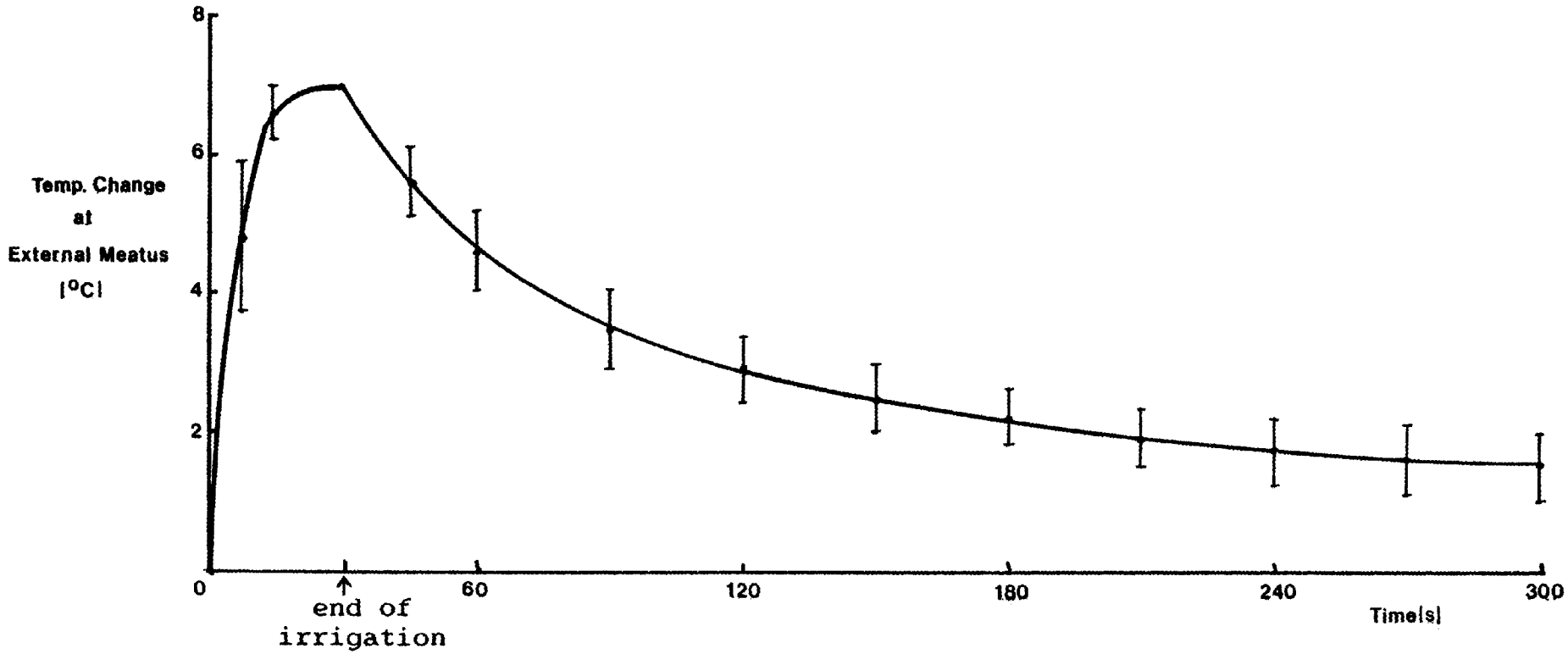


Fig. 5.14 Average temperature change at the external meatus from a standard caloric irrigation in seven human cadaveric temporal bones (± 1SD).

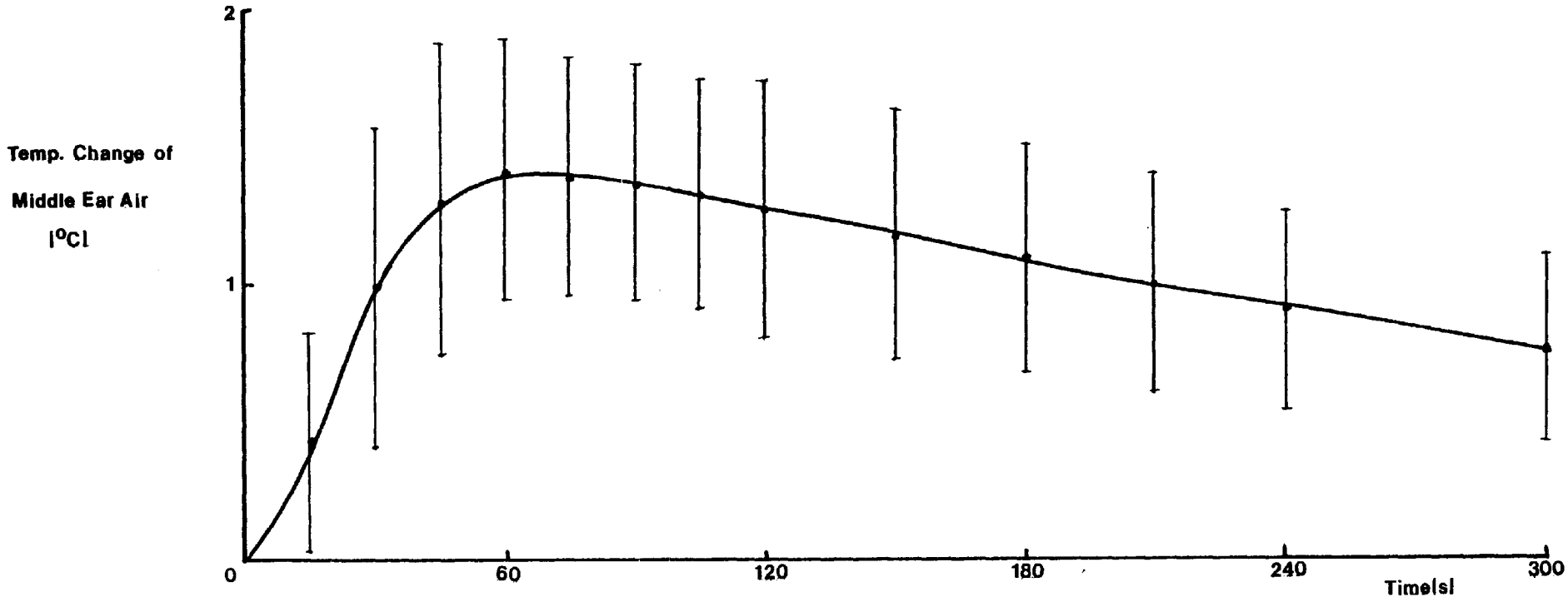


Fig. 5.15 Average temperature change of the middle ear air from a standard caloric irrigation in six human cadaveric temporal bones (± 1SD).

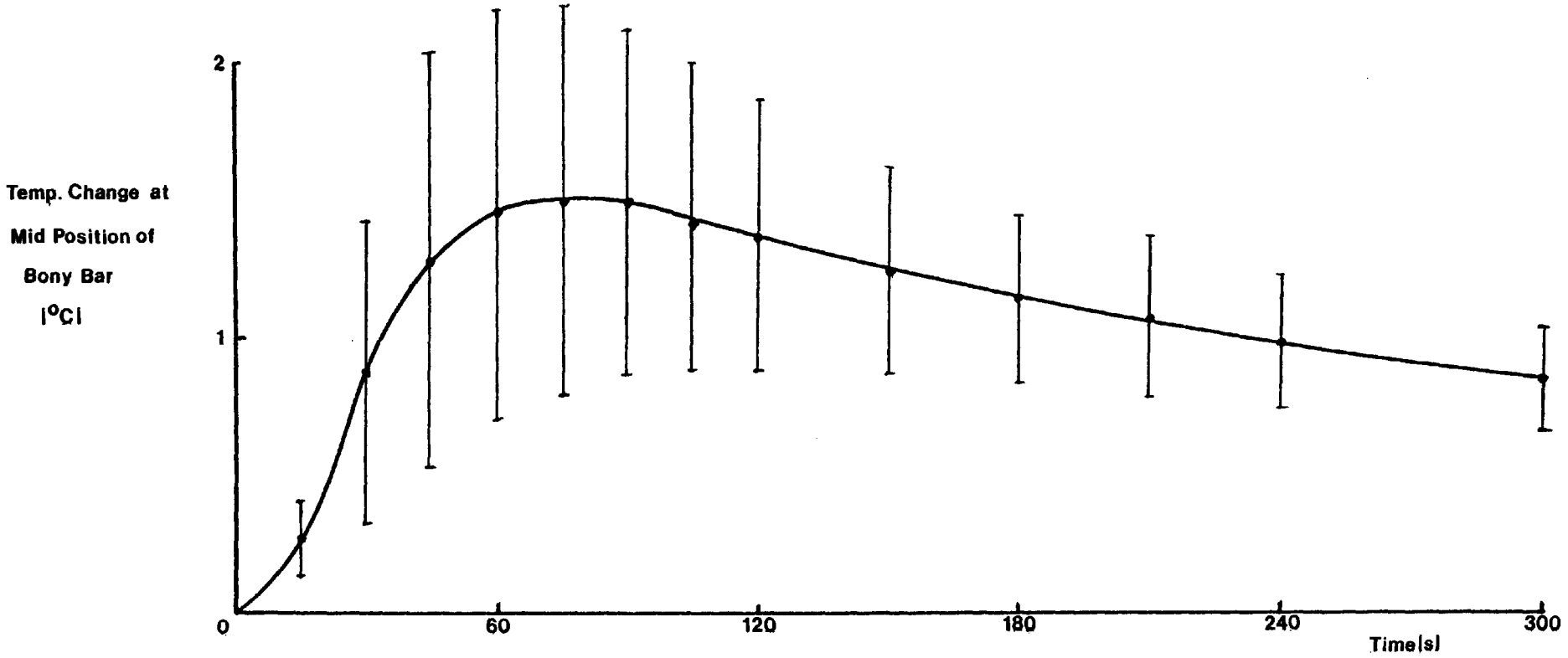


Fig. 5.16 Average temperature change at the mid-position of the 'bony-bar' from a standard caloric irrigation in six human cadaveric temporal bones (± 1SD).

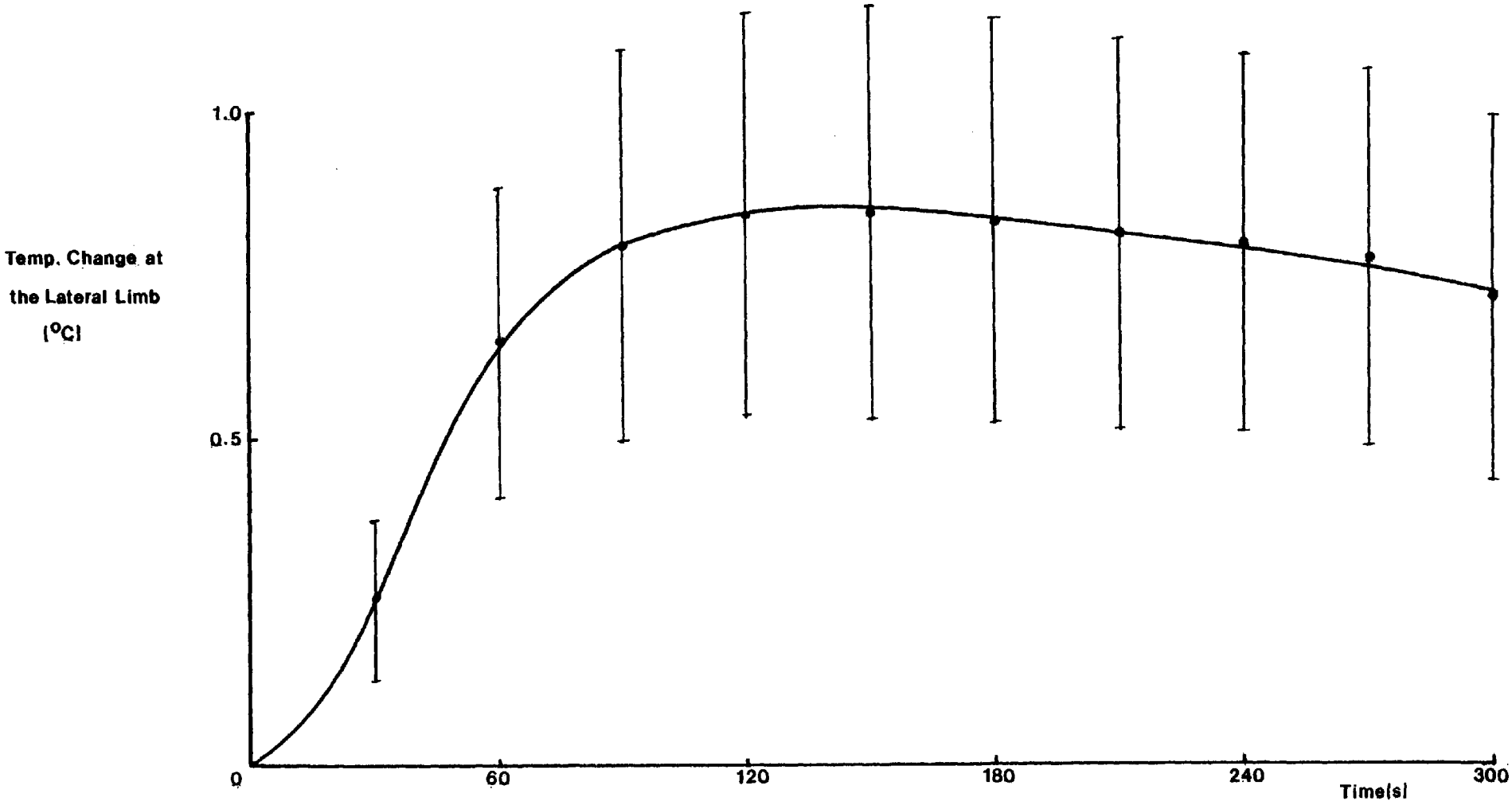


Fig. 5.17 Average temperature change at the lateral limb of the lateral semicircular canal from a standard caloric irrigation in seven human cadaveric temporal bones (± 1SD).

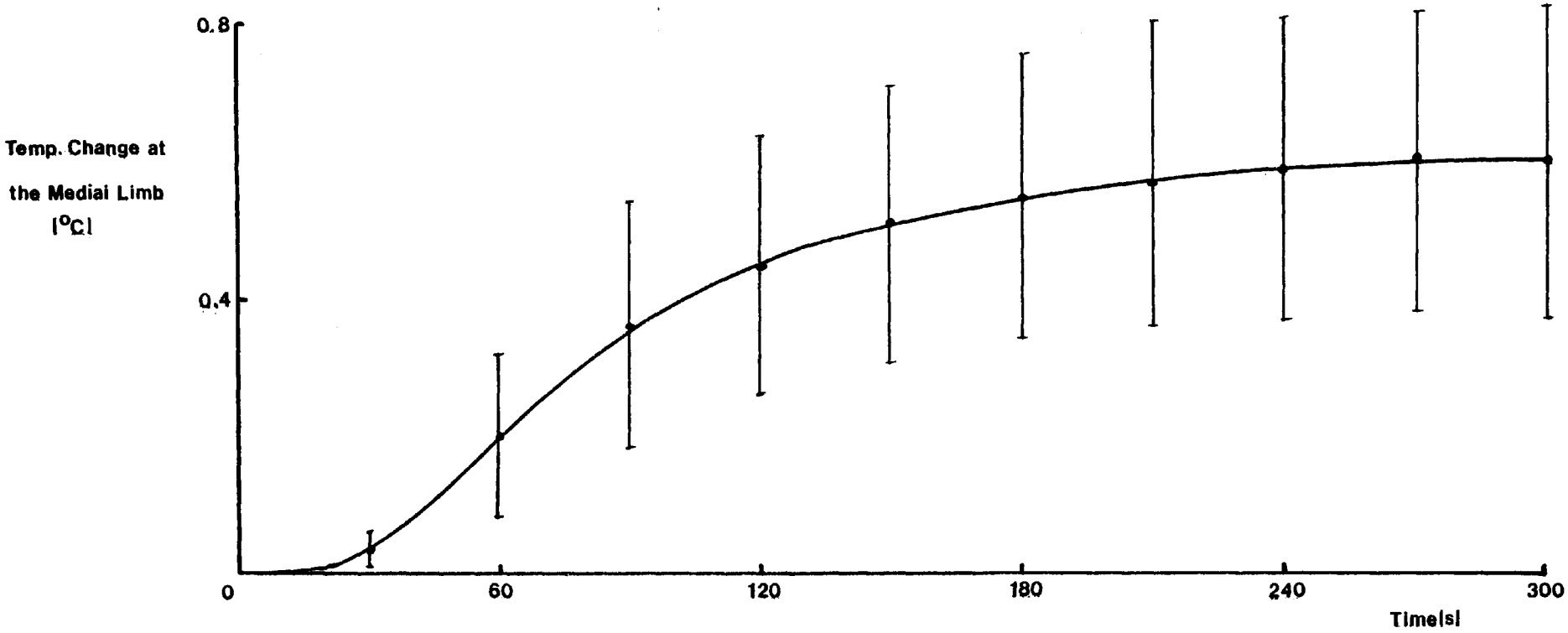


Fig. 5.18 Average temperature change at the medial limb of the lateral semicircular canal from a standard caloric irrigation in seven human cadaveric temporal bones (± 1SD).

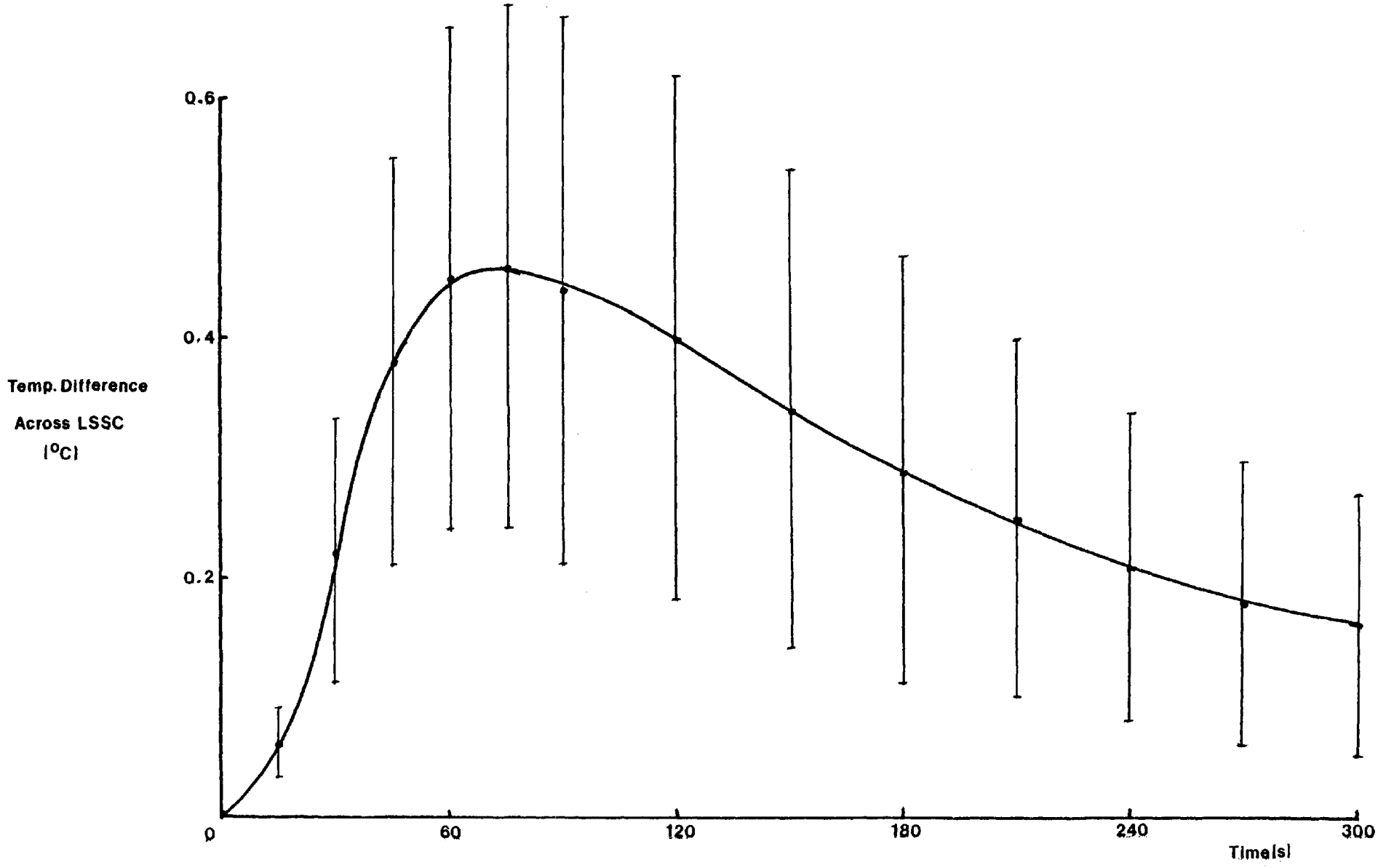


Fig. 5.19 Time-course of average temperature difference across the lateral semicircular canal from a standard caloric irrigation in seven human cadaveric temporal bones (± 1SD).

CHAPTER 6

MATHEMATICAL MODELLING OF THE VESTIBULAR SYSTEM RESPONSE TO CALORIC STIMULATION

6.1 Nomenclature

- a - small radius of canal duct
- f - frequency
- g - acceleration due to gravity
- K_n - cupula pressure difference-to-nystagmus gain
- K_{T1} - thermal gain
- K_{T2} - " "
- M - steady-state torque on endolymph
- N - nystagmus intensity
- P - pressure difference
- P_c - pressure difference across cupula
- Q - flowrate
- R - large radius of canal
- t - time
- T_a - adaptation time constant
- T_b - temperature at external meatus
- δT_c - temperature difference across semicircular canal.
- T_i - input temperature to external meatus
- T_L - high frequency time constant
- T_l - temperature at lateral limb of lateral ssc
- T_m - " " medial " " " "
- T_1 - canal long time constant
- T_2 - canal short time constant
- T_3, T_4, T_5 - thermal time constants

α - angular acceleration of the skull

Δ - torque coefficient ('cupular stiffness') about the centre of the canal per unit of angular deflection of endolymph in the duct

Θ - moment of inertia of endolymph

θ_{max} - maximum input angular displacement

μ - viscosity

ξ - angular displacement of endolymph in the semicircular canal duct

Π - viscous friction coefficient - torque about the centre of the canal per unit angular velocity of endolymph flow in the duct

ρ - density

ϕ - angle between the plane of the thermal gradient and the perpendicular to the direction of gravity

6.2 Introduction

The similarity between the hydrodynamics of the semicircular canals and the damped torsion pendulum was highlighted by Steinhausen (1931) following his experiments on fish. Rotational accelerations of the skull cause viscous and elastic forces to be generated on the endolymph. Whereas the viscous force is produced by the relative motion between endolymph and the membranous wall, the elastic force is due to the elastic property of the cupula. For the situation in which rotation occurs about an axis perpendicular to the plane of the lateral semicircular canal, the system may be mathematically represented as follows [using the notation of van Egmond et al. (1949)].

$$\Theta\ddot{\xi} + \Pi\dot{\xi} + \Delta\xi = \alpha\Theta$$

If the system is highly damped then $\frac{\Delta}{\Theta} \ll \frac{\Pi}{\Theta}$ and the system equation in Laplace notation may be written as follows:

$$\frac{\xi(s)}{\alpha(s)} = \frac{T_1 T_2}{(T_1 s + 1)(T_2 s + 1)} \qquad \text{Eqn. 1}$$

where $T_1 = \frac{\Pi}{\Delta}$ = long time constant

$T_2 = \frac{\Theta}{\Pi}$ = short " "

By the use of rotational stimuli on humans, van Egmond et al. (1949) determined the value of the long time constant as 10 seconds and that of the short time constant as 0.1 seconds. It has since been shown however, that the value of the long time constant was in error because no account had been taken of the effect of adaptation upon behavioural responses. A value of T_1 = 20 seconds seems to be a more accurate estimate of this time constant, [Young and Oman (1969), Schmid et al. (1971), Oman and Young (1972)].

The value of the short time constant T_2 can be verified using an analysis similar to that of van Egmond et al. (1949) in which the value of $\prod$ was determined by consideration of laminar flow in a semicircular duct. From subsequent studies on the dimensions of the vestibular end-organ, it would seem that a more accurate value for the radius of the duct than that used by van Egmond et al. is approximately 0.015cm [Igarashi (1967)]. Also, Dohlman (1980) refers to the work of Vilstrup (1951) and states

> "it is obvious that the 'endolymph stream' from the ampulla does not enter the utricular space towards the macula or its overlying utricular membrane but is instead diverted towards the space above the otolite membrane. Injection experiments have also given the impression that a relatively narrow path-way exists and is used from the ampulla to the duct, which leaves the otolite membrane chiefly unaffected by the endolymph displacements in the angular acceleration system of the canals. The utricle must therefore from this point of view be regarded only as part of - and mainly of the same width as - the toroidal ring."

From Poiseuille's equation, the pressure difference P required to maintain a flowrate of Q throughout a

duct of length $2\pi R$ and radius a is $P = 16\mu RQ/a^4$. Considering the hypothetical flowrate Q within the duct for unit angular velocity $\dot{\xi} = 1$ rad/s then $Q = \pi a^2 R$ and thus $P = 16\mu\pi R^2/a^2$.

Since $\prod$ = viscous torque/unit angular velocity

$= P\pi a^2 R$

then $\prod = 16\pi^2\mu R^3$

Taking the moment of inertia of the duct Θ as that of a complete toroidal ring $= 2\pi^2 a^2 R^3 \rho$

then $T_2 = \Theta/\prod = a^2\rho/8\mu$

taking $\rho = 1$ gm/cm^3; $\mu = 7 \times 10^{-3}$ dyne. s/cm^2 and

a = 0.015 cm.

then $T_2 = 0.004$s, which is in good agreement with currently accepted values for this time constant [Oman and Young (1972), Sills et al. (1978)].

A mathematical model based on the previous system equation and including the effect of adaptation upon subjective vestibular responses to rotational stimuli was presented by Young and Oman (1969) in which a term of the form $T_a s/(T_a s + 1)$ was used to provide the effect of adaptation, where T_a = 30 seconds = adaptation time constant for subjective response. The use of the same term but with T_a = 120 seconds provided the effect of adaptation upon nystagmus slow phase velocity. Malcolm and Melvill Jones (1970) deduced basically the same adaptation term and found from experiment that the mean adaptation time constant was 82 seconds. The model of Schmid et al. (1971) in which T_1 = 20 seconds and T_a = 70 seconds shows a good correlation with nystagmus slow

phase velocity for an input which involved a ramp increase in velocity followed by a period of constant velocity and then a ramp velocity decrease.

Regarding modelling of nystagmus response to caloric stimulation, Steer (1967) developed an equation relating the torque induced on a thin torus of fluid in a uniform temperature gradient field. The steady-state torque on the endolymph is shown to be:

$$M = 4.0 \times 10^{-8} \; g \cos\phi \; \delta T_c \qquad \text{dyne cm}$$

The semicircular canal temperature gradient was modelled using a first order lag term based on experimental results by Cawthorne and Cobb (1954). [The accuracy of the results presented by Cawthorne and Cobb (1954) regarding the time course of temperature change across the lateral semicircular canal will be discussed later in this chapter where it will also be shown that the actual temperature change is represented more accurately by the use of three first order lag terms]. Having calculated the torque on the endolymph and the equivalent angular acceleration which would produce the same torque, Steer calculated the cupula displacement using van Egmond's differential equation for the hydrodynamics of the canal system. The effect of adaptation was not included in the model.

Young (1972) and Demers (1975) both represented the heat transfer in the temporal bone by a model based on one-dimensional heat conduction through a homogeneous semi-infinite solid. However, since the results of the

experimental work presented in chapter 5 of this thesis show that there is significant heat transfer through the temporal bone by routes other than bone, the validity of these models must be questionable.

A model of caloric nystagmus by Baertschi et al. (1975) incorporates effects of the thermal characteristics of the skin, bone and blood circulation.

Bock and Bromm (1977) modelled the heat transfer to the lateral semicircular canal by a first order lag to represent heat transfer from irrigation fluid to external meatal wall, a further first order lag to represent transfer from meatal wall to the lateral limb of the semicircular canal and another first order lag representing transfer from the lateral to the medial limb of the semicircular canal. The temperature difference across the canal could thus be computed and the resulting nystagmus determined using the hydrodynamic model described previously. Once again, the results of the model were compared to the experimental temperature measurements of Cawthorne and Cobb (1954) and a degree of similarity achieved.

At present, no mathematical models exist which use temperature profiles as measured in the cadaveric temporal bone as their input to the hydrodynamic system of the semicircular canal. The use of such profiles in a model however would not only indicate the ability of the complete model to predict caloric nystagmus response, but would also provide information on the temperature changes which are likely to occur 'in-vivo'. With this in mind, the

following analysis will be concerned firstly with the determination of the cupula pressure difference - to - nystagmus gain. A mathematical model of temperature generation in the cadaveric temporal bone, based on the results of chapter 5, will then be shown. Finally, the response of the complete model will be presented.

6.3 Cupula Pressure Difference - to - Nystagmus Gain (K_n)

The pressure difference across the cupula can be evaluated by considering rotational acceleration of a simple 'fluid-filled' torus containing an elastic membrane. For moments about the centre of the torus,

$$\Delta\xi = P_c \pi a^2 R$$

Dividing through by Θ and noting that $\Theta/\Delta = T_1 T_2$ then

$$\xi = T_1 T_2 P_c \pi a^2 R/\Theta$$

Substituting for ξ in Eqn 1 and taking $\Theta = 2\pi^2 a^2 R^3 \rho$ gives

$$\frac{P_c(s)}{\alpha(s)} = \frac{2\pi R^2 \rho}{(T_1 s + 1)(T_2 s + 1)}$$

Taking into account an adaptation term as described previously and in addition a high frequency phase lead term $(T_L s + 1)$ as described by Fernandez and Goldberg (1971) where $T_L \triangleq 0.05$ second, the equation relating nystagmus to head angular acceleration is as follows:

$$\frac{N(s)}{\alpha(s)} = \frac{2\pi R^2 \varrho T_a s(T_L s + 1)K_n}{(T_1 s + 1)(T_2 s + 1)(T_a s + 1)}$$

Where N(s) = nystagmus output from stimulation of two canals and K_n = cupula pressure difference - to - nystagmus gain for two canals.

For values of $T_1 = 20s$; $T_2 = 0.005s$;

$T_a = 100s$; $T_L = 0.05s$

$\varrho = \varrho_{water} = 1.0\ gm/cm^3$;

$R = 0.3$ cm [Igarashi (1967)].

$$\frac{N(s)}{\alpha(s)} = \frac{56.5s(0.05s + 1)K_n}{(20s + 1)(0.005s + 1)(100s + 1)}$$

Sinusoidal Input: The value of K_n may be determined by comparison of the output of the model to that of experimental results for a sinusoidal input. Thus for the input:

$$\alpha(t) = \theta_{max}(2\pi f)^2 \sin 2\pi ft$$

It can be shown that $\theta_{max} = \dot{\theta}_{max}/2\pi f$

for $f = 0.05Hz$, $\alpha(t) = 0.3\ \dot{\theta}_{max} \sin 0.3t$

$$\text{and } \alpha(s) = 0.3\ \dot{\theta}_{max}\left\{\frac{0.3}{s^2 + 0.3^2}\right\}$$

$$\text{Thus } N(s) = \frac{56.5s(0.05s + 1)K_n}{(20s + 1)(0.005s + 1)(100s + 1)}\left[0.3\ \dot{\theta}_{max}\left\{\frac{0.3}{s^2 + 0.3^2}\right\}\right]$$

Ignoring $(0.05s + 1)/(0.005s + 1)$

$$N(s) = 2.54 \times 10^{-3} K_n \dot{\theta}_{max} \left\{ \frac{s}{(s + 0.05)(s + 0.01)(s^2 + 0.3^2)} \right\}$$

Solving by Laplace transforms gives:

$$N(t) = 28 \times 10^{-3} K_n \dot{\theta}_{max} \cos(2.9 - 0.3t)$$

from which $N(t)_{max} = 28 \times 10^{-3} K_n \dot{\theta}_{max}$

$$\text{hence } K_n = \frac{N(t)_{max}}{28 \times 10^{-3} \dot{\theta}_{max}}$$

Table 6.1 shows values of K_n calculated from the equation above by using the experimental results of Baloh et al (1979). By this means, the average value for K_n is found to be 1.14×10^3.

It can be shown that if the adaptation time constant T_a is taken as 50 seconds instead of 100 seconds, the value of the gain K_n would not be significantly altered. The transfer function thus becomes:

$$\frac{N(s)}{\alpha(s)} = \frac{644\ T_a s(0.05s + 1)}{(20s + 1)(0.005s + 1)(T_a s + 1)}$$

The time course of pressure difference across the cupula as determined by the model for the sinusoidal stimulus is shown in Fig 6.1.

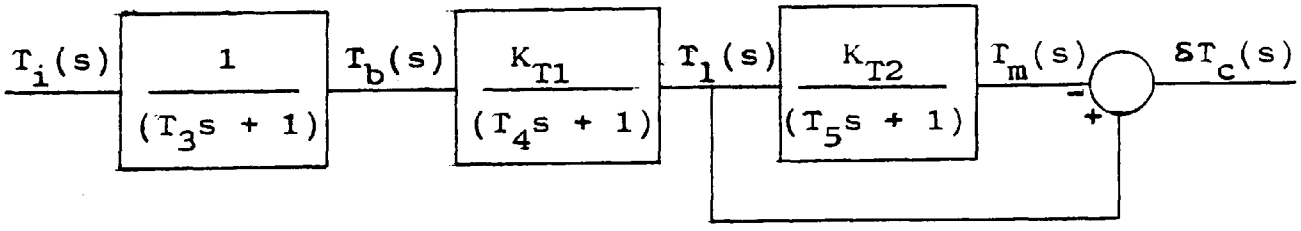
Model Response to Step Acceleration Input: Figs.6.2 to 6.5 show a comparison between the model nystagmus output and experimental results for a series of step acceleration inputs. Experimental responses to an input of $1.5^{o}/s^{2}$ are those from Guedry and Lauver (1961). For the higher accelerations of $5^{o}/s^{2}$, $8^{o}/s^{2}$ and $10^{o}/s^{2}$, the results of Brown and Wolfe (1969) have been used. For each acceleration two model responses are shown, one for T_a = 100 seconds, the other for T_a = 50 seconds. It can be seen that the use of T_a = 50 seconds provides a much better correlation with the experimental results than does T_a = 100 seconds. There is very good agreement between model and experiment at the lower accelerations of $1.5^{o}/s^{2}$ and $5^{o}/s^{2}$. At $8^{o}/s^{2}$ and $10^{o}/s^{2}$ however, the model overestimates the experimental results by about 25%. The time course of the pressure difference across the cupula as determined from the model for accelerations of $1.5^{o}/s^{2}$, $5^{o}/s^{2}$ and $8^{o}/s^{2}$ is shown in Fig.6.6.

Model Response to Impulsive Input: Fig.6.7 shows the modelled pressure change across the cupula resulting from an acceleration impulse of 1 rad/s. In Fig.6.8 is seen the modelled nystagmus output from the same stimulus. The three nystagmus curves show what effect the adaptation time constant has on the response. Where there is no adaptation, the nystagmus declines to zero asymtotically. The inclusion of adaptation gives rise to secondary phase nystagmus after approximately 30 to 40 seconds.

One important difference between the model output and experiment is that in practice, only relatively high levels of stimulation give rise to measurable secondary nystagmus [Sills et al.(1978)].

6.4 Model of Temperature Change in the Temporal Bone

Because of the complex anatomical structure of the human temporal bone and the probability that convective as well as conductive mechanisms are involved in heat transmission from caloric irrigation of the external meatus, it was not considered feasible to attempt a purely theoretical analysis of heat transfer. However, since many physical processes can be modelled by the use of first or second-order differential equations in the form of single or cascaded transfer function blocks, it was thought advantageous to use this method, albeit empirical, to represent temperature changes at different locations within the temporal bone. The respective time constants and gains were adjusted to provide an acceptable degree of fit to the experimental results of chapter 5 where temperature changes were measured in isolated cadaveric temporal bones. The transfer function block diagram is shown below:



For a step input of T_i, the model allows for a steady-state temperature of $T_b = T_i$. This is considered a very reasonable assumption for temperature generation in the immediate vicinity of the irrigation fluid. During the period of irrigation, T_3 is set at a relatively low value to give the fast increase of T_b under conditions of forced convection heat transfer. When the irrigation ceases however, there is no longer forced convection at the external canal surfaces and the decrease of T_b is much slower than its rise. This has been achieved in the model by setting T_3 to a higher value at the point of the cessation of irrigation. Heat transfer from external canal surfaces to the lateral limb of the semicircular canal is represented by one first-order lag term. The steady-state attenuation resulting from three dimensional diffusion and possible heat sinks is accommodated by the inclusion of the thermal gain K_{T1}. Similarly, heat transfer from the lateral to the medial limb of the semicircular canal is represented by a single first-order lag term with steady-state attenuation K_{T2} and time constant T_5. The temperature difference across the canal is simply the difference between the temperatures in the respective limbs.

The system differential equations were solved with the use of an 'ISIS' programme which was available on a PDP 11-23 computer at the Polytechnic of Wales. Adjustment of the model parameter values was performed by a 'trial-and-error' method in order to provide an

acceptable degree of fit to the experimental results of chapter 5 where temperature changes were recorded in isolated cadaveric temporal bones. Figs.6.9 to 6.12 show a comparison between the results of the model and experiment for the following values for time constants and gains:

T_3 = 7s(0-30s) = 120s(30s-) T_4 = 200s T_5 = 50s
K_{T2} = 0.39 K_{T3} = 0.72

Regarding the temperature change at the external meatus following the cessation of irrigation, it would seem that the actual temperature change would be more accurately modelled by the use of a 'double' rather than a single exponential term. The observed difference between model and experiment at this location indicates a more complex heat exchange than that which is implied in the model. The modelled temperature changes at the other locations however, compare very favourably with the experimental results. The difference between model and experiment for the temperature change across the semicircular canal (Fig.6.12) can be explained in part by the obvious combination of modelling errors for the respective limbs from which the temperature difference is calculated. Even so, the temperature change over six minutes is well represented.

6.5 Complete Model of Caloric Nystagmus

Because of the thermal lag effect of heat transfer in the temporal bone, the end-organ is subjected to a

relatively slowly changing stimulation from caloric irrigation of the external meatus. Under this condition, the high frequency lead term ($T_L s + 1$) as described by Fernandez and Goldberg (1971) and also the term involving the short time constant of the semicircular canal can be neglected. The complete system of stimulation and response for one canal is thus represented by the block diagram transfer function shown in Fig. 6.13. The cupula pressure difference - to - nystagmus gain (K_n) is halved to represent the gain of one canal. Use has also been made of the equation by Steer (1967) to allow the determination of the 'equivalent angular acceleration' input to the semicircular canal $\alpha(s)$. Combining this with the equation $M = \Theta\alpha$ gives $0.33\ ST_c = \alpha$ as shown.

Fig. 6.14 shows the output of the complete model for an input temperature profile $T_i(s)$ as previously modelled and shown in Fig. 6.9. Three model responses are shown, one where adaptation is not present, one where the adaptation time constant is 100 seconds and one where it is 70 seconds. Also shown is the nystagmus slow phase velocity response from warm water irrigation of eight normal male subjects [Barnes and Benson (1978)]. The output of the model with no adaptive term shows the magnitude and latency of maximum response and total duration to be significantly in error. By contrast, although the use of an adaptive term overestimates the magnitude of secondary phase nystagmus, a much better comparison exists for primary nystagmus. With an adaptation time constant of 70 seconds, the model

underestimates the magnitude of maximum slow phase velocity by only 4%. Although the latency of this maximum is overestimated by approximately 25%, much of this error can be explained by the error in prediction of the latency of maximum temperature change across the lateral semicircular canal as is shown in Fig. 6.12. The pressure difference across the cupula for the caloric stimulus is shown in Fig. 6.15.

Fig. 6.16 shows the modelled output for a 40 seconds caloric irrigation. Whereas the absence of an adaptive term gives large errors in the magnitude and latency of maximum response and also total duration of primary phase nystagmus, the response with adaptation gives a much better comparison with experimental results.

6.6 Discussion

The mathematical model presented in this chapter is based on several hypotheses, namely, i) representation of the hydrodynamics of the semicircular canal by the Steinhausen (1931) concept of the mathematical similarity to the damped torsion pendulum. ii) assumption of endolymph inertia being equivalent to that of a simple torus. iii) the equivalence of the cupula pressure difference - to - nystagmus gain in rotational and caloric stimulation, accepting that this value must be halved in the situation of the caloric response where only one canal is stimulated. iv) the accuracy of the equation of Steer (1967) in calculating the 'equivalent torque' induced on a torus of fluid in a temperature gradient field. v) the use of

temperature profiles as recorded in the isolated human cadaveric temporal bone as an approximation to those temperatures occurring in-vivo. vi) the inclusion of an adaptation term.

In particular, it is remarkable, considering the number of simplifications made, that the use of temperature profiles based on those occurring in the cadaveric temporal bone gives such a good model response of caloric primary nystagmus. [The overestimation of the intensity of secondary phase nystagmus is considered to be an inevitable result of the inclusion of the adaptation term]. This is strong evidence to indicate that for the 'in-vivo' situation, the effect of blood perfusion on heat transfer is of secondary importance to the effect of the anatomical condition of the temporal bone. This statement may be supported by the observations of Hood (1973) who concluded from his findings of the persistence of caloric nystagmus when subjects were re-positioned that a temperature gradient can exist across the lateral semicircular canal for over ten minutes following a caloric irrigation. If, as some maintain, blood perfusion were to play a major role, it may be argued that the small temperature gradient produced by a standard caloric irrigation should decay much faster than was found to be the case by Hood. Also, McLeod and Meek (1962) produced nystagmus response in 75% of subjects using a stimulus of only $\pm$ 0.5^{o}C relative to the temperature of the external meatus, irrigated for 40 seconds. This extremely small stimulus would arguably be easily dissipated

within the temporal bone if blood perfusion was a significant influence upon heat transfer.

Regarding the modelling of temperature changes, several previous investigators have used the data of Cawthorne and Cobb (1954) as a reference for purposes of comparison [Steer (1967), Bock and Bromm (1977), Barnes and Benson (1978)]. In their study, Cawthorne and Cobb measured temperature changes in several positions of the temporal bone in patients undergoing surgery for Meniere's disease. Their stimulus was irrigation of the external meatus with water at $\pm$ 7^{o}C relative to body temperature for 40 seconds and also 360 seconds. The temperature curves illustrated in Fig. 3 of their publication show the temperature change across the lateral semicircular canal to increase to approximately 0.6^{o}C during the 40 seconds of irrigation, after which the temperature change immediately begins to decrease and at a slower rate than the initial increase. Since it has been shown in this present chapter that caloric primary nystagmus can be predicted with reasonable accuracy by a model of temperature generation in the isolated cadaveric temporal bone in which the peak value of temperature change across the lateral semicircular canal occurs approximately 30-40 seconds after the cessation of the stimulus, it is difficult to accept that the temperature profile presented by Cawthorne and Cobb is typical of that which occurs in the majority of patients in the clinical situation. In order to investigate this further, the temperature profile of Cawthorne and Cobb was modelled and

used as an input to the hydrodynamic model of the semicircular canal, allowing comparison of the output of this model with available experimental results for the same stimulus. Fig. 6.17 shows the modelled temperature profile together with the data of Cawthorne and Cobb. Fig. 6.18 shows the output of the complete model using this temperature profile. It can be seen that this model provides a very poor prediction of caloric nystagmus. Without adaptation the nystagmus intensity is extremely large, the latency of maximum intensity is predicted to occur too early, and the duration of primary nystagmus is significantly overestimated. With the inclusion of adaptation, nystagmus intensity is still much greater than that which occurs in practice, the prediction of latency is in greater error than before, and an intense secondary phase nystagmus is generated very early. Since the hydrodynamic model of the vestibular end-organ has been extensively studied and found to be accurate, albeit with further improvements undoubtedly to be made in the future [Young and Oman (1969), Malcolm and Melvill Jones (1970), Schmid et al. (1971)], the above errors in the model must be attributable, in the main, to an error in the input temperature profile of Cawthorne and Cobb. Use of their temperature profile is thus to be avoided. By comparison, the model which uses temperature profiles based on measurements in cadaveric temporal bones shows a good comparison with the experimental results for the stimulus duration of 40 seconds (Fig. 6.16).

Regarding adaptation, it can be seen that the inclusion of an adaptive term in the model has the effect

of reducing the magnitude of nystagmus maximum intensity, shortening the latency of this maximum and producing secondary phase nystagmus. Although this gives a better comparison with experimental data than does the model which excludes adaptation, a problem arises when the model is used to predict response to long-term caloric irrigations. The results of Baertschi et al. (1975) and Bock et al. (1979) indicate that a primary nystagmus of small amplitude is still present after continuous irrigation for over 15 minutes. The adaptive term used in the model would produce complete decay of nystagmus for such a stimulus. Since Hood (1973) and Barnes and Benson (1978) have shown by experiment that adaptation is present in the caloric response, it would seem that although the present model of adaptation as originally described by Young and Oman (1969) can be used with reasonable accuracy for certain profiles of vestibular stimulation, it is nevertheless an over-simplification of the true physiological process.

It was shown earlier in this chapter, by comparing model response with available experimental results from step acceleration inputs, that greater errors were produced by the model as the stimulus magnitude increased (Figs. 6.2 - 6.5). In the model, successively higher levels of stimulation require a corresponding shortening of the adaptation time constant to produce results closer to experiment. It may be postulated then, that adaptation is dependant upon the strength of the stimulus - a view also held by Bock et al. (1979). Since in the caloric test

the stimulus strength, as represented by the temperature gradient across the lateral semicircular canal, is slowly, but constantly changing, then adaptation will be modified during the stimulation of the end-organ.

The results of chapters 3 and 4 showed differences in both the intensities and latencies between the warm and cold caloric responses in that, on average, the cold stimulus produced responses which were greater in intensity and shorter in latency than those for the warm. However, the difference in intensities cannot necessarily be attributed to a difference in heat transfer arising from physiological response to different thermal stimuli since the cold stimulus was greater than the warm by approximately 20% relative to skull temperature. Also, if as proposed, adaptation is dependant upon stimulus strength, then there exists the possibility that the observed difference in latencies may be explained as an effect purely of adaptation. Clearly, a better understanding of the mechanism of adaptation is required for more accurate modelling of caloric nystagmus. The subject of 'velocity-storage' [Raphan et al. (1979)] also warrants further study in relation to caloric responses.

An improvement to the existing model with regard to the prediction of the intensity of secondary phase nystagmus and response to long-term stimulation may be made by consideration of two additional factors. Firstly, as indicated in the previous chapter, there may be a direct thermal effect upon the vestibular neuroepithelium which results in modulation of the neural activity of the vestibular nerve. The inclusion of such an effect in the model,

possibly based upon the temperature change at the medial limb of the lateral semicircular canal [Oman (1984)], although providing nystagmus output to sustained stimulation, would unfortunately, for a standard irrigation, give a primary nystagmus lasting far in excess of the time indicated by experiment. This would be due to the slow rate of decline of the temperature at the medial limb. Secondly, the results of Goldberg and Fernandez (1971a) and Precht (1978, p16) indicate the existence of a non-adapting population of neural units in the vestibular end-organ. Theoretically, nystagmus would be produced as long as a temperature difference existed across the semicircular canal. The inclusion of this effect would thus give a primary nystagmus for sustained caloric stimulation. Again, however, due to the slow decline of the temperature difference across the canal, then for a standard irrigation, a primary nystagmus would be produced during the period when experiment indicates complete absence of nystagmus. Because of the problems described, these possible additional influences have not been incorporated into the present model.

Regarding the input temperature stimulus at the external auditory meatus, the characteristics of this do not resemble anything which is considered a suitable test stimulus in control theory. There is seen to be a relatively fast change of temperature reaching a plateau which then begins to decline slowly upon cessation of irrigation. The stimulus is therefore neither a step nor a pulse and thus provides a poor input for evaluation of the transfer function of the system under investigation. The use of Pseudo-

Random Binary Sequence (PRBS) as an alternative thermal input may possibly result in better evaluation of vestibular function by providing the system impulse response, and is therefore a method which warrants further study.

--- oOo ---

$\dot{\theta}_{max}$ (rad/s)	$N(t)_{max}$ (^{o}/s)	$K_n = \frac{N(t)_{max}}{28 \times 10^{-3} \dot{\theta}_{max}}$
0.26	8.5	1168
0.52	16.8	1154
1.05	34.1	1160
2.09	63.6	1087
		Mean 1142
		SD 37

Table 6.1 Values of K_n calculated from the model using experimental data of Baloh et al. (1979).

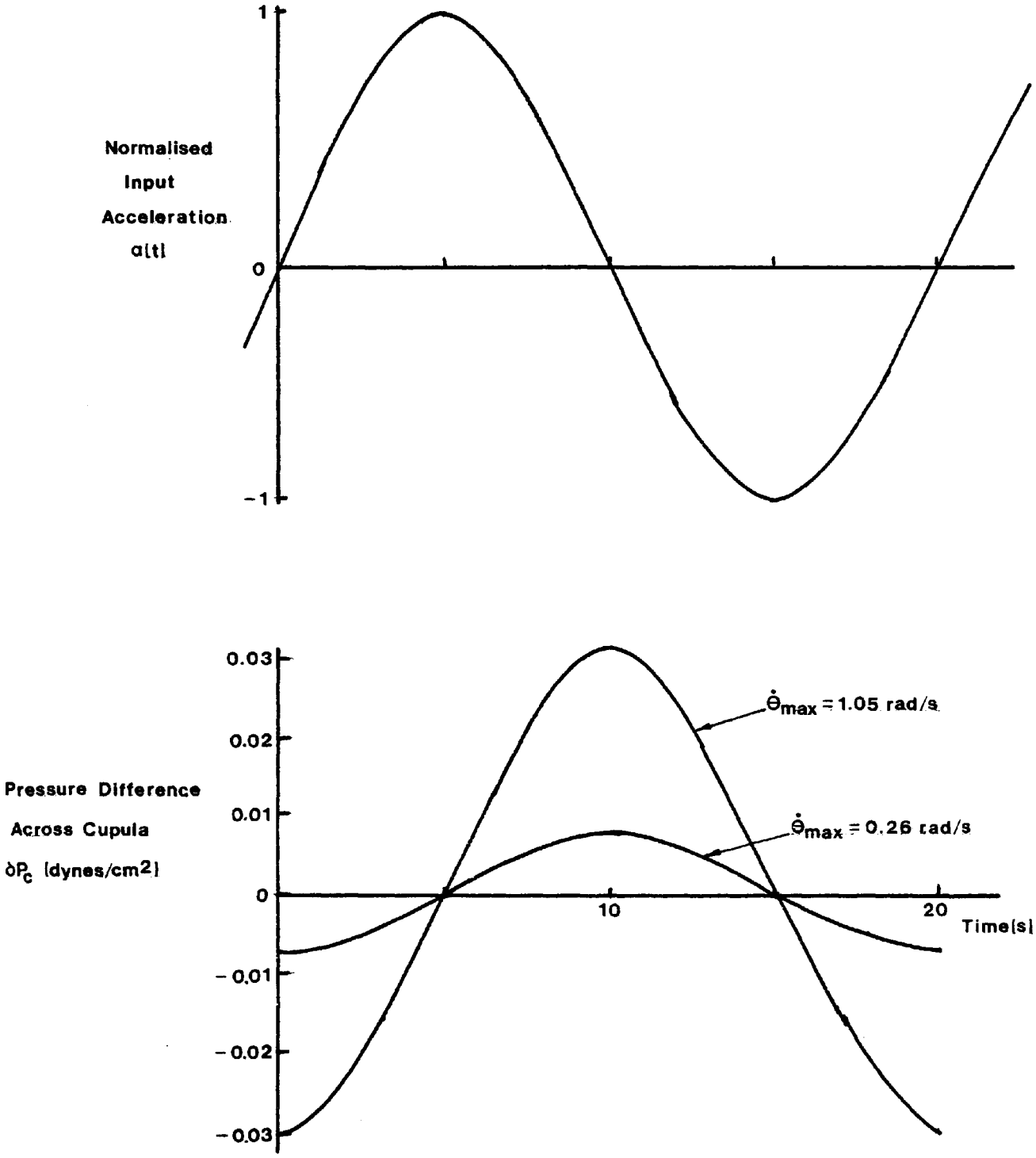


Fig. 6.1 Modelled time course of pressure difference across the cupula for sinusoidal stimulus (f = 0.05 Hz).

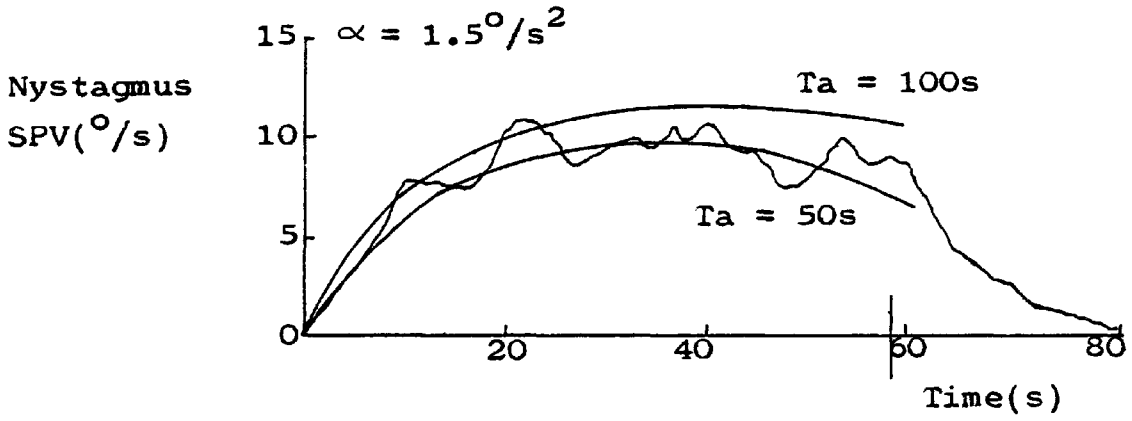


Fig. 6.2 Comparison of model output (Ta = 50s and Ta = 100s) with experimental results of Guedry and Lauver (1961) for step acceleration input of $1.5^{\circ}/s^2$.

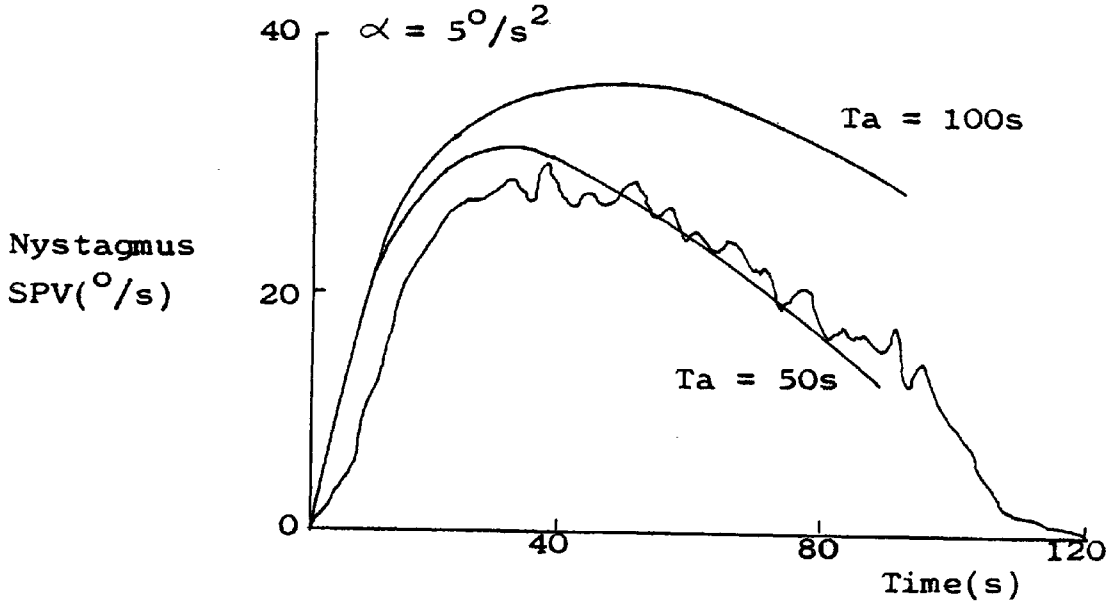


Fig. 6.3 Comparison of model output (Ta = 50s and Ta = 100s) with experimental results of Brown and Wolfe (1969) for step acceleration input of $5^o/s^2$.

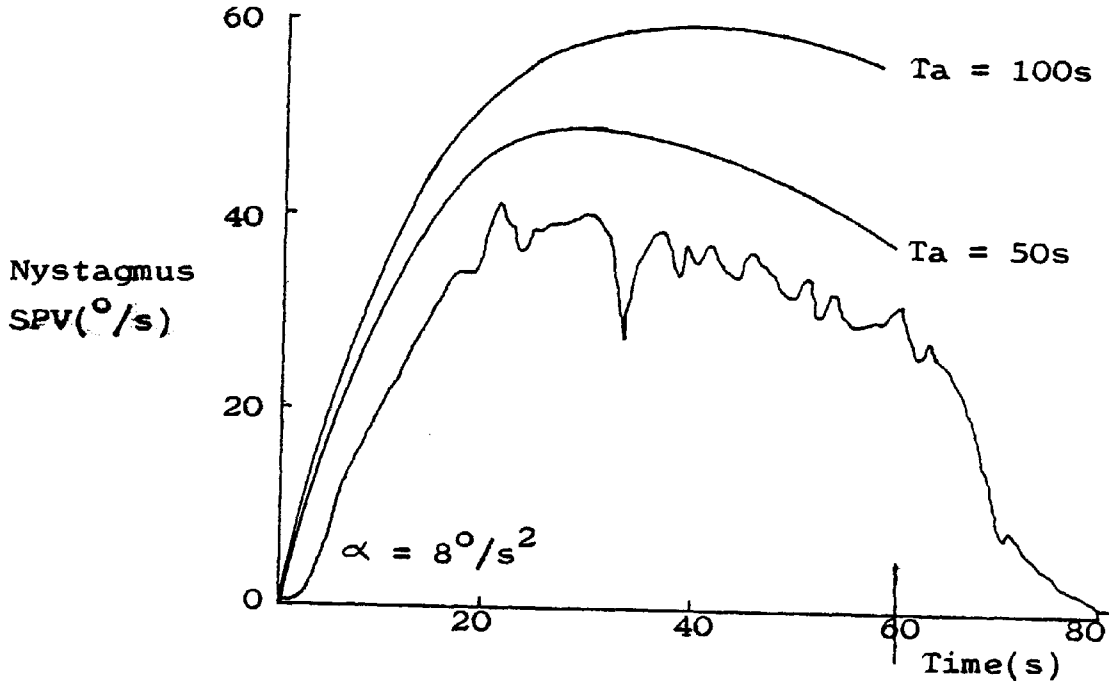


Fig. 6.4 Comparison of model output (Ta = 50s and Ta = 100s) with experimental results of Brown and Wolfe (1969) for step acceleration input of $8^{\circ}/s^{2}$.

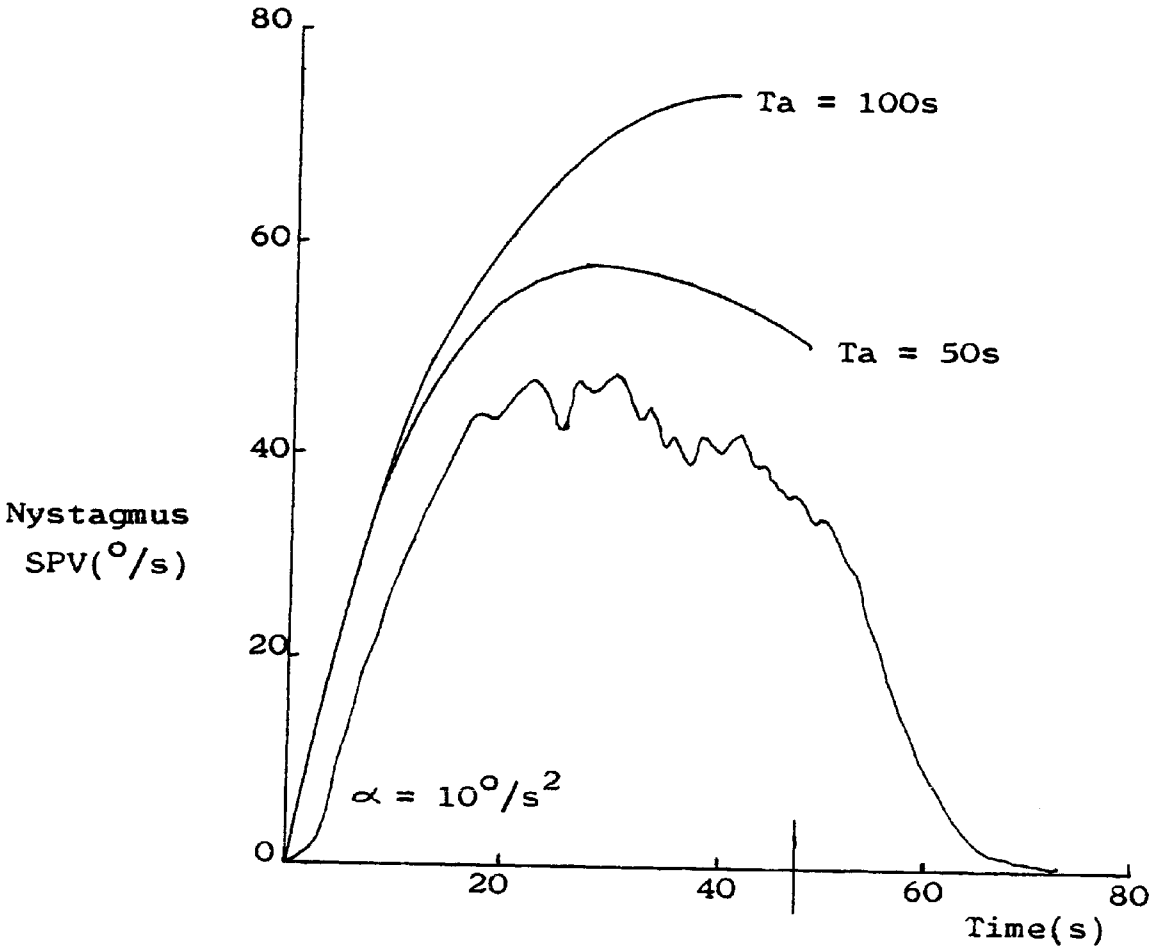
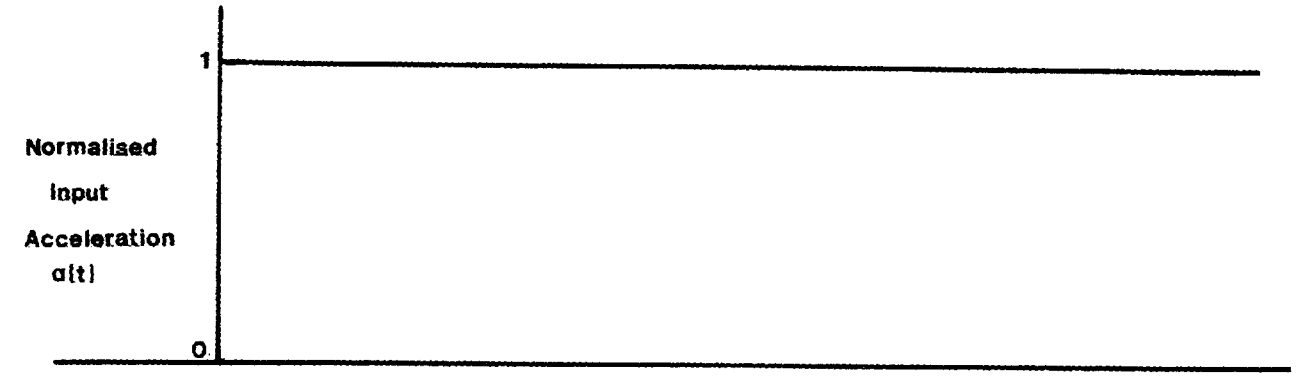


Fig. 6.5 Comparison of model output (Ta = 50s and Ta = 100s) with experimental results of Brown and Wolfe (1969) for step acceleration input of $10^{o}/s^{2}$.



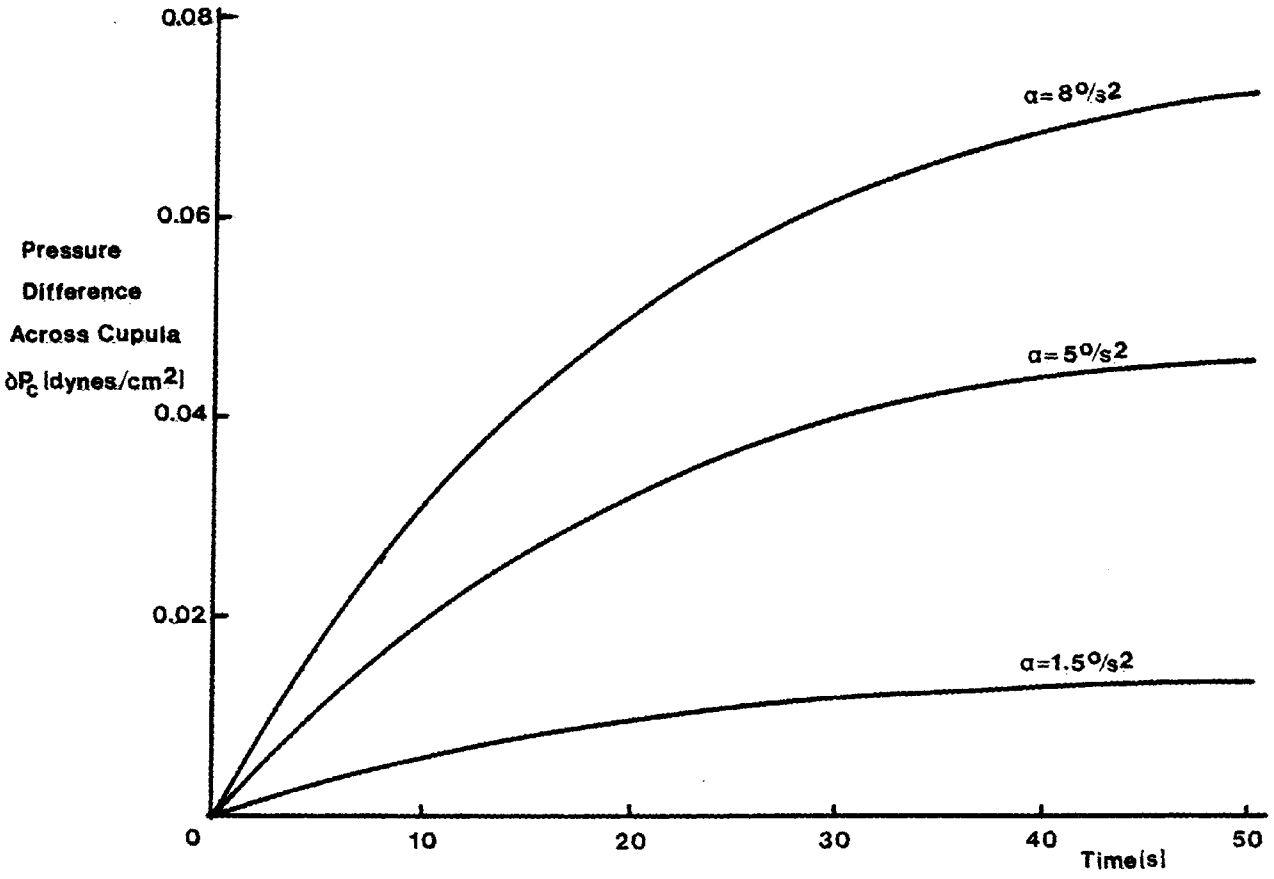


Fig. 6.6 Modelled time course of pressure difference across the cupula for step acceleration input.

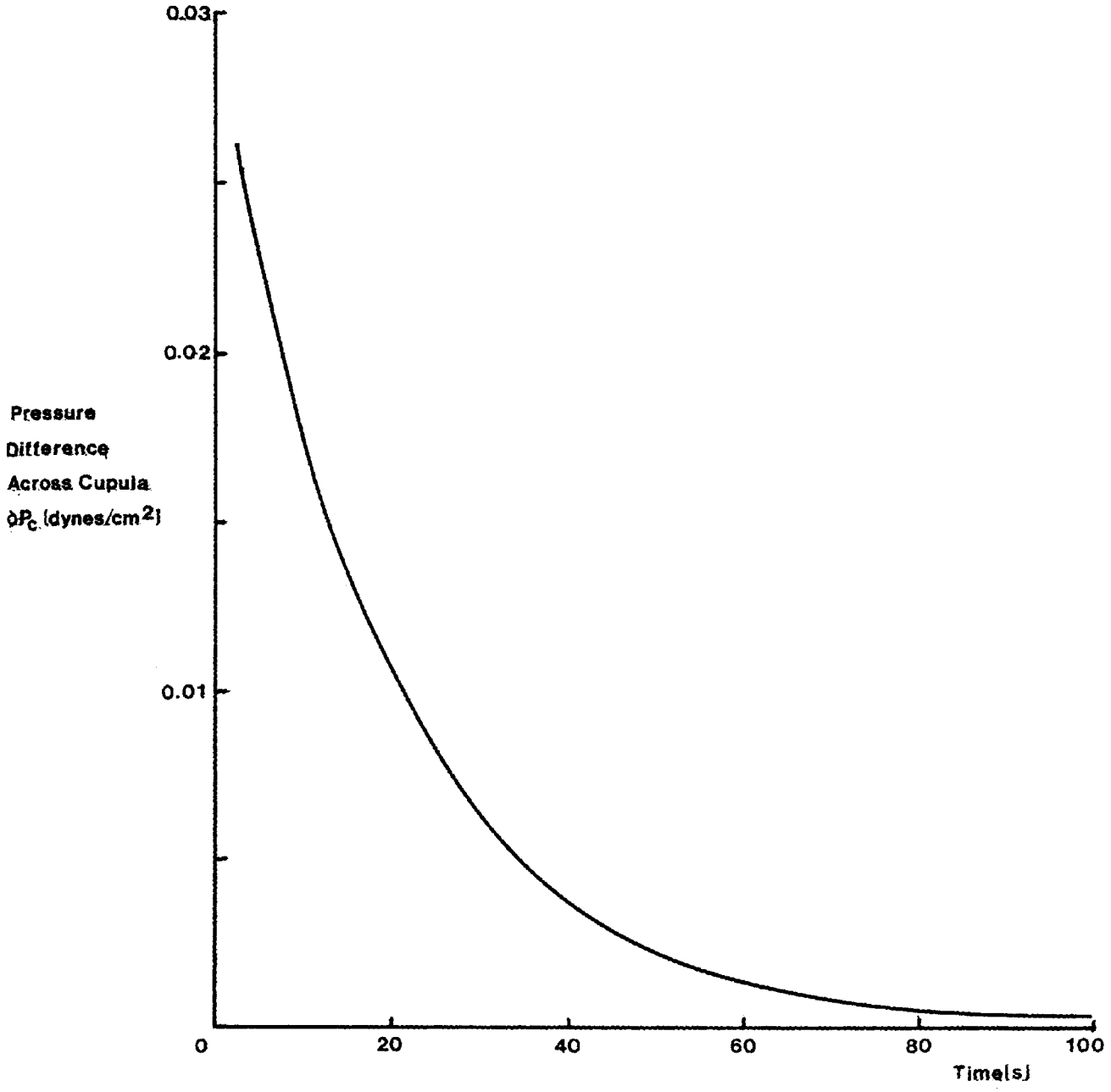


Fig. 6.7 Modelled time course of pressure difference across the cupula from an acceleration impulse of 1 rad/s.

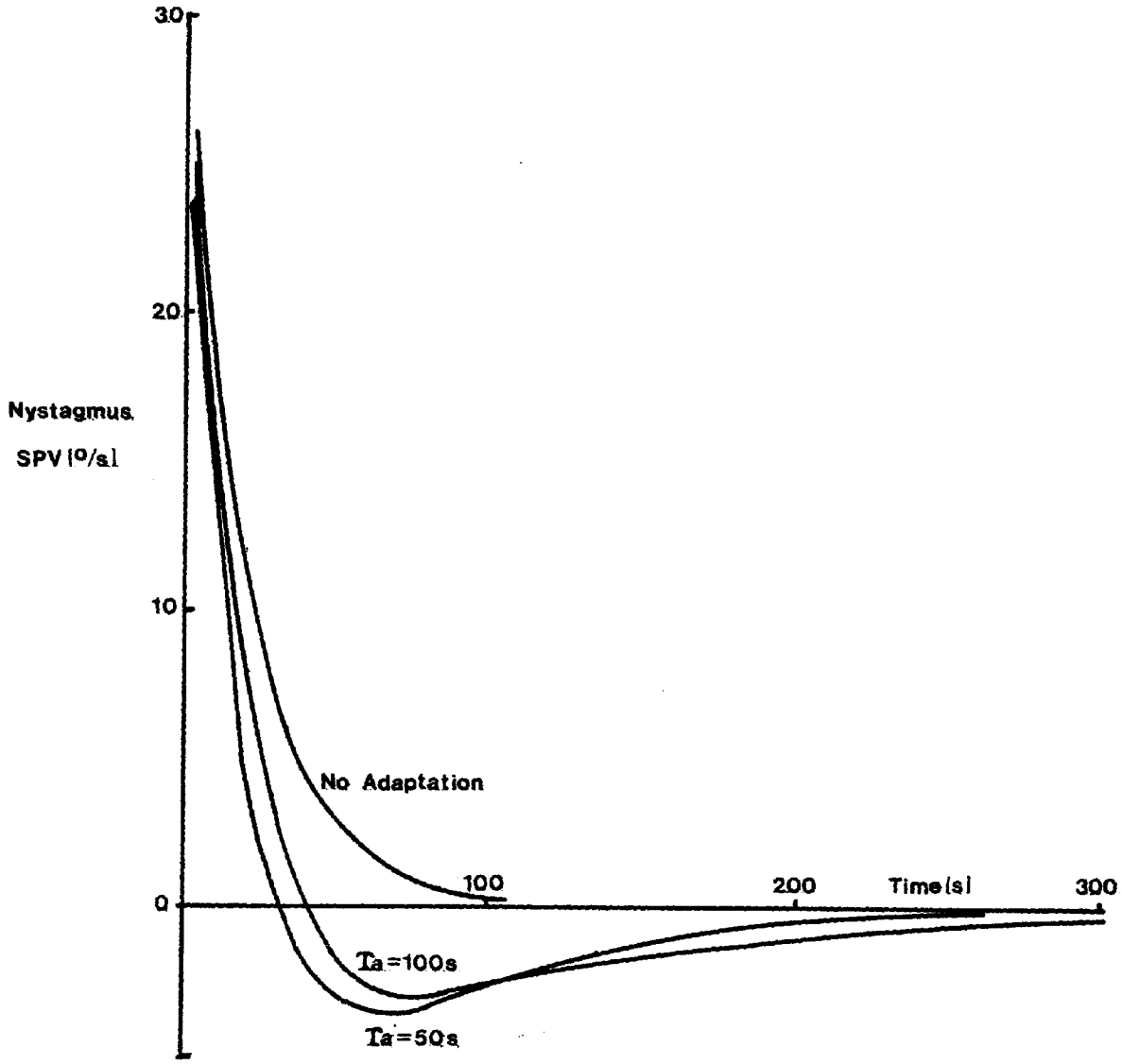


Fig. 6.8 Modelled nystagmus response resulting from an acceleration impulse of 1 rad/s.
(Ta = adaptation time constant).

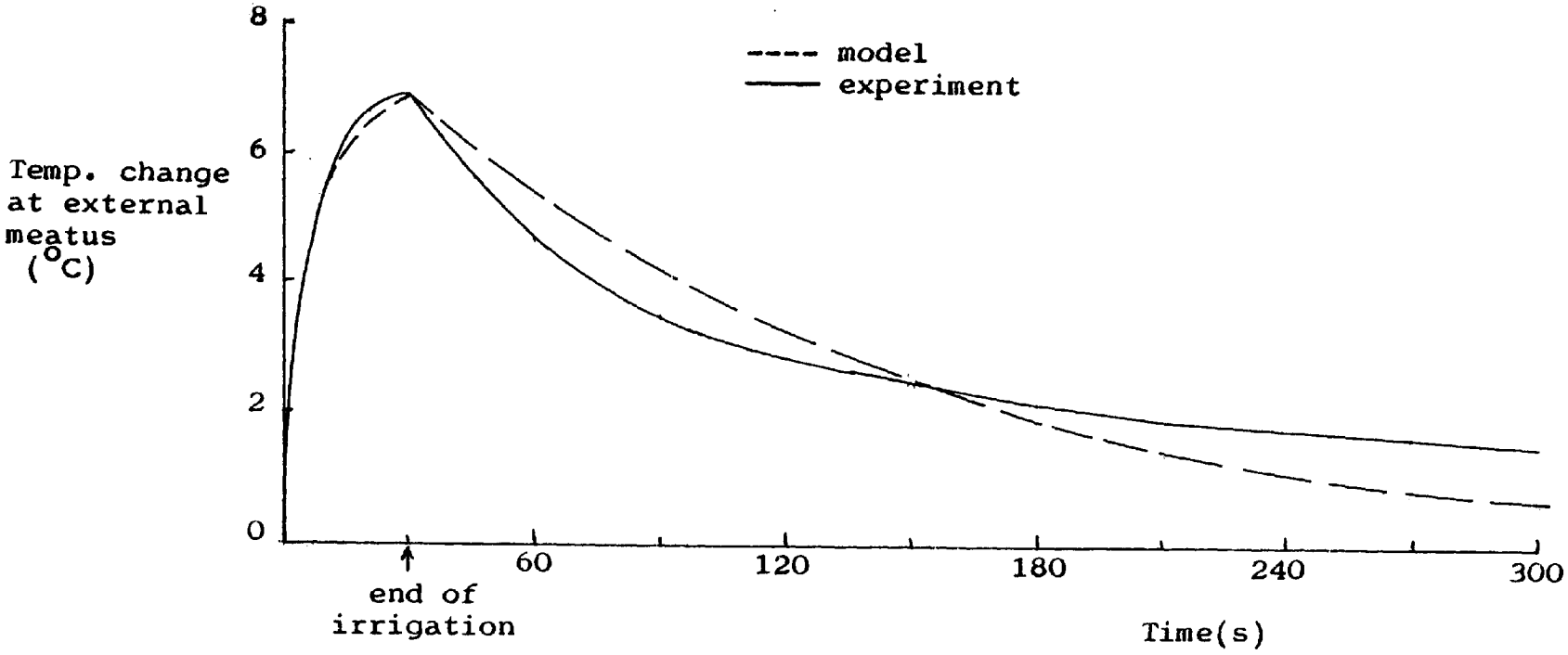


Fig. 6.9 Temperature change at the external meatus from a standard caloric irrigation - comparison of model output with experimental results in cadaveric temporal bones.

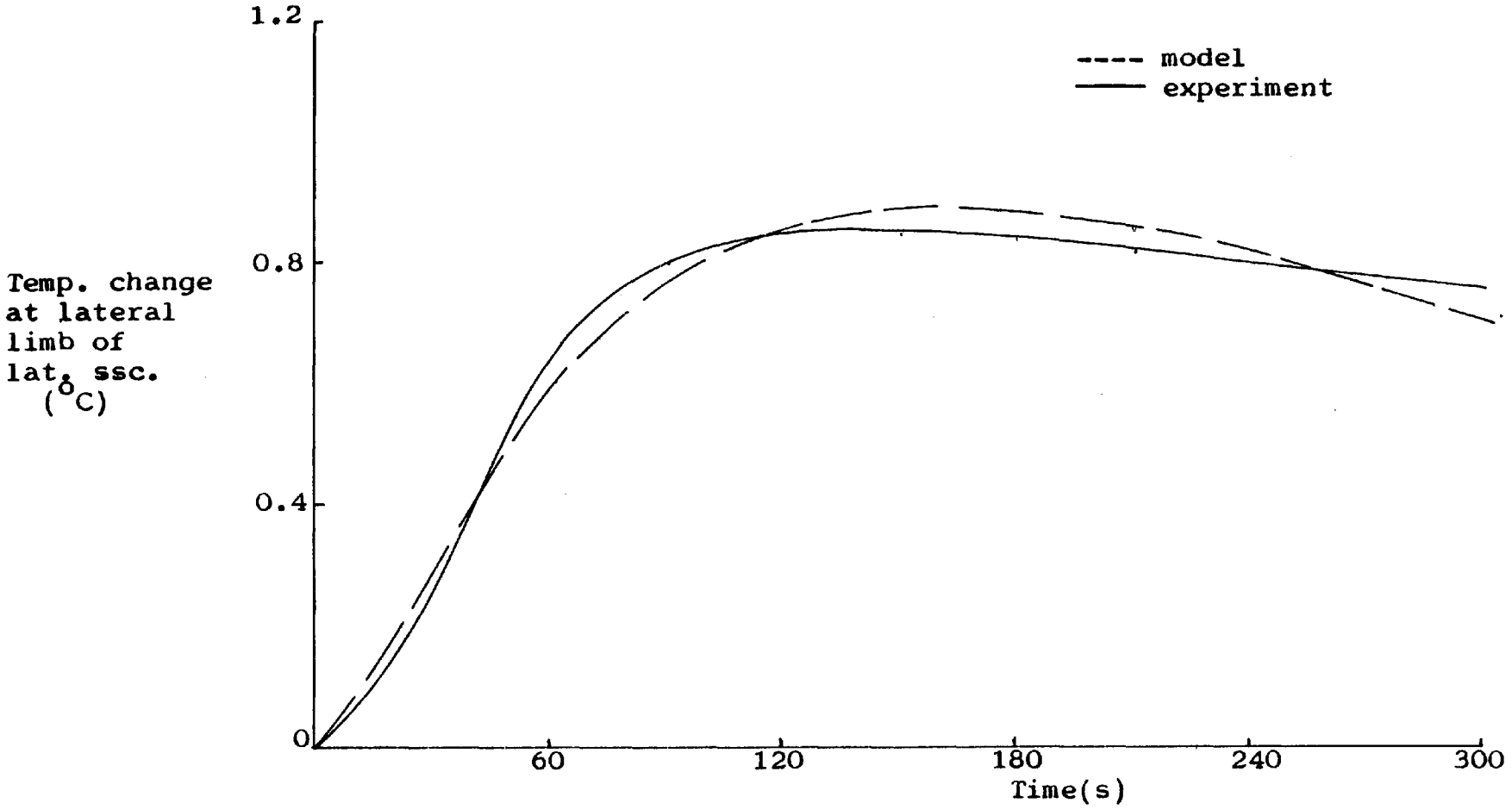


Fig. 6.10 Temperature change at the lateral limb of the lateral semicircular canal from a standard caloric irrigation - comparison of model output with experimental results in cadaveric temporal bones.

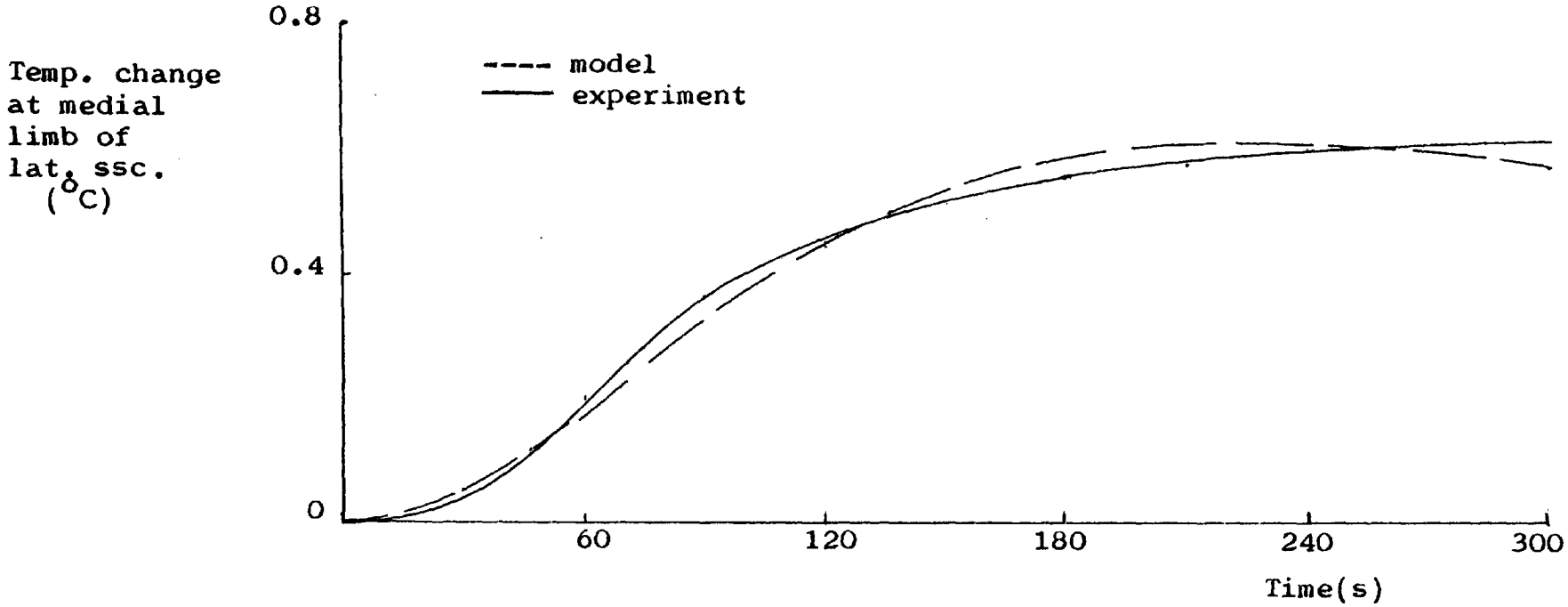


Fig.6.11 Temperature change at the medial limb of the lateral semicircular canal from a standard caloric irrigation - comparison of model output with experimental results in cadaveric temporal bones.

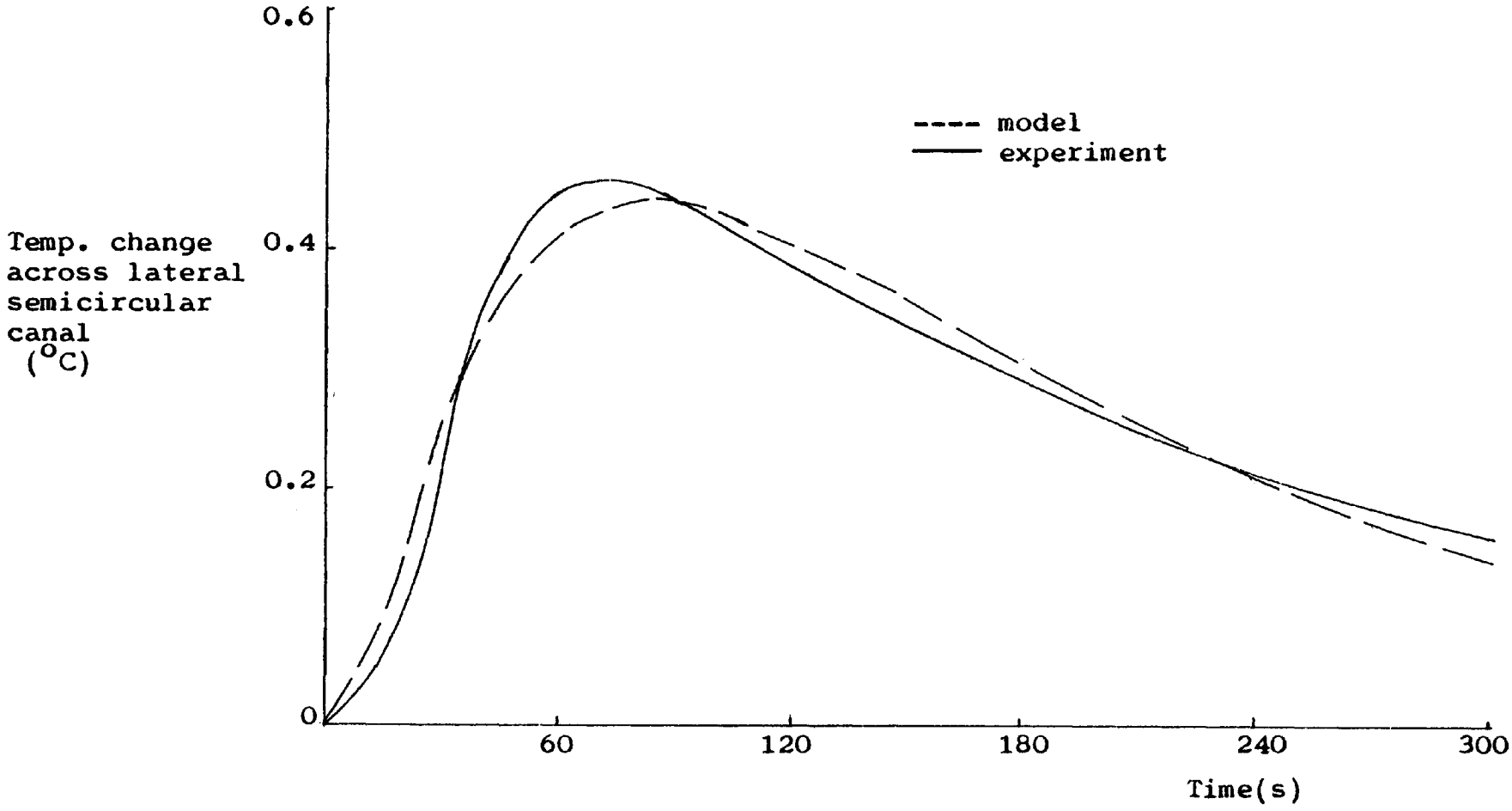


Fig. 6.12 Temperature change across the lateral semicircular canal resulting from a standard caloric irrigation - comparison of model output with experimental results in cadaveric temporal bones.

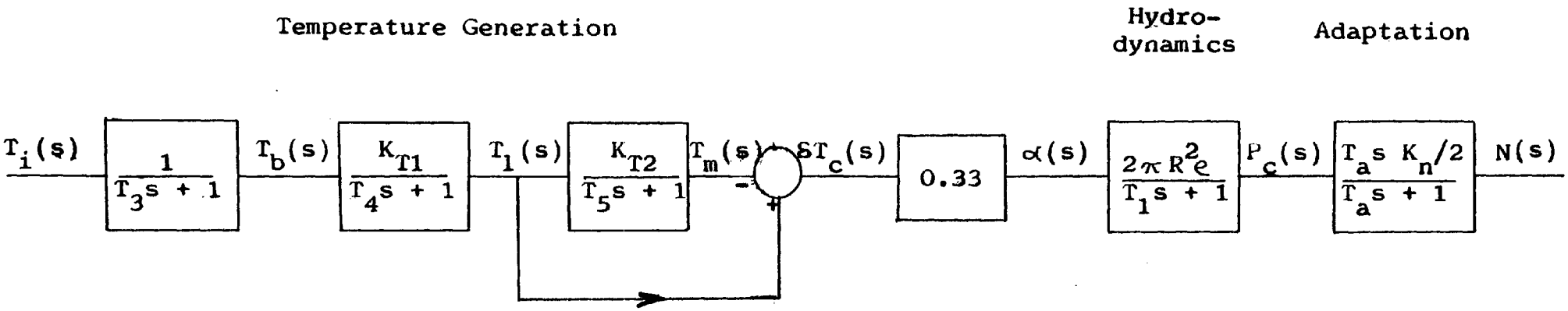


Fig. 6.13 Complete model of caloric nystagmus including temperature generation, end-organ hydrodynamics and adaptation. The cupula pressure difference - to - nystagmus gain (K_n) is shown divided by 2 to represent the gain of one canal.

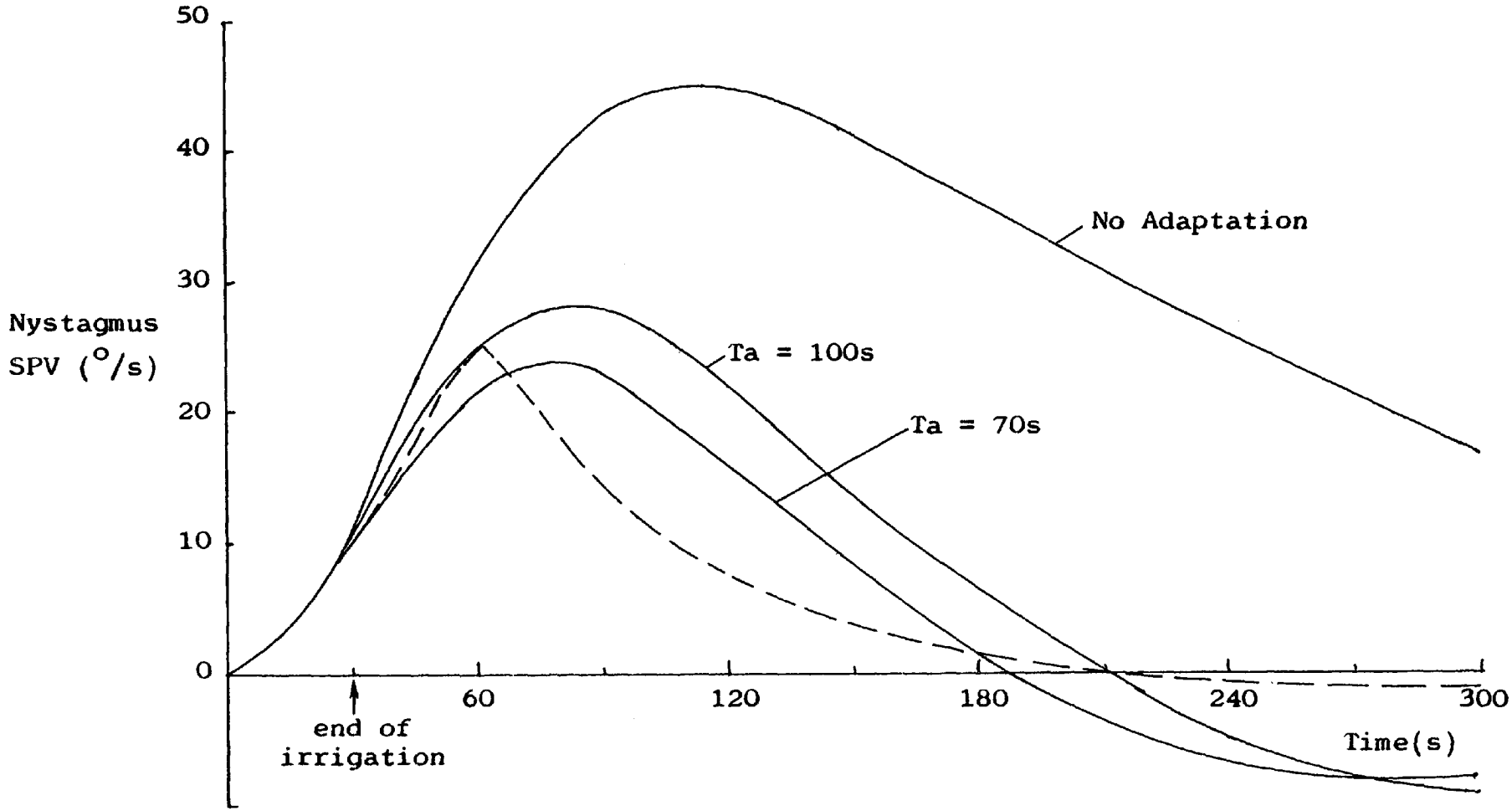


Fig. 6.14 Output of complete model for caloric irrigation of 30 seconds with water at + 7°C re. skull temperature. Experimental results (----) are those from warm water irrigation of eight normal male subjects [Barnes and Benson (1978)].

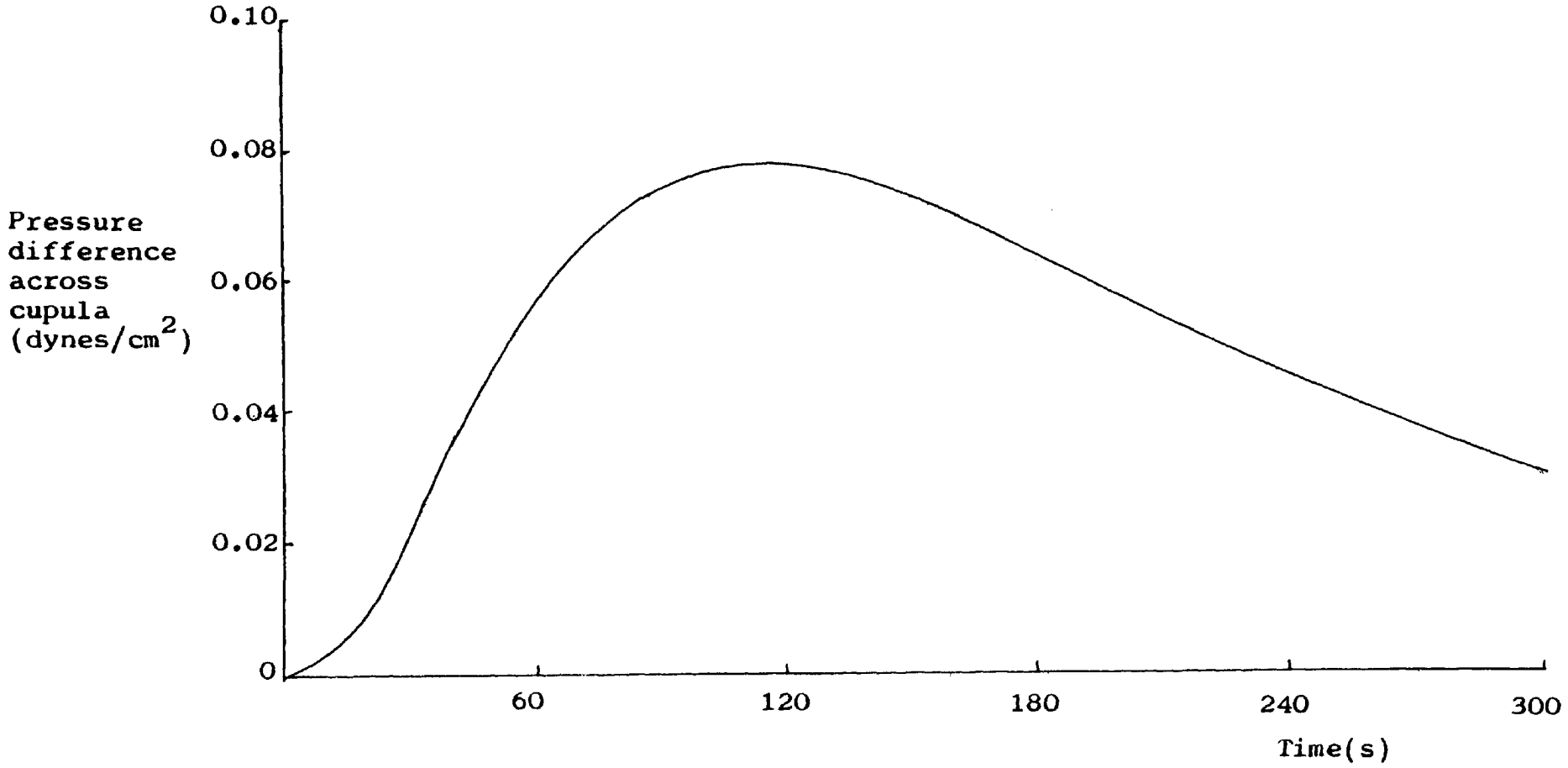


Fig. 6.15 Modelled pressure difference across the cupula resulting from a 30 second caloric irrigation of water at + 7^{o}C re. skull temperature.

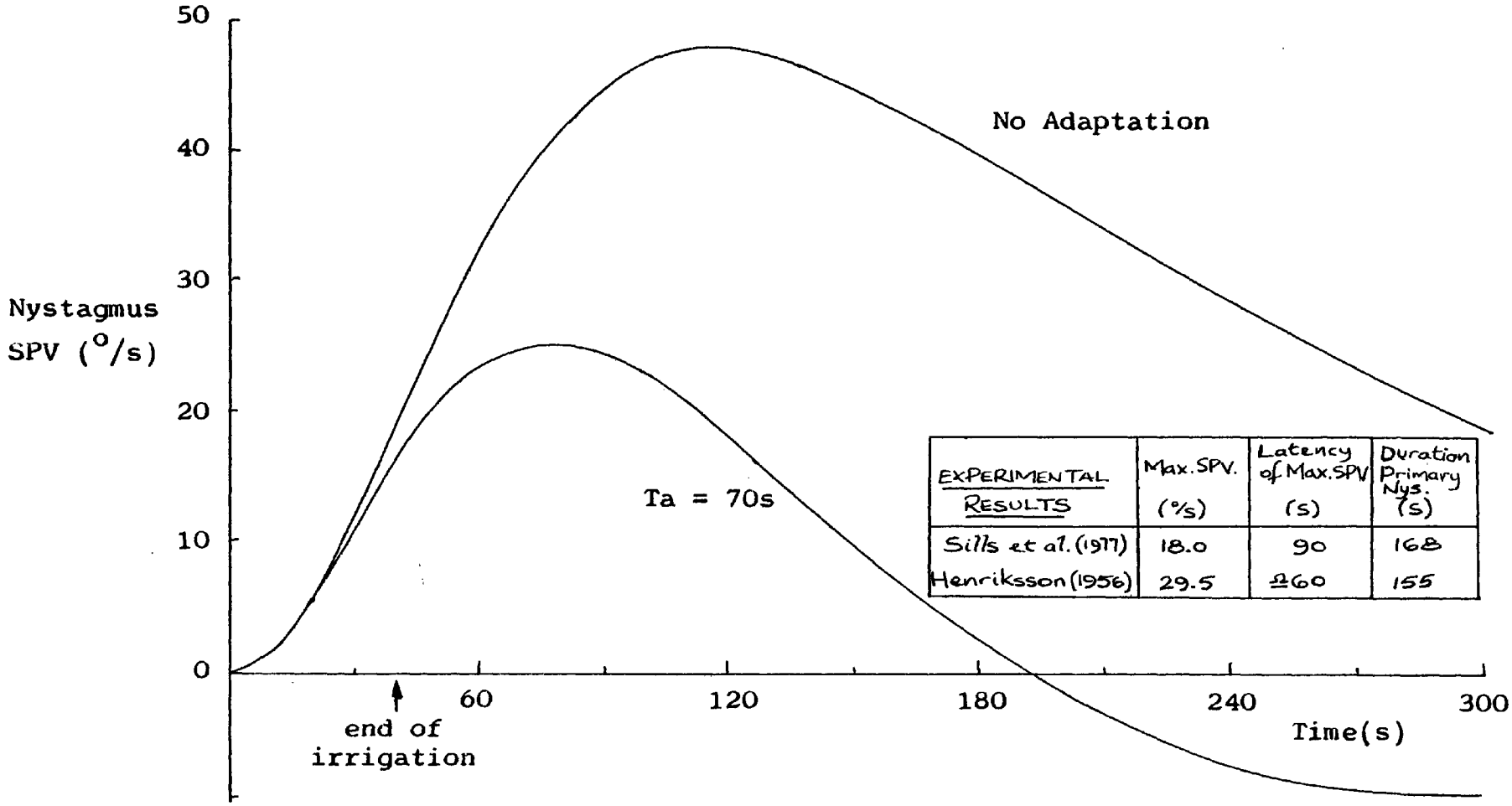


Fig. 6.16 Output of complete model for caloric irrigation of 40 seconds with water at + 7°C re. skull temperature.

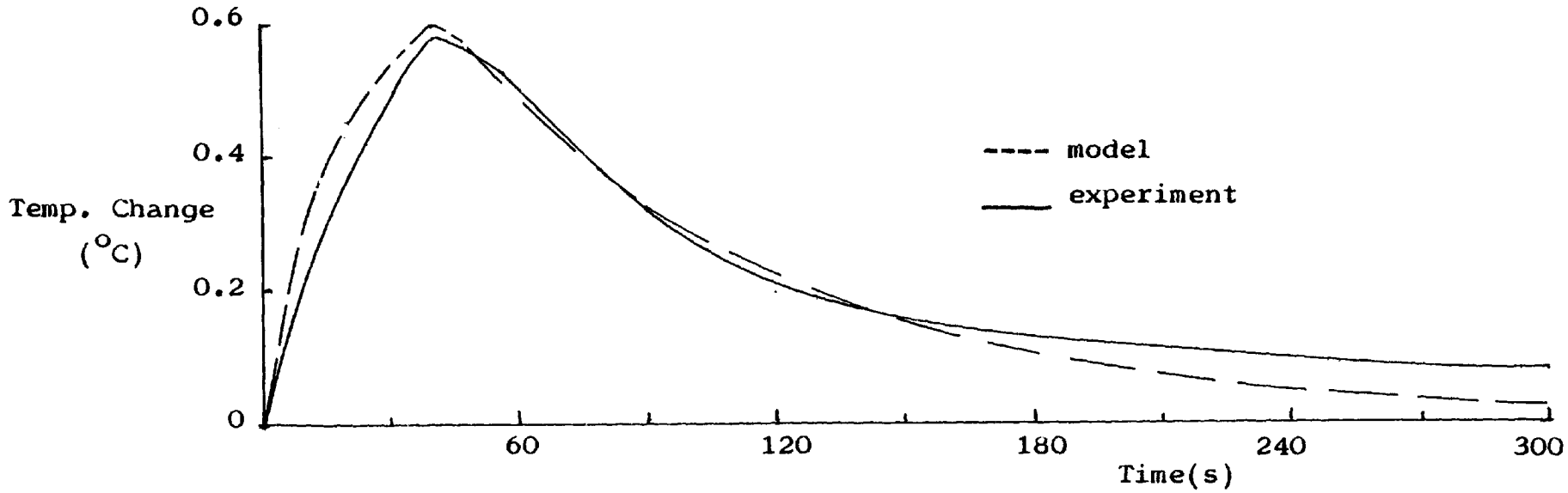


Fig. 6.17 Modelled temperature change across the lateral semicircular canal from caloric irrigation, based on results obtained in the living human by Cawthorne and Cobb (1954).

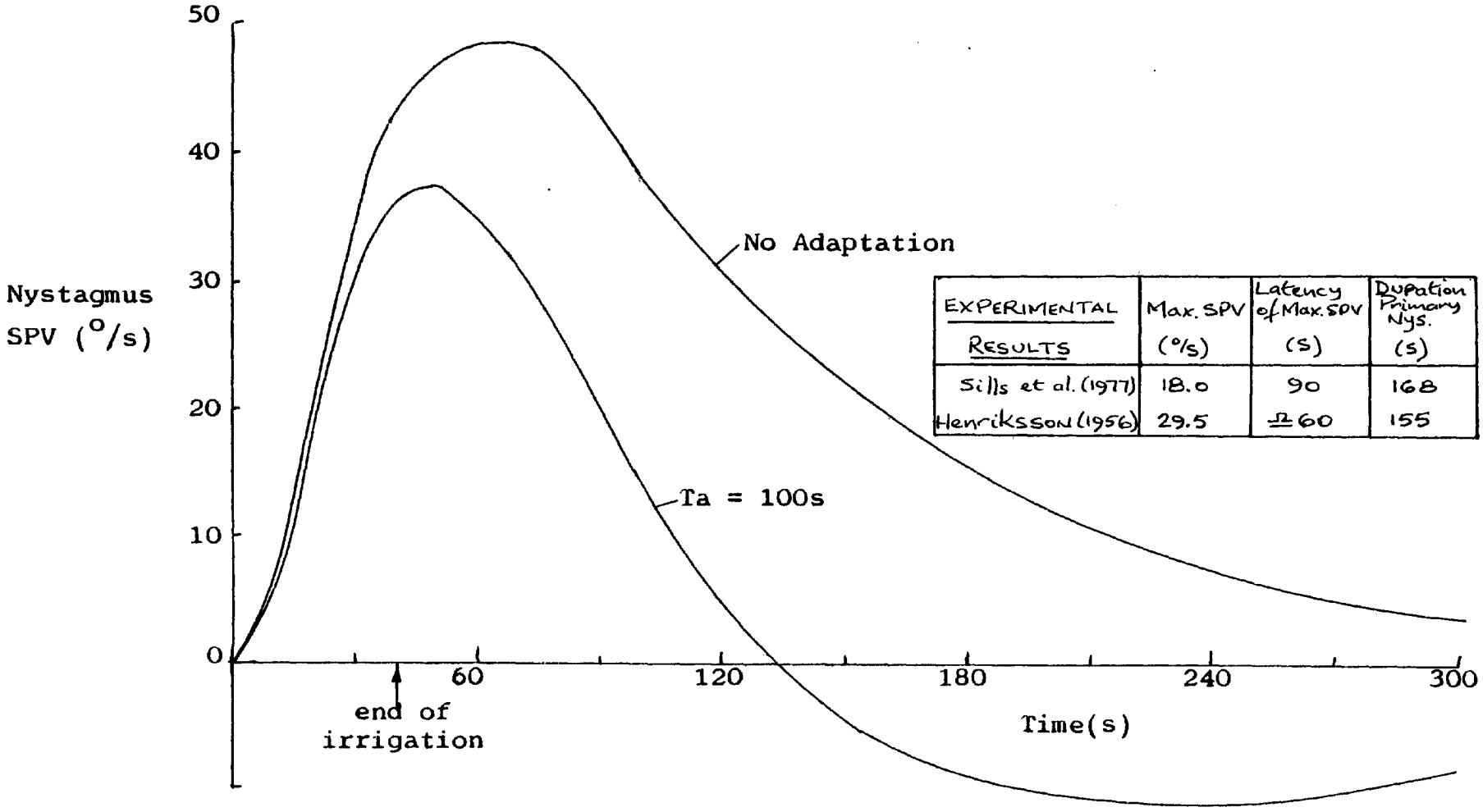


Fig. 6.18 Output of complete model of caloric nystagmus using temperature profile of Cawthorne and Cobb (1954).

CHAPTER 7

CONCLUSIONS AND SUGGESTIONS FOR FURTHER WORK

It has been shown that the large normal range for percentage canal paresis and percentage directional preponderance is, in the main, attributable to the numerous random and systematic errors which are present in caloric testing rather than to vestibular imbalance in the normal population. Some important considerations in this respect are fluctuations of the temperature of the irrigating fluid, effectiveness of irrigation, changes in corneo-retinal potential, alertness of the subject, anatomical asymmetry, position of the eyes and marking errors.

Regarding systematic errors, it has been shown that under the testing conditions as described in this thesis, there exists a sequential response decline in the four caloric responses. The effect of this is a bias in the overall caloric pattern in that, on average, the second ear to be irrigated will show an 'apparent' canal paresis of 4%. Using this value in re-classifying caloric results, it was found that 11% of patients originally classified as outside normal limits were subsequently found to be false positive. Because of the several factors which are likely to be involved, it was not possible to provide a precise explanation for the observed

response decline. As a progression of the work, it would seem useful to determine what effect different mental tasks have on this decline. A more difficult task than that used in this study may, through the influence of arousal, maintain caloric responses so that the bias is either reduced or removed completely.

It is suggested that strict adherence to a set irrigation sequence, taking into account the bias value for that sequence is a procedure which should be adopted for routine caloric testing in the clinical situation. A 'random' sequence, beginning in either ear (usually the 'worst'), which is a method presently adopted at some centres, should clearly be avoided.

The results of this study also showed that, on average, the cold caloric stimulus produced a greater nystagmus activity in terms of maximum slow phase velocity and a shorter latency of this maximum than did the warm stimulus. The fact that the cold stimulus, relative to skull temperature, was greater than the warm may account for much of the difference in nystagmus intensities. The difference in latencies, however, is not so easily explained. Apart from the possible influence of blood perfusion upon the time-course of the stimulus at the end-organ and hence the latency of response, the influence of adaptation cannot be overlooked. In the mathematical model of caloric nystagmus presented in this thesis, it was shown that a change in the adaptation time constant results in a change in the latency of nystagmus response.

Since there is evidence which suggests that the degree of adaptation is dependent upon stimulus strength, then this effect may to a large degree explain the difference in latencies between the two responses. More work upon the effect which stimulus strength has upon the degree of adaptation in both rotational and caloric tests is clearly warranted.

Regarding temperature generation in the cadaveric temporal bone from a standard caloric irrigation, it was found that, on average, the maximum temperature change produced across the lateral semicircular canal was 0.47^{o}C with a standard deviation of 0.23^{o}C. The latency of this maximum, measured from the beginning of irrigation, was 74 seconds with a standard deviation of 15 seconds.

The profile of the temperature change for the middle ear air was very similar to that for the mid-position of the bony-bar. The average maximum temperature change at these locations was approximately 1.5^{o}C with a latency of 75 seconds. Temperature changes for the lateral and medial limbs of the lateral semicircular canal occurred more slowly with average maximum changes of 0.8^{o}C and 0.6^{o}C respectively. The relatively small temperature changes which are generated in the inner ear can be explained by i) the poor thermal conduction characteristics of the temporal bone ii) the transient nature of the stimulus and iii) three-dimensional diffusion of heat energy.

The fact that caloric primary nystagmus was found to be modelled reasonably well using temperature profiles

from cadaveric temporal bones, indicates a degree of similarity of these profiles to those which occur in-vivo. Additionally, the findings by Hood (1973) that the caloric stimulus at the end-organ can persist for over ten minutes, indicates the weak effect of blood perfusion and lends support to this view.

Regarding heat transfer pathways, it has been shown that, contrary to popular belief, the bony ridge which extends from the posterior-inferior wall of the external meatus across the middle ear cleft to the inner ear is not solely the main route of heat transfer. Complete removal of this structure still resulted in a substantial temperature difference being generated across the lateral semicircular canal, presumably by heat transfer through the only obvious route available - the air of the middle ear cleft. Furthermore, significant temperature changes of the order of 1.5^{o}C were found to occur in the cleft, indicating significant heat transfer by natural convection between the outer and middle ear. Since the lateral semicircular canal forms a prominence on the medial wall of the middle ear cleft, then it may be postulated that significant heat transfer takes place by natural convection at this boundary also. In support of this, study of horizontal serial sections of the temporal bone shows the bony-bar to be a very indirect route between the outer and inner ear. The bar is encountered at a level well below that of the lateral limb of the lateral semicircular canal and is, in the majority of bones, made up of numerous air cells. It is conceivable, however, that in

sclerotic temporal bones, this bar being more dense, would constitute a better conductor of heat. It would be interesting to study temperature changes across the lateral semicircular canal in conjunction with information gained from radiology of the temporal bone such as the size of the middle ear cleft and the degree of pneumatisation of the mastoid and perilabyrinthine areas. This may have significance subsequently in the clinical situation where caloric responses may be evaluated in the light of available radiological information.

In the mathematical model of caloric nystagmus it was found that the use of temperature profiles based upon results in the cadaveric temporal bone, together with an adaptive term with a time constant of 70 seconds gave prediction of the intensity of nystagmus maximum slow phase velocity to within 4% for the case of a 30 seconds irrigation. Although the model over-estimated the latency of this maximum by approximately 25%, this error can be attributed to the error in the prediction of the latency of the peak temperature change produced across the lateral semicircular canal. This in turn was due to the combination of modelling errors for the temperature changes at the lateral and medial limbs respectively. Comparison of the model output with available experimental data for a 40 seconds irrigation gave results for nystagmus maximum intensity and it's latency well within the normal range. The use of the adaptation term, although providing a better prediction of primary nystagmus than

was the case when it was excluded, resulted in over-estimation of the intensity of secondary phase nystagmus. By comparing the model output with available experimental results for rotational tests involving step acceleration inputs, it was seen that larger stimulus inputs required shortening of the adaptation time constant in order to achieve a better comparison. It was thus concluded that the present linear term used for adaptation is an over-simplification and that the true mechanism is probably non-linear. As indicated previously, further investigation of the relationship between stimulus strength and the degree of adaptation is required for better modelling of caloric nystagmus. It is interesting to note, however, that the use of an adaptation time constant of 70 seconds for caloric nystagmus is comparable to that used for modelling response to rotational stimulation. This seems to indicate a degree of similarity between the mechanism of adaptation in both types of stimulation.

Other possible factors which may influence caloric nystagmus were considered to be i) direct thermal stimulation of the vestibular neuroepithilium producing a modulation of neural activity ii) the presence of a non-adapting population of neural units. Although these considerations would result in a better model output for long-term caloric stimulation by providing sustained nystagmus, the errors introduced by their use for short-term stimulation, together with the present lack of detailed information, excluded their inclusion into the model. Hopefully, further Spacelab experiments in a

microgravity environment will provide information upon the basic mechanisms involved in caloric stimulation of the vestibular labyrinth, perhaps resulting in modification of the present theory.

It is hoped that however small the contribution of this thesis to vestibular research may be, that the work undertaken has provided a further insight into the many complexities which are associated with the vestibular system.

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APPENDIX

INSTRUMENTATION USED FOR TEMPERATURE MEASUREMENT IN THE TEMPORAL BONES - SPECIFICATIONS AND CALIBRATION

1. Thermocouples

manufacturer:	Universal Thermosensors Ltd., Sittingbourne, Kent.
material:	Chromel/Constantan conductors with mineral insulated Inconel sheath.
diameter:	0.5 mm.
length:	200 mm.
hot junctions:	several exposed junctions and several insulated.
time constant (T):	for thermocouples in water moving at a velocity of 5ft/s. T = 0.25s (insulated) T ≏ 0.025s (exposed)
sensitivity:	59 $\mu v/^{o}C$

2. Amplifiers

manufacturer:	Bell and Howell Ltd, Basingstoke, Hampshire.
type:	1 - 190 high gain d.c. differential amplifier.
gain:	switched 40, 100, 200, 400, 1000, 2000.
accuracy:	± 1% maximum.

linearity:	<0.1% deviation from best straight line.
stability:	better than 0.02%/^{o}C, better than 0.1% long term.
input impedance:	>2MΩ
output voltage:	± 8 volts maximum.
common mode rejection:	>100 dB.
Bandwidth:	d.c. to 50 Hz (-3 dB) 1000 gain.

3. Recorder

manufacturer:	Bell and Howell Ltd., Basingstoke, Hampshire.
type:	U-V recording oscillograph.
number of channels:	12.
chart width:	16 cms.
chart speed:	0.2 cm/s -160 cm/s in 12 steps.
galvanometers:	type 7-349 magnetically damped, 10 Hz undamped natural frequency; system sensitivity- 3.27 cm/mv.

4. Water Bath

manufacturer:	Grant Instruments Ltd., Barrington, Cambridge.
type:	temperature controlled water bath with pump and delivery nozzle.

capacity:	approx. 9 litres.
temperature stability:	$\pm$ 0.2°C.

5. Standard Thermometer

manufacturer:	Comark Electronics Ltd., Rustington, Sussex.
type:	1604 analogue electronic thermometer.
range:	-60°C to +170°C in 23 steps of 10.
resolution:	0.1°C.
material:	Ni-Cr/Ni-Al.

System Linearity, Calibration and Stability

a) Linearity: The linearity of the thermocouple-recorder system was investigated by measuring the recorder beam deflection for different step changes of temperature at the hot junctions of the thermocouples. In practice, this was achieved by the use of two stirred water baths at predetermined temperatures, the thermocouples being moved quickly from one bath to the other and the resulting beam deflection measured. The thin probe of the electronic thermometer was attached to the bundle of the hot junctions in order to provide a standard of measurement for the temperature change occurring at the thermocouple junctions. The results, which are presented in Figs. A1 and A2, show

the system to be highly linear.

b) Calibration: The results from the previous investigation of linearity also enabled calculation of the system sensitivity. Additional tests performed 18 months later also enabled the evaluation of long-term changes in system sensitivity. For a particular temperature change at a given amplifier setting, the sensitivity of each channel was calculated by dividing the resulting beam deflection by the temperature change as measured by the standard thermometer. The results are shown in Table A1. Averaged for all the thermocouples, the maximum percentage change in sensitivity is 10% with a SD of 4%.

c) Stability: System stability was investigated by measuring the output drift when both hot and cold junctions of the thermocouples were placed in a vacuum flask containing insulating material at room temperature. All amplifiers were set on maximum gain (x 2000). Table A2 shows the values of drift for each channel in terms of percentage full-scale-deflection over a five minute period. No data is included for channel 8 which was inadvertently excluded from the tests. However, since this channel was used with a much lower gain (x 100) than the rest (x 400 and x 1000), then its drift during temperature measurement was considered negligible. Maximum drift for the averaged values of Table A2 is 1.5%FSD/5 mins.

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	Channel Number					
	1	3	4	6		8
Amp. Gain	x400	x1000	x400	x1000		x100
Date					Date	
14.4.81	3.90	12.31	4.27	11.23		
15.10.82	4.22	-	4.31	11.56	19.10.82	1.02
19.10.82	3.68	11.17	4.15	10.00	11.4.83	1.10
Maximum absolute change (%)	13	9	4	13	*	

*The original thermocouple for channel number 8 was damaged half way through the temperature measurement studies and was replaced. There is therefore no value for the change in sensitivity for this channel.

Table A1 System sensitivty - cm/^{o}C.

	Channel Number			
	1	3	4	6
Test 1	1.3	1.9	2.2	1.3
" 2	0.3	1.3	1.0	1.0
" 3	0.3	1.9	1.6	2.2
" 4	0.3	1.0	1.0	1.0
Mean	0.6	1.5	1.5	1.4
SD	0.5	0.5	0.6	0.6

Table A2. System stability; values for drift as percentage FSD over five minutes. Amplifiers were set on maximum gain (x 2000).

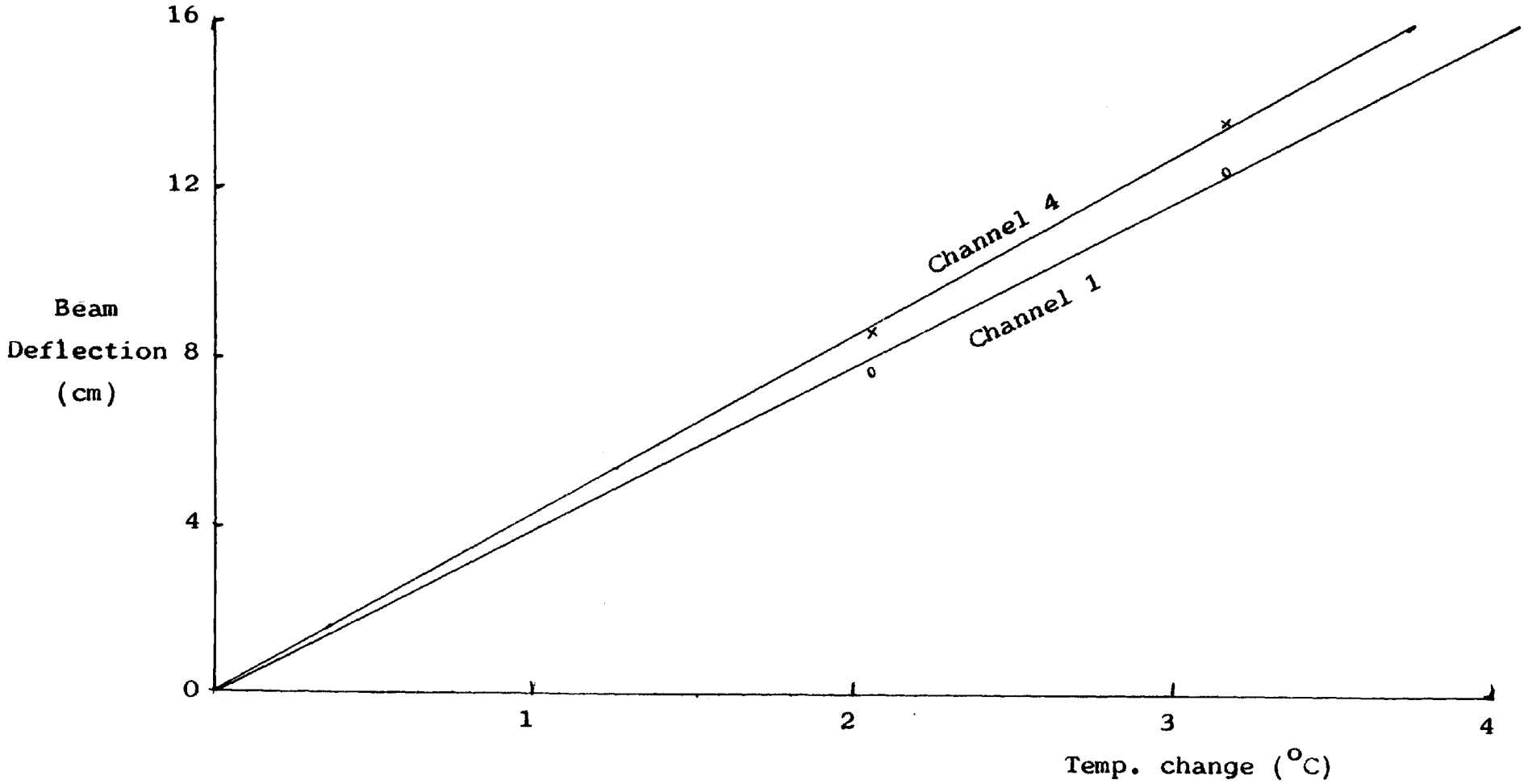

Fig. A1 Temperature measurement system linearity - results for Channels 1 and 4.

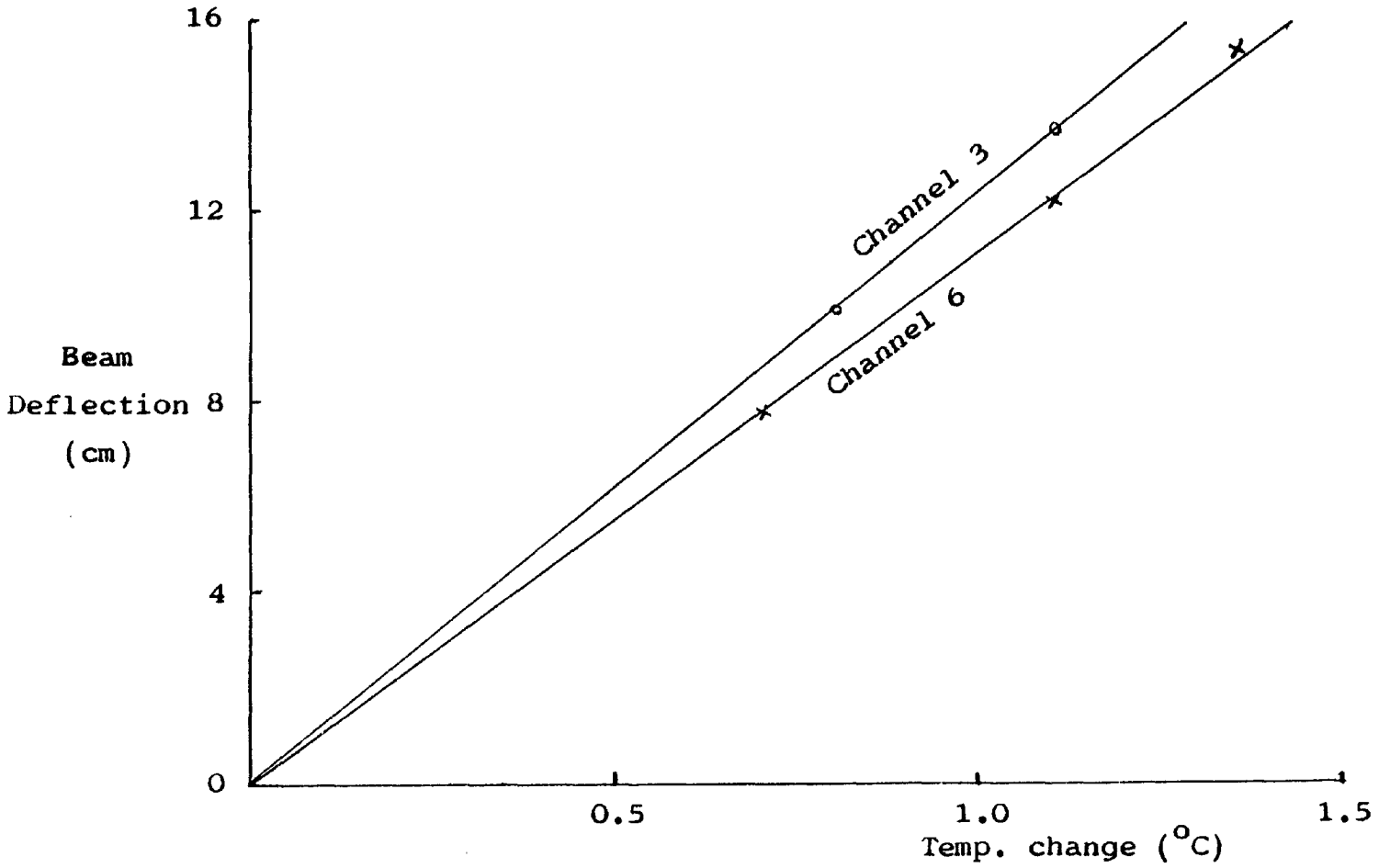

Fig. A2 Temperature measurement system linearity - results for Channels 3 and 6.