LINEAR ACCELERATION-DRIVEN NEURONS IN DEITERS' NUCLEUS: THEIR DYNAMIC RESPONSE CHARACTERISTICS AND POSSIBLE ROLE IN LOCOMOTOR CONTROL

by

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Linear acceleration-driven neurons in Deiters' nucleus

ABSTRACT

The response of single neurons to sinusoidal linear acceleration at physiologically important frequencies was studied in Deiters' nucleus of the cat.

Roughly equal numbers of units were sensitive to static (14/27) and dynamic (11/27) tilt (2/27 tilt unknown), with most of these units excited by ipsilateral side down tilt. Axons of 2/27 units (possibly 3/27) projected directly to spinal levels via the lateral vestibulospinal tract.

The orientation of functional polarization vectors (direction along which cell is most responsive) appeared to be broadly distributed. Threshold of all units was approximately 0.004 'g'. Mean bias (resting firing rate) was 24 ± 2 AP/sec, S.E. There was no significant difference in threshold or bias between units responding preferentially in the X, Y, or Z axes.

The response to dynamic stimulation was not dependent on the acceleration amplitude (studied at 0.2 Hz). With increasing stimulus frequency (range 0.1-4.0 Hz), a significant attenuation in response gain was observed ($P < 0.05$). Phase behaviour, however, remained relatively flat.

The present results indicate that at frequencies which can be experienced during locomotion, meaningful otolith signals are represented at least at the level of the vestibular nuclei. In some cases, these signals can then be transmitted directly to spinal levels. The full extent of otolith contribution to locomotor control, however, remains to be determined.

RESUME

La réponse de simples neurones situés dans le cortex de Deiter, chez le chat, exposés à des accélérations sinusoïdales dont les fréquences sont physiologiquement significatives fût étudiée.

Un nombre approximativement égal d'unités furent trouvées sensibles aux inclinaisons statiques (14/27) et dynamiques (11/27) (2/27 inclinaison inconnue), la majorité de ces unités furent stimulées par une inclinaison ipsilatérale. Les axones de 2/27 des unités (possiblement 3/27) projetèrent directement aux niveaux spinaux via la trachée vestibulospinal latérale.

L'orientation des vecteurs de polarisation fonctionnelle (direction le long de laquelle la réponse cellulaire est la plus grande) semble avoir une distribution étalée. Le seuil de sensibilité pour toutes les unités était d'environ 0.004 'g'. La polarisation moyenne (taux d'activité au repos) était de 24 ± 2 AP/sec, S.E. Le seuil et la polarisation des unités ne diffèrent pas de façon significative et ne semblent pas être affectés par leur réponse préférentielle le long des axes X, Y, ou Z.

La réponse à un stimulus dynamique fût indépendante de l'amplitude de l'accélération (étudiée à 0.2 Hz). Une atténuation significative du gain de la réponse ($P < 0.05$) fût observée lors de l'augmentation de la fréquence du stimulus (gamme 0.1-4.0 Hz). Le comportement de la phase, par contre, demeura inchangé.

Les résultats indiquent que, lors de fréquences apparentées à la locomotion, des signaux otolithiques significatifs sont présents au moins au niveau des noyeaux vestibulaires. Ces signaux, dans certains cas,

peuvent ensuite être transmis directement aux niveaux spinaux. La pleine étendue de la contribution des organes otolithiques au contrôle locomoteur, par contre, reste à déterminer.

DEDICATION

to my parents

Ned and Helen Better

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LIST OF ABBREVIATIONS

AP	- Action potentials
C1	- First cervical vertebra
C2	- Second cervical vertebra
CNS	- Central nervous system
CVST	- Caudal vestibulospinal tract
DVN	- Descending (inferior) vestibular nucleus
EMG	- Electromyogram
FPV	- Functional polarization vector
'g'	- Acceleration due to gravity
H-reflex	- Hoffmann reflex
L2	- Second lumbar vertebra
L5	- Fifth lumbar vertebra
LVN	- Lateral vestibular nucleus (Deiters' nucleus)
LVST	- Lateral vestibulospinal tract
MVN	- Medial vestibular nucleus
MVST	- Medial vestibulospinal tract
P-value	- Probability that the difference between paired values is due to chance alone
RST	- Reticulospinal tract
SVN	- Superior vestibular nucleus
T1	- First thoracic vertebra
T12	- Twelfth thoracic vertebra
V.A.F.	- Variance accounted for
VOR	- Vestibulo-ocular reflex
V-S	- Vestibulospinal

X-axis - Fore-aft axis

Y-axis - Transverse axis

Z-axis - Dorsoventral axis

I INTRODUCTION

The otolith organs are the component of the vestibular labyrinth that sense linear motion and gravity, and have been described as low threshold linear accelerometers (Young, 1974; Wilson and Melvill Jones, 1979). This makes them well suited for a role in the control and maintenance of static posture.

Far less is understood, however, of the possible otolith contribution to locomotor control. Second and higher order neurons located in the vestibular nuclei have been shown to respond to dynamic linear accelerations (Melvill Jones and Milsum, 1969; Schor, 1974; Orlovsky, 1972b). Orlovsky (1972a) has shown that the activity of some cells in Deiters' nucleus is modulated during walking of a cat on a treadmill (with head fixed), with a peak during each stance phase of stepping. This indicates a close link between these cells and locomotor activity. Otolith-spinal reflexes, generated by sudden falls or possibly by hopping, have been shown to initiate and adjust muscular responses prior to contact of the animal or man with the ground (Melvill Jones and Watt, 1971a, b; Melvill Jones et al., 1973; Watt, 1976). Other studies by Watt (in cat: 1974, 1981a, b; in human: 1977), through the use of H-reflex testing, have investigated changes in spinal cord excitability induced by vertical linear acceleration. It was found that spinal cord excitability was systematically modulated by the accelerative stimulus. Finally, during normal locomotion, the linear accelerations resulting from vertical head movements are well above threshold for the otolith organs (Jongkees and Groen, 1942; Stuart et al., 1973; Watt and Wetzel, 1977). These findings

support the notion of a significant otolith contribution to locomotor control.

However, in order to fully understand how linear accelerations lead to motor outputs in limb muscles, it is often beneficial to first have an understanding of the workings of the individual components of the system being studied. There is therefore a need to characterize the response of individual neurons lying along this pathway before the vestibular component of the response in spinal motoneurons can be rationally interpreted.

The experiment described in this thesis was one step towards that goal. The aim was to quantify the response characteristics of neurons located in Deiters' nucleus of the cat, studied during sinusoidal linear acceleration. Relating this natural input to vestibular neuronal output allows an estimate of the extent to which the acceleration signal has been modified by central processing at this point in the chain of neurons leading eventually to limb muscles.

II LITERATURE SURVEY

1. Introduction

To put the present work into its proper context, it is necessary to begin with a general review of vestibular anatomy and physiology. This survey will be limited to the otolith organs, making reference to studies of the semicircular canals only when it helps clarify matters being discussed. In keeping with the emphasis on otolith contributions to locomotor control, studies dealing with static postural control will not be reviewed. As well, otolith interactions with the visual system (i.e., the vestibulo-ocular reflex, VOR) will not be discussed, nor will the conscious perception of linear acceleration in humans.

As the role and function of the vestibular system continue to be explored by many investigators, several excellent review articles and books have been written on this topic. These include publications by Kornhuber (1974a, b); Young (1974); Naunton (1975); Wilson & Peterson (1978); Wilson (1979); Wilson & Melvill Jones (1979); Goldberg & Fernandez (1984). Much of the material for the following sections was provided by these publications.

2. Anatomy

A) Otolith Organs

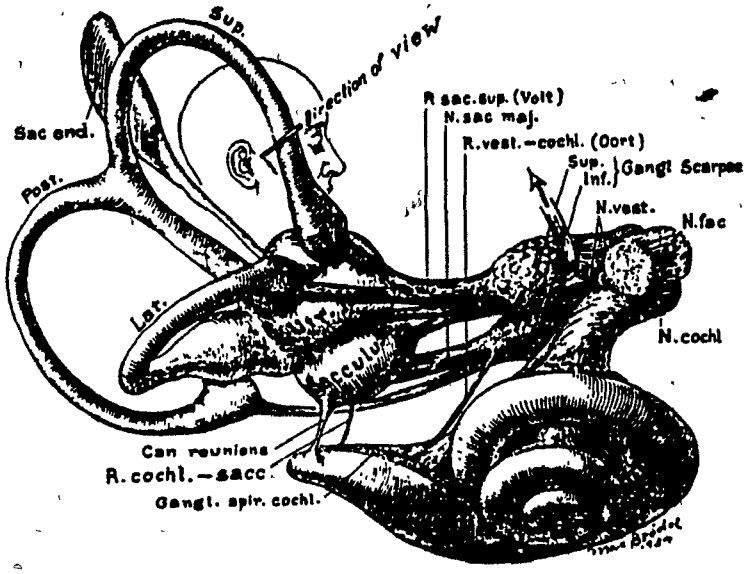
The otolith organs make up part of the nonauditory portion of each inner ear. They are located in two interconnecting endolymph-filled sacs, the utricle and saccule, that are part of the membranous labyrinth (Fig. 1a). The membranous labyrinth is bathed in perilymph and is

Figure 1

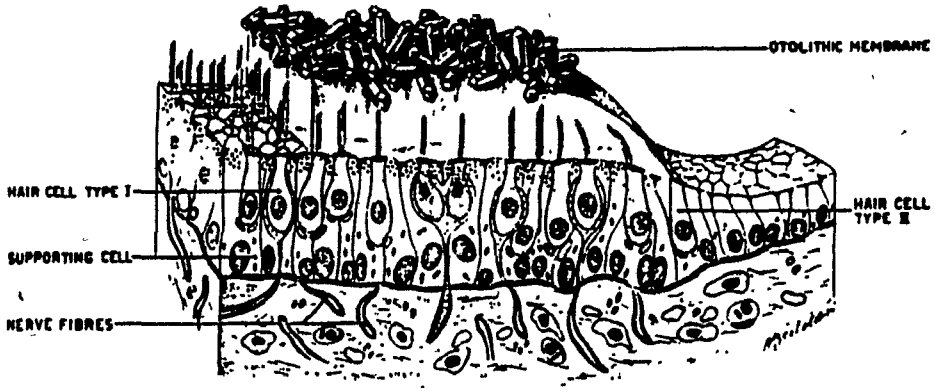
A. Anatomy of human membranous labyrinth and its innervation (from Hardy, 1934).

B. Schematic drawing of macular epithelium with the otolithic membrane (from Iurato, 1967).

A.


Sup.
Direction of view
Sac end.
Post.
Lat.
R sac.sup. (Volt)
N.sac maj.
R.vest.–cochl. (Oort)
Sup.
Inf.
Gangl Scarpae
N.vest.
N.fac
N.cochl
Can reuniens
R. cochl.–sacc.
Gangl. spir. cochl.

B.


OTOLITHIC MEMBRANE
HAIR CELL TYPE I
SUPPORTING CELL
NERVE FIBRES
HAIR CELL TYPE II

contained within the bony labyrinth (Young, 1974; Goldberg and Fernandez, 1984).

A specialized sensory region within each saccule and utricle is known as the macula. The utricular macula lies on the floor of the utricle, in approximately the same plane as that of the horizontal semicircular canals (Lowenstein, 1974; Wilson and Melvill Jones, 1979; Goldberg and Fernandez, 1984). The saccular macula lies in an approximately orthogonal plane to the utricular macula on the medial wall of the saccule. The sensory epithelium of each macula consists of sensory hair cells and supporting cells. The otolithic membrane, which is a thin fibrous structure, overlies each macula (Wilson and Melvill Jones, 1979; Goldberg and Fernandez, 1984). Sensory hairs (cilia) from the hair cells project into the lower surface of the membrane. Embedded in the upper surface of the membrane are the otoconia, which consists of crystals of calcium carbonate (Fig. 1b). These crystals form the otoliths.

Two types of cilia are found in the hair bundles which are located on the surface of the sensory hair cells, the stereocilia and a single kinocilium. The kinocilium has a basal body and tubular structure similar to motile cilia in other cells (Spoendlin, 1966; Lowenstein, 1974). The stereocilia have a much simpler structure consisting of a central filament surrounded by cytoplasm and a typical cellular membrane. The stereocilia are arranged in rows of increasing length, terminating with the kinocilium. The kinocilium is always located on one side of the hair bundle (Young, 1974; Wilson and Melvill Jones, 1979). Bending of the hair bundles towards the kinocilium is associated with a depolarization (excitation) of the cell, while bending away from the kinocilium is associated with

hyperpolarization (inhibition or suppression) of the cell (Fig. 2a). The eccentric location of the kinocilium and the staircase arrangement of the stereocilia define a morphological polarization of each hair cell (Spoendlin, 1966; Wilson and Melvill Jones, 1979). Figure 2b diagrammatically shows the orientation and distribution of this polarization in the utricular and saccular maculae. The striola is a slightly curved band going through the middle of the maculae, where the sensory cells are especially large (Spoendlin, 1966). The striola also marks the dividing line of sensory hair polarization in the maculae. In the utricular macula, the polarization vectors point toward the striola, while in the saccular macula the polarization vectors point away from the striola (Spoendlin, 1966; Wilson and Melvill Jones, 1979; Goldberg and Fernandez, 1984).

The orientation within the skull and the distribution of polarization vectors within the maculae should enable both of the otolith organs together to detect inertial acceleration or gravity in any direction in 3-dimensional space (Wilson and Melvill Jones, 1979).

B. Innervation of the Otoliths

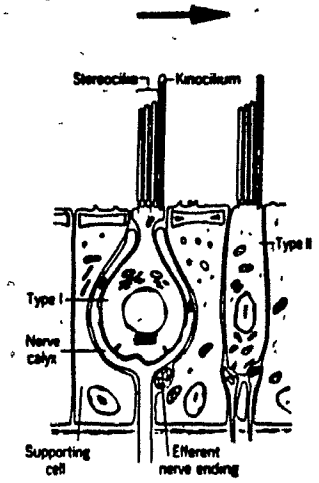
Two kinds of sensory hair cells can be found within the vestibular sensory epithelium (Spoendlin, 1966; Wilson and Melvill Jones, 1979; Engström and Engström, 1981; Goldberg and Fernandez, 1984). Type I cells are typically flask-shaped and surrounded by an afferent terminal in the form of a nerve chalice. Type II cells are cylindrical in shape and receive bud-shaped afferent terminals at their basal ends (Fig. 2a). Type I hair cells are more numerous within the macular striola, though both

Figure 2

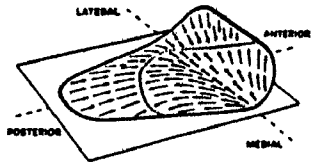
A. Ultrastructural organization of type I and type II hair cells and their innervation, with typical arrangement of stereocilia and kinocilium. Bending the cilia in the direction of the arrow is excitatory (adapted from Brodal, 1969).

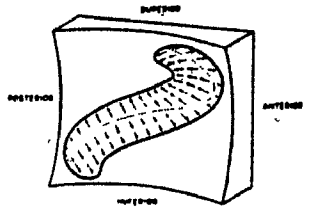
B. Schematic representation of hair cell polarization vectors in the utricular macula (top), and saccular macula (bottom). For adjacent hair cells, each vector points to the side of the cell where the kinocilium is located. Note that in the utricular macula the polarization vectors face each other, while in the saccular macula the polarization vectors face away from each other. The dotted line on each macula where the polarization reverses corresponds with the striola (from Spoendlin, 1966).

A.


Stereocilia
Kinocilium
Type II
Type I
Nerve calyx
Supporting cell
Efferent nerve ending

B.


LATERAL
ANTERIOR
POSTERIOR
MEDIAL



types are found in relatively equal proportion within the rest of the macula (Goldberg and Fernandez, 1984).

The afferent innervation of the labyrinth comprises bipolar neurons which make up most of the vestibular branch of the eighth cranial nerve. These fibers are distributed in roughly equal proportions to the three canals, with somewhat larger and smaller proportions distributed to the utricular and saccular maculae, respectively (Gacek, 1975). Centrally, the fibers terminate in the vestibular nuclei and the vestibulocerebellum.

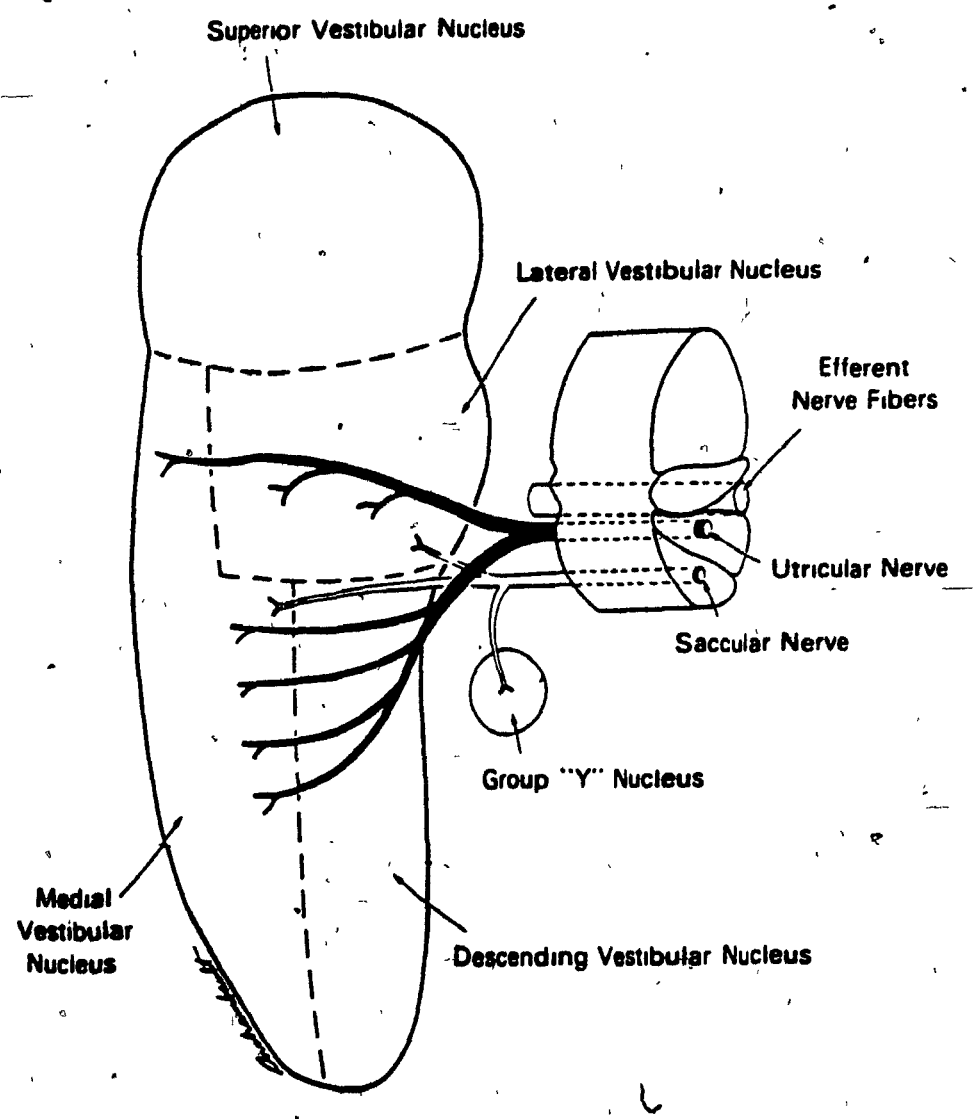
A small branch of the vestibular nerve consists of efferent fibers whose cell bodies are located near the central vestibular nuclei. Efferent fibers branch extensively and terminate on both the nerve chalice of Type I hair cells and the cell body of Type II hair cells in all vestibular end organs (Gacek, 1975; Goldberg and Fernandez, 1984).

C. Labyrinthine Input to the Vestibular Nuclei

The central vestibular nuclear complex consists of four principal vestibular nuclei as well as some smaller groups of cells, and is located in the pontomedullary region of the brainstem (Wilson and Melvill Jones, 1979; Gacek, 1981). The four principal vestibular nuclei are: the superior (SVN), lateral (LVN) or Deiters', descending (DVN) or inferior, and medial (MVN) vestibular nuclei. Macular afferents project to the LVN, DVN, and the MVN, with the LVN and then the DVN receiving the largest portion of these fibers (Fig. 3), (Gacek, 1969; Goldberg and Fernandez, 1984). Canal afferents project primarily to the MVN, as well as to the SVN, DVN, and LVN. Primary afferents terminate largely rostroventrally in the LVN, rostrolaterally in the MVN, rostrally in the DVN, and centrally in the SVN.

Figure 3

Utricular and saccular afferents' termination in the vestibular nuclei. Note that afferent termination in the DVN is not shown (from Gacek, 1975).


Superior Vestibular Nucleus
Lateral Vestibular Nucleus
Efferent
Nerve Fibers
Utricular Nerve
Saccular Nerve
Group "Y" Nucleus
Medial
Vestibular
Nucleus
Descending Vestibular Nucleus

The small groups of cells include the interstitial nucleus and the cell groups f, l, x, y, and z (Brodal, 1974). Of the small groups of cells only the y group and the interstitial nucleus receive direct vestibular nerve inputs (Gacek, 1969, 1981; Brodal, 1974; Goldberg and Fernandez, 1984), with the y group receiving input primarily from the saccular macula while input to the interstitial nucleus derives from the canals and possibly the otoliths as well (Gacek, 1975, 1981). Cells responding polysynaptically to vestibular stimulation are found throughout the central vestibular nuclei.

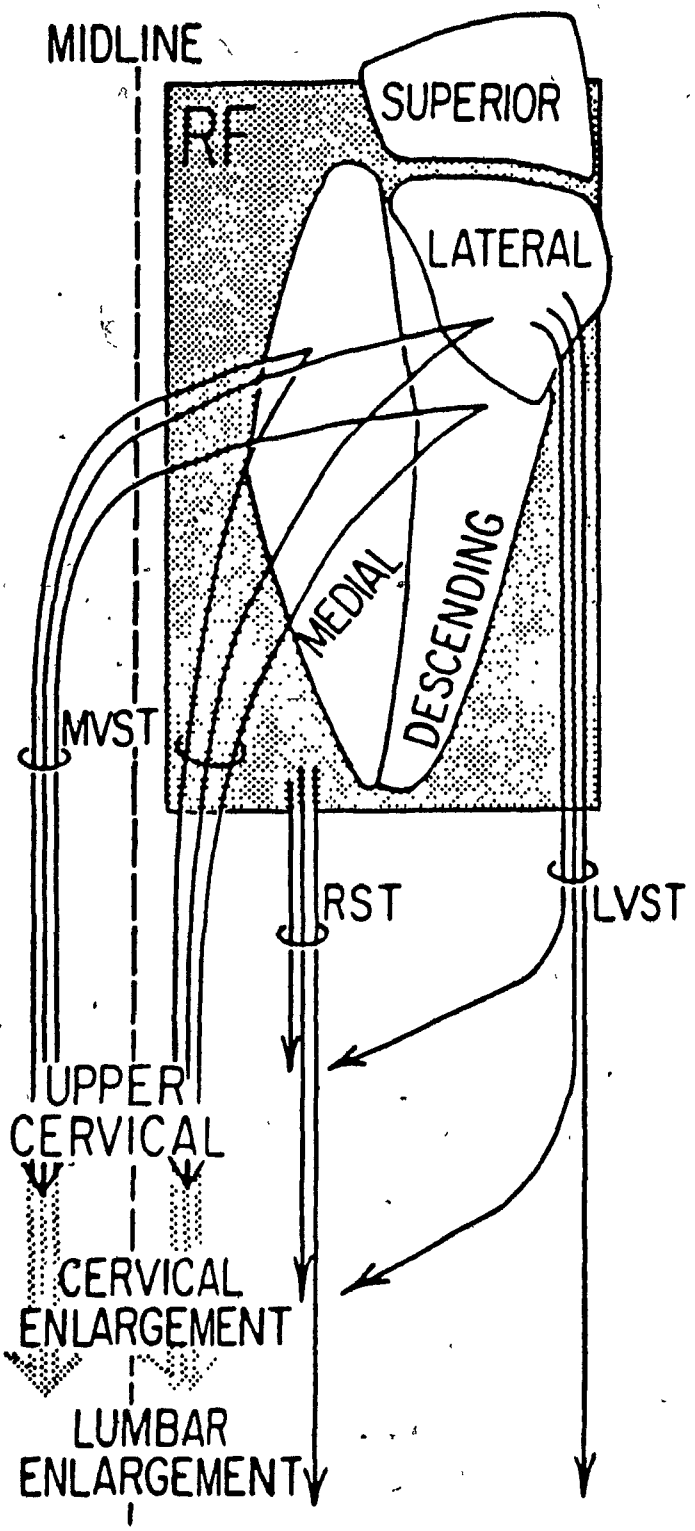
D. Spinal Projections of the Vestibular Nuclei

Signals from the vestibular nuclei can be relayed to various levels of the spinal cord via a number of pathways. The two major direct pathways are the lateral vestibulospinal tract (LVST), and the medial vestibulospinal tract (MVST), (Brodal, 1974; Wilson, 1979). A third is the caudal vestibulospinal tract (CVST), while a less direct pathway is the reticulospinal tract (RST), (Wilson and Melvill Jones, 1979).

The LVST originates largely in Deiters' nucleus (Fig. 4), with a minor contribution from the DVN (Wilson and Melvill Jones, 1979; Goldberg and Fernandez, 1984). It projects primarily ipsilaterally to all levels of the spinal cord, and single axons may branch to widely separate spinal levels (Wilson and Peterson, 1978; Wilson and Melvill Jones, 1979). Studies have shown that Deiters' nucleus is organized somatotopically (Wilson et al., 1967; Peterson, 1970): cells projecting to the lumbosacral cord are generally located in the dorsocaudal region of the nucleus, while cells projecting to the cervical cord are generally located in the rostroventral region of the nucleus.

Figure 4

Origin of LVST and MVST in the vestibular nuclei and their projections to different levels of the spinal cord. DVN input to LVST not shown, nor is the lateral RST and CVST (from Wilson and Melvill Jones, 1979).


MIDLINE
RF
SUPERIOR
LATERAL
MEDIAL
DESCENDING
MVST
RST
LVST
UPPER
CERVICAL
CERVICAL
ENLARGEMENT
LUMBAR
ENLARGEMENT

The MVST originates largely in the MVN and in the DVN, with some axonal input from Deiters' as well (see Fig. 4), (Wilson and Peterson, 1978; Wilson and Melvill Jones, 1979; Goldberg and Fernandez, 1984). It projects both ipsilaterally and contralaterally down the spinal cord, and terminates largely in the cervical spinal cord.

The CVST originates in the caudal regions of the MVN, DVN, and in the f group, and projects as far as the lumbar cord (Peterson and Coulter, 1977; Wilson and Melvill Jones, 1979). Little is known, however, of its functional properties.

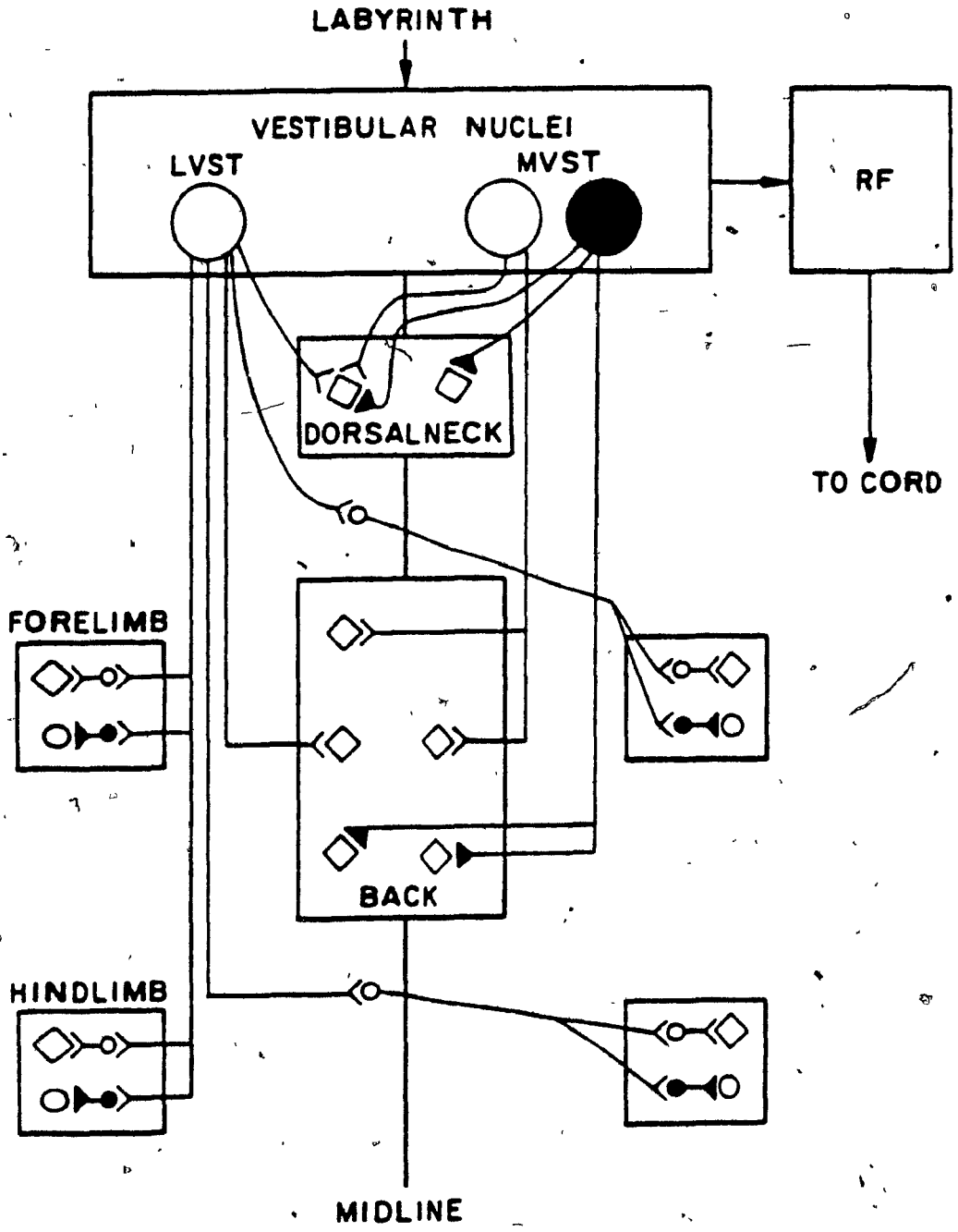
The RST originates in the pontomedullary reticular nuclei, which receive input from the vestibular nuclei (Wilson, 1979; Wilson and Melvill Jones, 1979). There are two tracts, one medial and the other lateral, and they project bilaterally to all levels of the spinal cord. As with the LVST, single axons of RST fibers may branch to widely separate spinal levels (Wilson and Peterson, 1978; Wilson and Melvill Jones, 1979).

E. Spinal Connections of the Descending Tracts

Axons of the LVST and MVST terminate primarily in the medial part of the ventral horn of the spinal cord (Goldberg and Fernandez, 1984). While there is no anatomical evidence of direct synaptic linkage of these axons with motoneuron cell bodies, physiological studies have demonstrated mono as well as polysynaptic connections. Activation of the LVST results in excitation of extensor motoneurons and inhibition of flexors in limb and some neck and back muscles (Wilson, 1979; Wilson and Melvill Jones, 1979; Goldberg and Fernandez, 1984). Activation of MVST fibers results in both excitation and inhibition of extensor motoneurons in the neck and back (Fig. 5). It appears that the LVST is the most direct pathway to limb

Figure 5

Connections between the vestibulospinal tracts (LVST and MVST) and motoneurons at different spinal cord levels. RF denotes reticular formation. ◊ , extensor motoneurons; ○ , flexor motoneurons; ○ , ● , interneurons. Filled symbols signify inhibitory neurons (from Wilson and Melvill Jones, 1979).


LABYRINTH
VESTIBULAR NUCLEI
LVST
MVST
RF
DORSALNECK
TO CORD
FORELIMB
BACK
HINDLIMB
MIDLINE

motoneurons, while the MVST is the predominant pathway to axial motoneurons (Wilson and Peterson, 1978).

RST fibers terminate in the ventral horn as well as the basal aspect of the dorsal horn of the spinal cord (Wilson and Melvill Jones, 1979). There are extensive mono and polysynaptic connections between these axons and motoneuron cell bodies. Activation of the RST results in widespread excitation and inhibition of flexor and extensor muscles (Wilson, 1979; Wilson and Melvill Jones, 1979).

F. Cerebellar-Vestibular Connections

A very close inter-relationship exists between the vestibular system and the cerebellum. Both primary afferents and fibers from the vestibular nuclei project to and terminate in the vestibulocerebellum (flocculus, nodulus, uvula, and ventral paraflocculus), as well as the vermis and anterior lobe (Wilson and Peterson, 1978; Wilson and Melvill Jones, 1979; Goldberg and Fernandez, 1984). Fibers from the vestibulocerebellum project to the vestibular nuclei, though Deiters' is poorly supplied (Angaut and Brodal, 1967; Walberg, 1975). Deiters' receives most of its cerebellar input from the anterior lobe, with some slight input from the posterior lobe (Brodal, 1974).

G. Vestibulo-Vestibular Connections

An extensive system of commissural fibers link the vestibular nuclei of the two sides. Commissural neurons run between the SVN, DVN, and y group (Brodal, 1974; Gacek, 1981). A moderate number of commissural fibers originate in the MVN, projecting to the contralateral MVN, SVN, and sparsely to Deiters'. Fibers from DVN also project sparsely to the

contralateral Deiters' nucleus (Ito et al., 1985). Commissural fibers do not appear to originate within Deiters' nucleus (Gacek, 1981). It is believed that commissural inhibition is primarily a property of canal-related central vestibular neurons, but not otolith-related neurons (Precht, 1974). The crossed connections of central otolith-related neurons are not as well defined. It is believed that the facilitation or inhibition of Deiters' neurons caused by stimulation of the contralateral labyrinth is carried by deep reticular pathways (Shimazu and Smith, 1971; Precht, 1974).

H. Non-Labyrinthine Inputs to the Vestibular Nuclei

Neurons within the vestibular nuclei are influenced by activity arising in many regions of the central nervous system. These include somatosensory inputs ascending via spinal pathways to reach the nuclei directly, or indirectly via the cerebellum or reticular formation (Wilson and Peterson, 1978). Descending inputs can arise from the cortex, visual system, and the interstitial nucleus of Cajal. The somatic inputs originate in a broad spectrum of cutaneous, joint, and muscle receptors.

3. Studies using Electrical Stimulation

A. Introduction

In order to gain an overall understanding of the vestibular system, it is necessary first to study the synaptic events in, or organization of various regions of that system. Electrical shocks, either orthodromic or antidromic, have often been used as a means of stimulation. However, a number of limitations must be considered.

As described by Wilson and Yoshida (1969), it is difficult to localize the stimulus on to individual cell bodies or their axons. Stimulation and

activation of neurons and fibers belonging to other cell groups will no doubt result. The simultaneous stimulation of units from more than one semicircular canal may also influence the reflex response. Lastly, vestibular cells responding to different directions of linear acceleration have been found to be clustered close together (Daunton and Melvill Jones, 1982). Natural stimulation of these cells by head movements in a given direction should result in excitation of some cells and inhibition of others. Electrical stimulation, on the other hand, would cause all cells to be activated simultaneously, creating a very unnatural response.

Nevertheless, electrical stimulation can still be a useful tool for the analysis of the synaptic actions of vestibular afferent fibers on second and higher order neurons (Wilson and Melvill Jones, 1979), as well as for studying the distribution of postsynaptic activity.

B. Primary Afferents

The galvanic response of canal afferents in the anaesthetized monkey was described by Goldberg et al. (1982). The electric currents were delivered by two chlorided silver wires; one wire was fit into the perilymphatic space of the vestibule, the other placed in the hypotympanic space of the middle ear. Single unit responses were recorded from the superior vestibular nerve. The response gain and phase were relatively flat, with a phase lead, and were not systematically affected by a change in stimulus magnitude. Galvanic responses of otolith afferents have not yet been described in the literature.

C. Central Vestibular Nuclei Neurons

Electrical stimulation of the whole vestibular nerve evokes field potentials in the brainstem (orthodromic stimulation). If the stimulus strength is not excessive, the field potentials are essentially restricted to the vestibular nuclei (Wilson and Melvill Jones, 1979).

Distribution of neuronal activity, as revealed by electrical stimulation, has been studied in detail for MVN and Deiters' nucleus only. Monosynaptic field potentials within Deiters', evoked by stimulation of the whole vestibular nerve, are more prominent ventrally than dorsally (Ito et al., 1969). Polysynaptic potentials appear to be more widely distributed. Stimulation of utricular afferents (Sans et al., 1972) and of the saccule (Hwang and Poon, 1975) show termination of their axons primarily within Deiters' nucleus.

Within the vestibular nuclei there exist both mono and polysynaptically driven neurons. All monosynaptic connections between primary afferent and second-order neurons are excitatory; inhibitory potentials are at least disynaptic (Wilson and Melvill Jones, 1979).

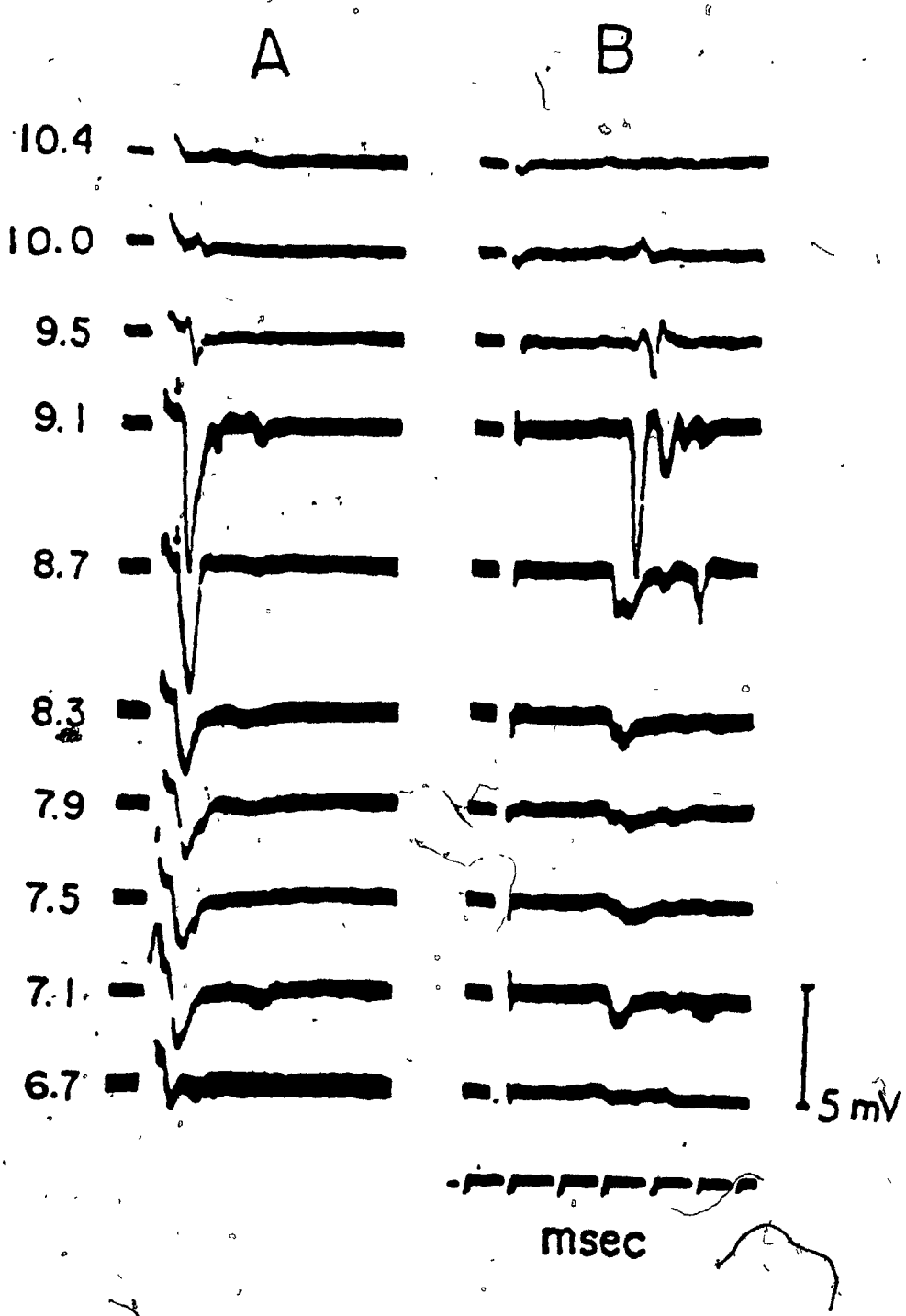
Antidromic activation has been widely used in the vertebrate central nervous system (CNS) as a reliable method of identifying a selected neuron group (Ito et al., 1964). Field potentials within the vestibular nuclei can be produced by antidromic stimulation of the vestibulospinal (V-S) tracts. Activation of the LVST results in field potentials primarily within Deiters' nucleus (Fig. 6). The pathway for producing the field potential in Deiters' nucleus is on the ipsilateral side of the spinal cord, which is in agreement with anatomical findings.

Figure 6

Field potentials recorded along a track through Deiters' nucleus. Downward arrows mark the small positive phase preceding the negativity. Figures to the left of each record indicate the depth (in mm) of microelectrode tip from the medullary surface.

A. Antidromic stimulation of ipsilateral LVST at cervical level of spinal cord.

B. Antidromic stimulation of ipsilateral lumbar LVST (adapted from Ito et al., 1964).


A
B
10.4
10.0
9.5
9.1
8.7
8.3
7.9
7.5
7.1
6.7
5 mV
msec

The majority of LVST neurons with projections to the lumbar cord originate in the dorsocaudal region of Deiters', while cells with projections to the cervical cord originate primarily in the rostroventral region (Ito et al., 1964; Wilson et al., 1966, 1967). These borders are not strictly defined, and there is a considerable overlap in their location.

D. Motoneurons

Electrical stimulation of Deiters' nucleus neurons revealed that the spinal projecting fibers can exert mono and polysynaptic facilitatory effects on extensor motoneurons, and polysynaptic inhibitory effects upon flexor motoneurons (Kato and Tanji, 1971). Most facilitatory effects on extensor motoneurons are polysynaptic. Of those linkages which are monosynaptic, most are found in neck motoneurons though there are some monosynaptic linkages from Deiters' neurons to hindlimb extensor motoneurons, particularly in quadriceps and gastrocnemius-soleus motoneurons (Wilson and Yoshida, 1969; Wilson, 1979). Limb extensor motoneurons activated monosynaptically by stimulation of Dieters' nucleus are activated via axons in the LVST and not the MVST.

In some instances the pattern of potentials evoked in motoneurons by electrical stimulation of individual vestibular nerve branches is in agreement with the pattern of vestibulospinal reflexes evoked by natural stimulation (Wilson and Melvill Jones, 1979). However, the short-latency pathways revealed by electrical stimulation may only be a part of the circuitry involved in the production of vestibulospinal reflexes.

E. Cerebellar Interactions

Electrical stimulation of cerebellar fibers revealed that the cerebellar influence on V-S tract neurons is exerted primarily by the anterior lobe and to a lesser extent (if at all) by the vestibulocerebellum (Ito et al., 1968; Akaike et al., 1973). The cerebellar vermis of the anterior lobe exerts a powerful monosynaptic inhibition of Deiters' nucleus neurons, though Shimazu and Smith (1971) did not observe any projection from the anterior lobe vermis to the ventral region of Deiters' nucleus.

4. Studies using Natural Stimulation

A. Introduction

The otoliths are linear accelerometers, and as such respond to linear accelerations and to changes in orientation of the head with respect to gravity (Young, 1984). A variety of methods to provide a natural stimulus to the otolith organs have been used by other investigators. Two such methods are dynamic linear acceleration and roll tilt. The former stimulus does not include an angular component, and the semicircular canals could only react if they possessed significant sensitivity to linear acceleration. With roll tilt, the restrained animal is dynamically tilted relative to the gravity vector. However, there is an angular component to this accelerative stimulus. If you wish to study the effects of otolith stimulation only, you must eliminate canal responses. One method for accomplishing this is to plug the canals, thereby making them insensitive to the angular component of the accelerative stimulus. However, this is still not a "clean" solution. The otoliths would be undergoing off-axis rotation, thereby exposing the maculae to both radial and tangential linear

acceleration (Fernandez and Goldberg, 1976c; Watt, personal communication). These additional accelerations, which are significant at frequencies akin to locomotion, would complicate interpretation of the results.

B. Response of Primary Afferents

On the basis of primary afferent fibers' discharge patterns, two types of fibers have been described. "Regular" fibers tend to be of small diameter (slow conducting) and innervate large peripheral receptor fields in the sensory epithelia, while "irregular" fibers tend to be of large diameter (fast conducting) and innervate small centrally located receptor fields (Wilson and Melvill Jones, 1979). The high average spontaneous firing rate of both these fibers permit a bidirectional response. Regular afferents show a tonic response pattern, in that these fibers show little, if any, adaptation to maintained linear force. Irregular afferents show a phasic response pattern, in that they adapt relatively quickly to a maintained linear force (Goldberg, 1981). In mammals, many otolith neurons can be considered phasic-tonic in the sense that they exhibit some adaptation but do respond in a sustained manner to maintained linear forces (Goldberg and Fernandez, 1984). However, in regularly discharging neurons the tonic response components predominate, while phasic responses predominate in irregular units. As described by Mayne (1974), the adaptation of some cells may be a means of separating gravitational inputs from other linear acceleration inputs. While regular and irregular units have been identified in all species examined (Wilson and Melvill Jones, 1979), there is a somewhat higher proportion of regular units projecting from the maculae (Fernandez et al., 1972; Fernandez and Goldberg, 1976a), at least in mammals.

Studies of macular afferent response characteristics using natural stimulation have been performed in the anaesthetized, partially decerebellate monkey by Fernandez and Goldberg (1976a, b, c), and in the anaesthetized, partially decerebellate cat by Anderson et al. (1978) and Tomko et al. (1981). Their results are in general agreement, indicating some consistencies between the otolith primary afferent systems in these two species.

A majority of isolated fibers responded with an increase in their resting firing rate to ipsilateral side-down tilt. Saccular afferents generally responded in a fashion analogous to utricular afferents. The regular fibers' frequency response, over a frequency range of dc-1.0 Hz, showed a slight increase in gain and a relatively flat phase with increasing frequency (Fernandez and Goldberg, 1976c; Anderson et al., 1978). Fernandez and Goldberg also showed that at frequencies between 1.0-2.0 Hz there was an increase in phase lag. Those authors assumed that the phase lags reflected the mechanisms of the end organ. The gain for irregular units is larger than that for regular units, and the difference between the two groups becomes more conspicuous at higher frequencies. The average phase curves for regular units may be taken as representative for all units (Fernandez and Goldberg, 1976c). Fernandez and Goldberg (1976c) and Anderson et al. (1978) also showed that in general otolith afferents respond in a linear fashion to a change in stimulus magnitude, at least at the single frequencies used in the 2 experiments (0.1 Hz and 0.25 Hz respectively). Orientation of polarization vectors of macular afferents, determined using static tilts (Fernandez and Goldberg, 1976a; Tomko et al., 1981), correlated well with the morphological polarization vectors of

sensory hair cells of the maculae. The response characteristics of the saccular and utricular afferents confirm that the otolith primary afferent neural signal encodes linear (or gravitational) acceleration (Wilson and Melvill Jones, 1979).

C. Response of Vestibular Nuclei Neurons

Many studies have investigated the response of higher order neurons located in the vestibular nuclei to natural stimulation. Their response to tilt reveals that a majority of the units' resting firing rates increase when exposed to ipsilateral side-down tilt, although there did not appear to be a strong tendency towards pitch up or down (Peterson, 1970).

Studies of the dynamic response of neurons using roll tilt have resulted in sometimes conflicting observations. Schor (1974) described the behaviour of neurons (including some V-S units) located in the DVN and Deiters' in decerebrate, canal-plugged cats. With increasing frequency (range 0.1-1.0 Hz) there was either a corresponding slight increase or a large increase in response gain. Response phase was not determined. Boyle and Pompeiano (1980), using sinusoidal tilt on decerebrate cats, observed two different populations of neurons located within Deiter's nucleus (also including V-S units). A majority of neurons exhibited a stable or slightly reduced sensitivity and stable phase response with increasing stimulus frequency (range 0.008-0.325 Hz). The second group of neurons exhibited an increase in sensitivity with a phase response that was closely related to the velocity signal during increases in angular acceleration. It should be noted, however, that this stimulus also activated the vertical semicircular canals and no action was taken to remove their input from the response. In experiments using roll tilt in decerebrate, canal-plugged cats Schor and

Miller (1982) and Schor et al. (1985) examined the response of vestibular neurons (again including some V-S units) in and around the DVN and Deiters'. They observed two different types of responses in cells located within the central vestibular nuclei. With increasing stimulus frequency (range 0.01-1.0 Hz), one group of neurons exhibited a slight increase in response gain and a relatively flat phase lead. The second group of neurons showed a large increase in gain with a progressive phase lag of 180°.

A horizontal linear accelerative stimulus was used by Melvill Jones and Milsum (1969) to examine the phase behaviour of MVN neurons (Melvill Jones, personal communication) in the decerebrate cat . They observed a large increasing phase lag with increasing stimulus frequency (range 0.3-3.0 Hz) in these neurons. Response gain was not determined. Perachio (1981) recorded from cells in and around the DVN and Deiters' nucleus during horizontal linear oscillation in the alert monkey. With an increasing stimulus frequency (range 0.2-1.2 Hz) there was a decrease in response gain and a relatively flat phase lag. Xerri et al. (1987) used vertical linear acceleration to study cells in and around Deiters' nucleus in the alert cat. A decrease in response gain and a relatively stable phase lead was observed with an increase in stimulus frequency (range 0.05-0.75 Hz).. The diversity of these results may be a consequence of the different experimental procedures used in each study. However, one class of neurons appear to act as simple relays of otolith afferent activity (Schor et al., 1985), while a second class of neurons appear to be involved with information processing (Wilson and Melvill Jones, 1979; Schor et al., 1985).

The dependency of the response of the system to stimulus magnitude (the linearity of response) was examined by Schor (1974) at 0.2 Hz and 0.3 Hz and Xerri et al. (1987) at 0.1 Hz. At these specific frequencies the response of the system was demonstrated to be independent of the stimulus magnitude, at least over the range of stimuli employed.

Daunton and Melvill Jones (1982) have shown that the functional polarization vectors (FPV, the direction in 3-dimensional space along which a cell is most sensitive to linear acceleration) of otolith-driven units in the vestibular nuclei are broadly distributed, with what appears to be a tendency for concentration of responses in the horizontal and vertical planes. This might be expected for units responding to utricular and saccular stimulation, respectively (Wilson and Melvill Jones, 1979). Schor et al. (1984) using a bi-axial stimulus produced by independent roll and pitch tilts in decerebrate, canal-plugged cats, however, noted an absence of neurons with fore/aft directed vectors. This may be due to a limited ability of their stimulus to activate neurons in that direction.

D. Response of Motoneurons

Vestibulospinal fibers may terminate on motoneurons either directly or indirectly through spinal interneurons (Wilson and Melvill Jones, 1979). Relatively few studies have investigated the response of motoneurons or interneurons to natural stimulation. It appears, however, that motor or interneurons are modulated by labyrinthine activity.

Evidence of this modulation in animals was described by Lacour et al. (1978) using the H-reflex (Hoffmann reflex) test to examine spinal motoneuron pool excitability during free fall in the awake baboon. Facilitation of the H-reflex occurred approximately 40 ms after release

(i.e., upon entering free fall), and continued as long as the animal was in free fall. After bilateral vestibular neurectomy no facilitation of the H-reflex was observed. Watt (1981b) examined spinal motoneuron pool excitability during vertical sinusoidal oscillation by means of the H-reflex technique in decerebrate cats. In cats with a functioning labyrinth, modulation of the H-reflex amplitude was seen over a frequency range of 0.5-2.5 Hz. Maximum H-reflex amplitude occurred at the point of maximum downward acceleration. There was no obvious change in response gain or phase with increasing stimulus frequency. No significant modulation was seen in acute bilaterally labyrinthectomized cats. The elimination of H-reflex facilitation or modulation after bilateral labyrinthectomy is an indication of some macular effect on the motoneuron pool, at least at the level of the lumbosacral spinal cord.

Wilson et al. (1984) examined the response of cervical spinal interneurons (and some likely motoneurons) to whole body tilt in the decerebrate cat. Over a frequency range of 0.02-0.5 Hz there was an increase in response gain with a constant slight phase lead. No significant modulation was seen in acute bilaterally labyrinthectomized cats, indicating that there is some macular effect on the interneuron pool at the level of the cervical spinal cord as well.

E. Response of Muscles

The effects of labyrinthine signals on muscle can be studied by observing the electrical responses of the muscle through the use of electromyographic (EMG) recordings.

Berthoz and Anderson (1971) examined the forelimb extensor EMG response of decerebrate, spinal cats to sinusoidal angular rotations about

the X axis. With increasing stimulus frequency from 0.1-1.0 Hz, there was a slight decrease in gain and a relatively unchanging phase lag. Using roll tilt in decerebrate, canal-plugged cats, Schor (1981) observed a relatively stable gain with an increase in phase lag up to 180° as the stimulus frequency increased from 0.1 Hz to 1.0 Hz. Cats with intact labyrinths showed no such increasing phase lag, indicating that at the higher stimulus frequencies there is an increasing contribution from the canals. Responses of forelimb and contralateral neck extensor muscles were shown to be very similar.

Sinusoidal linear acceleration was used by Anderson et al. (1977) to study forelimb extensor muscle response in the decerebrate, spinal cat. Over a stimulus frequency range of 0.15-1.0 Hz, there was a corresponding decrease in gain and an increase in phase lag above 0.4 Hz. The response was similar in all three axes, indicating that the dynamic behaviour of the utricular and saccular receptors are similar. Lacour et al. (1987) used vertical linear acceleration to study the response of splenius capitis muscle in the neck of the alert cat. The head of the animal was immobilized throughout the recording sessions and its trunk was wrapped in a secured hammock to minimize relative motion of the head and trunk, thus eliminating postural reflexes originating in the neck. As well, visual motion cues were prevented by oscillating the animal in total darkness. With increasing stimulus frequency (range 0.25-1.0 Hz) there was a corresponding decrease in response gain and an increase in phase lag. At the level of muscle, then, there do not appear to be many differences in response to a linear acceleration stimulus between a decerebrate and an alert cat.

Taken together, these results suggest that the motor output may not result simply from vestibular afferent activity being relayed directly to the spinal motoneurons via the V-S tracts (Anderson et al., 1979). Other as yet unidentified systems may be involved.

F. Otolith-Spinal Effects in Humans

Studies of the vestibular system in humans have confirmed the existence of otolith-spinal reflexes. A sudden fall can be used to provide a step input of acceleration to stimulate the otoliths (and specifically the saccule). Melvill Jones and Watt (1971b) showed a short-latency EMG response occurring in the human gastrocnemius muscle about 74 ms after the start of sudden unexpected falls. This reflex was considered to be of otolith origin, and was abolished by labyrinthectomy in cats (Watt, 1976) and in baboons (Lacour et al., 1978). It is also absent in labyrinth-defective humans (Greenwood and Hopkins, 1976). Canal-plugging in cats (Watt, 1976), however, has no effect on the response.

Further evidence of otolith-spinal effects has been provided by studies of changes in excitability of the lumbosacral spinal motoneuron pool as measured by H-reflex testing. Greenwood and Hopkins (1977) examined the behaviour of the human H-reflex during sudden falls, and observed a facilitation of the response which began between 30 and 40 ms after the onset of a fall. Presumably, this facilitation of the H-reflex reflects a progressive increase in the excitability of the lumbosacral motoneuron pool, which leads to EMG activity in the lower limb muscles. Using sinusoidal vertical linear acceleration, Watt (1977) observed a non-adapting modulation of the H-reflex amplitude. Over a stimulus frequency range of 0.002-3.0 Hz, there was little change in response gain and phase.

Differences which appear in the results of animal and human studies may be due to different experimental paradigms. However, they might also reflect the significantly different functional requirements of quadrupeds and bipeds.

5. Studies during Locomotion

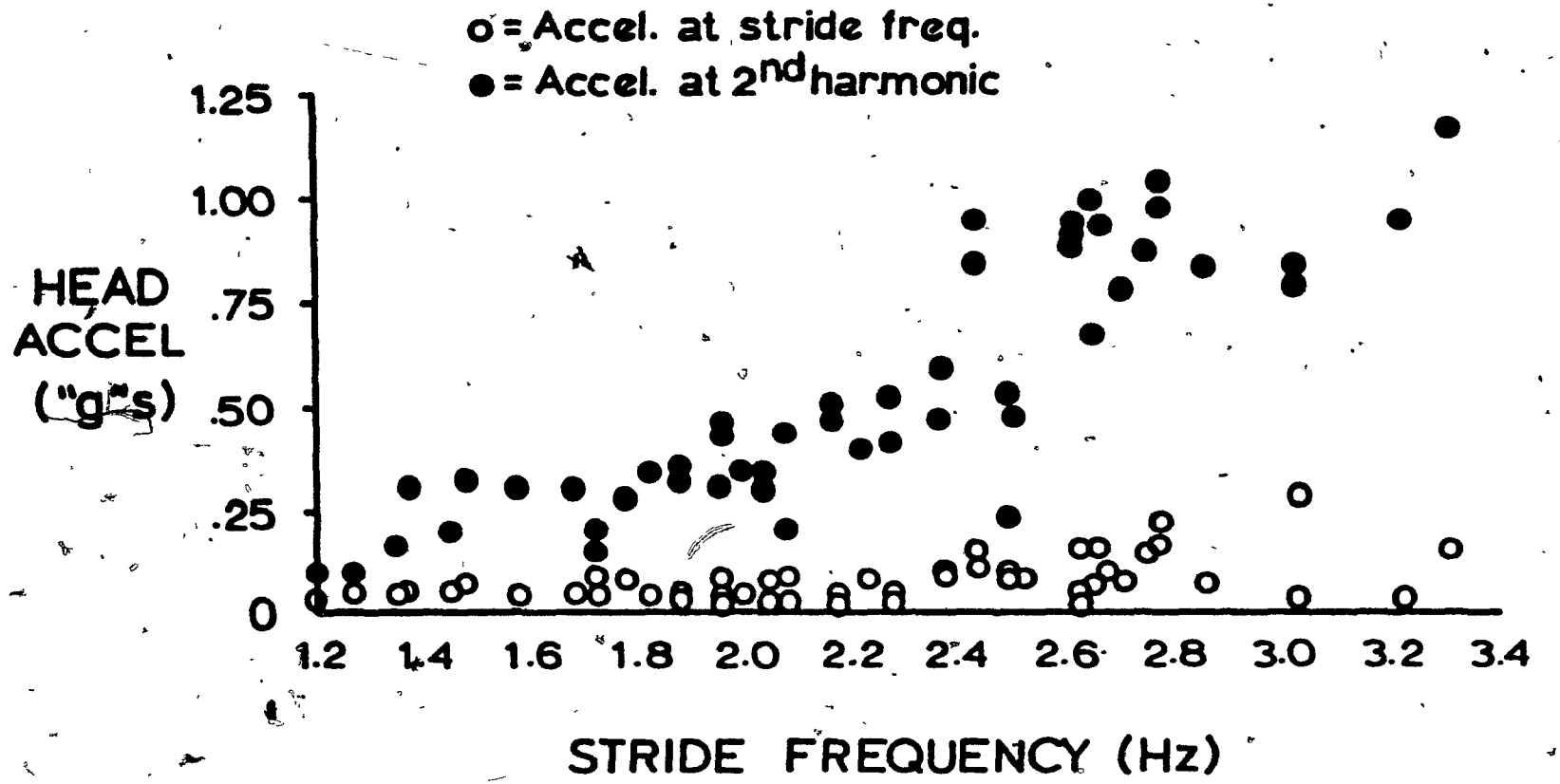
A. Acceleration Stimulus

In the previous section it was shown that natural stimulation of the otolith organs induces changes in lumbosacral spinal cord excitability. Vestibulospinal reflexes resulting from the linear accelerations experienced during normal locomotion might contribute to locomotor control if the stimulus is large enough to activate the otolith end-organs, and if there is an appropriate temporal relationship between such activation and EMG activity in the extensor muscles (Stuart et al., 1973).

Studies of cats walking or trotting on a treadmill showed that while lateral head accelerations were minimal during locomotion, accelerations in the fore-aft and vertical directions were substantial (Watt and Wetzel, 1977). Head vertical acceleration and head oscillation frequency (which is twice the stride frequency) ranged from 0.07 'g' at 2.5 Hz (slow walk) to 0.8 'g' at 6.0 Hz (fast trot) (Fig. 7). These values of head acceleration are orders of magnitude above the reported thresholds of central vestibular neurons (Melvill Jones and Milsum, 1969; Xerri et al., 1987), indicating that the otoliths should be activated by vertical head movements during locomotion.

Figure 7

Vertical head accelerations of alert cat walking or trotting on treadmill, plotted as a function of stride frequency. Head accelerations occurring at twice the stride frequency due to alternating forelimb movements (filled circles) increased rapidly as stride frequency increased (from Watt and Wetzel, 1977).


o = Accel. at stride freq.
● = Accel. at 2nd harmonic
HEAD ACCEL ("g"s)
1.25
1.00
.75
.50
.25
0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
STRIDE FREQUENCY (Hz)

B. Interactions between Deiters' Nucleus Neurons and Extensor Motoneurons during Locomotion in Cats

As described previously, signals from the otolith organs are known to be relayed to spinal levels via the V-S tracts during electrical or natural stimulation of those organs (Wilson and Melvill Jones, 1979; Wilson, 1985). However, it is not certain how these signals are modified during active movements. In a series of experiments, Orlovsky (1972a, b) studied the interaction of Deiters' neurons and hindlimb extensor motoneurons during locomotion in mesencephalic and thalamic cats. Extensor muscles are active during the stance phase of the limb. Electrical stimulation of Deiters' nucleus during this stance phase increased the activity of the extensor muscles, but did not change the timing of the locomotor cycle (Orlovsky, 1972a). Destruction of Deiters' nucleus resulted in the disappearance of the stepping movements of the ipsilateral limb, or in a decrease of extensor muscle activity during locomotion. The discharge pattern of Deiters' neurons was correlated with the beginning of the stance phase of the ipsilateral hindlimb (Orlovsky, 1972b). The phasic modulation would disappear if the limbs were prevented from moving.

Reduction of the response of Deiters' nucleus neurons to static tilt was observed by Orlovsky and Pavlova (1972) during electrically stimulated walking in the mesencephalic or thalamic cat. In these procedures the animal's head was immobilized during locomotion. It should be noted, however, that the vertical head accelerations experienced during normal locomotion (Watt and Wetzel, 1977) are much larger than the accelerations associated with the small angles of whole body tilt used in the former experiments. Locomotor movements are also dynamic, not static, in nature.

Further studies of Deiters' neurons in controlled locomotion were performed by Kanaya et al. (1985), also in mesencephalic cats. In these studies it was observed that in many Deiters' neurons the tonic discharge property seen during slow walk would change to a phasic discharge property during fast walk.

These results demonstrate a relationship between Deiters' nucleus and locomotor activity, and imply that labyrinthine inputs would be passed on to the spinal cord. They also suggest that the functional role played by Deiters' neurons may change depending on the relative requirements for static or dynamic postural control during locomotion (Kanaya et al., 1985).

C. Otolith-Spinal Contributions to Locomotor Control in Humans

The otolith-originating EMG response to sudden falls (Melvill Jones and Watt, 1971b) suggests that otolith-spinal pathways might contribute to the organization of motor control during landing from these falls (Wilson and Melvill Jones, 1979). These pathways may contribute during active locomotion as well. This is supported by the following observations. Melvill Jones et al. (1973) noted that EMG activity in the gastrocnemius muscle commences approximately 75 ms after the foot leaves the ground, i.e., upon entering a short period of free fall. This response is time-locked to the onset of free fall even when hopping at simulated reduced 'g' levels, which significantly increases the time until the subsequent landing (subjects suspended horizontally, with bungee cords substituting for gravitational pull; Backman and Watt, 1978). Furthermore, the amplitude of the response decreases as 'g' levels are reduced.

These results indicate that otolith stimulation due to vertical linear acceleration can bring a functionally effective influence to bear upon the

extensor muscles of the leg (Melvill Jones et al., 1973). Since large cyclical changes in vertical linear acceleration of the head occur during normal locomotion, especially during running, it seems reasonable to speculate that periodic vestibulospinal influences might contribute to the neuromuscular organization of normal locomotor control (Wilson and Melvill Jones, 1979).

6. Summary

While the results discussed in the previous sections were not always in complete agreement, they do support the notion of an otolith contribution to dynamic motor control since there was a corresponding motor output for a given linear acceleration input.

The studies have shown that many second and higher order neurons located in the vestibular nuclei do respond to dynamic linear accelerations. However, few of these studies have examined otolith-driven neurons using a pure linear acceleration stimulus over a wide range of frequencies, especially the higher frequencies associated with locomotion (2-6 or 7 Hz; Watt and Wetzel, 1977).

The aim of these experiments was to quantify the dynamic response characteristics of otolith-driven neurons located in Deiters' nucleus of the cat. The fidelity of the transfer of information from the peripheral receptor to Deiters' nucleus was examined, using sinusoidal linear acceleration at physiologically important frequencies.

III METHODS

1. Introduction

Twenty-seven cats weighing 2.05-2.95 kg were used in these experiments. In four cats, the anatomical locations of the isolated cells were confirmed histologically.

Given the sometimes violent acceleration stimulus, it was particularly important to monitor the extracellular recordings obtained from single neurons. While the oscilloscope was used to isolate and identify cells in the usual fashion, it was also necessary to continuously view a triggered and expanded display of the single unit during testing. This ensured that spikes were not lost at any point in the oscillation cycle, and that no other units were being recorded. In general, units with a signal to noise ratio of less than 5 or 10:1 could not be expected to survive the experiment.

2. Anaesthesia

Gaseous agents were used for the initial induction of anaesthesia. The cat was placed in a dark plexiglass box, and a mixture of 2.5% Fluothane (Halothane, Ayerst) in nitrous oxide/oxygen (60:40) was introduced. Excess gas was vented outdoors via a suction line. The animal's respirations were constantly monitored. When the animal was determined to be well anaesthetized, it was removed from the box. Xylocaine (Lidocaine, Astra), as an endotracheal aerosol, was sprayed into the larynx to prevent laryngeal spasms and the animal was then intubated. The gaseous anaesthetic, now using a 1% Halothane mixture, was then

administered by way of the endotracheal tube. The right cephalic vein was exposed and cannulated, and the gaseous anaesthetic discontinued. The animal was then maintained on 10 mg/kg methohexital (Brietal, Eli Lilly), with doses given intravenously as needed until the decerebration was performed. A minimum of 2.5 to 3.0 hours was always allowed from the time of the last dose until actual extracellular recording commenced.

3. Care and Maintenance of Experimental Animal

The animal was shaved dorsally head to tail, and ventrally on the neck. The left carotid artery was exposed and cannulated. A manometer was then connected to the carotid cannula which allowed for the continuous monitoring of the animal's blood pressure. Clotting of blood was prevented by filling the cannula with a solution of heparin (Abbott) in isotonic saline (1 ml:10 ml). Care was taken not to infuse significant amounts of heparin into the animal. Blood pressure generally remained between 100-120 mm Hg. In two experiments blood pressure was maintained at this level with a slow drip of 1 mg/ml norepinephrine bitartrate (Levophed, Winthrop) in Normosol-M (Abbott, 1 ml:250 ml). In all cases, however, a prolonged fall of blood pressure to below 80 mm Hg was considered to be an indication of serious deterioration of the preparation. This could also be seen as a marked decrease in brainstem activity as recorded by the inserted microelectrode, as well as in a change in the quality of respiration. This often occurred late in the experiment, which would be terminated soon afterward.

Rectal temperature was monitored throughout the experiment.

Temperature was maintained between 36-38°C by an electric heating ribbon wrapped around the animal's torso, and when needed, by a heating lamp.

In all experiments the animals breathed spontaneously and were not paralyzed by drugs or artificially ventilated.

4. Surgical Procedures

The surgical procedures used in the preparation of the animal for electrophysiological recording will be described below in the order in which they were carried out. A detailed description of the stimulating and recording electrodes will be given in subsequent sections.

A. Placement of Animal in Stereotaxic Holder

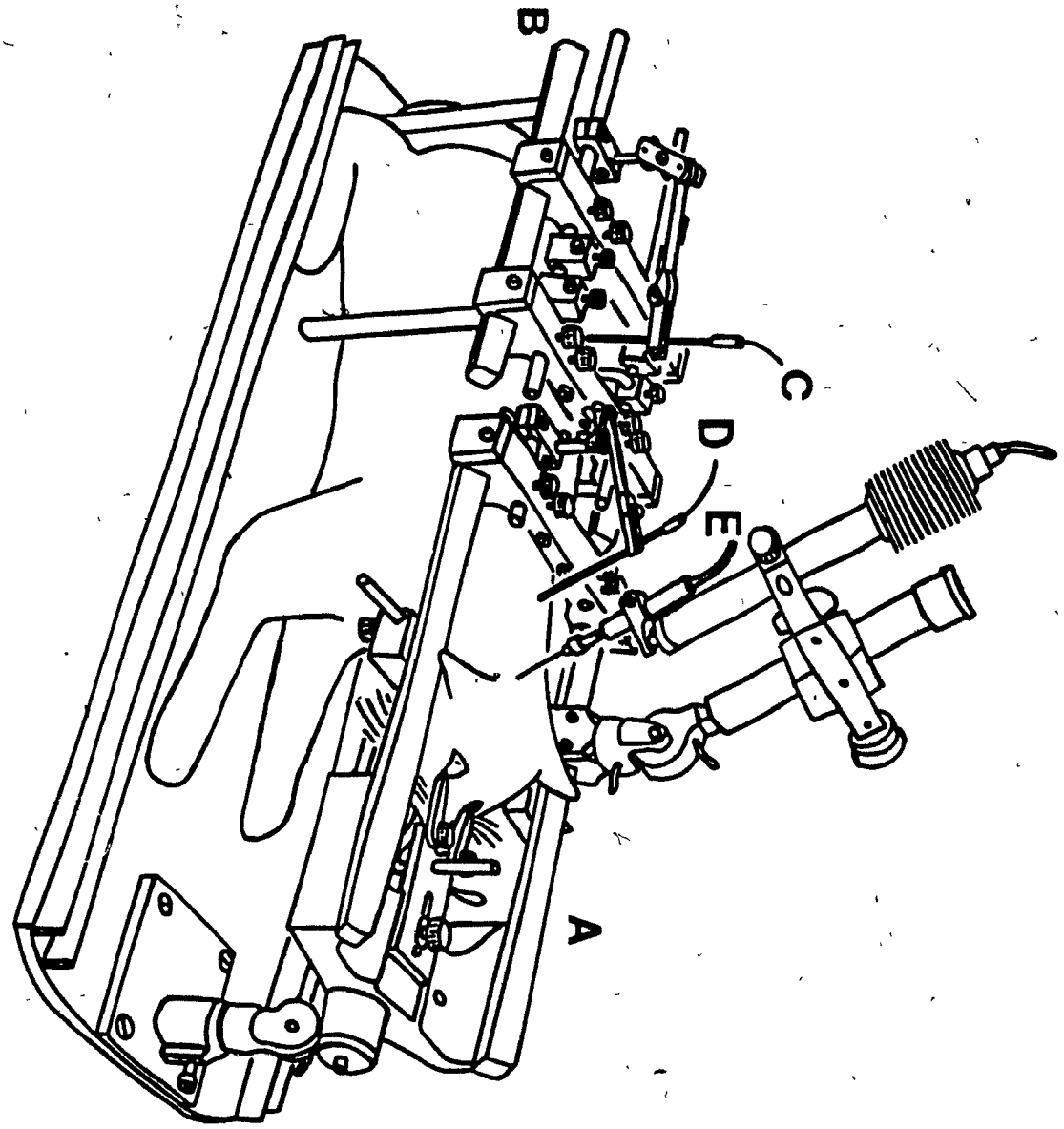
After connecting the manometer to the carotid cannula, the animal was placed prone on the base of a portable platform upon which were mounted head and spinal stereotaxic frames. The T1 dorsal vertebral spine was exposed. The cat's head was then fixed into the Kopf stereotaxic frame using conventional ear, eye and mouth bars. The T1 dorsal process was clamped and fixed to the frame with the neck extended (Fig. 8). This arrangement maintained a rigid alignment of the brainstem and upper spinal column during oscillations conducted later in the experiment.

B. Exposure of Cerebellum

With the cat's head held in the stereotaxic frame, the top of the skull was exposed from the frontal to the occipital bones. A stereotaxically positioned pointer was used to locate 3 trephine holes to be used for decerebration and recording from Deiters' nucleus. The first of these, for recording, was made in the right occipital bone, exposing a

Figure 8

Diagram of cat fixed into portable stereotaxic holder, with recording and stimulating electrodes in place. A, head stereotaxic frame, with spinal clamp affixed to T1 vertebral spine. B, spinal stereotaxic frame, with spinal clamps affixed to T12 and L5 vertebral spines. Note that head and spinal stereotaxic frames are isolated from each other. C, lumbar (L2) LVST stimulating electrode, held in place by clamp attached to spinal stereotaxic frame. D, cervical (C1-C2) LVST stimulating electrode, held in place by clamp attached to head stereotaxic frame. E, recording microelectrode coupled to holder. The microelectrode holder is attached to an electrically-driven microdrive, which advances or retracts the microelectrode in steps of 1.25 μm. The microdrive is attached to a micromanipulator which is clamped to the head stereotaxic frame, thereby minimizing displacement of the electrode relative to the head during oscillation.


B
C
D
E
A

small part of the cerebellum. The hole was then lightly packed with an isotonic saline-soaked gauze pad.

C. Exposure of Cerebral Cortex for Decerebration

The remaining pair of trephine holes were made in the parietal bone on either side of the midline overlying the posterior part of the cerebral cortex. The exposed dura in these two locations was then opened, and a precollicular postmammillary decerebration was performed using an expanding wire leukotome. The decerebration was performed in four steps. The leukotome, inclined backwards 19° from vertical and with the wire loop facing towards the right side of the skull, was inserted into the brain until its tip reached a predetermined stereotaxic location just above the floor of the skull. The wire loop was opened, raised 5 mm, retracted, and the leukotome withdrawn and moved to the next penetration site on the other side of the midline, where the procedure was repeated. Once this was completed, the wire loop was adjusted to face towards the left side of the skull and the above two steps were repeated. Upon completion of the decerebration, anaesthetics were discontinued.

In a few cases excess bleeding at the decerebration site, indicated by acute swelling of the cerebral cortex and/or by cardiorespiratory instability, necessitated rapid decompression of the brainstem. This was achieved by partial removal of the forebrain by suction. In some cases this proved successful with resulting stabilization of the animal, while in others it was unsuccessful and was followed by rapid deterioration of the animal. In the latter cases the experiment was soon terminated. At the end of all experiments, the level and condition of decerebration were determined by visual inspection of the carefully removed brain.

D. Laminectomies

After decerebration, dorsal laminectomies were performed at spinal segment levels C2 and L2. These allowed access to the spinal cord for insertion of stimulating electrodes, which will be discussed in a following section. The exposed areas of the spinal cord were kept moist with isotonic saline-soaked gauze pads.

E. Spinal Clamps

To prevent the cat's torso from swaying during oscillations, spinal clamps were used to rigidly hold the lower spinal column. The dorsal vertebral spines T12 and L5 were exposed, and clamps placed around the transverse processes prevented any spinal column movement at those points (see Fig. 8).

The forepaws were then taped to the base of the apparatus, a heater cord was wrapped around the torso, and a rectal thermometer was inserted.

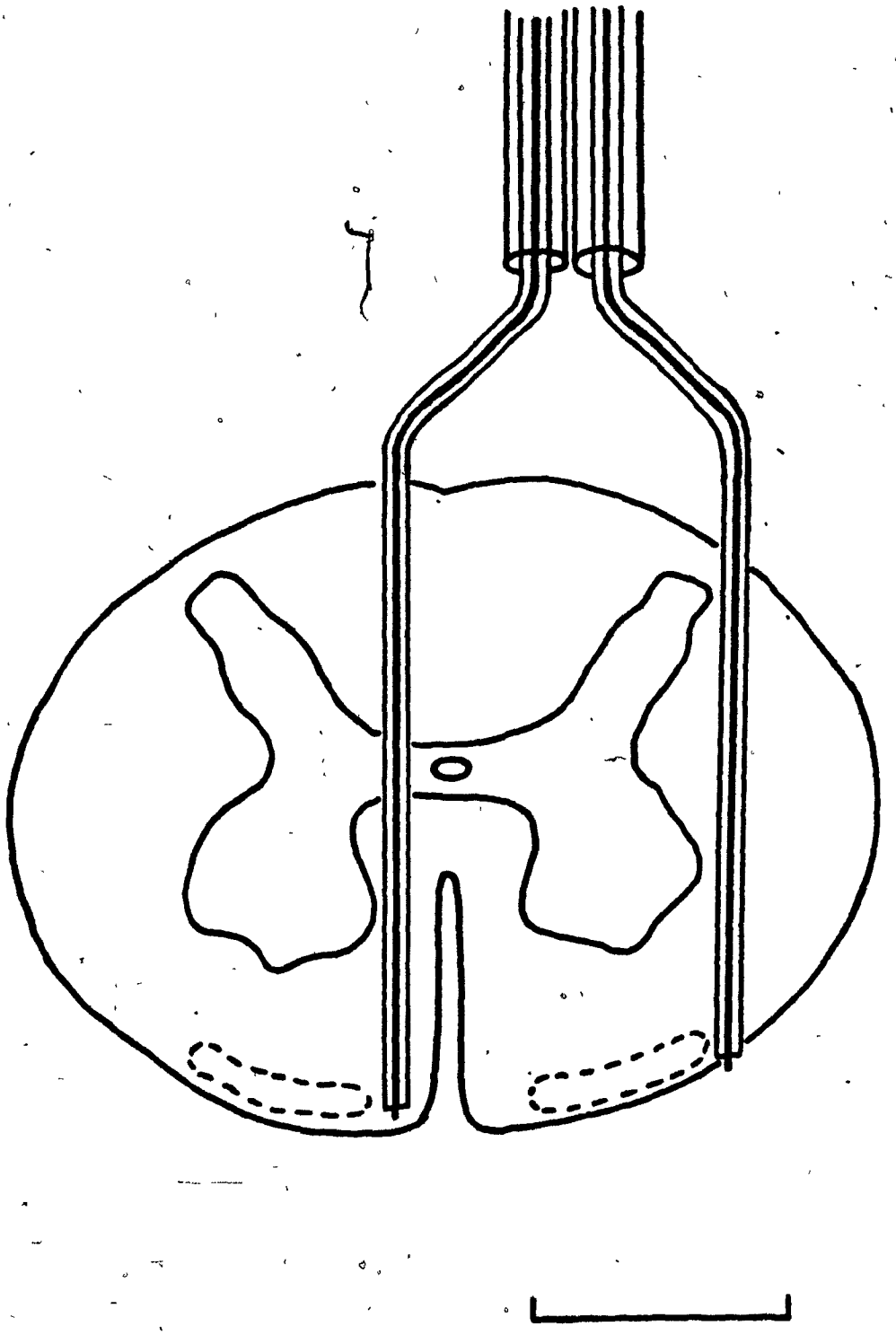
F. Insertion of Stimulating Electrodes

The platform, with the cat secured in the stereotaxic frames, was then transferred onto the oscillation device. The following procedures to insert the electrodes were carried out with the aid of an operating microscope.

The dura over the exposed portion of the cerebellum, as well as over the two exposed sections of the spinal cord, was opened. The stimulating electrodes were then secured in their holders over the C2 and L2 spinal segment levels. One wire of each electrode was placed just contralateral to the midline of the cord and the second was placed ipsilaterally, just lateral to the entry point of the dorsal root fibers (Fig. 9). Both wires

Figure 9

Representative diagram of stimulating electrode placement in the spinal cord. Teflon-coated stainless steel wires pass through capillary tubes to prevent sway during oscillation. Dashed line indicates approximate locations of LVST. Scale approximately 2 mm, depending on cervical or lumbar location of stimulating electrodes (adapted from Netter, 1983).



were inserted until they touched the floor of the spinal canal. They were then pulled back up approximately 0.5 mm. This placed the electrodes in a position that would allow for antidromic stimulation of the ipsilateral ventral quadrant of the spinal cord, including the lateral vestibulospinal tract (LVST).

G. Insertion of Recording Electrode

A 13 gauge hypodermic needle was used as an indifferent, or ground electrode. This needle was inserted into the deep muscle layers of the neck, and connected to the recording instruments. A tungsten microelectrode was coupled to a stepping motor-driven microdrive capable of step increments of 1.25 μm. The microdrive and microelectrode were inclined backwards 30° from the vertical. The stereotaxic coordinates for the center of Deiters' nucleus were determined, and the microelectrode was inserted through the cerebellum to a point 2 mm above the predetermined aiming point.

5. Stimulating and Recording Electrodes

Each stimulating electrode consists of two teflon-coated, braided stainless steel wires (0.21 mm diameter) which were passed through two capillary tubes. The capillary tubes prevented sway of the wires during oscillation, thereby minimizing spinal damage (and resultant spinal block) that would otherwise occur with electrode movement. The capillary tubes were held in place by clamps which were secured onto the stereotaxic apparatus (see Fig. 8). Only the tips of the wires were devoid of insulating material.

Extracellular recording in Deiters' nucleus was achieved using an insulated tungsten microelectrode with an uninsulated tip diameter of approximately 1-2 μm (Frederick Haer, 9-12 MΩ at 1000 Hz, 10^{-8} A). As mentioned above, the microelectrode was advanced or retracted with an electrically-driven microdrive, in steps of 1.25 μm/step.

6. Linear Oscillation Apparatus

The accelerative stimulus was provided by a linear motion device specially designed by Dr. D.G.D. Watt, and constructed in the Aerospace Medical Research Unit at McGill University. The platform with the cat and stereotaxic apparatus was fixed to a carriage. Suitable gimbals and pivot points allowed the cat to be rotated about any axis, through its center of gravity. Pitch and roll are illustrated in Figure 10. The bed upon which the carriage was mounted could also be rotated between 0-90 degrees from vertical. Figure 11 shows how a combination of bed and cat rotation, adjusted prior to oscillation, would allow for linear oscillation in 3 orthogonal directions, with the cat always remaining upright. The oscillation was driven by a servo-controlled 0.5 HP motor (Small Electric Motors Ltd, Servomex motor controller type MC.47), and air-bearings minimized carriage vibration during movement. Different oscillation frequencies and acceleration magnitudes were achieved by readjusting the motor speed and changing stimulus amplitude.

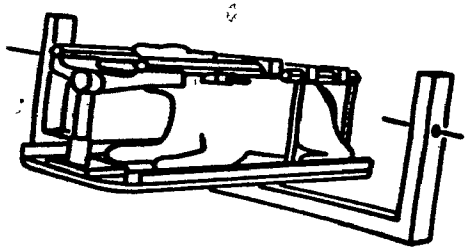
7. Electronic Equipment

The electronic apparatus used for stimulation, recording and data processing is shown in the block diagram of Figure 12. The spinal cord

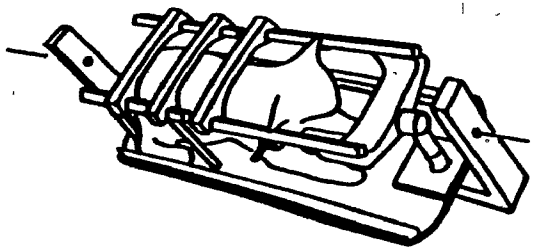
Figure 10

Illustrations of pitch and roll of cat fixed in stereotaxic apparatus, which is attached to the carriage of the linear oscillator. Rotation is through the cat's center of gravity. A, pitch up. B, Roll right (ipsilateral side down). C, Upright. D, Roll left (contralateral side down). E, Pitch down.

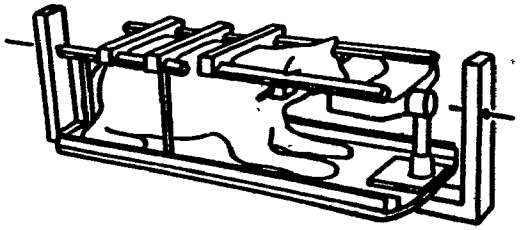
A



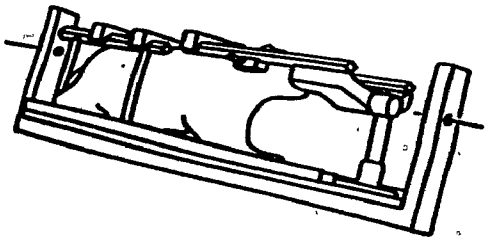
B



C



D



E

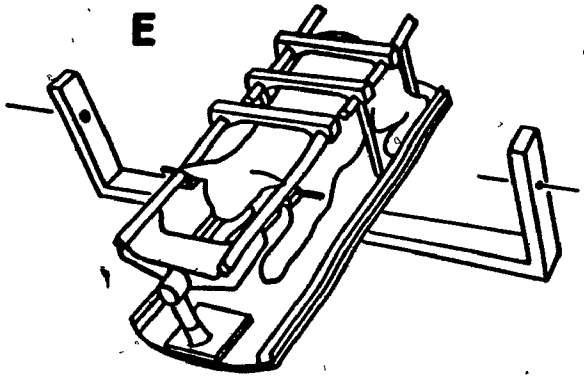
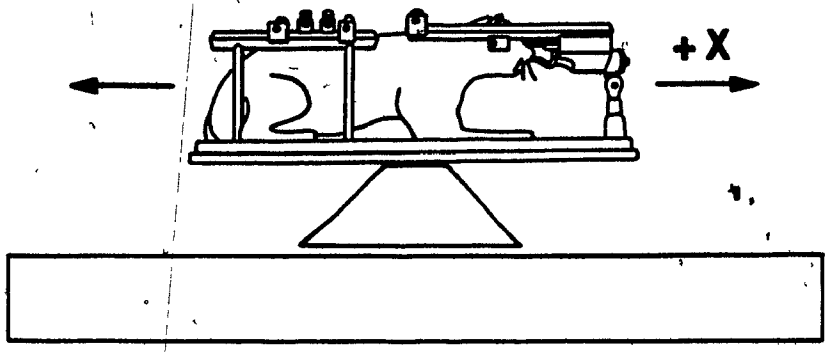
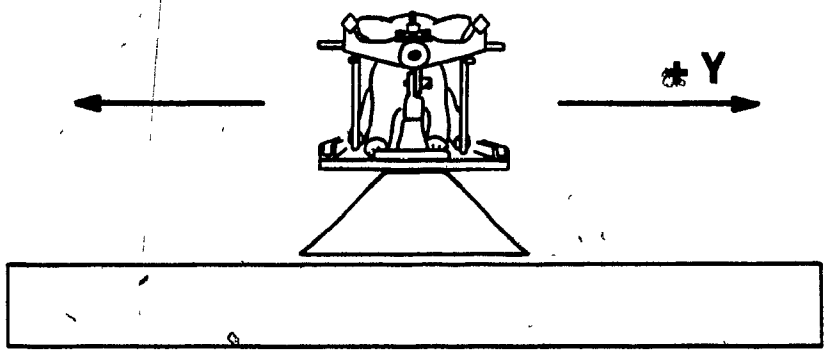


Figure 11

Illustrations of combinations of bed and cat rotation which would allow for linear oscillation in 3 orthogonal directions. Cat always remains upright. Direction of positive acceleration is indicated.


+X


+Y

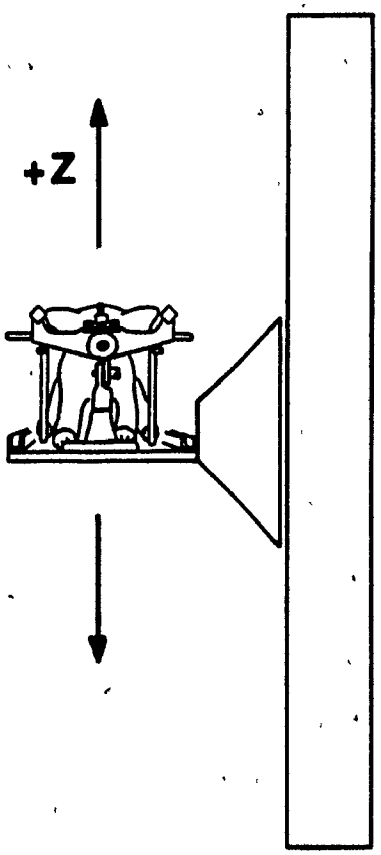
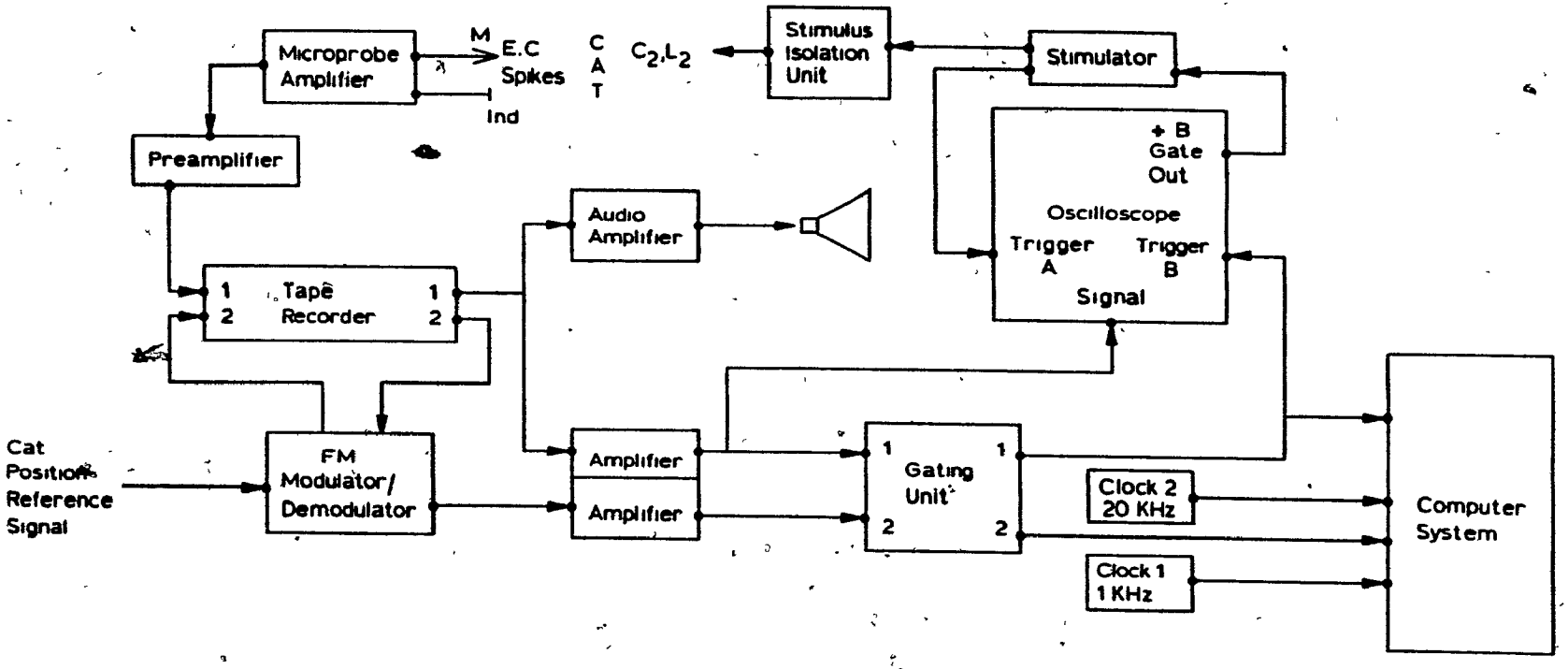

+Z

Figure 12

Schematic diagram of electronic stimulating and recording apparatus. C2,L2 denotes position of stimulating electrodes at the level of the 2nd cervical and lumbar vertebrae. E.C. spikes, extracellular spikes. M, recording microelectrode. Ind, indifferent (ground) electrode. For further description of apparatus, see text.


Microprobe Amplifier
M
E.C
Spikes
Ind
C
A
T
C_2,L_2
Stimulus Isolation Unit
Stimulator
Preamplifier
+ B Gate Out
Oscilloscope
Trigger A
Trigger B
Signal
Audio Amplifier
1
2
Tape Recorder
1
2
Cat Position Reference Signal
FM Modulator/ Demodulator
Amplifier
Amplifier
1
2
Gating Unit
1
2
Clock 2 20 KHz
Clock 1 1 KHz
Computer System

stimulation was generated by one channel of a Grass model S88 stimulator through a stimulus isolation unit (Grass SIU5). A selector switch routed the stimulus to either the cervical or lumbar stimulating electrodes. The stimulator could be run at a predetermined pulse rate or triggered by the extracellular spike.

A microswitch, which was closed as the carriage passed a specific point in the oscillation cycle, was used to provide a position reference signal to the data processor.

Impedance matching of the recording microelectrode to the electronics was achieved using a microprobe amplifier (W-P Instruments, Model 725). The extracellular spikes recorded by the microelectrode were amplified and filtered with a Grass P15 preamplifier (band pass filtered between 30 Hz and 3 kHz). This signal was sent to both an audio speaker (for monitoring of modulation of firing rate of cell), as well to a Tektronix Type 2A63 amplifier. The amplified output was displayed on a Tektronix Type 565 oscilloscope, and passed through a Ferch Electronics gating unit (Model 119). The gated output was used to trigger the oscilloscope display, and provided a series of standardized pulses to the data processing unit.

8. Experimental Procedures

A. Location of Recording Electrode

When preparation of the animal was completed and all the mechanical apparatus was in place, microelectrode tracking began. The microelectrode was inserted to 2 mm above the stereotaxically determined aiming point, which was the center of Deiters' nucleus as described by Snider and Niemer, 1964. While advancing the microelectrode, field potentials produced by the

antidromic stimulus (0.2 ms square pulse, 4-12 volts at 2 Hz) were monitored on the oscilloscope display. Shape and size of the field potentials provided an indication of the location of the microelectrode in relation to Deiters' nucleus. Tilting of the animal resulted in modulation of the background cells' firing rate if vestibular units were nearby. This was monitored through the audio speaker and the number and loudness of the modulating neurons also provided an indication of the relative location of the microelectrode.

The microelectrode was advanced until a position was reached where the extracellular spikes of a single neuron could be discriminated very clearly above the background neural activity and noise.

B. Antidromic Stimulation

Modulation of a cell's firing rate to roll or pitch of the animal indicated vestibular input to the isolated unit. If no modulation of firing rate occurred, a new cell would be isolated. If modulation did occur, antidromic stimulation was then used to determine whether a neuron was a vestibulospinal (V-S) unit. A 0.2 ms square pulse at 2 Hz and varying voltage was used to test the neural unit. The following criteria were used to prove the antidromic character of the evoked spikes (Lipski, 1981): Constant latency of firing, all-or-none firing, the unit's ability to follow a high stimulation rate ($>$ 200 Hz for a very short period of time), and spike collision. Where possible, the refractory period (ms), antidromic latency (ms), and the critical delay (ms) were measured. A collision confidence level, as described by Fuller and Schlag (1976), and Schlag (1978), was calculated using these recorded values. A result $<$ 0.5 would indicate a good confidence of collision.

The original intent of this experiment was to study only otolith-driven V-S units. However, the excellent isolations required in this experiment were quite rare, and V-S units were even more scarce in this sample, so all otolith-driven neurons isolated were studied.

C. Response to Tilt

To determine whether an isolated unit received otolith input, the unit's response to tilt was examined. The animal would be rolled laterally and pitched up and down to determine whether the unit was statically or dynamically sensitive to tilt. Modulation of the firing rate was determined by listening to the spike train played through an audio speaker. The direction of sensitivity (ie, ipsilateral side down, contralateral side down, pitch up or down), was also noted. If the isolated neural unit was deemed to receive otolith input (see RESULTS), a further study of the unit's dynamic response characteristics was undertaken.

D. Standard Test Sequence of Oscillations.

Table 1 shows the complete test sequence of oscillations used during the experiment. The animal would initially be oscillated in the vertical (+Z=up), lateral (+Y=left), and fore-aft (+X=forward) directions at 0.3 Hz. After each run along one axis, the gain (AP/sec/g), phase re acceleration (degrees), maximum firing rate (AP/sec), bias (AP/sec), and variance accounted for (V.A.F., used to indicate how much of the relationship is due to the factors we are comparing, in this case the smoothed, averaged response curve to the stimulus profile) were calculated by the computer. This entailed the fitting of a sine wave to the smoothed, averaged response curve and comparing it to the stimulus profile. The curve was smoothed with

Table 1

Standard Sequence of Oscillation

Axis	Frequency (Hz)	Displacement (cm)	Cycles	Acceleration (g)
Z	0.3	10.0	25	0.0363
Y	0.3	10.0	25	0.0363
X	0.3	10.0	25	0.0363
*	0.2	10.0	25	0.0161
	0.1	10.0	25	0.0040
	0.1	21.5	25	0.0087
	0.2	21.5	25	0.0346
	0.6	2.6	25	0.0377
	1.0	1.0	25	0.0403
	2.0	0.5	25	0.0806
	3.0	0.2-0.3	50	0.0725-0.1088
	4.0	0.2-0.3	50	0.1289-0.1934

* - indicates remainder of sequence used the axis along which cell was most responsive.

an 11 bin Hanning filter (a digital filter which uses a weighted average to smooth out the harmonics of the spectral frequency) and fitted using the method of least squares. Any curves which were "cut-off" (see RESULTS) were fitted only over that portion of the cycle during which the cell was actively firing.

The objective at this point was to obtain data which would allow the determination of the direction in 3-dimensional space along which the cell was most sensitive to linear acceleration (the functional polarization vector, FPV). The actual vector was calculated after the experiment. For the remainder of testing, the animal was oscillated along the axis (X, Y, or Z) providing the greatest modulation of cell firing. The threshold and dynamic response of the cell were determined by varying the amplitudes and frequencies of oscillation. Frequencies ranged between 0.1 Hz and 4.0 Hz. These limits were determined by the desire to cover the widest possible range of frequencies, bounded by the threshold of acceleration sensitivity at the low end and the ability to control small displacements of the oscillation apparatus at the high end. After each oscillation run, the gain, phase and other parameters were determined by the computer.

Approximately 2.5 hours were required to perform all tests on one cell. Upon completion of full runs, or if the cell was lost prematurely, a new cell was isolated and the entire procedure repeated. A single experiment could last upwards of 17 hours, usually limited by the neurons becoming too sensitive to direct mechanical stimulation.

9. Histological Procedures

At the termination of all but four experiments, the animal was perfused with 100 ml of Perfix (Fisher) via the carotid artery cannula. The brain was removed and the level and condition of the decerebration were determined by visual inspection.

The location of the microelectrode aiming point was determined histologically in the remaining four experiments during which 12 cells were studied. Prior to the termination of the experiment, a stainless steel microelectrode was substituted for the tungsten recording electrode and inserted into the presumed center of Deiters' nucleus. A 1 mA current was passed through this microelectrode for 20 seconds, leaving minute iron deposits in the tissue (this was not possible with the original tungsten electrode). The animal was then given a euthanizing dose of pentobarbital (Somnotol, M.T.C. Pharmaceuticals). The thorax was opened, the descending aorta clamped, the right atrium cut, and perfusion through the left ventricle of 500 ml of saline followed by 600 ml of a potassium ferri/ferrocyanide solution was carried out. This solution was used to develop a visible blue spot at the site of the iron deposits. The appropriate section of the brainstem was cut under stereotaxic control and removed. It was eventually stored in a 30% sucrose/formalin solution for up to 3 months.

Serial frozen sections of the brainstem were cut transversely at 40 μm thickness. Sections were mounted on gelatin-coated slides and stained with a cresyl violet solution. The blue spots were then located under a microscope, and their position noted.

IV RESULTS

1. Anatomical Distribution of Cells

A total of 39 central vestibular neurons were isolated and studied. Of these, 32 units received input from the otolith organs while 7 units were suspected of receiving input from the semicircular canals (Fig. 13). Of the 32 units that received otolith input, the data from 5 cells were discarded due to gradually deteriorating signal to noise ratio or modulation of spike amplitude during oscillation (see DISCUSSION).

As explained in METHODS, the brainstems of 4 cats were marked stereotaxically for histologic examination (Fig. 14). The coordinates of the microelectrode tip were recorded for each isolated cell and during placement of the electrolytically-produced spot. After the experiment, the location of the blue-green spot was determined by microscopic examination and the position of the cells isolated in that brainstem were calculated relative to the coordinates of that spot. Anatomical landmarks within the brainstem were identified with reference to Snider and Niemer (1964), and Berman (1968).

The locations of 12 cells were confirmed histologically. 11/12 cells were otolith-dependent, with 1/12 cells being canal-dependent. Figure 15 is a pictorial representation of the location of these 12 cells within Deiters' nucleus, where each circle represents the location of one cell and each asterisk represents one electrolytically-placed blue-green spot. All 12 cells were located within Deiters', primarily in the dorsal region of the nucleus. In one instance, the spot was located just anterior to the

Figure 13

Summary of cells isolated and studied.

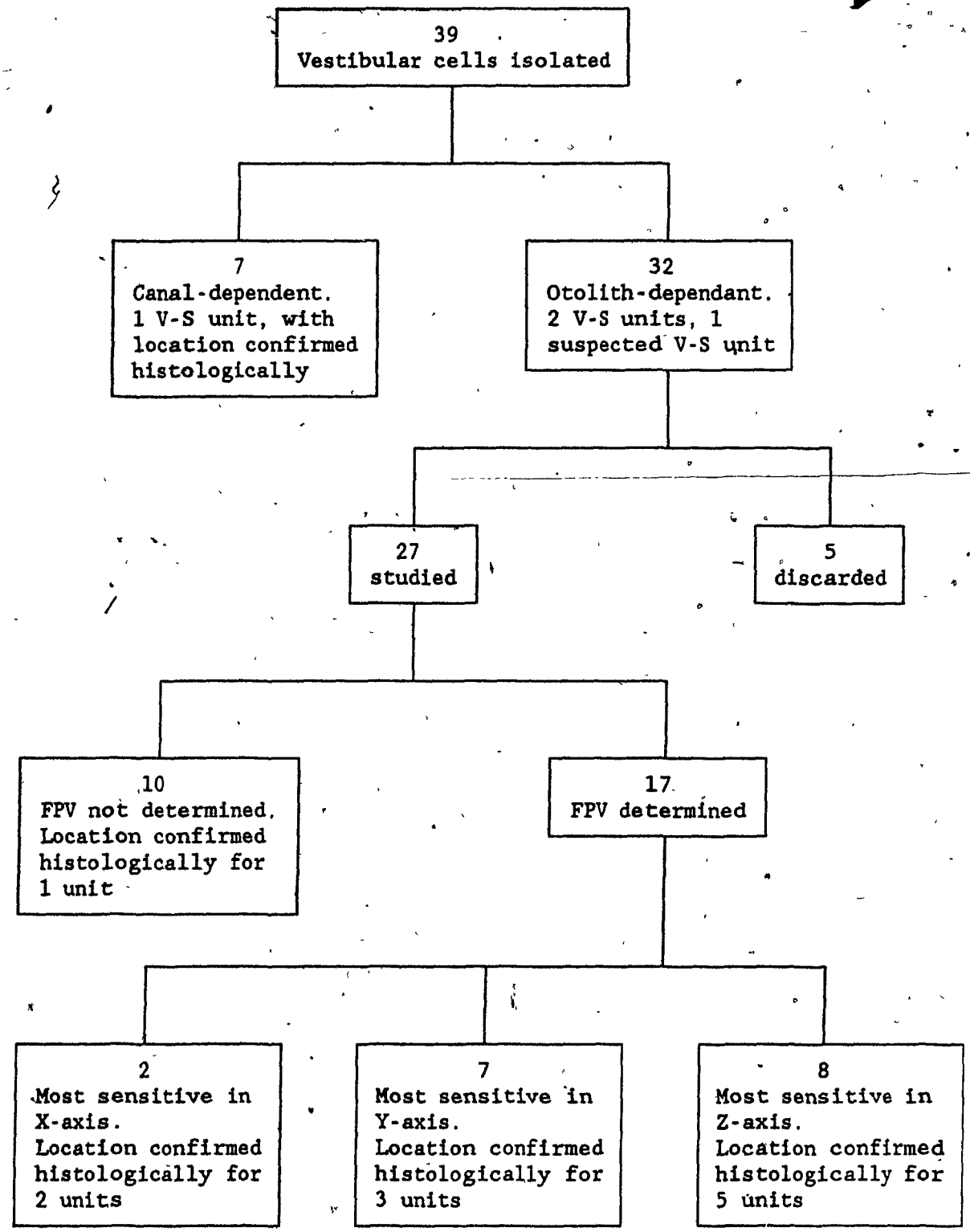

39
Vestibular cells isolated
7
Canal-dependent.
1 V-S unit, with
location confirmed
histologically
32
Otolith-dependant.
2 V-S units, 1
suspected V-S unit
27
studied
5
discarded
10
FPV not determined.
Location confirmed
histologically for
1 unit
17
FPV determined
2
Most sensitive in
X-axis.
Location confirmed
histologically for
2 units
7
Most sensitive in
Y-axis.
Location confirmed
histologically for
3 units
8
Most sensitive in
Z-axis.
Location confirmed
histologically for
5 units

Figure 14

Microphotographs of transverse section of brainstem at level of caudal Deiters' nucleus.

A. Location of electrolytically placed spot (arrow) on lateral edge of Deiters' nucleus.

B. Close-up of spot (arrow) within Deiters' nucleus. Same spot as in A. Note giant cell bodies, which are characteristic of Deiters' nucleus.

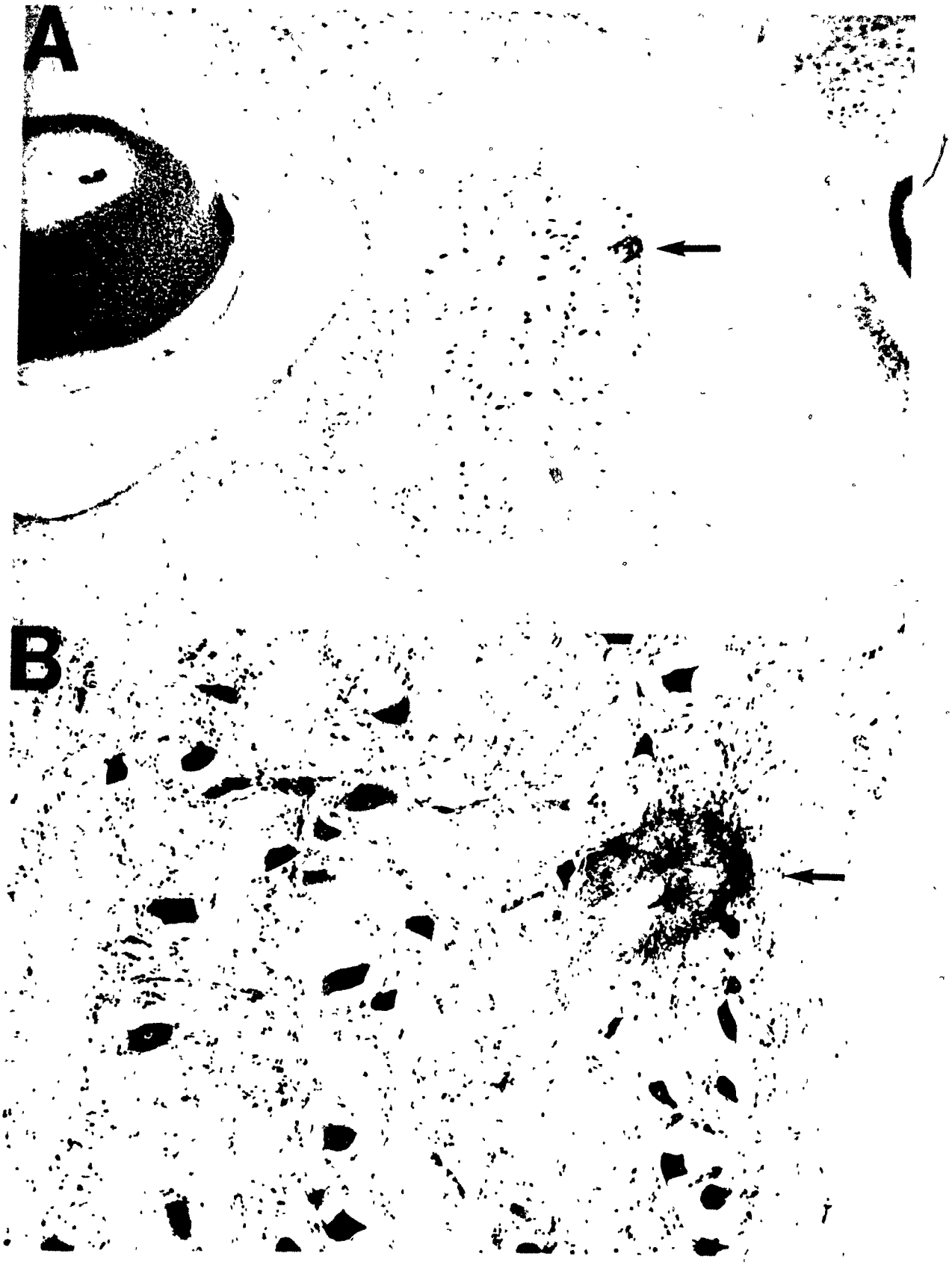

A
B

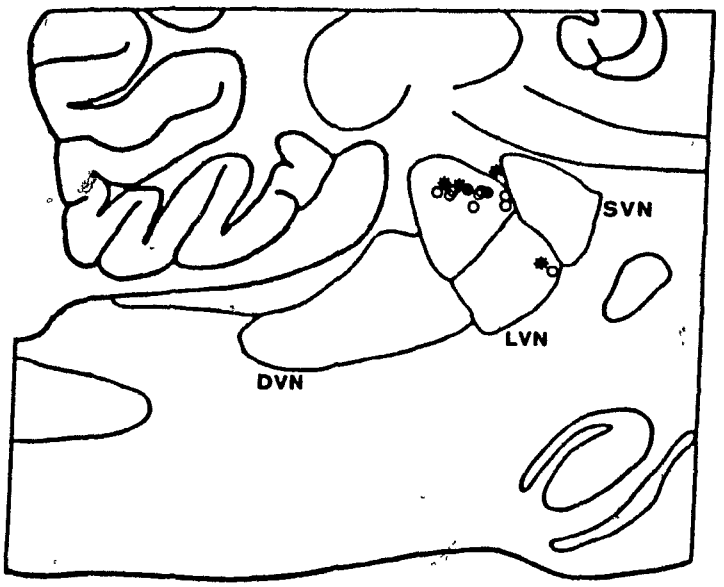
Figure 15

Diagrams indicating approximate locations of 12 units within Deiters' nucleus. Each section represents a small segment in that region of the brainstem, and not a specific slice at that level. Electrode track is inclined 30° from vertical. ✱ , denotes electrolytically placed spot. ● , V-S units. ○ , non-VS units. Crossed circles indicate units located very close to each other.

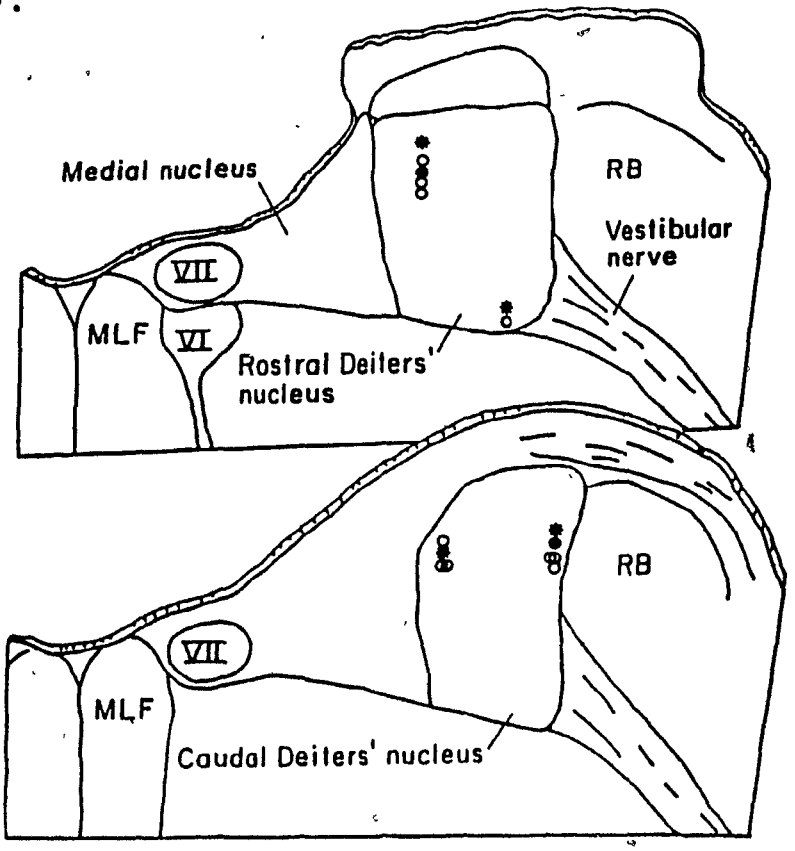
A. Sagittal view of the location of spots and cells in and around Deiters' nucleus. Note that in one instance the spot is located anterior to Deiters'. However, all units recorded in this case were located posterior to the spot, within the nucleus. SVN, superior vestibular nucleus. DVN, descending vestibular nucleus. Deiters' (LVN) is divided into dorsal and ventral divisions (adapted from Chan et al., 1985).

B. Transverse sections showing locations of spots and cells in and around rostral (top) and caudal (bottom) Deiters'. Spot located in the dorso-medial region of rostral Deiters' is actually anterior to the nucleus (i.e. out of the page). RB denotes restiform body. MLF, medial longitudinal fasciculus. VI, abducens nucleus. VII, motor nucleus of the facial nerve (adapted from Peterson, 1969).

A.


SVN
LVN
DVN

B.


Medial nucleus
RB
Vestibular nerve
VII
MLF
VI
Rostral Deiters' nucleus
RB
VII
MLF
Caudal Deiters' nucleus

nucleus. However, the cells isolated in this case were found 1-2 mm posterior to the spot, placing them within Deiters'.

2. Identification of Vestibulospinal Units

All cells isolated in this experiment were classified according to their response to antidromic stimulation of the LVST. A total of 3 isolated cells were considered to be likely V-S units, with 1 of these cells thought to be receiving input only from the semicircular canals. All 3 demonstrated a constant antidromic latency, with all-or-none firing and the ability to follow a high stimulation rate (> 200/sec) for a short period of time. Collision appeared to be evident on the oscilloscope display. One additional cell was suspected of being a V-S unit, however due to many nearby actively firing cells this could not be demonstrated conclusively. All 4 units appeared to project only to the cervical level of the spinal cord, as none were driven antidromically from the lumbar level of the spinal cord.

3. Responses to Tilt

Isolated neurons responded to tilting of the animal (in roll or pitch) with either a modulation of that unit's firing rate, or no reaction at all. If no modulation was observed, the unit was deemed not to receive a vestibular input. If modulation of the firing rate was observed, the direction of change for specific tilts was noted. All extracellular recordings in these experiments were from the right LVN, hence ipsilateral side down denotes right side down.

Two types of otolith-dependent neurons were observed in this experiment. In one group, the neurons were sensitive to static tilt, as their firing rates continued to be altered as long as there was a deviation from the upright position. It should be noted that although these neurons are said to be sensitive to static tilt, they were not purely statically sensitive units. When the animal was tilted (in roll or pitch), an even greater modulation of the firing rate occurred as soon as there was a deviation from the upright, i.e. during the roll or pitch itself and not just when a static tilt was maintained. The firing rate of the second group of observed neurons returned to its resting value whenever the tilt (roll or pitch) remained unchanged for a short period of time. These neurons, which possessed no static sensitivity, were called dynamic units.

Table 2 indicates the number of isolated otolith-dependent cells which were classified as static or dynamically sensitive, as well as the relative numbers which responded with an increased firing rate to either ipsilateral or contralateral tilt and pitch up or down. Roughly equal numbers of units were classified as static (14/27) and dynamically (11/27) sensitive to tilt, with 2 units unclassified. Of these classified units, most were excited by ipsilateral side down tilt (23/25). Twice as many classified units responded with an increase in their resting firing rate to pitch down (15/25) as to pitch up (8/25), with 2 other units' responses to pitch uncertain.

One interesting observation was that of the two units that responded in a facilitatory manner to contralateral side-down tilt, one was an identified V-S unit and the second was suspected of being a V-S unit. (An additional V-S unit, which was presumed to be canal-dependent and was

Table 2

Responses of otolith-dependent neurons in Deiters' nucleus to tilt

	Total	Static	Dynamic
No. of Units	27	14	11
Ipsi. Tilt	23	12	11
Contra. Tilt	2	2	-
Tilt Unclassified	2	-	-
Pitch Up	8	5	3
Pitch Down	15	7	8
Pitch Unclassified	4	-	-

Values indicate number of cells classified in each category determined by the cell's sensitivity to tilt. Cell categorized according to an increase in its firing rate in response to stimulus. Ipsi.: ipsilateral (right) side down. Contra.: contralateral (left) side down. See text for explanation of static and dynamic behaviour.

therefore not included in the data analysis, was also excited by contralateral tilt.)

4. Dynamic Response Characteristics

A. Response Patterns

(i) Canal-dependent Units. As explained above, the response of an isolated cell to either static or dynamic tilt could be determined by exposing the animal to roll or pitch. If a unit was found to possess static sensitivity it had to be receiving an otolith input, since the semicircular canals are not expected to respond to static tilt (Goldberg and Fernandez, 1975; however, see Discussion, page 82). However, a 'dynamic' unit could in fact be receiving input from the otoliths, the canals, or both. To resolve this doubt the animal was oscillated in the 3 orthogonal directions, and the cell's response determined. Given that a pure linear acceleration stimulus was used, no response would be expected from a canal-dependent neuron. Figure 16 shows just such a lack of response in a 'dynamic' cell. This cell was thus presumed to be a canal-dependent unit and was not studied further.

(ii) Otolith-dependent Units. Isolated Deiters' nucleus neurons receiving an otolith input produced 3 different response patterns to the linear oscillations (Fig. 17). The largest number (15/27) demonstrated a highly sinusoidal response, while a smaller group (9/27) showed a somewhat distorted pattern. A small minority of units (4/27, including 2 distorted response units) exhibited a cut-off in their response. Presumably this was due to the cell being driven below its threshold, resulting in it being silent for part of the oscillation cycle. The response would have been

Figure 16

Response patterns for an isolated unit sensitive to dynamic tilt, oscillated in the 3 orthogonal axes. Sine wave fitted onto response curve using method of least squares. Lack of response in each axis indicates that this unit probably received input from the semicircular canals. Combined cell and test run number, direction of oscillation, frequency, displacement and acceleration level are indicated to the right of each plot.

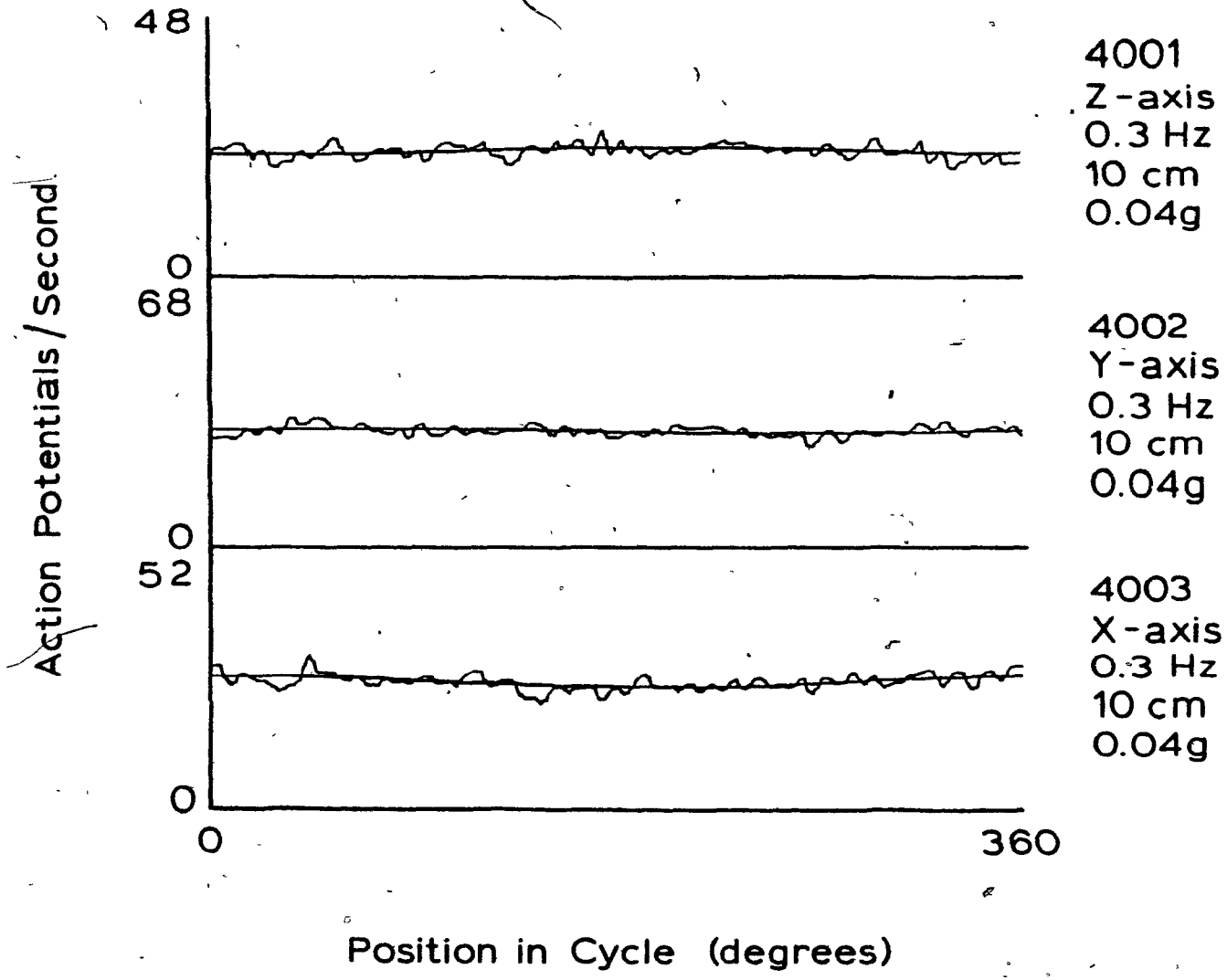
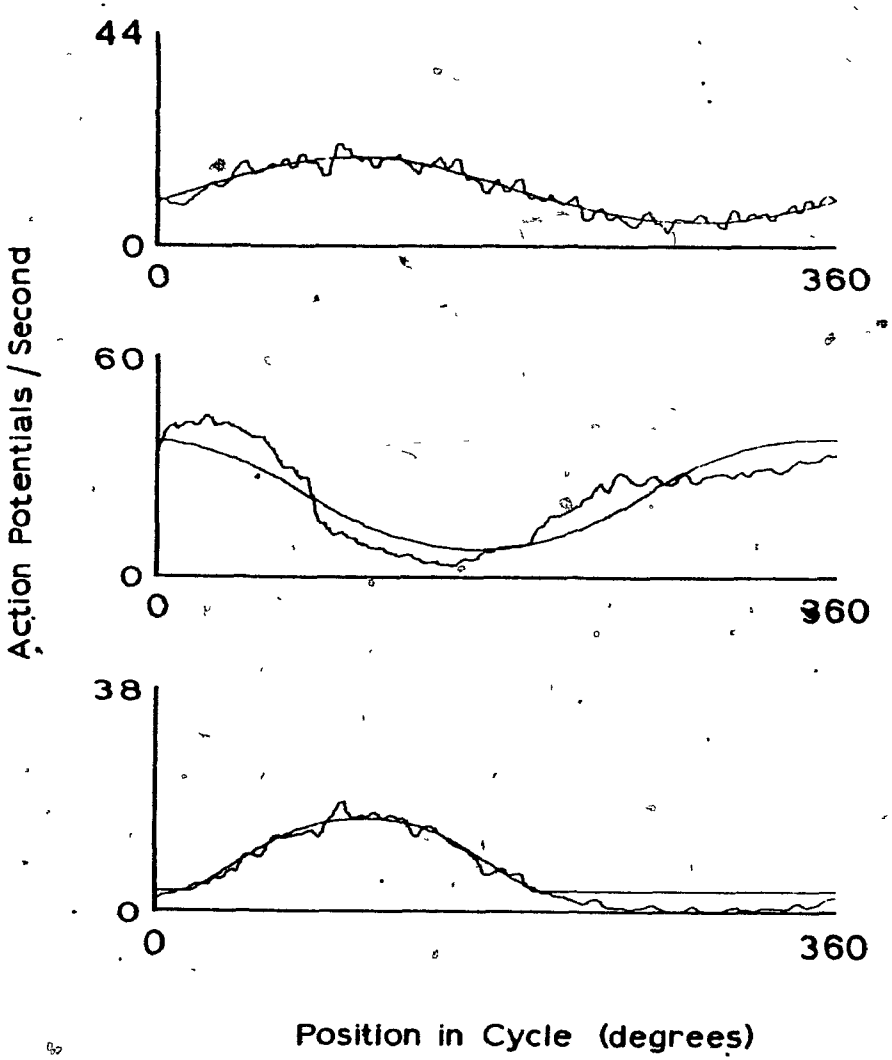

48
0
68
0
52
0
0
360
Action Potentials / Second
Position in Cycle (degrees)
4001
Z-axis
0.3 Hz
10 cm
0.04g
4002
Y-axis
0.3 Hz
10 cm
0.04g
4003
X-axis
0.3 Hz
10 cm
0.04g

Figure 17

Response patterns observed in otolith-dependent units (top to bottom): symmetrical, distorted and cut-off. Sine wave fitted using method of least squares. To fit a cut-off response curve, a sine wave was fitted over that portion of the cycle during which the cell was actively firing. Each response was recorded from a single unit during oscillations of 0.04 'g' at 0.3 Hz. Note lower V.A.F. value for distorted response, as well as low bias for cut-off response.


44
0
0
360
Gain = 190 (AP / sec / g)
Bias = 12 (AP / sec)
Phase = -15 (deg)
V.A.F. = 0.934
60
0
0
360
Gain = 411
Bias = 23
Phase = 102
V.A.F. = 0.773
38
0
0
360
Gain = 325
Bias = 4
Phase = -20
V.A.F. = 0.938
Action Potentials / Second
Position in Cycle (degrees)

sinusoidal in nature had the threshold not been reached. The location of each of the 3 units in Figure 17 was confirmed histologically to be within Deiters' nucleus.

The mean bias (resting firing rate) of cells studied was 24 ± 2 AP/sec, S.E. This resting firing rate is within the ranges observed by Wilson et al (1966), Schor (1974) and Boyle and Pompeiano (1980). The bias of cells which responded with a symmetrical pattern was significantly larger than the bias of cells which responded with a distorted pattern ($P < 0.05$) or cut-off pattern ($P < 0.05$).

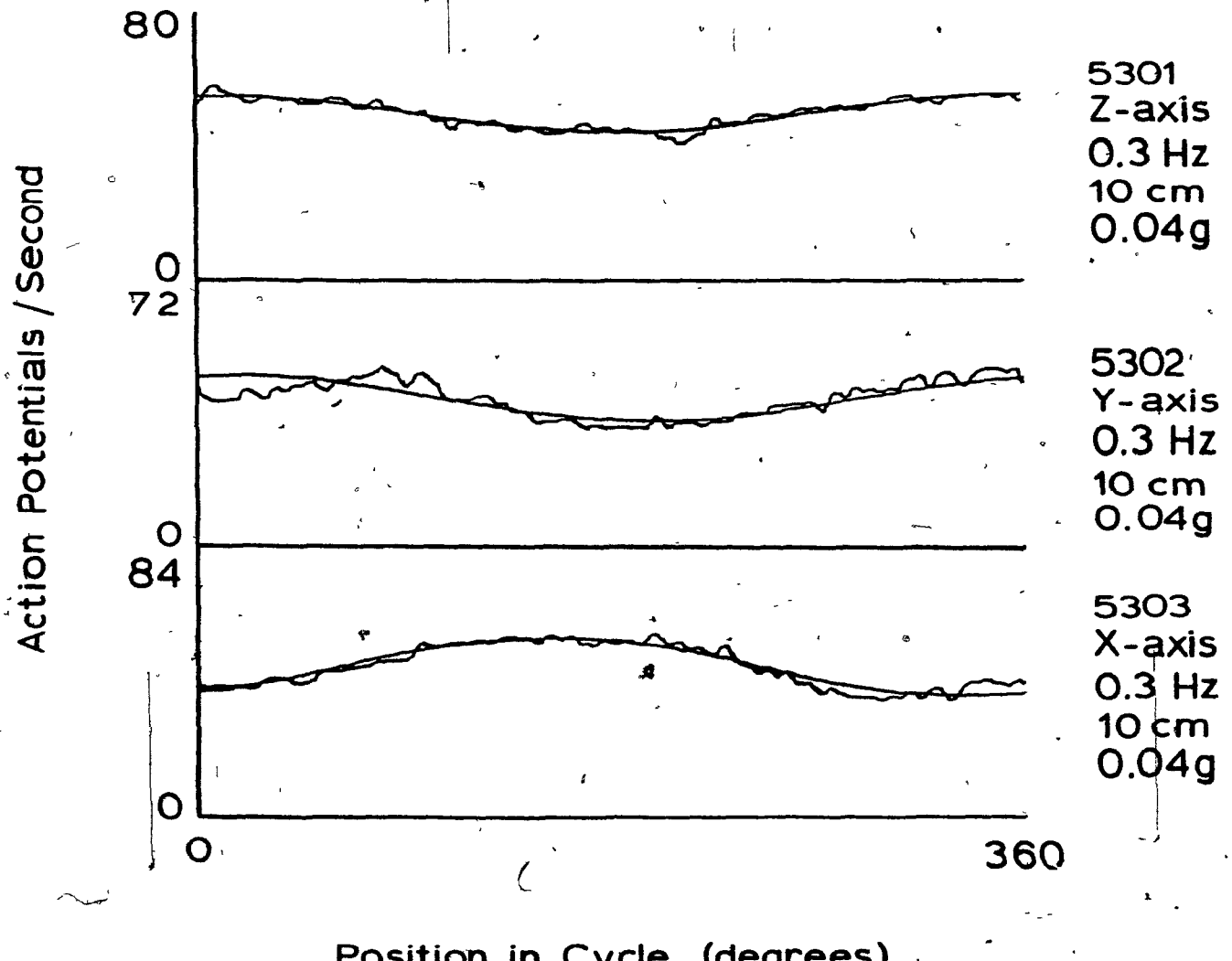
The statistical method used above and in the following sections was the Student-t test (Duncan et al., 1983). The P-value indicates the probability that the difference between the paired values is due to chance alone.

B. Determination of most sensitive axis

Initially, oscillation at a single frequency in the three orthogonal directions (see Table 1) was used to determine the axis along which the cell was most responsive. This axis was found in 18/27 isolated cells. In 9 cases, this was not accomplished as the cell was lost after oscillating along 1 or 2 axes. Maximum sensitivity was seen primarily along the Z (9/18) and Y (7/18) axes, with a small number showing greatest sensitivity along the X axis (2/18). Figure 18 shows a representative example of one unit's responses to the accelerative stimuli in the 3 orthogonal directions. This unit's location in Deiters' nucleus was confirmed histologically. The curve was smoothed with an 11 bin Hanning filter, and the result was plotted on an X-Y plotter (Hewlett Packard X-Y Recorder, Model 7041A). As can be clearly seen, this cell was most responsive to

Figure 18

Responses of an otolith-dependent unit to oscillation in the 3 orthogonal directions. Sine wave fitted by method of least squares. This cell was most responsive to linear acceleration in the X axis. Identification number, direction of oscillation, frequency, displacement and acceleration level are indicated to the right of each plot. The location of this unit in Deiters' nucleus was confirmed histologically.


80
0
72
0
84
0
0
360
Action Potentials / Second
Position in Cycle (degrees)
5301
Z-axis
0.3 Hz
10 cm
0.04g
5302
Y-axis
0.3 Hz
10 cm
0.04g
5303
X-axis
0.3 Hz
10 cm
0.04g

linear acceleration in the X axis. This was confirmed by comparing the gain and V.A.F. values that were computed for each axis after every oscillation run. To complete the test sequence, all further oscillations were conducted along the axis of maximum sensitivity, as determined above.

C. Functional Polarization Vector

(i) Calculation. Each cell can be said to have a direction of preferred response, or functional polarization vector (FPV). Following a successful oscillation run in each of the 3 orthogonal directions, the gains and phases of the cell's responses were determined (see METHODS). Each gain value was used as the magnitude of a vector for that axis. The vectors were assigned a directional sign (+ or -) according to the phase lag or lead of the response (i.e., up to ±90° would indicate a (+) direction). As will be discussed in a subsequent section, the phase curve over the range of frequencies used in the oscillations was relatively flat. Thus the phase should provide a correct indication of the directional sign of the response of a given cell.

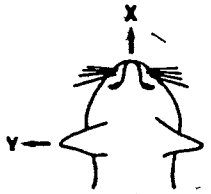
The gain and phase measurements along each axis were summed vectorially to determine the FPV of the cell. The locations of 7/18 units within Deiters' nucleus were confirmed histologically.

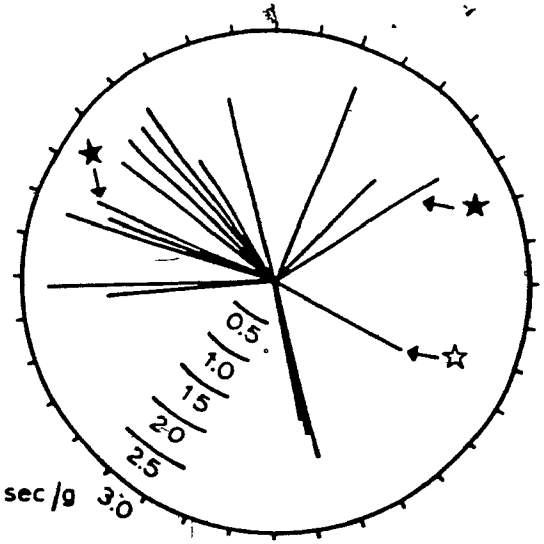
(ii) Distribution. In order to visualize the distribution in 3-dimensional space of the FPVs of isolated otolith-dependent neurons, polar coordinate plots were constructed (Fig. 19). The 3 graphs represent projections of the FPVs onto the horizontal (X-Y), frontal (Z-Y), and mid-sagittal (Z-X) planes. The magnitude of each vector represents the gain of the response on that plane, and the direction is that of maximum sensitivity of the cell.

Figure 19

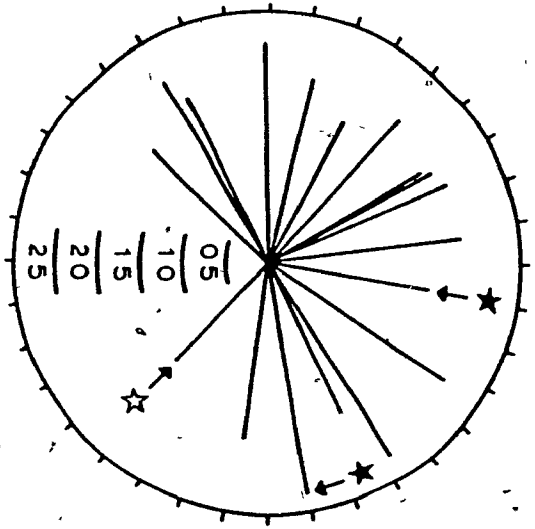
Distribution of 18 Deiters' nucleus units' polarization vectors as projected onto (clockwise from top) the horizontal (X-Y), frontal (Z-Y), and mid-sagittal (Z-X) planes. Spacing of tick marks is 10°. Arrows beside cat heads indicate direction of positive acceleration along that axis. Direction of vector is that of maximum sensitivity of the cell, and magnitude represents the response gain in that direction on that plane. Calibration marks indicate gain in terms of Log (AP/sec/g).

★ denotes V-S units. ☆, suspected V-S unit.

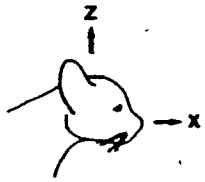


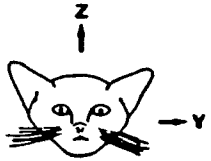


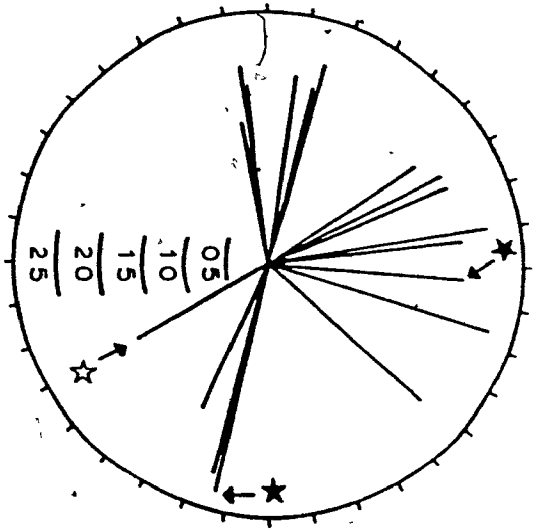
Log AP/sec/g



Log AP/sec/g







In order to confirm that the assigned phases and hence directional sensitivities were correct, the FPVs determined during oscillation were compared with the cells' responses to tilt. In most instances, the static response to both roll and pitch could be predicted from the FPV. In a few cases, however, the vector was so close to the sagittal or frontal plane that the cell responded equally to roll right or left, or pitch up or down, respectively.

The FPVs appear to have a relatively broad distribution in space. In the horizontal (X-Y) plane there is also a hint of vector concentration along diagonal axes close to the planes of the vertical canals (Melvill Jones and Daunton, 1973; Daunton and Melvill Jones, 1982), though with the small sample size this cannot be stated with certainty.

(iii) Correction of data. The response gain of individual neurons was measured while the animal was oscillated at several frequency/amplitude combinations along the X, Y, or Z axis. Since each otolith-dependent cell is most sensitive to linear acceleration along its FPV, however, these values would have been greater had they been obtained while with the animal was being oscillated along that vector (Melvill Jones & Milsum, 1969; Loe et al, 1973). In order to correct for this error, the gain values for 18/27 units were trigonometrically adjusted to compensate for the difference in orientations of the FPV and the most sensitive axis. This adjustment was made by dividing the gain measured along the most sensitive axis by the sine of the angle made by the FPV and the plane perpendicular to the most sensitive axis.

Nearly all further analyses of the dynamic response characteristics were conducted using the corrected data from these 18 units. Threshold measurements were not adjusted, however, since they constituted rough and rather arbitrary estimates at best.

D. Threshold

The approximate threshold of each cell was determined by visually inspecting the average response curves and noting at which acceleration level modulation of the cell firing rate ceased (Fig. 20). Average threshold for these isolated cells was about 0.004 'g'. Comparing the variance accounted for of each fitted curve also helped confirm the threshold; a V.A.F. < 0.4 generally indicated a lack of modulation of the cell's response.

E. Effects of Acceleration Amplitude on Response Phase and Gain

To determine whether the response of the system is dependent on the stimulus magnitude, each isolated cell was studied at 0.1 Hz or 0.2 Hz with oscillation amplitudes of 10 and 21.5 cm, when feasible. The two gain and phase measurements were then compared at each stimulus frequency. Figure 21 shows such a comparison for 10 units tested at 0.1 Hz, and 8 units at 0.2 Hz. At a frequency of 0.1 Hz, there is a significant difference between the response gain ($P < 0.02$) and phase ($P < 0.02$) at the two acceleration amplitudes. It is important to note, however, that as mentioned above the average threshold of the cells was approximately 0.004 'g'. Therefore the responses seen at this acceleration level may not be representative, as many of the cells were at or below their thresholds. In contrast, at a frequency of 0.2 Hz, there is no significant difference

Figure 20

Determination of threshold by varying acceleration at low oscillation frequencies. Acceleration level at which modulation of the cell firing rate ceased was considered the approximate threshold of the cell. Threshold for this unit appeared to be between 0.009-0.02 'g'. Same cell, and data presented as in Figure 18.

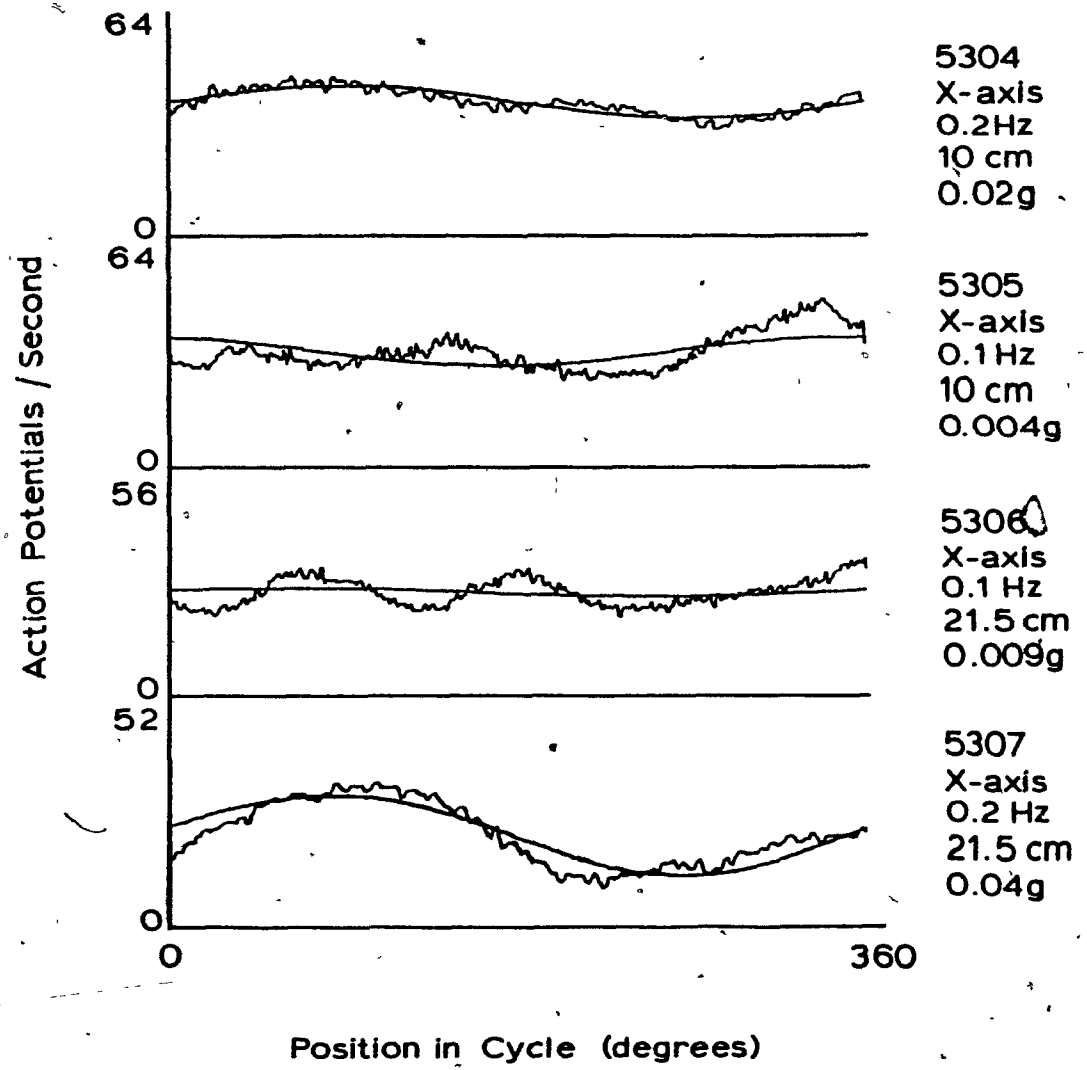
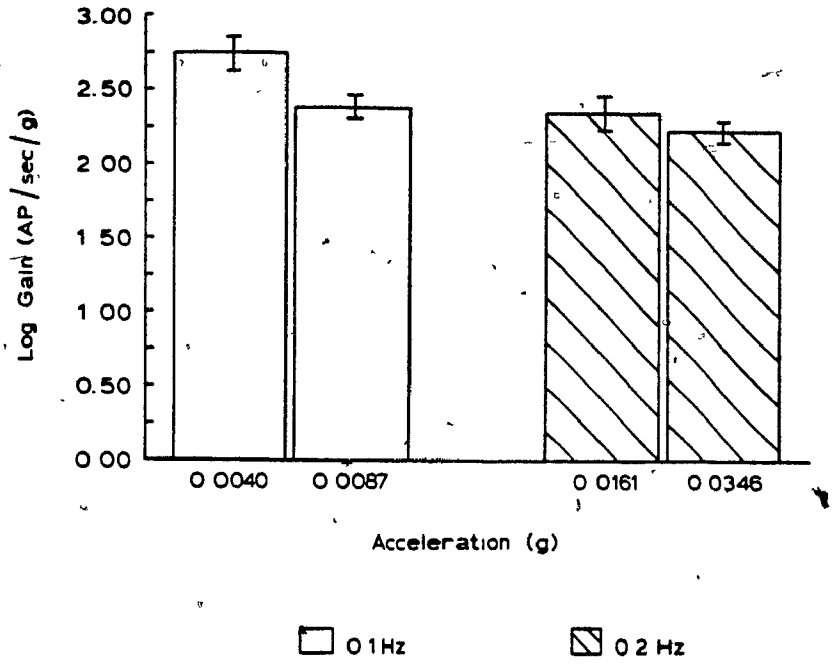

64
0
64
0
56
0
52
0
0
360
Action Potentials / Second
Position in Cycle (degrees)
5304
X-axis
0.2Hz
10 cm
0.02g
5305
X-axis
0.1Hz
10 cm
0.004g
5306
X-axis
0.1 Hz
21.5 cm
0.009g
5307
X-axis
0.2 Hz
21.5 cm
0.04g

Figure 21

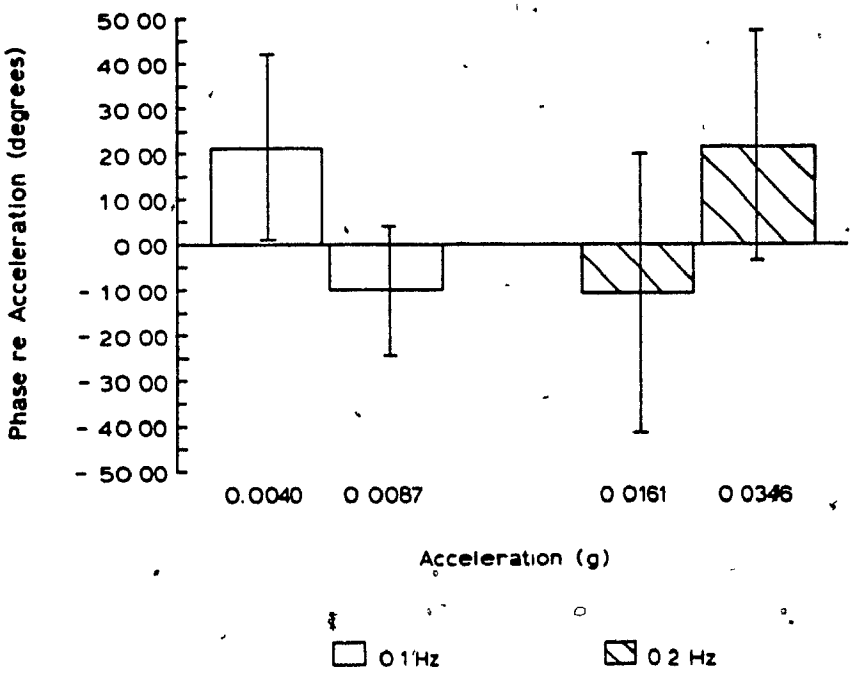
Comparison of the effects of change in acceleration amplitude on response gain (A) and phase (B).

10 units studied at 0.1 Hz, 8 units studied at 0.2 Hz. Note that some units are at or below threshold at 0.1 Hz. Error bars indicate ±1 standard error of the mean.

A


3.00
2.50
2 00
1 50
1 00
0.50
0 00
Log Gain (AP/sec/g)
0 0040
0 0087
0 0161
0 0346
Acceleration (g)
0 1 Hz
0 2 Hz

B


50 00
40 00
30 00
20 00
10 00
0 00
- 10 00
- 20 00
- 30 00
- 40 00
- 50 00
Phase re Acceleration (degrees)
0.0040
0 0087
0 0161
0 0346
Acceleration (g)
0 1 Hz
0 2 Hz

between the response gain ($P > 0.2$) and phase ($P > 0.4$) measured at the two stimulus amplitudes. This suggests that the response of the system is independent of the magnitude of stimulus (Schor, 1974; Xerri et al, 1987).

F. Effects of Acceleration Frequency on Response Phase and Gain

Each isolated otolith-dependent neuron was tested by oscillating the animal at increasing frequencies, from 0.1 Hz up to and including 4.0 Hz when feasible. Figure 22 depicts a representative example of one cell's responses to such an oscillation run, in this case with a frequency range of 0.1-3.0 Hz (same cell as in Fig. 18 & 20). In general, there was a consistent symmetrical response while the cell was above threshold.

The response of a system to varying stimulus frequencies can be expressed as Bode plots, in which gain and phase of the response are displayed as a function of frequency. A trend of decreasing gain with increasing stimulus frequency can be seen quite clearly in Figure 23a. This decrease is significant over the range of 0.1-3.0 Hz ($P < 0.05$). (There was no significant change in gain between 0.1-4.0 Hz ($P > 0.7$). As only 3 units were oscillated at 4.0 Hz, however, it cannot be said whether this result shows an actual trend of increasing gain at these higher frequencies, or whether it is a statistical anomaly due to the extremely limited number of data points at this frequency.)

Figure 23b plots response phase as a function of frequency. There is no significant change in phase over the entire frequency range of 0.1 and 4.0 Hz ($P > 0.1$). One unusual unit had a consistent phase shift of approximately 180°, indicating that it would respond maximally to an

Figure 22

Response of single unit to oscillations of 0.1-3.0 Hz. Same cell, and data presented as in Figure 18.

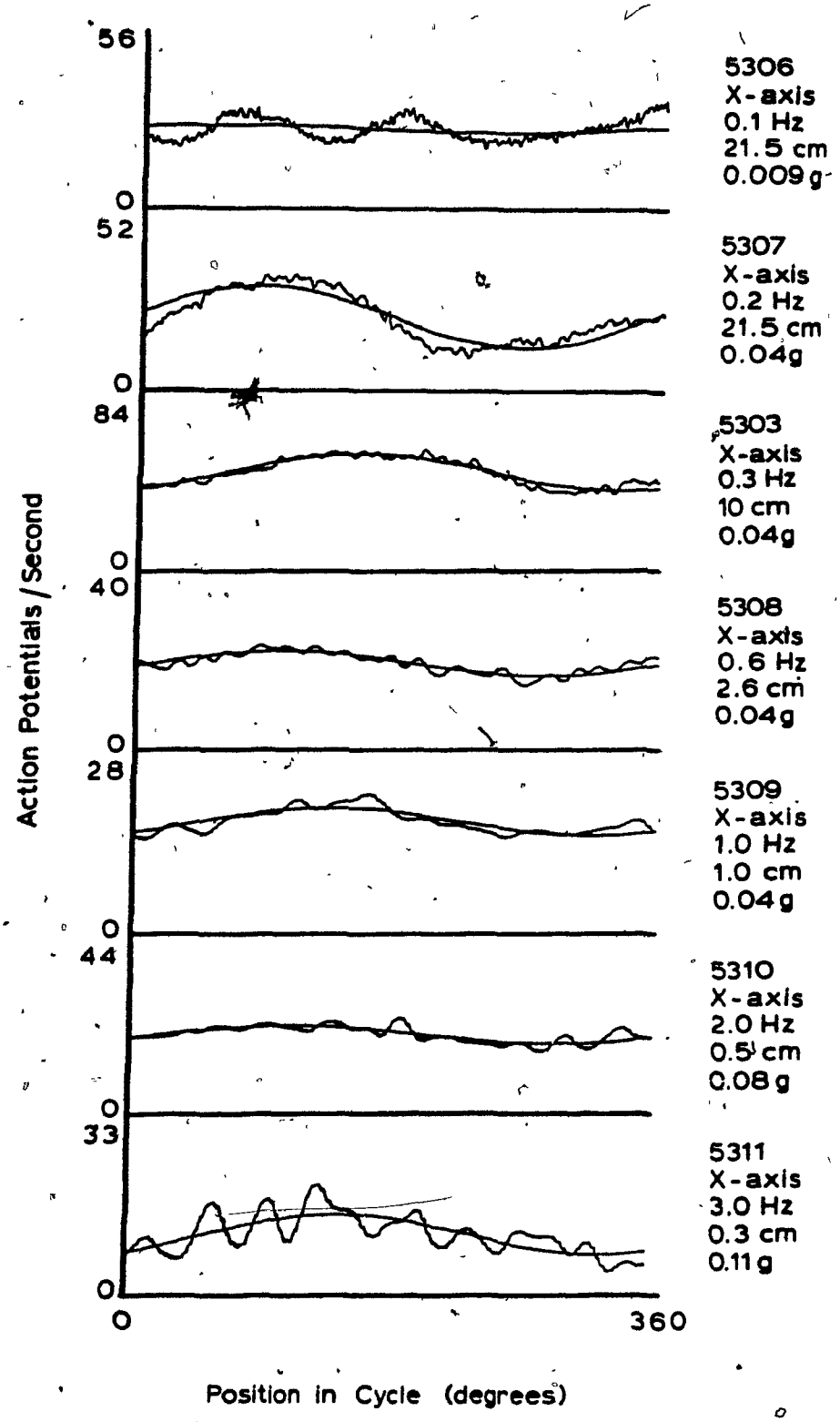

56
0
52
0
84
0
40
0
28
0
44
0
33
0
0
360
Action Potentials / Second
Position in Cycle (degrees)
5306
X-axis
0.1 Hz
21.5 cm
0.009 g
5307
X-axis
0.2 Hz
21.5 cm
0.04g
5303
X-axis
0.3 Hz
10 cm
0.04g
5308
X-axis
0.6 Hz
2.6 cm
0.04g
5309
X-axis
1.0 Hz
1.0 cm
0.04g
5310
X-axis
2.0 Hz
0.5 cm
0.08 g
5311
X-axis
3.0 Hz
0.3 cm
0.11 g

Figure 23

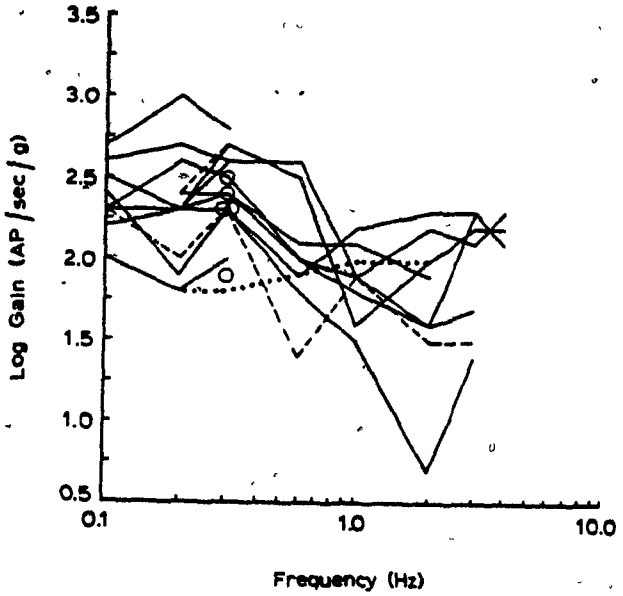
Gain and phase plotted as a function of oscillation frequency for 18 Deiters' nucleus units.

Dashed lines denote V-S units. Dotted line, suspected V-S unit. ○, units oscillated at just one frequency (0.3 Hz). Crossed circles indicate units with similar gain values.

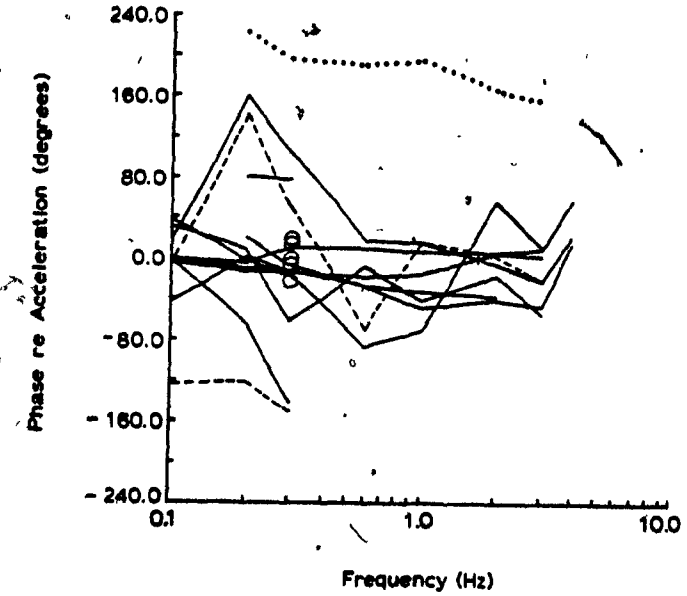
A. Response gain as a function of stimulus frequency. Attenuation of gain with increasing frequency (up to 3.0 Hz) is statistically significant ($P < 0.05$).

B. Response phase (re acceleration) as a function of stimulus frequency. Note relatively flat phase behaviour. As well, one unit had a consistent phase shift of approximately 180°.

A


3.5
3.0
2.5
2.0
1.5
1.0
0.5
Log Gain (AP/sec/g)
0.1
1.0
10.0
Frequency (Hz)

B


240.0
160.0
80.0
0.0
-80.0
-160.0
-240.0
Phase re Acceleration (degrees)
0.1
1.0
10.0
Frequency (Hz)

accelerative stimulus in the opposite direction to most other cells. It should also be noted, however, that this unit had one of the lowest gains measured, and a particularly low V.A.F. along all axes.

V DISCUSSION

1. Evaluation of Methods

Before discussing the results presented in the previous chapter, limitations imposed by the methods employed in this experiment will be considered. Single cell extracellular activity was recorded from decerebrate cats. This well-established procedure was adopted since it was expected to give results that could be related to previously available information on vestibular neuron response. It is understood, however, that since decerebration results in the transection of major CNS tracts, the neural activity in a decerebrate cat could differ from that of a normal alert animal.

A. Anaesthesia

(i) Introduction. It is known that different anaesthetics can have various effects on the CNS. Anaesthetics tend to reduce the spontaneous activity of vestibular cells in the brainstem and decrease the responsiveness of these cells to stimulation (Kimm and Luschei, 1971). Each anaesthetic has its own advantages and disadvantages in a specific application, and when choosing an anaesthetic to be used during an experiment it is necessary to consider how these factors may influence the results.

(ii) Halothane/Nitrous Oxide. Halothane is a potent CNS depressant (Green, 1979). As an inhalant mixed with nitrous oxide and oxygen it does not cause irritation to the respiratory mucosa, thus

avoiding respiratory problems. Halothane is fairly soluble in blood and recovery is quite rapid.

At the flow rates necessary for anaesthetic maintenance in this experiment, however, the equipment that was available was unable to provide a stable concentration of halothane. For this reason the gaseous anaesthetic was used only as a convenient and painless method of anaesthesia induction.

(iii) Brietal (Methohexital). This short acting barbiturate was used in the maintenance of anaesthesia. Though a CNS depressant (Green, 1979), the relatively quick recovery time (2-3 hours) allows for recording in the CNS with minimal concern for anaesthetic effects on the neural response. In the present experiment a minimum of three hours normally passed between the time of the last supplemental dose of Brietal and the commencement of extracellular recording.

On one occasion only, extracellular recording was attempted two and a half hours after the last dose of barbiturate. Very few cells were found to be firing spontaneously though the presence of large field potentials, caused by antidromic stimulation, indicated that cell bodies were located in the vicinity. In a short while more cells began to fire, including in areas where there had previously been no spontaneous activity. Presumably this reflected decreased effect of the anaesthetic on the CNS as it was metabolized (Kimm and Luschei, 1971), although no direct levels of anaesthesia was measured.

(iv) Decerebration. The level at which the decerebration was performed (precollicular postmammillary) allowed for the complete transection of ascending sensory fibers, with little or no decerebrate

rigidity. A successful decerebration resulted in few, if any complications. In some cases the animal would remain stable in this condition for more than twenty-four hours. One consequence of such a high level decerebration was a reflex "walking" movement (primarily in the forelimbs) observed in a few animals. This "walking" was temporary, lasting only a few minutes, though occasionally reappearing some time later. Unfortunately, this movement would usually result in the loss of an isolated cell.

As mentioned previously, upon completion of the experiment the level and condition of decerebration were examined by visual inspection of the removed brain. Only the most ventral part of the rostral midbrain was not completely transected. This included a small section of the crus cerebri, and occasionally a small section of substantia nigra pars compacta and oculomotor nerve.

Evidence of bleeding was usually seen in the area of the transections; though in general this did not seem to be of any consequence. In animals who deteriorated rapidly after decerebration, however, large clots were often found in the area of the transections. This relatively large volume of blood probably caused compression of the brainstem, resulting in compromised cardiovascular and respiratory function.

B. Extracellular Recording

While small and medium sized cells can be found within Deiters' nucleus, there is also a population of giant cells with diameters upwards of 60 μm (Walberg, 1975). Such intermixing within the nucleus may result in the prominent spikes of the large cells obscuring the smaller spikes of the small cells (Peterson, 1969). A large cell is also more likely to

survive mechanical pressures exerted by the approaching microelectrode (Schlag, 1978). Before recording from a cell, one of the criteria used for acceptance of the cell isolation was to observe a clean signal-to-noise ratio of approximately 5 or 10:1 (as measured directly from the oscilloscope display). Taken together, these factors would lead to a bias in favour of recording from the large cells. The majority of units isolated in the present experiment and whose locations were determined histologically, were located in the dorsal region of the nucleus. Brodal (1974) observed that giant cells were more predominant in the dorsocaudal region of Deiters'. This also suggests that most recordings in the present experiment may have been from the larger cells of Deiters' nucleus.

Care was taken to detect any distortion of the properties of the neurons by the microelectrode. If mechanical stimulation of the cell by the microelectrode was suspected, the microelectrode would be backed off until the spontaneous firing rate returned to normal. Any systematic fluctuation of spike amplitude during tilt or an oscillation run also suggested movement of the microelectrode relative to the unit. The microelectrode would be advanced and retracted slightly to try to improve stability of the recording. If amplitude fluctuation still occurred, the cell would not be studied further.

As described in the previous chapter, a small number of units were observed to respond in a distorted manner. While this could be the result of convergence of non-otolith inputs onto the cell, or a tendency of the cell to fire in bursts, it could also be caused by a deteriorating neuron, mechanical stimulation of the cell by the microelectrode during oscillation or a distorted acceleration stimulus due to inadequate fixation of the cat

in the oscillating device. The relative importance of these various factors could not be determined in the present experiments.

Removal of the cerebellum would alter the background activity and tilting responses of vestibular neurons (Peterson , 1970). In the present experiment the microelectrode was passed through the cerebellum prior to reaching Deiters' nucleus in the brainstem. Due to the small shaft diameter of the microelectrode, it is unlikely that the limited number of cerebellar fibers damaged would result in any noticeable change in the responses of Deiters' nucleus neurons.

In summary, while the extracellular recording technique used in the present experiment probably resulted in a bias towards recording from large cells within Deiters' nucleus, it is unlikely that the method itself influenced the responses of these vestibular neurons (Peterson, 1969).

C. Stimulation of Vestibulospinal Tracts

The stainless steel wires used for stimulating the LVST were designed to provide a stable antidromic stimulus throughout the experiment. Field potentials produced by antidromic stimulation of the lumber LVST, however, were usually smaller than those produced by stimulation at the cervical level. Possible reasons for this will be discussed in section 2A, following.

Stimulus spread would result in the stimulation of other tracts located in the ipsilateral lower quadrant of the spinal cord (see Fig. 9 for location of electrodes). However, the criteria listed in section 8B of METHODS eliminated the possibility that activation of vestibular units was occurring by way of orthodromic pathways.

The stimulus pulse duration (0.2 ms) and voltage (range 4-12 volts) were in accordance with antidromic stimuli used by other investigators (Ito et al., 1964; Schlag, 1978). As well, the antidromic responses observed in the present experiment were similar to those described in the literature (see Fig. 6).

D. The Acceleration Stimulus

The linear motion device used in the present experiment was intended to provide a sinusoidal acceleration stimulus. Distortion of the sine wave was a possibility at the higher stimulus frequencies ($\geq$ 2.0 Hz), due to resonances of the carriage or of the whole apparatus caused by the severity of the high frequency motion. Other potential sources of distortion included backlash of the device, or deformation of non-rigid structures associated with the stereotaxic apparatus. These effects were minimized by suitable bracing.

Neck proprioceptive clues as to the motion of the carriage were minimized by using spinal clamps to suspend the animal, thereby keeping the torso and neck rigid. At the higher stimulus frequencies, however, tactile inputs could not be avoided even though the sides of the cat were supported with foam pads. Despite best efforts at stabilizing the animal, modulation of some somatosensory input can occur. However, in view of the fact that deafferentation of the cat forelimb does not significantly change the dynamic response of forelimb extensor muscles to sinusoidal linear acceleration (Anderson et al., 1977), it is not likely tactile inputs would significantly affect the dynamic response of central vestibular neurons.

E. Histology

The size of the electrolytically placed spot ranged from being visible with the naked eye, to microscopic. This variation was likely due to the changing condition of the steel microelectrode, which was used several times for marking. Despite variability in cat size, errors caused by exchanging the tungsten recording microelectrode for one made of steel, and other inherent inaccuracies of the stereotaxic technique, all 12 cells which were localized histologically were found to be within Deiters' nucleus. This suggests, but does not prove, that all units studied were in that nucleus.

2. Responses of Deiters' nucleus neurons

A. V-S Units

The very small number of V-S units included in the sample of cells which were studied was disappointing. Certainly, large field potentials were seen within Deiters' nucleus. These were similar to those described by Ito et al. (1964) and Wilson et al. (1966). Nevertheless, very few V-S units were identified. Why might this be the case? As mentioned above, the majority of the units isolated were located in the dorsal region of Deiters'. Studies have shown that neurons originating in the dorsocaudal region of Deiters' project primarily to the lumbar region of the spinal cord (Peterson, 1970; Wilson and Melvill Jones, 1979). Peterson (1969) observed that 56% of cells isolated in Deiters' were not antidromically activated. In some cases he attributed the failure to excite axons in the V-S tract to mechanical damage to the spinal cord. Since large field potentials were not often observed from stimulation of the lumbar V-S tract

in the present experiment, it is possible that damage to the spinal cord (due to insertion of the stimulating electrodes) prevented full stimulation of the V-S tract at that level or that it blocked transmission at the cervical level. An alternate explanation is that the V-S tract may originate from the small or medium size cells within Deiters' nucleus. A bias towards isolating the large cells within Deiters' would then lead to the rarity of V-S units in our sample.

B. Response to Tilt

Tilting of the animal in a given direction facilitated the firing rate of some cells and inhibited the firing rate of others (Duensing and Schaefer, 1959; Peterson, 1970). Cells facilitated by ipsilateral side-down tilt have been classified as alpha cells, with cells facilitated by contralateral side-down tilt known as beta cells. Units facilitated or inhibited by both ipsilateral and contralateral side-down tilts are known as gamma and delta, respectively. Cells facilitated by pitch up are labeled as type 1, while a positive response to pitch down is called type 2. Units facilitated or inhibited by both pitch up and down are labeled types 3 and 4, respectively (Duensing and Schaefer, 1959).

Classifying the neurons isolated in the present experiment showed that approximately 90% responded as alpha units to lateral tilt, with 10% responding as beta units. The observation that all beta units were proven or suspected V-S neurons may or may not be significant. A roughly equal proportion of neurons responded as type 1 and type 2 to pitch. Peterson (1970) categorized approximately 54% of neurons as alpha units, with the majority of these located in the ventral region of Deiters' nucleus. Twice as many units were classified as type 1 than as type 2, though the relative

number of pitch sensitive neurons were much less than lateral tilt sensitive neurons. Peterson also identified gamma, delta, type 3 and 4 units, though these were very few in number. Differences in the proportion of responses may only reflect the limited sample of the present experiment, or they may be due to the different animal preparations, since Peterson's studies were conducted in chloralose-urethane anaesthetized, decerebellate cat.

C. Response to Dynamic Stimulation

(i) "Canal" versus "otolith" units. Each neuron isolated in Deiters' nucleus reacted in one of three ways when the cat was tilted: 1) it responded to static and dynamic components of tilt (14/32 units), 2) it responded to dynamic components only (18/32, of which 11 were determined to receive otolith input), or 3) it did not respond at all (many cells).

Units in the first category were considered to receive at least some otolith inputs, although convergence from the canals could not be ruled out (Gacek, 1969; Baker et al., 1984b). While convergence may have been present, it should be noted that when purely dynamically responding units were studied with our pure linear acceleration stimulus, many showed no modulation whatsoever. Though some would argue otherwise (Benson et al., 1967; Clegg et al., 1982), this suggests that the canals are not generally sensitive to linear acceleration. However, the possibility cannot be ruled out by this work.

Units in the second category required further evaluation. Rotation in pitch or roll exposes the animal to both angular acceleration and change of head position with respect to gravity. Thus a cell sensitive to dynamic tilt may be activated by either the semicircular canals, the otoliths, or

both. In these cases, dynamic linear acceleration stimulation was used to discriminate between otolith-dependent and canal-dependent units. If there was no response, the neuron was assumed to receive semicircular canal inputs only.

Units in the final category were isolated frequently. Since they had no labyrinthine input, they were discarded immediately.

(ii) Directional sensitivity. FPV orientation was determined using a stimulus frequency of 0.3 Hz. This frequency was used to provide a consistent, suprathreshold stimulus. Since the vector orientation for a given unit does not alter with a change of stimulus frequency (Schor et al., 1985), it is sufficient to determine the FPV at a single stimulus frequency.

The orientation of the FPVs observed in the present study had a relatively broad distribution in space. Though the majority of these units responded to positive acceleration (i.e., in the direction of +X, +Y, and +Z), this confirms that each side of the brainstem receives information representing all directions of acceleration of the head. This is in general agreement with the orientation of FPVs in central vestibular nuclei neurons observed by Melvill Jones and Daunton (1973), and Daunton and Melvill Jones (1982). In those experiments the polarization vectors were determined from unidentified vestibular nuclei cells in the decerebrate cat, using a parallel swing to provide a linear acceleration stimulus. When the latter vectors were projected onto the horizontal plane those authors also observed a tendency of vector concentration along diagonal axes close to the planes of the vertical canals and close to the horizontal plane. A slight trend of vector concentration along the diagonal axes may

also be seen in the present study (see Fig. 19). However, with the small sample size this is certainly not a conclusive finding.

Schor et al. (1984) determined the polarization vectors of units located in and around Deiters' nucleus using a bi-axial stimulus produced by independent roll and pitch tilts in the decerebrate, canal-plugged cat. These authors noted a conspicuous absence of units with fore/aft directed vectors. However, as mentioned previously, this may be due to limitations of their stimulus to activate neurons in that direction.

Polarization vectors of central vestibular neurons receiving semicircular canal input were determined by Baker et al. (1984a). While these authors observed a relatively broad distribution of vector orientation, they also noted a clustering of vectors around the planes of the canals. These trends may indicate that the central representation of both rotational and linear vestibular information tends to be coordinated along the same three orthogonal planes (Daunton and Melvill Jones, 1982).

(iii) Thresholds. Varying the stimulus amplitude at the lower stimulus frequencies allowed a rough estimation of thresholds for Deiters' nucleus neurons. An average threshold of approximately 0.004 'g' is in close agreement with the 0.002-0.005 'g' thresholds of central vestibular neurons reported by Melvill Jones and Milsum (1969) in the decerebrate cat using horizontal linear acceleration, and with the approximately 0.003 'g' threshold of otolith-dependent central vestibular neurons reported by Xerri et al. (1987) in the alert cat using vertical linear acceleration.

(iv) Effects of changing stimulus amplitude. In the present experiment the stimulus amplitude was varied during oscillation runs at frequencies of 0.1 Hz and 0.2 Hz. As mentioned previously, since many

cells were at or below threshold at 0.1 Hz the results at this frequency are questionable. At 0.2 Hz, however, there was no significant change in gain or phase of the response at the two acceleration amplitudes. This result corroborates observations of both Schor (1974) and Xerri et al. (1987). At frequencies of 0.2 Hz and 0.3 Hz, Schor observed no change in gain or phase of the response during changes in stimulus amplitude. Xerri et al. also observed no change at a stimulus frequency of 0.1 Hz. Unfortunately, the same test has not been carried out at higher frequencies of oscillation.

(v) Effects of changing stimulus frequency. Previous studies on the dynamic response characteristics of central vestibular neurons have yielded varying results.

Horizontal linear acceleration was used by Melvill Jones and Milsum (1969) to study MVN neurons in the decerebrate cat. With increasing stimulus frequency (range 0.1-3.0 Hz) they observed a large increase in phase lag (Fig. 24a). Response gain was not determined. Differences in phase behaviour of these neurons compared to those of the present experiment may be due to the fact that they were located in different vestibular nuclei.

As described previously, Schor and MiPler (1982) and Schor et al. (1985) using roll tilt in decerebrate, canal-plugged cats, observed two patterns of response in units located in DVN and Deiters' (including some V-S units). In one group of neurons, there was a slight increase in response gain with increasing stimulus frequency (range 0.1-1.0 Hz), and a relatively flat phase lead (Fig. 24b). The second group of neurons demonstrated a large increase in gain with increasing stimulus frequency,

Figure 24

Bode plots for central vestibular neurons (from the literature).

A. Response phase of 8 MVN neurons, studied during horizontal linear acceleration in the decerebrate cat. Stimulus frequency range approximately 0.1-2.0 Hz. Parallel swing rotation (open circles) produced a rotating linear acceleration vector rather than angular movement of the platform (from Melvill Jones and Milsum, 1969).

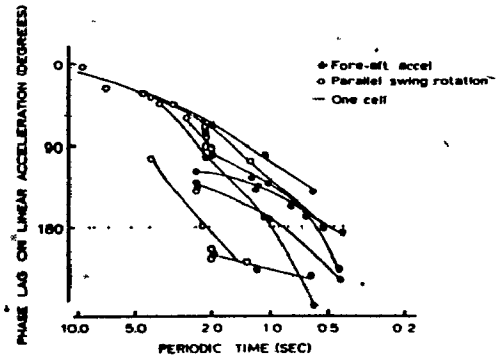
B. Gain (upper graphs) and phase (lower graphs) of the responses of central vestibular neurons (solid lines), and extensor muscles (triceps, dashed line; biventer, dotted lines) studied in canal-plugged, decerebrate cats using roll tilt. Note alpha (i) and beta (ii, iii) type units, with phase response of some beta units approximating that of extensor muscles (ii). Error bars represent ±1 S.E. (from Schor and Miller, 1982).

C. Sensitivity of the responses of two populations of neurons located in Deiters' nucleus (n=25) studied using roll tilt in labyrinth-intact decerebrate cats. Note that input from the canals was not prevented in any way. Error bars represent standard deviation (from Boyle and Pompeiano, 1980).

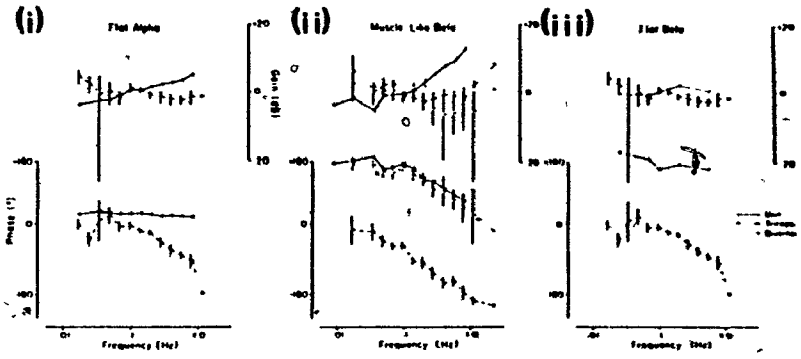
D. Gain response of 4 neurons located in the region of Deiters' nucleus, studied in the alert monkey. X⁻ designates peak firing associated with backward-directed linear acceleration along the fore/aft plane (from Perachio, 1981).

E. Gain (upper graph) and phase (lower graph) of the responses of 7 units (4 represented by dashed line, 3 by solid line) located in and around Deiters' nucleus in the alert cat (from Xerri et al., 1987).

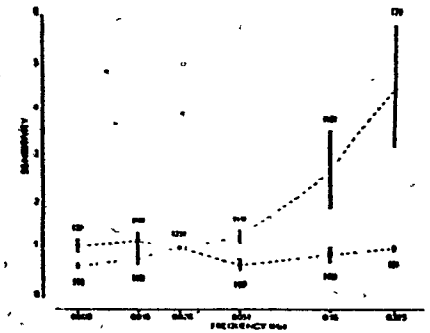
A


PHASE LAG ON LINEAR ACCELERATION (DEGREES)
0
90
180
10.0
5.0
2.0
1.0
0.5
0.2
PERIODIC TIME (SEC)
Fore-aft accel
Parallel swing rotation
One cell

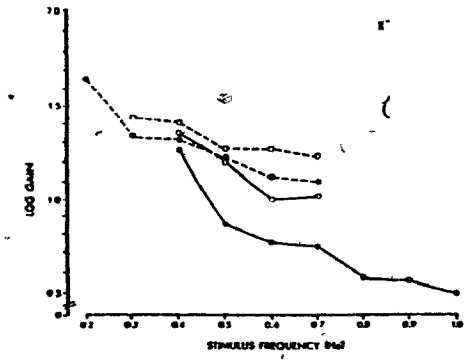
B


(i)
(ii)
(iii)

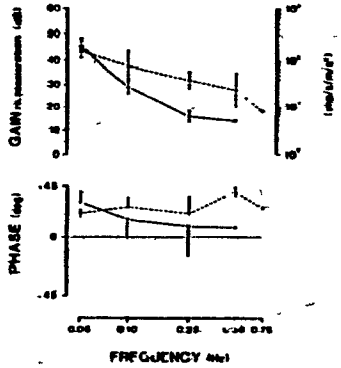
C



D


LOG GAIN
STIMULUS FREQUENCY (Hz)

E


GAIN
PHASE (deg)
FREQUENCY (Hz)

with a progressive phase lag towards zero phase shift. Schor and Miller described this second group's response as "muscle-like". The term "muscle-like" derives from the similarity of the response to that of the phase behaviour of neck and forelimb extensor muscles to tilt (Schor and Miller, 1982).

Boyle and Pompeiano (1980), using sinusoidal tilt on decerebrate, labyrinth-intact cats observed two different populations of neurons located within Deiters' nucleus (including V-S units). At a stimulus frequency range of 0.008-0.325 Hz, a majority group of neurons exhibited a stable or slightly reduced sensitivity (Fig. 24c) and stable phase response. The second group of neurons exhibited an increase in sensitivity (Fig. 24c) with a phase response that was closely related to the velocity signal during increases in angular acceleration. As noted previously, however, input from the semicircular canals was not excluded and probably influenced the responses of the latter group at the higher stimulus frequencies.

Horizontal linear acceleration was used by Perachio (1981) to record from cells in and around Deiters' nucleus in the alert monkey. A decrease in response gain (Fig 24d) and a relatively flat phase lag was observed with increasing stimulus frequency (range 0.2-1.2 Hz). A small number of units were observed to have an increase in phase lag with increasing stimulus frequency, similar to the "muscle-like" units of Schor and Miller. Whether these units projected to the spinal cord was not determined.

Xerri et al. (1987) used vertical linear acceleration to study cells in and around Deiters' nucleus in the alert cat (Fig. 24e). They also observed a decrease in response gain and a relatively stable phase lead with increasing stimulus frequency (range 0.05-0.75 Hz).

As far as response gain is concerned, with the exception of the results of Schor and Miller (1982), Schor et al. (1985), and a minority of units observed by Boyle and Pompeiano (1980), the results of the present experiment are in general agreement with those just described: with increasing frequency there is a reduction in response gain. Since the gain attenuation at higher frequencies is not seen in primary otolith afferents (Fernandez and Goldberg, 1976c; Anderson et al., 1978; Goldberg et al., 1982), this reduction must occur centrally. Does this gain attenuation serve a useful purpose? Otolith-driven units that respond to the small, low frequency stimuli encountered during postural sway may also have to respond to the large, high frequency accelerations experienced during locomotion. Without this reduction in gain the unit would saturate, thus limiting its useful operating range.

According to Schor and Miller (1982), central vestibular neurons exhibit two types of phase behaviour. These include flat and "muscle-like" responses. The flat phase response observed in the present experiment appears to be similar to that described by Boyle and Pompeiano (1980), Perachio (1981), Schor and Miller (1982), Schor et al. (1985) and Xerri et al. (1987). "Muscle-like" responses have been observed by Melvill Jones and Milsum (1969), Boyle and Pompeiano (1980), Schor and Miller (1982), Schor et al. (1985), and in small numbers by Perachio (1981). It should be noted that the flat phase response seen in some vestibular nuclei neurons is similar to the phase behaviour of otolith primary afferents (Fernandez and Goldberg, 1976c; Anderson et al., 1978). These results tend to indicate that one class of neurons may act as simple relays of otolith

afferent activity, while a second class may be involved with information processing (Wilson and Melvill Jones, 1979; Schor et al., 1985).

In the present experiment, one unit was observed to have a phase shift of approximately 180° throughout the entire stimulus frequency range. This unit was one of two excited by contralateral side down tilt, and also exhibited one of the lowest response gain and VAF values of all units studied. Schor and Miller (1982) also observed a small number of units exhibiting a flat phase shifted approximately 180°, which they categorized as "beta" units, indicating they responded to contralateral side down tilt. The sensitivity of these "beta" units was not significantly different from that of "alpha" units. It is possible that the low gain and VAF values of the former unit were a consequence of the unit being driven from the contralateral labyrinth through the deep reticular pathways (Shimazu and Smith, 1971; Precht, 1974).

D. <u>"Utricular" versus "Saccular" Units</u>

The directional sensitivity of the maculae can be attributed to their orientation within the membranous labyrinth and the direction of polarization of the sensory hairs (see Fig. 2b). Thus the utricular macula will respond most readily to a linear acceleration stimulus projected along the X/Y plane, and the saccular macula will respond primarily to vertical (Z axis) linear acceleration. It should be noted, however, that a fore/aft (X axis) linear acceleration stimulus may also stimulate some saccular macula sensory hair cells (Perachio, 1981). Nevertheless, cells responding most strongly along the X or Y axis have been termed "utricular", and those responding along the Z axis have been called "saccular".

In the present experiments, both utricular and saccular units have been shown to possess static and dynamic sensitivity. Thus both maculae should be able to distinguish between gravitational and inertial forces (Goldberg and Fernandez, 1984), since the adaptation of dynamic units would allow for the separation of gravitational inputs from other transient linear accelerations (Mayne, 1974).

Sensitivity to linear acceleration of units in both populations appeared similar, with a threshold of approximately 0.004 'g'. This threshold is similar to that observed by Melvill Jones and Daunton (1973) in unidentified central vestibular neurons, where the threshold of the most sensitive unit studied was 0.002 'g'.

As mentioned previously, the mean bias (resting firing rate) of units studied in the present experiment was within the range described in the literature. In agreement with the observations of Daunton and Melvill Jones (1982), there was no significant difference in the bias of cells which were most responsive in either the X, Y, or Z axes, nor between units responding in the +Z and -Z directions. This suggests some form of compensation correcting for the constant effects of gravity on the otolith organs (Daunton and Melvill Jones, 1982), especially on the saccule.

There did not appear to be any significant difference in the gain and phase responses of utricular versus saccular units. Though the number of units studied in the present experiment was small, this too is in general agreement with the observations of Daunton and Melvill Jones (1982). Anderson et al. (1977) studied extensor muscle EMG response to sinusoidal linear acceleration in the decerebrate cat. In this study the authors also

concluded that the dynamic behaviour of utricular and saccular receptors was the same.

Studies on the response behaviour of utricular and saccular afferents in the cat (as opposed to central vestibular units) have provided some conflicting results. Tomko et al. (1981), using static tilt and roll tilt in the barbiturate anaesthetized decerebellated cat, observed that saccular afferents possessed a lower resting firing rate and lower response sensitivity than utricular afferents. Using a similar procedure, Anderson et al. (1978) also noted a lower sensitivity in saccular afferents. However, the latter authors noted no significant difference in the resting firing rate. This is in agreement with Fernandez and Goldberg (1976a) who, using static tilt and long-duration centrifugal force in the anaesthetized, partially decerebellate monkey, observed a lower sensitivity in saccular afferents but no difference in the resting discharge.

The different results of the latter studies may be due to the different experimental procedures used, or they may reflect an actual difference in the dynamic behaviour of otolith afferents versus higher order neurons.

E. Comparison to Previously Collected Data

During development of the current experiment, the dynamic responses of 12 units receiving otolith input were studied by D. Watt and A. Budning. These units were presumed to be located within Deiters' nucleus although this was not confirmed histologically. As with the present results, the response gains of these 12 units were corrected for actual FPV direction (see RESULTS, section 4C(iii)). Comparison of this previously collected data with that of the present experiment revealed some similarities.

Of the 12 units studied, 4 responded maximally to linear oscillation in the X axis (including 1 V-S unit), 3 in the Y axis, and 5 in the Z axis (including another V-S unit). There was no significant difference in the bias of units responding maximally in any of these axes, nor between units responding maximally in the +Z or -Z directions. While the mean bias of these units was approximately 15 AP/sec, this was not significantly different from the bias of units studied in the present experiment (t-test for two means, $P > 0.05$).

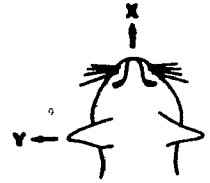
Threshold, which was determined for only 4/12 units (including 1 V-S unit), fell between 0.004-0.0161 'g'. This is within the range of thresholds described in the literature (Wilson and Melvill Jones, 1979), and close to the values measured in the present experiment.

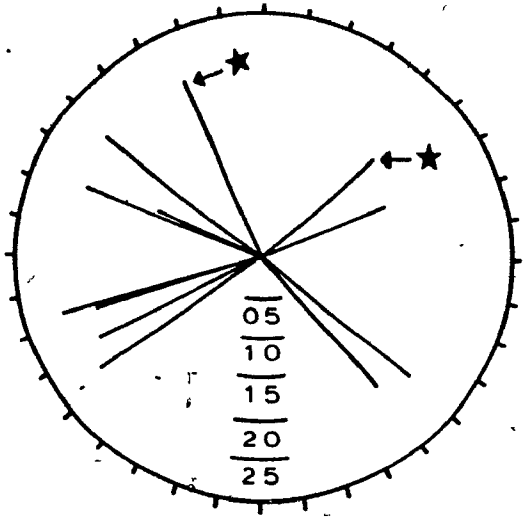
The distribution of FPVs appeared broadly distributed when projected onto any of the 3 planes (Fig. 25). Comparing these plots with those of the present experiment (see Fig. 19) and those of Melvill Jones and Daunton (1973) lends support to the notion that the otoliths on each side of the skull contain responses representing all directions of linear acceleration of the head.

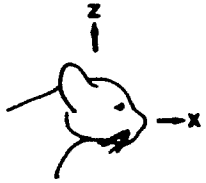
While there is considerable scatter in the measurements of response gain, there is a trend toward gain attenuation with increasing stimulus frequency (Fig. 26a). No significant change in response phase was observed with increasing stimulus frequency (Fig. 26b). Both of these results are in agreement with the present observations (see Fig. 23). As well, units with large phase shifts generally had the lowest VAF values, and in some instances lower gain values.

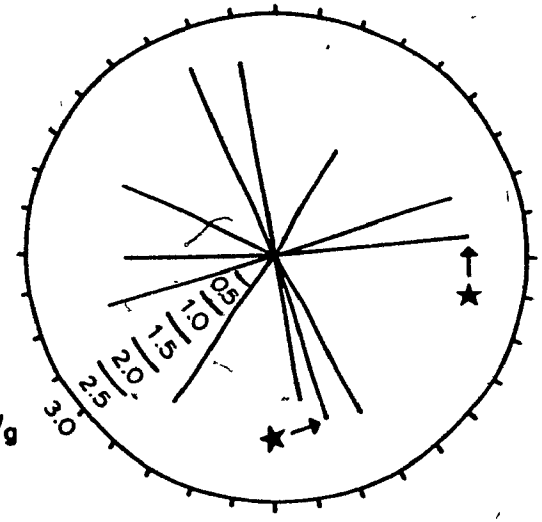
Figure 25

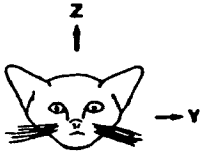
Distribution of the polarization vectors of 12 presumed Deiters' nucleus units as projected onto (clockwise from top) the horizontal (X-Y), frontal (Z-Y), and mid-sagittal (Z-X) planes. Spacing of tick marks is 10°. Arrows beside cat heads indicate direction of positive acceleration along that axis. Direction of vector is that of maximum sensitivity of the cell, and magnitude represents the response gain in that direction on that plane. Radial marks indicate gain calibration in terms of Log (AP/sec/g). ★ , V-S units (Watt and Budning, unpublished data).


X
Y


05
10
15
20
25
3.0
Log AP / sec / g


Z
X


05
10
15
20
25
3.0
Log AP / sec / g


Z
Y

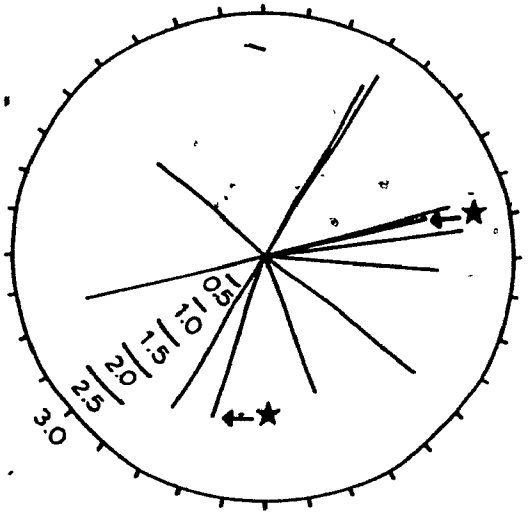

05
10
15
20
25
3.0
Log AP / sec / g

Figure 26

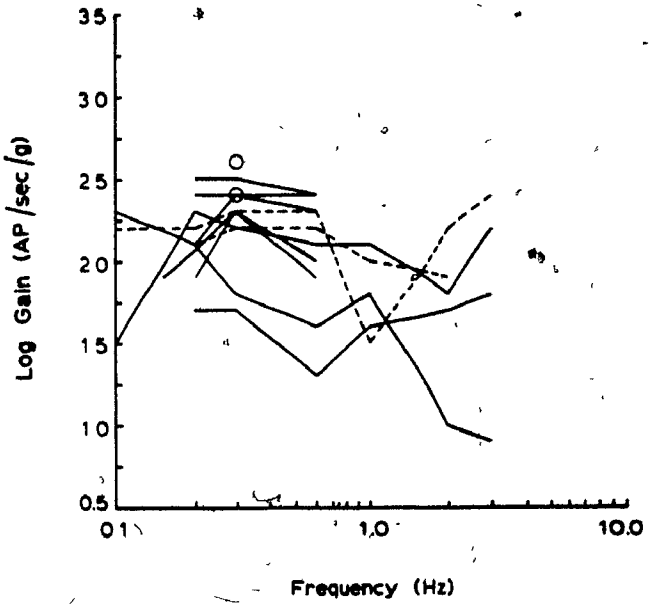
Bode plots for 12 presumed Deiters' nucleus units.

O indicates unit oscillated at only one frequency (0.3 Hz). Dashed lines signify V-S units.

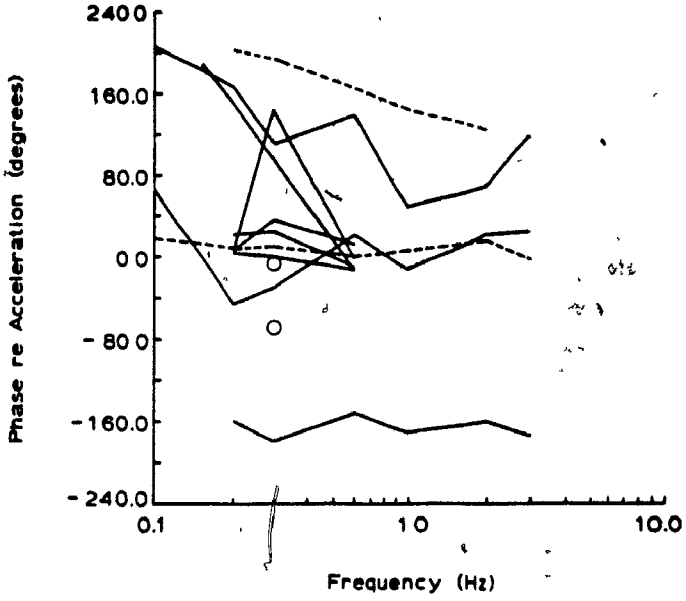
A. Response gain as a function of stimulus frequency. Note trend of gain attenuation with increasing stimulus frequencies.

B. Response phase (re acceleration) as a function of stimulus frequency. No significant change in phase occurs with increasing stimulus frequency. Note large phase shifts exhibited by a small number of units (Watt and Budning, unpublished data).

A


35
30
25
20
15
10
0.5
Log Gain (AP/sec/g)
0.1
1.0
10.0
Frequency (Hz)

B


2400
160.0
80.0
0.0
-80.0
-160.0
-240.0
Phase re Acceleration (degrees)
0.1
1.0
10.0
Frequency (Hz)

While the number of units tested in the previous study was small, the results do tend to confirm the present observations. The combined results support the notion that the dynamic behaviour of utricular and saccular units is similar, and that otolith signals, both "processed" and "unprocessed", can be relayed to spinal levels via V-S neurons.

3. Vestibular Contributions to Locomotor Control

Given the above results, how might otolith signals assist in locomotor control? As described by Stuart et al. (1973), an otolith-spinal reflex may periodically reinforce stepping provided there is: 1) sufficient change in linear acceleration during locomotion to activate the otoliths; and 2) an appropriate time delay between otolith activation and the onset of EMG activity in the extensor muscles.

As discussed previously, Watt and Wetzel (1977) examined the linear head movements of walking and trotting cats (frequency of head oscillation approximately 2-7 Hz). These authors found that vertical and fore/aft head accelerations were several orders of magnitude larger than the thresholds of the otolith organs (see Fig. 7). Thus the stimulus required to produce these otolith-spinal reflexes is present during normal locomotion.

The present experiments demonstrate that in at least part of this frequency range (up to 4.0 Hz), these linear accelerations will be transduced and that this information can be relayed to the spinal cord. With increasing stride frequency, the vertical head acceleration is known to increase substantially (Watt and Wetzel, 1977). This would result in a corresponding increase in otolith output. The attenuation of response gain observed at the higher stimulus frequencies in the present experiments may

be useful in preventing saturation of the system as the acceleration amplitude increases.

Responses to step inputs of linear acceleration have been demonstrated at the level of the spinal cord and muscle (in cats: Watt, 1976, 1981a; baboons: Lacour et al., 1978; man: Melvill Jones and Watt, 1971b; Greenwood and Hopkins, 1977). Modulation of spinal motoneuron excitability has been observed immediately following the step change, as well as a fixed latency EMG burst occurring before a voluntary muscle response is possible. The latency of this burst in the cat is approximately 55 ms after onset of the vertical acceleration stimulus (Watt, 1976). Stuart et al. (1973) observed that in the walking cat, at least 59 ms elapses between the moment there is a sharp change in vertical head acceleration and the subsequent moment of contact of the paw with the ground. This interval was generally longer in faster gaits. Taken together, these results indicate that for vestibulospinal reflexes in the cat at least , the time delay between end-organ activation and the onset of EMG activity is compatible with the timing constraints of stepping.

The situation appears to be similar in the case of humans. The latency of the response to a sudden change in vertical acceleration in gastrocnemius is approximately 74 ms (Melvill Jones and Watt, 1971b). In a rhythmically hopping human (Melvill Jones and Watt, 1971a), EMG activity controlling landing on the ground begins approximately 75 ms after the sudden transition into weightlessness which occurs as the feet leave the ground. This timing is essentially unchanged when hopping under conditions of reduced gravity (Backman and Watt, 1978), even though the time spent in the air is greatly increased and the next landing is delayed.

Responses to sinusoidal linear acceleration have also been demonstrated at the level of the spinal cord and muscle (in cat: Anderson et al., 1977; Watt, 1981b; Lacour et al., 1987; in human: Melvill Jones and Watt, 1971a; Melvill Jones et al., 1973; Watt, 1977). In the decerebrate cat, modulation of H-reflex amplitude was observed during vertical oscillation (Watt, 1981b). Maximum amplitude occurred at the point of maximum downward acceleration, i.e. when 'g' force is minimal. These signals would be timed so as to enhance the landing phase of activity in hindlimb extensor muscles, especially during walking or trotting (Stuart et al., 1973).

H-reflex amplitude is also modulated by vertical oscillation in human subjects (Watt, 1977), with the largest responses also occurring at the point of maximum downward acceleration. Given this timing, human otolith-spinal reflexes could contribute to muscle activity controlling landing from each step.

These results indicate that otolith stimulation due to vertical linear acceleration associated with locomotion could bring a functionally effective influence to bear upon the extensor muscles of the leg (Melvill Jones et al., 1973). An important potential advantage of this V-S contribution is the control of muscle contraction prior to contact with the ground.

While there is evidence that periodic vestibulospinal activity might contribute to the neuromuscular organization of locomotor control (Wilson and Melvill Jones, 1979), the process whereby the acceleration input is transformed into a motor output is complex and generally poorly understood. Some areas still at issue will be mentioned below.

Head acceleration pattern has been shown to vary with gait frequency in cats (Watt and Wetzel, 1977). During a slow walk head acceleration follows a nearly sinusoidal pattern. At faster gaits (trotting, galloping), however, head acceleration patterns resemble a series of steps (Watt, personal communication). How this change in acceleration pattern might affect control of limb movement is uncertain.

The phase relationship between head and hindlimb movement in quadrupeds varies considerably with gait frequency (Stuart et al., 1973; Watt and Wetzel, 1977). This phase relationship is more constant in the forelimbs of quadrupeds and in bipeds (Watt and Wetzel, 1977), but the question remains as to how hindlimb locomotor control may be influenced by periodic acceleration input, if at all.

As mentioned previously, head oscillation frequency during locomotion is twice the stride frequency (Watt and Wetzel, 1977). How then can a vestibular reflex provide appropriate control of the gait cycle of any single limb? While the exact nature of the information sent from the otolith organs to the spinal cord remains controversial, it has been suggested that limb position signals could act as a neural transmission "switch" or "block" until the limb is in its proper phase of locomotion (Grillner, 1975). This was observed by Forssberg et al. (1975) as a hindlimb reflex reversal in spinal cats that was dependent on the angle of the hip during locomotion (walking). It is not known, however, whether joint or muscle afferents are responsible for this "switch" or "block" (Grillner, 1975).

Otolith-spinal reflexes which would result from a sudden fall do not occur if a subject initiates the fall himself (Greenwood and Hopkins,

1976), or if he chooses not to respond to the landing (during horizontal falls; Tomi, 1986). These results indicate that the contribution of these reflexes to locomotor control may vary depending on whether the movement is self-generated, or externally applied. Under normal circumstances when the movement proceeds exactly according to a central locomotor plan (Grillner, 1975), they may not play a part, only coming into operation to compensate for a disturbance in locomotor movements.

Given these issues, then, it is apparent that while much is known of the input to the vestibular system and its final motor output, the physiological basis of the sensorimotor transformation and its interaction with other systems remains unclear. An understanding of the workings of the individual components of the locomotor system will be necessary before the vestibular component of locomotor control can be fully understood.

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