THE EFFECTS OF NATURAL OTOLITH STIMULATION ON MYOTATIC AND CUTANEOMUSCULAR REFLEXES IN HUMAN LOWER LIMB MUSCULATURE

by

© TONY JOSEPH SZTURM

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A thesis submitted to the Faculty of Graduate Studies of the University of Manitoba in partial fulfillment of the requirements of the degree of

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ABSTRACT

The purpose of this thesis work was to attempt to develop a human model of otolith-spinal function. To this ends, it was a desirable first step to examine whether known vestibulospinal synaptology as derived from animal experiments is present and detectable in humans. Experiments were designed to examine the effects of static tilt, a practical form of natural otolith stimulation, on myotatic and cutaneomuscular reflex excitability of human lower limb motoneurons.

The first series of experiments, addressed the effects of natural otolith stimulation on connections to amble extensor motoneurons from Deiters' nucleus (DN), the site of second order neurons of the primary otolith afferents. By stimulating the posterior tibial nerve with paired (S_1-S_2) shocks, both the monosynaptic pattern of excitability of the soleus motoneuron pool and the H-reflex recovery curve was examined during whole body tilts in the pitch axis. The outcome of this study revealed no dependence between angle of tilt and the magnitude of the soleus H-reflex. However a highly significant effect was observed between angle of tilt and the recovery of a test H-reflex (H_2) preceded by a conditioning H-reflex (H_1). These results support the view that with surface EMG recordings, the soleus H-reflex method does not provide a sensitive measure of the central effects of static tilt. With respect to the tilt-dependent response (the conditioned H_2 response), unfortunately little information is available as to the neural elements involved (segmental or supraspinal).

These results were followed up with a second series of experiments designed to test for a convergent effect in lower limb muscles of static tilt and the reflex action of cutaneous nerve stimulation. The latency and magnitude of the reflex responses in lower limb flexor and extensor muscles evoked by sural nerve stimulation were examined during whole body tilts in the pitch axis. A highly significant tilt-dependent modulation of the magnitude of the cutaneomuscular reflex response for; the contralateral tibialis

anterior (coTA), ipsilateral hamstrings (iH), and ipsilateral quadriceps (iQ) was demonstrated. It was concluded that a step toward an identification of the spinal neural elements involved in the central effects of static tilt has been made.

CONTENTS

LIST OF FIGURES

PAGE

LIST OF FIGURES (cont'd)

PAGE

LIST OF TABLES

PAGE

CHAPTER 1

INTRODUCTION

The vestibular sense organs provide the central nervous system with information about the position and motion of the head in space. Although we are not normally aware of this dimension of our sensory experience, disorders of the vestibular system result not only in a significant functional impairment of balance and oculomotor control but also distressing sensations that all too quickly infringe on our consciousness.

In contrast to the semicircular canals, human otolith organ function is much more difficult to assess. This is probably due to the fact that activation of semicircular canals evokes reflex responses in extraocular eye muscles which are easily produced and recorded. In the case of human otolith end organs it is safe to say that few, if any, feasible test of function with the appropriate selectivity are available today. Substantial linear acceleration stimuli or off-vertical axis rotations are required to generate otolith mediated eye movements. However,in humans, these types of stimuli are difficult to produce and control. Static tilt with respect to the gravity vector, a powerful stimulus to the otolith organs, provokes small and inconsistent eye movements. Tests that measure, in humans, the ability to maintain balance have in general failed to yield information of physiological significance about otolith organ function in postural control. An otolith mediated reflex in lower limb muscle has been reported to occur in humans during vertical linear acceleration, but again, this does not make for a practical clinical test.

The objective of this thesis work was to obtain evidence for a physiological linkage between otolith end organs and human lower limb musculature and to characterize the pathway(s) mediating it. In this regard, it was a desirable first step to examine whether known vestibulospinal synaptology as derived from animal experiments is

present and detectable in humans. Only then will it be possible to: 1) establish a sensitive and feasible test of human otolith function; 2) investigate when and how activity originating in otolith receptors is normally used during postural control; 3) examine the process of vestibular compensation in people with selective vestibular disorders. To this ends the approach taken in this work was to examine the effects of natural otolith stimulation on the modulation of myotatic and cutaneomuscular reflex excitability in the lower limb musculature.

CHAPTER 2

LITERATURE REVIEW

2.1 - INTRODUCTION

This literature review will provide a concise overview of the relevant morphological aspects of the vestibular apparatus in particular the otolith end organs. Next an examination of the transduction process and physiological responses of vestibular primary afferents will be presented, focusing on linear acceleration stimuli. A detailed description of the vestibulospinal system will follow. In this regard, the effects of vestibulospinal signals on spinal reflex arcs, and muscle activity will be discussed.

A more detailed anatomical description and physiological analysis of the vestibular system can be found in reviews 266, 58, 70, 241, 139, 149, 269, 273, 274, 231, and 207.

2.2 - MORPHOLOGY OF THE VESTIBULAR APPARATUS

2.20 - General Anatomical Features

The fully formed inner ear has a complex geometry arising from the infolding, twisting, and fusion of the walls of the otic vesicle. The otic vesicle is derived from the otic placode - the first rudiments of the membranous labyrinth. The membranous labyrinth is a closed space of interconnecting ducts and sacs that comprise the vestibular and auditory peripheral organs. This space contains its own fluid - the endolymph. The walls of the membranous labyrinth are composed of two layers; an inner epithelial layer of ectodermal origin, and an outer mesenchymal layer. The inner layer consists

mainly of a single layer of squamous epithelial cells. In specialized regions the epithelium is considerably more differentiated. This differentiated epithelium constitutes the sensory hair cells. This is true for the organ of Corti, the maculae utriculi, the maculae sacculi, and the cristae ampullares.

The membranous labyrinth lies enclosed in the bony labyrinth which consists of a series of cavities in the petrous temporal bone. The membranous labyrinth is generally separated from the bony labyrinth by a perilymphatic space. This space holds its own fluid - perilymph.

The gross anatomical features and location of the internal labyrinthine system, which contains auditory and vestibular components are illustrated in Fig. 1. The vestibular labyrinth consists of two principle sets of structures: 1) a pair of sac like swellings - the otolith organs; and 2) three semicircular ducts - the semicircular canals.

There are two otolith organs, the utricle and the saccule. Each contains a specialized receptor region called the macula. The utricular macula lies on the floor of the utricle sac which has a horizontal orientation with the head tilted forward 20 to 30 degrees from the normal upright anatomical position. The saccular macula lies on the medial wall of the saccular sac and is orientated in a vertical plane, approximately orthogonal to the plane of the utricular macula.

The three almost orthogonal semicircular canals are the most prominent structures of the vestibular labyrinth and are termed the horizontal (lateral), anterior vertical (superior), and posterior vertical (inferior) canals. All three canals arise out of the utricular sac which provides endolymph fluid continuity. The ampulla, which is the receptor region of the individual canals, is a small enlargement of the duct where it joins the utricle. The structure and components of the ampulla are illustrated in Fig. 2. A thickened zone of epithelium producing a ridge like structure contains the hair

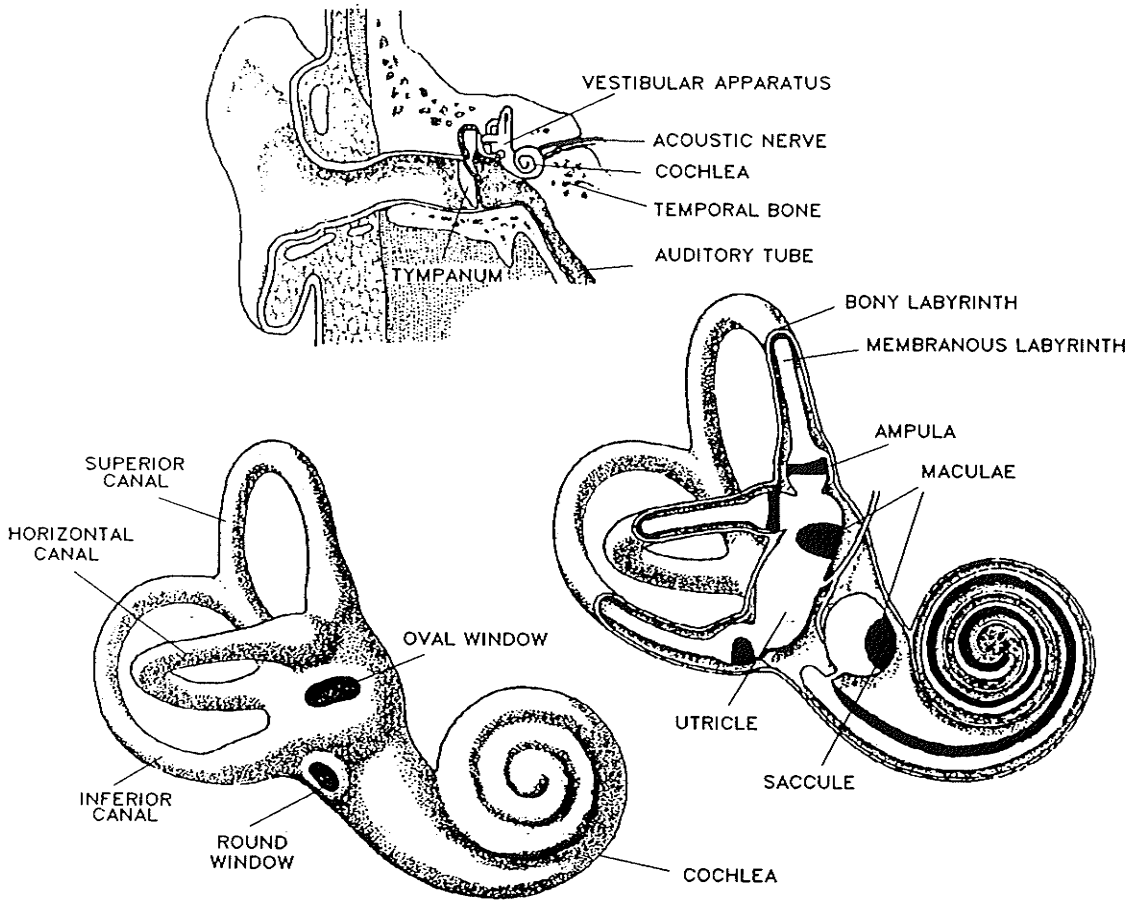

Fig. 1 Diagram illustrating the gross anatomy of the human inner ear. The upper panal is a section through the temporal bone where the vestibular and auditory sense organs (labyrinth) are embedded. The bottom left panal shows the isolated labyrinth. The bottom right panal shows the bony labyrinth opened to reveal the membranous labyrinth and specialized receptor regions of the sensory organs.

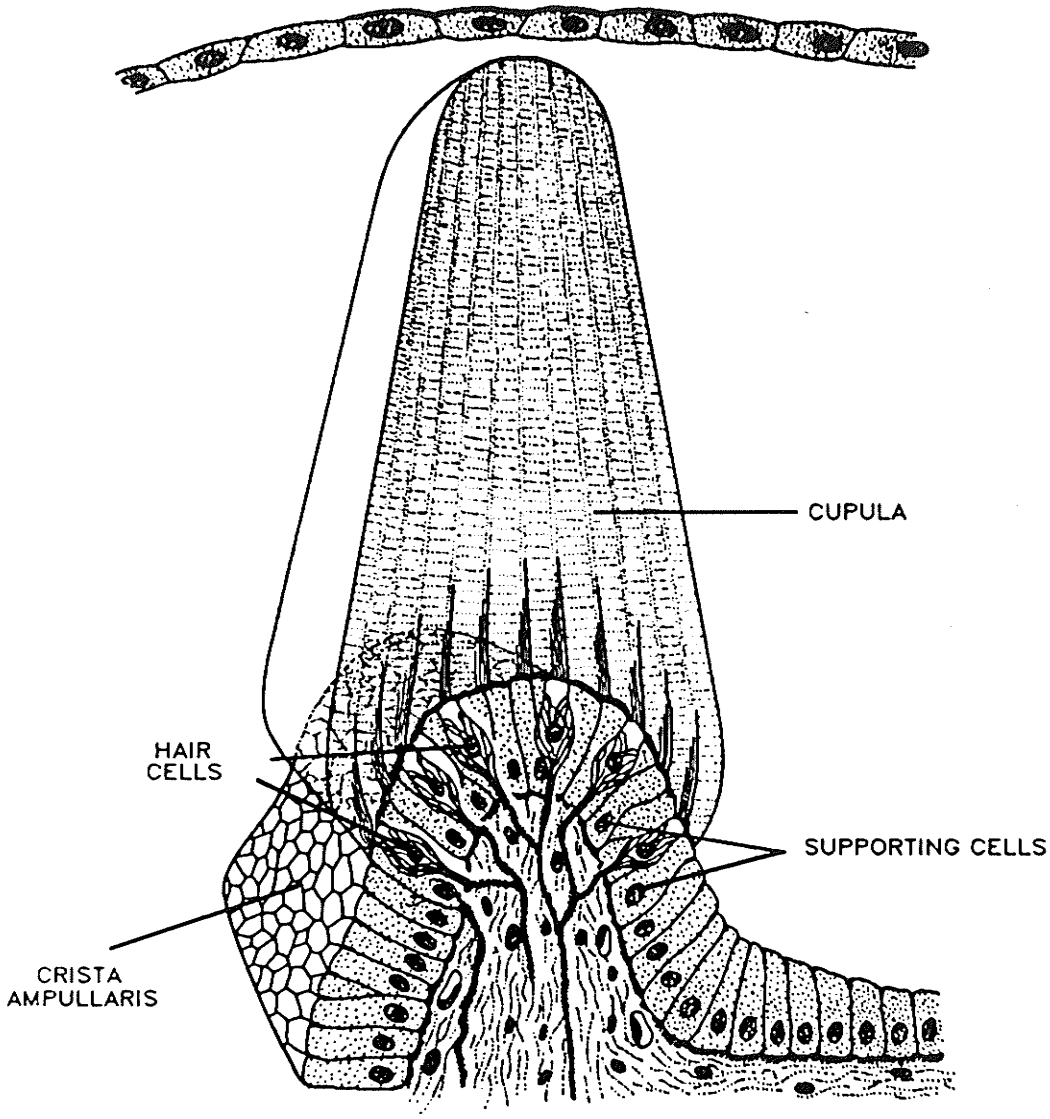

Fig. 2 Diagram illustrating the structure of the ampulla of the semicircular canals (Wersall 1956).

cells. This area is termed the crista ampullares. The arrangement of the hair cells and their hair bundles is integral to their function as receptors, which will be discussed in a later section. Extending from the crista towards the walls of the duct is a weakly elastic diaphragm structure of extracellular tissue material called the cupula. The cupula forms a watertight barrier across the ampullar lumen. The hair bundles project upwards and are inserted into the gelatinous cupula. The cupula moves relative to the epithelial surface in response to angular head accelerations, which results in bending of the hair bundles. Through a transduction process, the bending of hair bundles leads to membrane potential changes in the hair cells which is communicated to the associated nerve terminals. Functionally, the primary afferent innervation of the hair cells of the semicircular canal ampullae codes for angular motion of the head relative to space.

2.21 - Otolith Organ Ultrastructure

A number of investigations[266 58 2 119 240 241 139 137 149 268], using light/phase-contrast and electron microscopy have made detailed observations of the ultrastructure of the vestibular apparatus of fish, guinea pig, rabbit, cat, squirrel monkey and human . The figures referred to in this section (Fig. 4 - 6) are schematic representations of light-phase contrast and electron micrographs made from serial sections, and surface preparations of the sensory epithelium and statoconial membrane.

The orientation, shape, and subdivisions of the utricular and saccular maculae are illustrated in Fig. 3. Each macula is divided into two regions, the pars interna and pars externa, by the striola. The striola is a centrally located area, and in the guinea pig this area constitutes approximately 13% of the sensory epithelium in the saccule macula and 8% in the utriculae macula[139].

The sensory region of the otolith organs is not a homogeneous structure. Clear

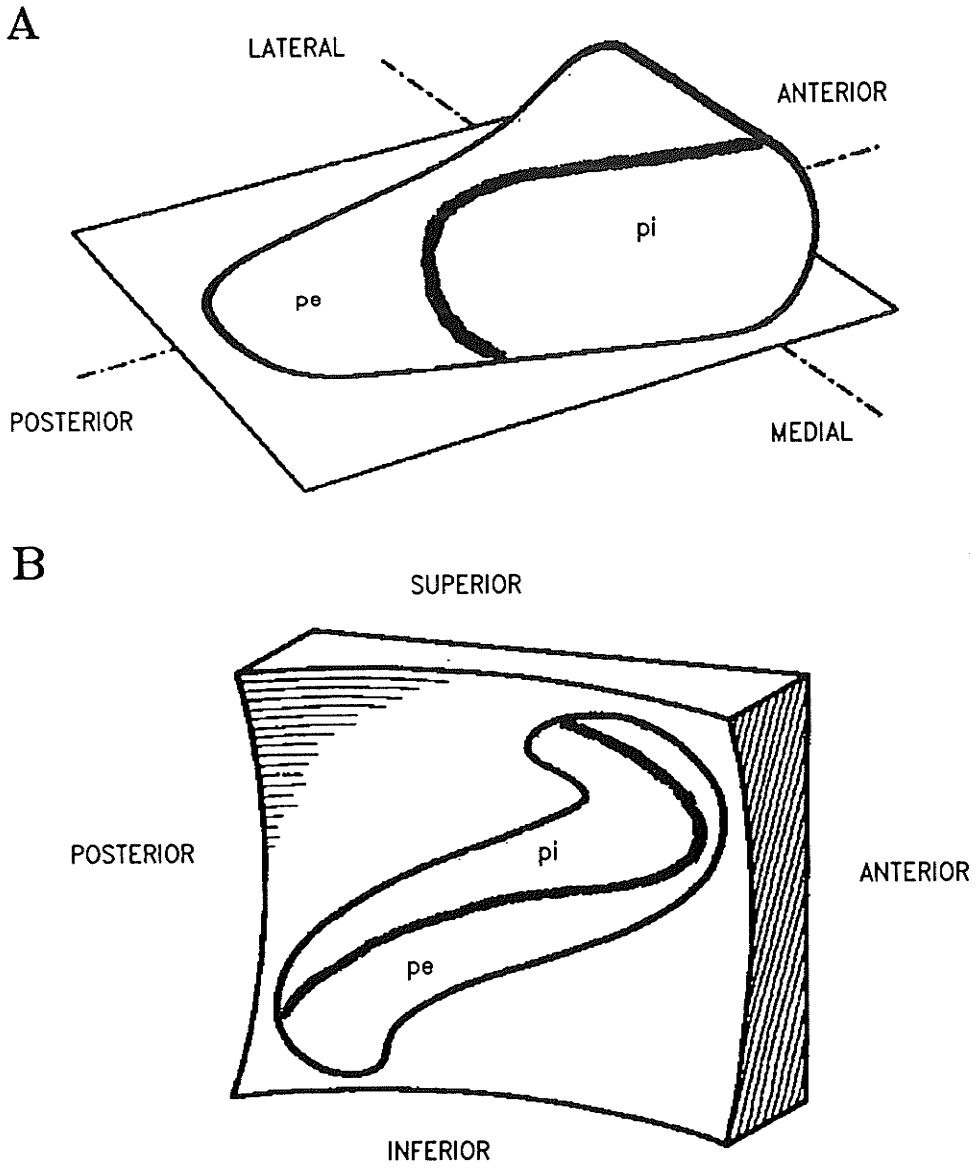

Fig. 3 Diagram illustrating the orientatiom and subdivisions of (A) utricular and (B) saccular maculae. Each maculae is divided into two areas, the pars interna (pi) and pars externa (pe) by the striola (central curved line).

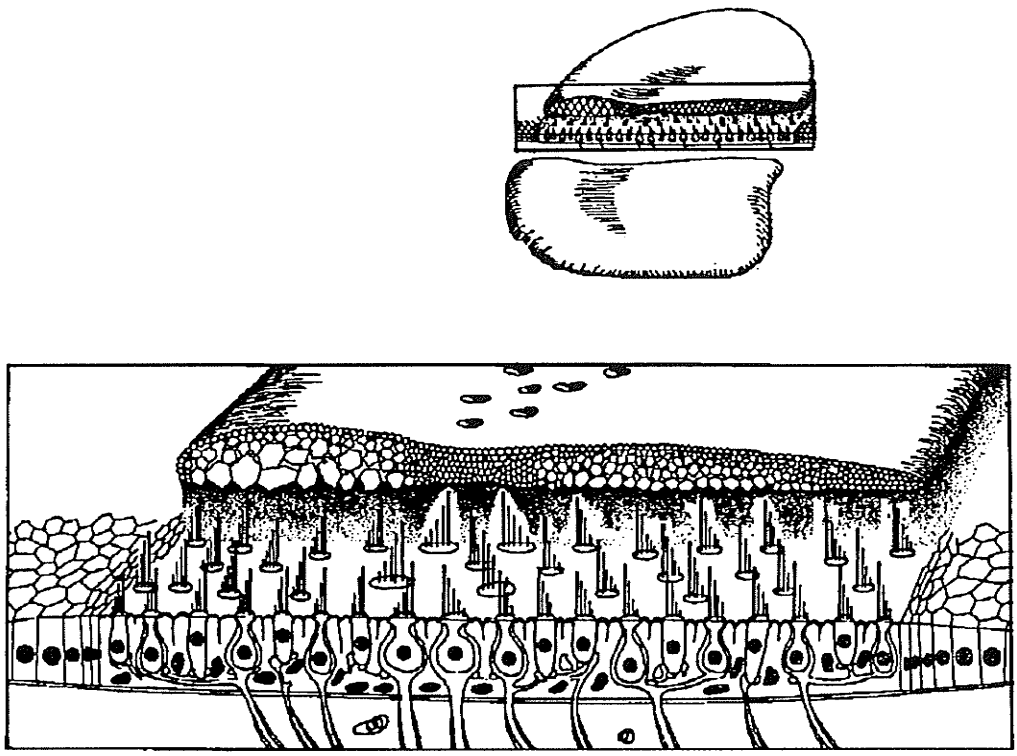

Fig. 4 Diagram illustrating the structure of the utricular maculae. Regional differences are shown of the thickness of the statoconial membrane, size of crystals, type and innervation of the sensory hair cells, and the polarization of the hair bundles i.e. the orientation of the kinociHum relative to stereocilia (Lindeman 1969).

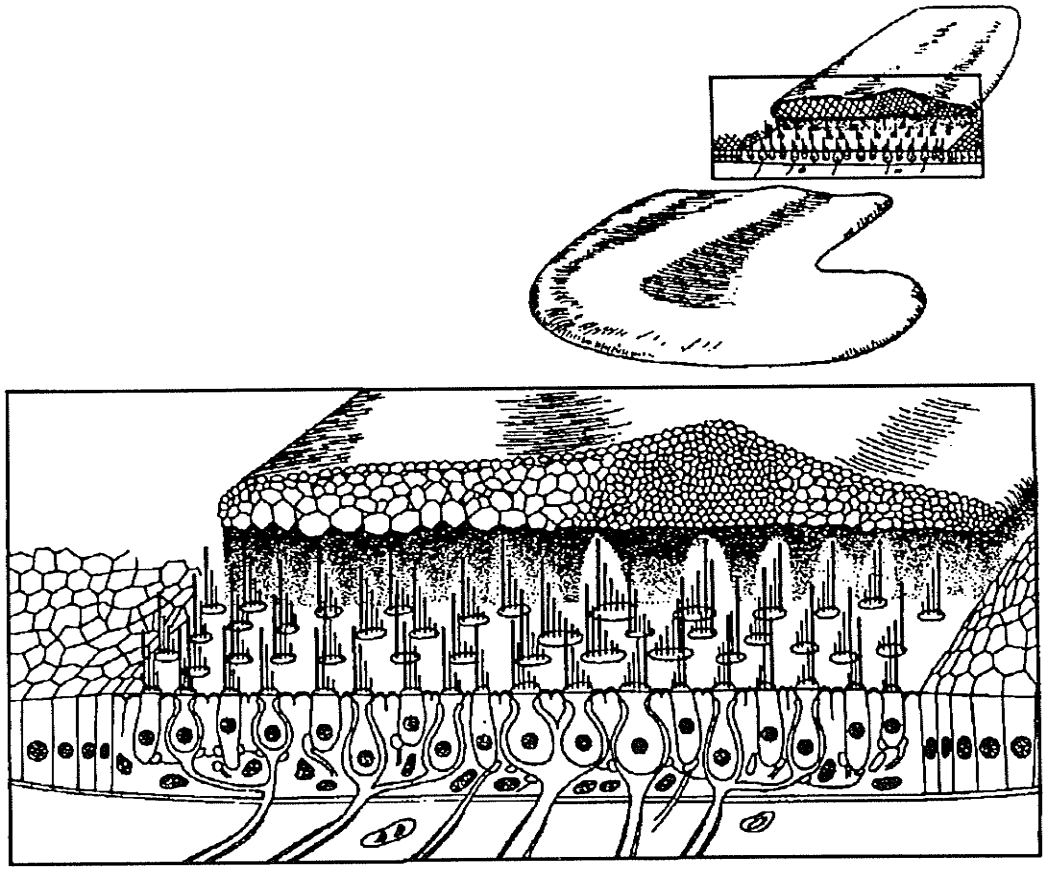

Fig. 5 Diagram illustrating the structure of the saccular maculae. Regional differences are shown of the thickness of statoconial membrane, size of crystals, type and innervation of sensory hair cells, and polarization of the hair bundles i.e. orientation of kinocilium relative to stereocilia. (Lindeman 1969)

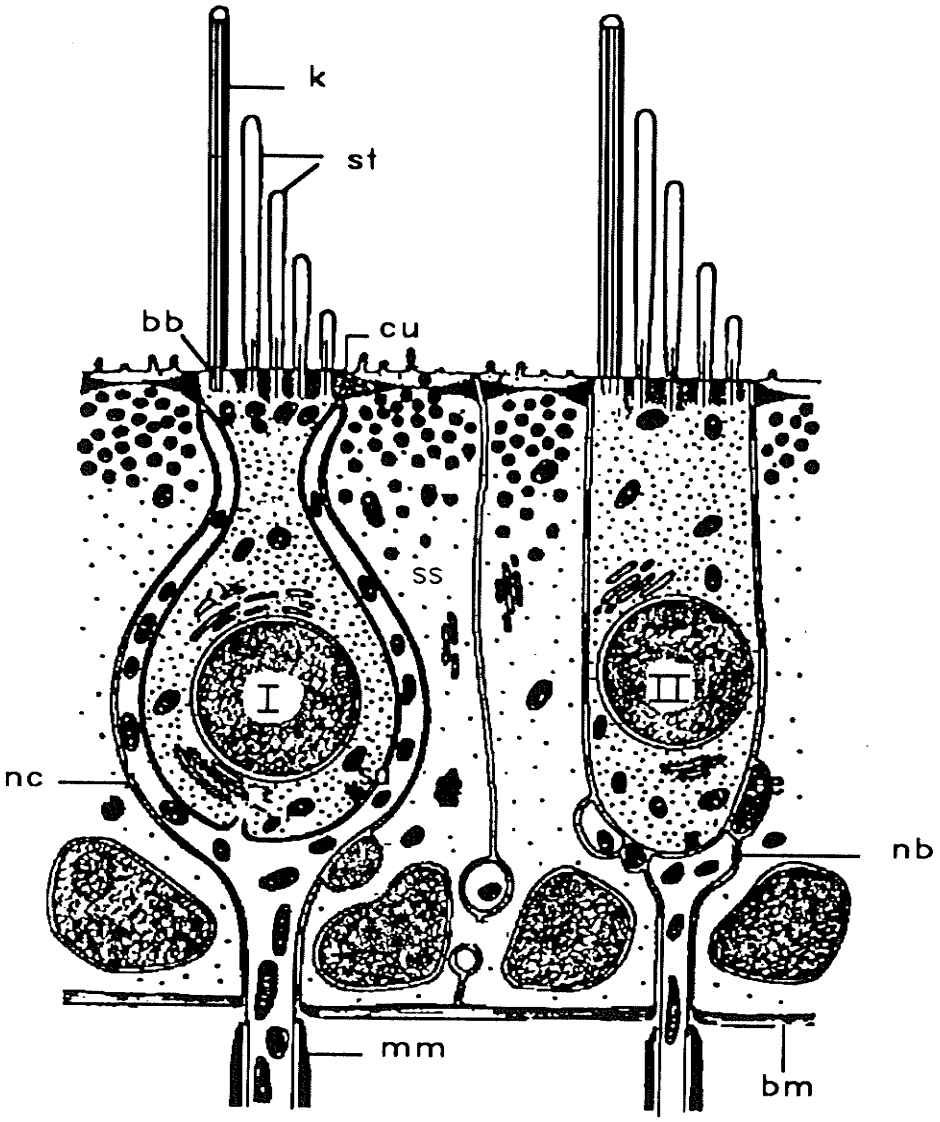

Fig. 6 General structure of vestibular sensory epithelium. Flask-shaped type I cell is surrounded by a nerve chalice (nc), the cylindrical type II cell innervated by bud-shaped terminals (nb). Kinocilium (k) and stereocilia (st) project from apical surface of hair cell into endolymphatic space. Basal body (bb) and cuticle (cu) anchor hair fibers to cell. Supportimg cell (ss), basement membrane (bm), myelinated nerve fibers (mm). (Lindeman 1969)

regional differences do exist in the structure of the sensory epithelium, its innervation, and the structure of the statoconial membrane[139]. The general arrangement of the sensory epithelium, and statoconial membrane of the saccular and utricular maculae is depicted in Fig. 4 and 5. It is these cells and non-neural elements that make possible the transduction of linear accelerations of the head into coded nerve signals. In the remaining section a description of the three component parts will be presented.

The receptor cell of the vestibular and auditory system is called the hair cell, so named because of the hair bundle which projects from its free surface. These hair cells are the main component of the sensory epithelium. Wersail[266], with the aid of the electron microscope, was able to distinguish two distinct populations of hair cells in the cristae ampullares of the guinea pig, which were named Type I and Type II hair cells. This is also true of the sensory epithelium of the otolith organs in vertebrates[58 139 241]. A schematic diagram of the sensory epithelium is presented in Fig. 6 to illustrate the general features of the hair cells and surrounding cells. The Type II hair cell is cylindrical and the Type I hair cell is flask shaped. Both are closely associated with nerve terminals, although they do not have axons or dendrites. The apical or upper end of the hair cell lies flush with the upper end of the surrounding supporting cells. The apical surfaces of the hair and supporting cells form a smooth surface which is in contact with the endolymph, and above which the hair bundles project.

The basic form and structure of the hair bundles is the same in all vertebrate animals[240 139 97 100]. Each hair bundle consists of 30 to 159 microvilli (stereocilia) and a single true

cilium (kinocilium). The hair bundle is circular in cross section and has a plane of bilateral symmetry i.e., along one diameter there is a progressive increase in the length of the stereocilia, but along any axis perpendicular to that diameter the stereocilia

are of equal length (see Fig. 6 and Fig. 7). The kinocilium is always found on the outer edge of the hair bundle occupying an eccentric position relative to the stereocilium.

The sensory regions of the otolith organs are covered by an extracellular substance of gelatinous nature. This substance also contains layers of crystals. The gelatinous substance together with the crystal layers forms a membrane like structure referred to as the statoconial membrane. Fig. 4 and 5 shows a cross section through utricular and saccular maculae illustrating the relationship between statoconial membrane and the hair cells, and the regional differences in the size of the crystals, and the thickness of the crystalline component of the membrane. The crystals are composed of calcite, a form of calcium carbonate. These calcite crystals have a specific gravity of about 2.7 times greater than the endolymph fluid that fills the utricular and saccular sac[35 36 180].

The gelatinous substance has a net-like structure, especially well developed in the striola[139 101 138]. The hair bundles project through canal-like pores in the gelatinous structure up into the crystalline layer[139 101]. The composition of the gelatinous substance is not known, although it has similar histochemical characteristics of the cupula[284].

A fluid filled space between the dense crystalline component of the statoconial membrane and the apical surface of the hair cell is maintained due to the presence of the gelatinous structure and the hair bundles.

The sensory regions of the mammalian vestibular organs are richly innervated by nerve fibers. The number of nerve fibers that project to the unilateral vestibular labyrinth has been determined to be about 18,000 in the monkey, 12,000 in the cat, and 8,000 in the guinea pig[77 78]. Roughly, they are distributed equally to the three canals, utricle, and saccule. The vestibular ganglion (Scarpa's ganglia) is situated in

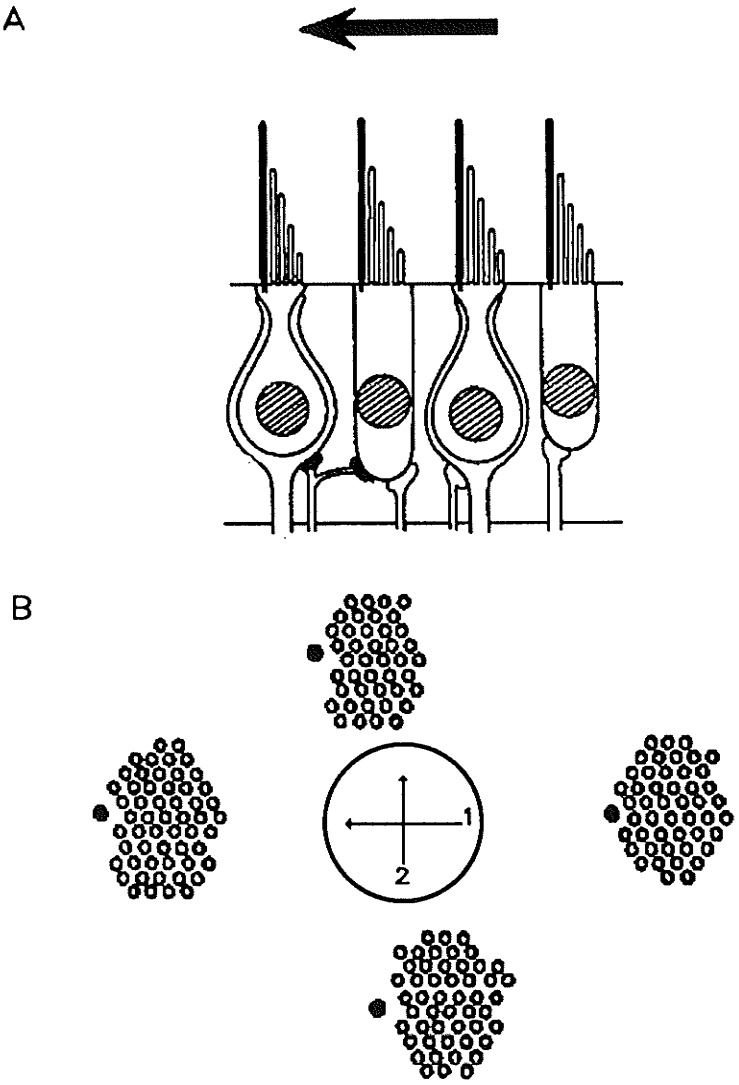

Fig. 7 Diagram illustrating the morphological polarization of the hair cells. A The direction of morphological polarization (top arrow) of hair cells is determined by position of kinocilium relative to stereocilia. B Cross section of hair bundles showing plane of bilateral symmetry. In center circle, along one diameter (arrow 1) there is a progressive increase in length of stereocilia, and perpendicular to this axis (arrow 2) the stereocilia are of equal length.

the bottom of the internal acoustic meatus and contains bipolar cells. The central extensions of these bipolar cells, which form the vestibular division of the VIIIth cranial nerve, enter the brain stem at the cerebello-pontine angle below the inferior border of the pons. The peripheral extensions from the bipolar cells form two main branches. The superior branch, which arises from the superior part of the ganglia, divides into the utricular nerve, the anterior and lateral ampullary nerves and Volt's nerve. Volt's nerve innervates the anterior part of the saccular macula. The inferior branch, which comes from the inferior part of the ganglia divides into the saccular and posterior ampullary nerves

The vestibular hair cells are innervated by myelinated fibers of different caliber[266 59 139]. These fibers are mainly afferent, but some somatic efferent fibers have been identified[76]. The cell bodies of the efferent fibers have been located in the brain stem lateral to the abducens nucleus in both the cat[80] and monkey[76]. These efferent fibers have been found to contain high levels of acetylcholinesterase[118 79].

In the sensory epithelium, the terminal branches of the nerve fibers make synaptic connections with the hair cells[59 2 240 241 139]. The nerve terminals end as enfolding chalices around Type I hair cells and bud or button shaped structures around type II hair cells (see Fig. 7). Sometimes the chalice like endings enclose several hair cells. Our knowledge of the pattern of afferent branching is rather limited, although there is often a large number of bud shaped terminals in contact with one type II cell originating in most cases from different nerve fibers[240 139]. Based on the morphological considerations it is suggested that chemically mediated signal transmission takes place at the contact sites between the hair cell and associated nerve terminals. There is some anatomical evidence that in some areas electrical rather than chemical transmission occurs between the nerve terminals and the hair cells[241].

2.22 - Morphological Polarization

It is generally believed that the adequate stimulus of the vestibular sensory cell is a force producing motion of the cupula or statoconial membrane relative to the sensory epithelium, and as a result, bending of the hair bundles. It has been shown that the vestibular organs are cable of encoding not only stimulus magnitude but also stimulus direction permitted by three-dimensional space. In regard to the directional selectivity of the vestibular system, of decisive importance is the orientation of the hairs on the hair cells.

Many studies[153 69 71 241 139 108] have shown that each hair cell is morphologically polarized as determined by the position of the kinocilium in relation to the stereociiium. Fig. 7 illustrates the morphological polarization of the hair cell. For the semicircular canals, the hair cells on the sane crista are polarized in the same direction. For example, on the crista of the horizontal canals the hair cells are all polarized towards the utricle i.e., the kinocilium is closer to the utricle than the stereocilium.

The situation on the maculae is more complicated[139]. The orientation of the corresponding polarization vectors in several species of mammals is presented in Fig. 8. Basically, each species has the same polarization pattern. Each macula is divided into two areas with opposite morphological polarizations. The dividing line coincides with the location and course of the striola. On the utricular macula the hair cells are polarized towards the striola, and on the saccular macula they are polarized away from the striola.

With respect to the planes of each macula the polarization vectors are orientated in all directions. Based on the morphological analysis, it has been implied that whereas a single receptor cell can provide information about the magnitude of one component of the stimulus (acting in the appropriate direction), the hair cells in total can provide measurements of an acceleration stimulus in any direction. Furthermore, it has been

shown in the earlier studies[152 153 70] that the morphological polarizations of the sensory cells could be correlated with electrophysiological observations (functional polarizations).

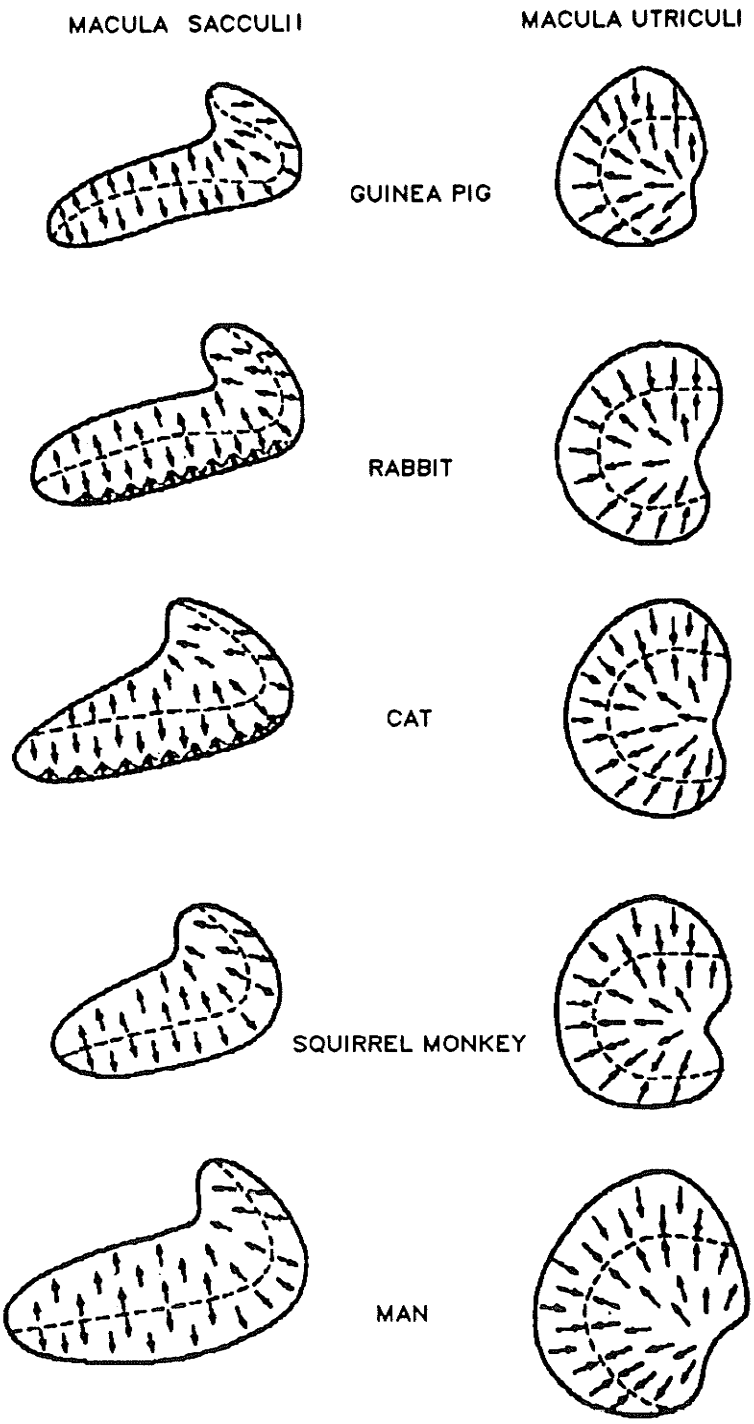

Fig. 8 Diagram illustrating the pattern of morphological polarization vectors in different species of mammals. (Lindeman 1969)

2.3 - RECEPTOR MECHANISMS AND THE PRIMARY AFFERENT RESPONSE

Before beginning the examination of the receptor mechanism and primary afferent response, a brief summary of the biophysics of the otolith organs will be presented.

Although the mechanics of the otolith organs is much less studied than that of the canals, it is generally established that the otolith organs act as linear accelerometer-like structures. The basic reaction of the otolith organs to linear acceleration stimuli is an inertial generated movement of the statoconial membrane relative the underlying sensory epithelium. Consequently hair fiber orientation is modified. In this regard three possibilities exist depending on the direction of the resultant force vector: 1) shearing movement of the statoconial membrane relative to the sensory epithelium which will produce hair bending; 2) an approximation of the statoconial membrane relative to the sensory epithelium which will produce compression of the hair bundles; 3) a separation of the statoconial membrane relative to the sensory epithelium which will produce a traction of the hair bundles. It should also be noted that due to the nature of the otolith receptors (inertial-gravitational system) that an ambiguity will exist between the effects of linear accelerations due to gravity and linear accelerations encountered during active movements or forces applied to the body. Here the otolith receptors will sense a change in position relative to the gravity vector but the direction of hair bundle deflection will be opposite to situations where the linear accelerations is the result of an active or a passive movement.

The physical response of the statoconial membrane to linear accelerations (gravitational and centripetal forces) has been studied by de Vries[48]. With the use of X-ray photography, quantitative measurements of the displacement of the statoconial membrane in the labyrinth of fish were made. Variations in the magnitude of the component of applied acceleration in the plane of the macula in question were obtained

by varying the position of the head relative to the vertical (line of gravity). The maximal displacements caused by gravitational forces was 1.0 mm. in both directions. It was also noted that large linear accelerations (centripetal force of 11 g.), produced by rotation of the platform, did not cause proportionally larger displacements of the statoconial membrane.

A critical stage in the transduction process is the displacement of the hair fibers which appears to mediate the coupling between mechanical events (the inertially generated movement of the statoconial membrane) and the electrical events (changes in the membrane potential of the hair cell). It has been proposed that the stereocilium can be modeled as a ridged lever attached to a short flexible beam clamped into the cuticular plate. Experimental evidence supports this model. In fresh preparations of frog ampulla Flock et al.[72] were able to visualize and photograph large displacements of the stereocilium and observe that the hair bundles moved as a ridged rod about its insertion into the surface of the cell. Also, on the hair cells of the lizard cochlea, Tilney et al.[252] have reported that excessive mechanical stimulation causes stereocilia to be severed near their insertion into the cell surface. This indicates that the major stress point occurs at the beam.

The process by which bending of the hair cells evoke electrical responses is largely unknown. However recent studies have shed some light on this subject[108 135].

Intracellular recording from the saccular hair cells of the frog shows that there exists a resting membrane potential of between -50 and -60 mv.[108]. A similar negative resting membrane potential of -35 to -45 mv. has been recorded intracellularlly in the hair cells of the molluscan statocyst, the basic form and structure of which is very similar to the vertebrate otolith organs[8 47]. It should be remembered that the apical surface of the hair cell and the hair bundle is in contact with the endolymph and that the basal end of the hair cell is surrounded by the supporting squamous

epithelial cells which are bathed in perilymph. The endolymph is peculiar because its ion concentration is similar to intracellular fluid i.e. approximately 15 mmol/litre of Na^+, 150 mmol/litre of K^+, and 120 mmol/litre of Cl^-[273]. On the other hand the composition of the perilymph is similar to that of plasma i.e. approximately 145 mmol-/litre of Na^+, 8 mmol/litre of K^+, and 130 mmol/litre of Cl^-[273]. Given the above considerations, the familiar electrochemical origin of the nerve membrane potential cannot account for the hair cell membrane potential.

The effects of artificially induced cupula movements on extracellular potentials recorded within the ampullae (ampullary potentials) have been investigated in the guinea pig by Trincker[254 255]. A consistent and significant modulation of the ampullary potential was observed, which depended on the direction of the cupula displacement. In the horizontal canals, cupula displacement towards the utricle (utriculopetal) resulted in a decrease in the amplitude of the ampullary potential, conversely a cupula deflection away from the utricle (utriculofugal) resulted in an increase in the amplitude of the ampullary potential. These findings are consistent with the known effects of natural semicircular stimulation on afferent nerve discharge rates[85 22].

Work done by Valli and Zucca[256] have extended these results. In this investigation an isolated preparation of the semicircular canal from the frog was used to examine the relationships among cupula deflection, modulation of the ampullary potential and the excitation and suppression of neural responses from primary afferents. In this experiment, a semicircular canal was isolated ,dissected and placed in a Tyrode Ringer bath. One end of a glass pipette was inserted into the cut end of the canal duct and the other end attached to a microsyringe device which could produce controlled, mainly sinusoidal deflections of the cupula. To record ampullary potentials an electrode was placed in the ampulla of the preparation near the hair cells. The primary afferent nerve trunk of the preparation was left intact to record action potentials and slow potential

changes. It was observed that the ampullary potential was modulated sinusoidally in response to a sinusoidal cupula displacement as was the mass discharge and slow potential changes recorded from the afferent nerves. A number of pharmacological manipulations were also performed during the experiments. It was shown that after reducing the Ca_2^+ concentration with or without increasing the Mg_2^+ concentration, both the modulation of the slow nerve potentials and afferent spikes were eliminated. In this situation the ampullary potential still exhibited a sinusoidal modulation. Similar findings were observed when dinitrophenol was added to the bath. These findings are indicative of Ca_2^+ mediated, energy dependent chemical transmission between the hair cell and the associated nerve terminal. Valli and Zucca[256] also reported that increasing the K^+ concentration in the bath to levels sufficient to block afferent fiber action potentials resulted in a significant increase in the amplitude of the ampullary potential. What are believed to be hair cell receptor potentials (intracellular recordings) have been examined during stimulation by mechanical means in the statocyt in molluscan[8 47], in lateral line organs of the mudpuppy[98], and in the saccule of the frog[108 135].

Hudspeth and Corey[108] developed an in vitro preparation which permitted intracellular recording from saccular hair cells during direct, precisely defined bending of the hair bundles (see also Shotwell, Jacobs,and Hudspath[237]). The hair bundles and the glass probe used to deflect the hair fibers were visualized under a microscope using a differential-interference-contrast optics. In this manner the degree of hair cell bending could be measured. Also the direction of bending relative to the axis of bilateral symmetry could be determined (see Fig. 2, ref. 237). It was shown that displacements of the hair bundles resulted in graded receptor potentials up to 20 mv. The hair cells responded to static deflections and to sinusoidal stimulation of frequencies up to 150 Hz. Both depolarizing and hyperpolarizing potentials were observed. The depolarizing potentials occurred when the stereocilium is displaced towards the kinocilium, conversely,

when the stereocilium was displaced away from the kinocilium a hyperpolarizing potential occurred. In general the amplitude of the hyperpolarizations were about one-fifth that of the depolarization. Furthermore, as the direction of the deflection changed from the axis of bilateral symmetry the size of the receptor potential decrease. The hair cell did not respond to displacements perpendicular to the axis of symmetry.

The input-output relationship (receptor potential amplitude as a function of the degree of hair fiber deflection), which was similar from cell to cell, is shown in Fig. 9. This relationship shows a more rapid saturation in the hyperpolarizing direction than in the depolarizing direction. The sensitivity of the hair cells, as calculated from the slope of the input- output curve is 20 mv. per micrometer of displacement.

From the intracellular studies on isolated hair cells it was concluded that the hair cell is quite responsive to hair fiber displacements directed along the axis of bilateral symmetry and unresponsive to displacements perpendicular to this axis.

Lewis and Hudspeth[136], using a whole cell voltage clamp technique, have studied the voltage and ion-dependent conductances in the isolated saccular hair cell of the frog. With the injection of depolarizing currents into voltage-clamped hair cells they reported several distinct ionic currents were able to characterize one inward and two outward currents. The inward current resembled a voltage dependent Ca_2^+ conductance that was non-inactivating. Taking into account the available morphological, pharmacological, and other electrophysiological observations previously described, it is likely that Ca_2^+ dependent chemical transmission occurs between the hair cell and the associated afferent nerve terminal. The two outward currents were characterized as a Ca_2^+ activated K^+ conductance, and an A- type K^+ conductance.

In order to characterize the physiological response of the vestibular receptors, many investigators[217 152 3 85 146 22 20 61 65 130] have studied the primary afferent activity of semicircular canals and otolith organs during natural stimulation. Generally,

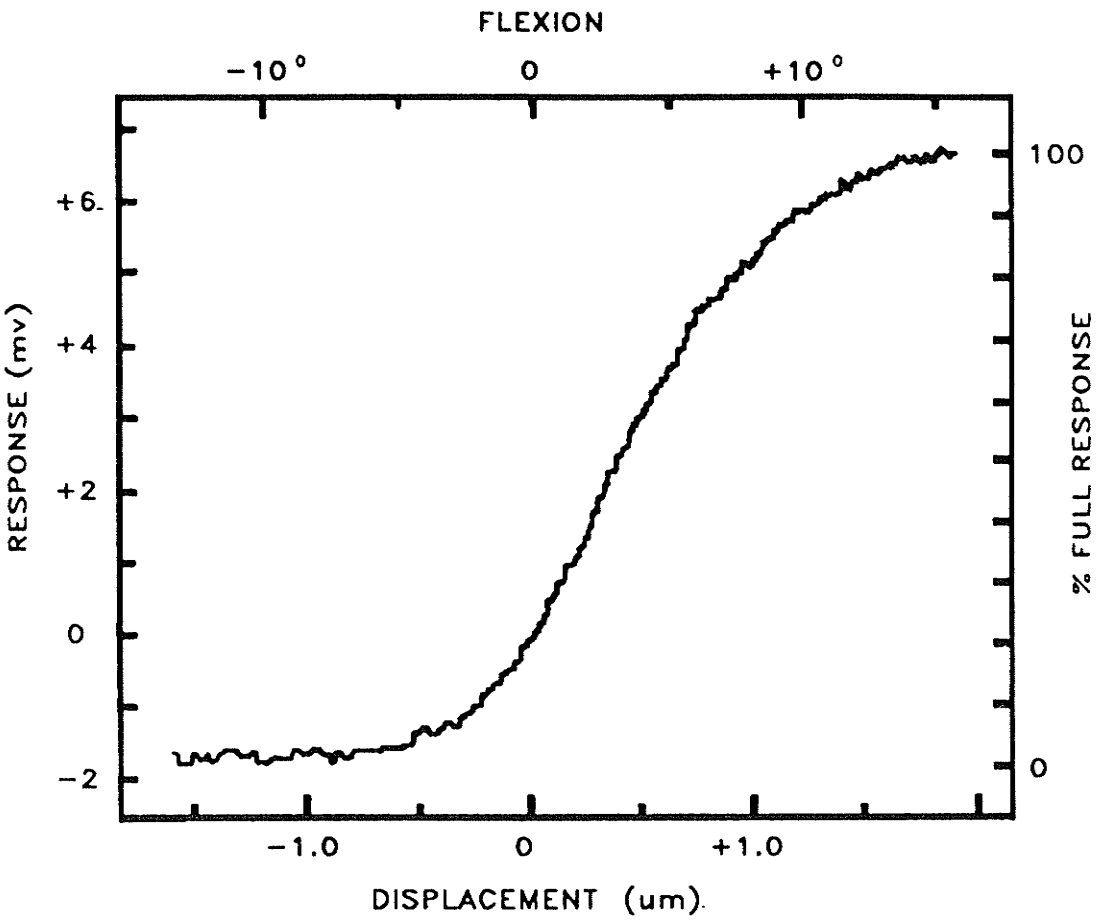

Fig. 9 Input–output relationship of bullfrog sacculus hair cell showing potential changes as a function of displacement of the hair bundle tips by a glass probe. Alternative scale (FLEXION VS % RESPONSE) represents the estimated angle of flexion of hair bundle on the assumption that it pivots at its base. (Hudspeth and Corey 1977).

it was found that both canal and otolith afferent nerves exhibited high levels of spontaneous activity, with a wide range of individual values, also that the vestibular units are functionally polarized, that is their discharge rate is modulated as a function of stimulus direction. It seems to be general principle that the functional polarization of the hair cells coincides with their morphological polarization.

In the earliest recordings of vestibular afferent activity in isolated preparations of the frog[217], dogfish[151], and Thorndike ray[152 150] it was shown that semicircular canal units were responsive to angular accelerations and otolith units were responsive to positional changes and linear translations. This has been confirmed in the cat[146 22 61 10] and the monkey[86 64 65], although there is some controversy as to the responsiveness of the semicircular canals to linear acceleration stimuli which will be discussed later. Adrian[3], recording from vestibular nucleus neurons in anesthetized and decerebrate cats, was the first to show that otolith end organs excited by static ipsilateral tilts invariably responded also to linear accelerations in the contralateral direction.

More recent work in the cat and monkey have made detailed observations of the directional selectivity, sensitivity and response dynamics of single otolith organ afferent units in the cat and monkey .

Unlike the canal afferents, the determination of the resting discharge of otolith afferents is complicated by the varying orientation of morphological polarization vectors on each macula and the constant presence of gravity. For these reasons each otolith unit should be characterized by a "functional" polarization vector which defines the axis of greatest sensitivity. The direction of the vector denotes the direction of a given acceleration which produced the maximum response, and the length of the vector represents the unit's response sensitivity (spikes/sec. per g.). The resting discharge for a unit can be defined as the spike frequency when the animal is positioned or tilted -90^{o} or $+90^{o}$ from the direction of maximum response about the axis of greatest

sensitivity. In this manner, Loe et al.[146] identified the directional characteristics and resting discharge of a population of single vestibular afferents, in the anesthetized cat, whose discharge frequency was dependent on head position. In this study, the discharge rate of the afferent units was recorded during slow (10^{o}/sec) rotations through 360^{o}. The responses of the afferent units examined closely resembled those of an idealized linear accelerometer, as a sinusoidal relationship between spike frequency and angular head position was observed. It was demonstrated, that starting from a head position where the unit spike frequency was maximal: 1) when the animal was tilted 18^{0o} the spike frequency was minimal; 2) when the animal was tilted $+90^{o}$ or -90^{o} the spike frequency was the same, being less than the maximal spike frequency and greater than the minimal spike frequency. Based on these findings, the resting discharge for the otolith units was taken as the recorded spike frequency with the animal tilted -90^{o} or $+90^{o}$ from the line of maximum sensitivity.

A series of studies by Fernandez and Goldberg[65 66 67] have extended the findings of Loe et. al[146]. In these investigations the physiological responses of primary otolith afferents, those responsive to static tilts and linear accelerations but not to angular accelerations, were examined. In this elegant work on the anesthetized squirrel monkey, care was taken to ensure that afferent nerve activity was sampled from both the utricular and saccular maculae. In this respect, afferent fibers were recorded from both the superior vestibular nerve (SN) or the inferior vestibular nerve (In). Remembering that the SN contains afferents that innervate not only the utricle , but also the saccule, controls were performed in which the superior nerve was sectioned.

In the first of the series of studies by Fernandez and Goldberg[65] the functional polarization vector of each otolith afferent unit was determined by using static tilts. It was observed that the polarization vectors for the 142 SN units were orientated close to the plane of the utricular macula, those for the 116 IN units near the plane

of the saccular macula. Within their corresponding planes, the SN force vectors had a wider distribution than IN force vectors . Furthermore most units were excited by ipsilateral force vectors. Also, in this study the degree of adaptation to prolonged stimulation was investigated using maintained centripetal force. Considerable variation was seen among units in their adaptive properties. However regular units (those classified as having regular resting discharge rates) showed little adaptation to maintained stimuli both in the excitatory and inhibitory phases. Irregular units (those classified by their irregular resting discharge rates) did show considerable adaptation. It should be noted that the majority of the afferent units studied were found to be regular units.

In the second series of experiments, Fernandez and Goldberg[66] examined the hypothesis that the hair cells respond to shearing displacements of the statoconial membrane relative to the sensory epithelium rather than to traction or compression. Here the direction of a centripetal force was varied with respect to the units function polarization vector and to the plane of the macula. Three types of centripetal force were used: 1) parallel shearing forces which were in the same direction as the functional polarization vector and in the plane of the corresponding macula; 2) orthogonal shear forces which were directed at right angles to the polarization vector, and in the plane of the corresponding macula; 3) orthogonal compression forces which were directed at right angles to the polarization vector and perpendicular to the plane of the corresponding macula. The results show that parallel shearing forces were most effective in modulating the spike frequency of otolith units. The sensitivity to orthogonal shears was about 10% of the sensitivity for parallel shearing forces. There was no significant response to orthogonal compression forces. By changing the magnitude of the centripetal force in the stimulus range $^{+}/_{-}$ 4.95 g. force-response functions of the afferent units were determined. The force-response function was found to be sigmoid shaped, saturating in both the excitatory (parallel) and inhibitory (anti-parallel) directions

(see Fig. 10). An asymmetry was observed in that the inhibitory saturation was attained at approximately 2 to 3 g., while excitatory saturation was just barely noted at 5g. These results conform with the findings of Hudspeth and Corey[108] who studied the relationship between the degree of hair cell bending and the amplitude of the receptor potential as discussed earlier and shown in Fig 9.

The purpose of the third series of experiments by Fernandez and Goldberg[67] was to characterize the response dynamics of the otolith afferent units. Centrifugal forces were used to produce sinusoidally varying forces in a frequency range from 0.006 to 2.0 Hz. The polarization vector of the afferent units were aligned and maintained in the horizontal plane (pivoted suprastructure) during exposure to the sinusoidal linear forces. The unit polarization vectors were orientated parallel and anti-parallel to the imposed centrifugal forces. The response dynamics of the regular units was found to be predominantly tonic, i.e., no more than a two-fold gain enhancement and only small (10^{o}) phase changes over the frequency spectrum of 0.006 to 2.0 HZ, These results indicate that the regular units carry a neural code that closely resembles the imposed acceleration below 2.0 HZ stimulation. On the other hand the response of irregular units was more phasic. These units exhibited a twenty-fold frequency-dependent gain enhancement with phase leads of 20^{o} to 40^{o} at the higher frequencies. This was interpreted as indicating that the otolith irregular units are responsive to statoconial membrane displacement and to the velocity of displacement, a feature which is also seen in the irregular semicircular canal units[22] (for review see 273). As to the functional significance of dynamic otolith responses, it was suggested that static tilts could be distinguished from linear movements by the predominate tonic responses of the regular units and the predominate phasic response of the irregular otolith units which is consistent with the adaptive characteristics of the regular versus the irregular otolith units. Anderson et al.[10] have examined the dynamics

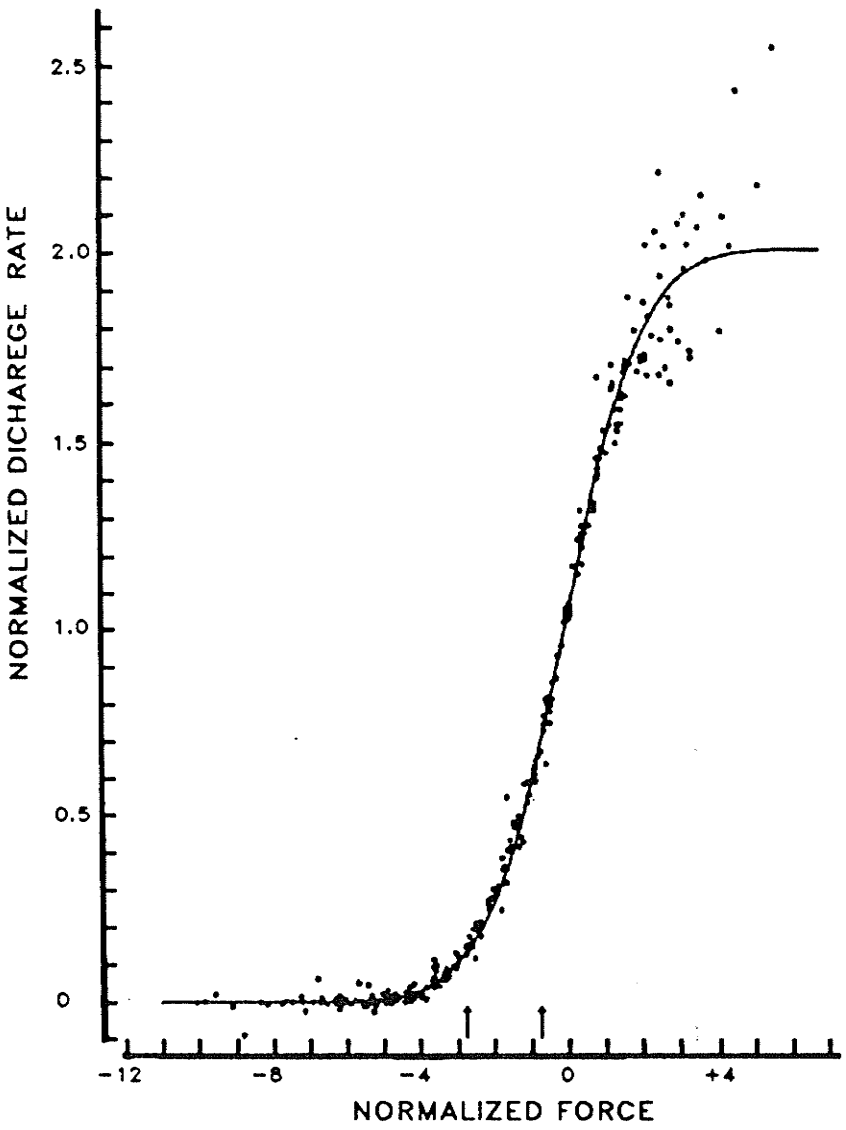

Fig. 10 Normalized force-response relation derived from the response characteristics of 17 saccular and utricular units to ± 4.95 g. forces. Arrows below curve represent average physiological range, i.e. ± 1.0 g. (Fernandez and Goldberg 1976b).

response of otolith primary afferents in the cat . The cat otolith afferents were found to behave in a similar manner as those described above in the monkey.

It is commonly thought that the adequate stimulus for the semicircular canals is rotational acceleration. However ,there is some physiological evidence which shows that the canals are capable of responding to linear accelerations, including nonadapting response to positional changes. Lowenstein[148] observed that some canal neurons in the isolated preparation of the ray were sensitive to head tilts. He noted, that because recordings were made from an opened labyrinth, this tilt dependent response could be artifactual. In this regard it should be noted that Ross[217], recording from the frog canal afferents with perilymphatic sac intact, did not find any effect due to gravity. Goldberg and Fernandez[86] have shown that peripheral neurons innervating intact canals in the squirrel monkey can respond to constant linear accelerations. They showed that this response was artifactual and arises from thermal gradients secondary to surgical exposure. However after canal plugging, which abolishes the response of canal neurons to angular accelerations[179 212], the canal units continued to respond to linear accelerations. This response could not be explained by the existence of thermal gradients because the caloric response, like the response to angular acceleration, requires the circulation of endolymph which should be prevented by the canal plugging procedure. Investigations in the cat by Estes et al.[61] and in the gerbil by Perachio and Correia[197], with the vestibular end organs intact, have also reported that canal afferents do respond to positional changes relative to the gravity vector.

It does appear that the canals are responsive to linear forces although the mechanism is unclear. It should be noted that these responses are considerably less than those observed in the otolith afferents[86 88 61]. Furthermore, with respect to cupular deflections, constant forces will become ineffective because the pressure on the two sides of the cupula will equalize in few milliseconds. However when subjected

to a rotating force vector, a sustained cupula deflection can occur[86].

2.4 - THE VESTIBULOSPINAL SYSTEM

The vestibulospinal system is one of the direct systems operating in descending skeletomotor control and considerable effort has been spent in examine its spinal organization and functional significance. From the classical postural reflex studies by Magnus (for review see ref. 165, 166) it has been observed that static tilts and head rotations could alter the extensor tonus of all four limbs. It was demonstrated that these effects were the consequences of the activation of vestibular and neck receptors. It was proposed that the macular labyrinth has an important role in the maintenance of balance, functionally to assist in the preservation of postural equilibrium during external perturbation. This view has gained experimental support from more recent animal studies[210 57 17 18 141 11 13 216 225 226 62 283], and a modified scheme of the directional pattern of tonic labyrinthine and neck reflexes has been proposed by Roberts[215] (see also Wilson et al.[283]).

In this section an analysis of the physiological role played by the otolith organs in the control of lower limb muscle activity or posture control will be presented. This will be preceded by an examination of the relevant morphological and physiological aspects of the vestibular nuclei and vestibulospinal tract.

2.40 - Vestibular Nuclei, Morphological And Physiological Considerations.

Activity originating from the hair cells of the vestibular organs is transmitted, via the VIIIth cranial nerve, to the brain stem terminating almost exclusively in the vestibular nucleus (VN). Anatomical studies (visualization of degenerating fibers) in the cat[147 261 184 77] and in the monkey[242] have examined the distribution and termin-

ation of primary vestibular afferents. In general it has been determined that afferent fibers to the VN all have their particular sites of termination, but no region of the nucleus receives fibers from only one vestibular end-organ. The results show that the macular afferents terminate in three of the four VN, Deiters' nucleus (DN), the inferior or descending nucleus and the medial nucleus. It was also found that canal afferents terminate in these nuclei, but for DN and the descending nuclei to a lesser extent.

The physiological properties of the vestibular afferent input to the VN have been investigated by electrical stimulation of the whole vestibular nerve or its branches, and during natural stimulation of the vestibular end organs.

Direct innervation of the VN by primary vestibular afferents has been substantiated in studies which recorded extracellular field potentials[211 74 282] and intracellular potentials[122 129] of neurons in the vestibular nuclei during stimulation of the whole vestibular nerve. These studies show that many neurons in the vestibular complex are excited by vestibular nerve stimulation. Both monosynaptic and polysynaptic EPSPs have been, with some cells exhibited both monosynaptic and polysynaptic potentials[122 129]. IPSPs have also been recorded and were found to be at least disynaptic. In regard to DN, the EPSPs of monosynaptic origin were located mainly in the ventral aspect while the EPSPs of polysynaptic origin were recorded throughout the nucleus[122].

Experiments with selective electrical stimulation of vestibular nerve branches have been employed to further examine the properties of central vestibular neurons receiving input from the canals and the otolith end organs. Most systematic studies have focused on the monosynaptic effects of ampullary nerve stimulation[168 272]. These investigations show little monosynaptic convergence from different canal afferents onto the same central vestibular neuron. A study by Sans et al.[220], recording extracellular potentials in the VN of the cat, examined the central effects of both ampullary and utricular nerve stimulation. It was reported that few neurons received direct

impulses from different receptors. They also found that during utricular nerve stimulation the distribution of field potentials was greatest in DN and to a lesser extent in the descending and medial VN. Other studies in the cat[115 280] have recorded orthodromic field potentials in the VN during saccular nerve stimulation. It was observed that saccular nerve stimulation evoked short latency field potentials mainly in DN and descending nucleus. With respect to DN cells, it was also noted that most short latency field potentials (indicative of monosynaptic connections) were located in the ventral aspect[280].

A number of investigators have examined the response of mammalian vestibular neurons during natural otolith stimulation[3 75 172 198 224 23 226 227 228]. In these experiments, selective elimination of possible contamination by canal stimulation has been achieved by recording steady state responses during maintained tilts, and in the case of dynamic stimuli with the canal plugging procedure developed by Money and Scott[179] (see also Raphen and Cohen[212]). As summarized by Wilson and Melvill-Jones[273], different types of central vestibular neurons have been identified during natural vestibular stimulation. Some neurons exhibit: 1) an increase in their discharge rate during ipsilateral tilts and a decrease in discharge rate during contralateral tilts (alpha response); 2) an increase in their discharge rate during contralateral tilts and a decrease in discharge rate during ipsilateral tilts (beta response); 3) an increase or decrease in their discharge rates to tilts in both directions (delta and gamma response respectively).

Peterson[198], recording extracellular potentials within the vestibular complex of the cat, has examined the distribution of neurons responsive to positional changes and steady maintained tilts. These same neurons were also classified according to their response to electrical stimulation of the labyrinth and vestibulospinal tract. In response to whole body tilts, the ongoing discharge rate of the neuron typically exhibited both phasic and tonic rate changes. The phasic rate changes adapted within 30 seconds of

tilt, while the tonic rate changes persisted. The tilt-dependent modulation of discharge rate was found to occur in many VN neurons, but was most prevalent in the ventral aspect of DN and the descending nucleus. It was also noted that neurons located in the ventral aspect of DN and the descending nucleus were driven antidromically by stimulation of the vestibulospinal tract and exhibited short latency potentials during stimulation of the labyrinth..

Melvill-Jones and Milsum[172] employed a parallel swing device similar to that described by Adrian[3] to examine the directional characteristics of central vestibular neurons in the cat during linear acceleration stimuli. They observed that the discharge rate of central vestibular neurons was dependent on the direction of the imposed linear acceleration. Each neuron had a maximal response when the animal was accelerated in one direction and a minimal response when accelerated at right angles to this line. Schor et al.[227] have systematically studied the directional selectivity of vestibular neurons during natural otolith stimulation. This investigation was done on canal plugged decerebrate cats. Stimulation of the otolith organs was achieved by: 1) slowly tilting the animal away from the horizontal about the roll or pitch axes in a sinusoidal fashion (0.05 or 0.1 Hz); 2) "wobble" stimulus, imposing a constant 10^{o} tilt, the direction of which was rotated around the animal by an appropriate combination of roll and pitch motions. The response of each neuron (extracellular recordings) could be characterized by a polarization vector whose orientation is given by the direction of the most effective stimulus about a given axis. They reported that the response vectors of 100 neurons, located mainly in DN, had a broad distribution in the horizontal plane (cats head in the normal anatomical position), being biased towards the roll direction. These findings contrast the uniform distribution (360^{o}) of otolith afferent polarization vectors recorded in the cat[253] and the monkey[65].

The dynamic behaviour of central vestibular neurons during natural otolith stim-

ulation has been examined in the decerebrate cat. Boyle and Pompeiano[23] have examined the frequency response characteristics of a large population of neurons located in the VN. Average firing rate of the neurons was recorded during sinusoidal tilt oscillations of 0.008 to 0.325 Hz, 10^{o} peak amplitude. It should be noted that at a peak frequency of 0.325 HZ, it would be difficult to differentiate pure otolith input from canal plus otolith input[273]. The gain was calculated as a ratio of the average firing rate (expressed in per cent of the base discharge frequency) to the stimulus amplitude in degrees. The phase angle of the first harmonic of the response was expressed in degrees with respect to the peak of the imposed tilt, ipsilateral to the recording side. The dynamic behaviour of 147 neurons, of which 102 were located in DN, was studied in this manner. Two populations of DN neurons were identified. The first population (about 60%) exhibited stable gain and phase angle over the frequency range studied, as would be expected if only macular afferents converged on these neurons. The second population (about 40%) was characterized by a progressive increase in gain as frequency increased and a phase lag (phase angle related to the angular velocity of the displacement). It was proposed that this type of response was indicative of semicircular canal input to the neurons.

Work by Schor and Miller[226] and Schor et al.[228] have obtained gain and phase response of central vestibular neurons in the canal plugged cat using extracellular recording techniques. Schor and Miller[226] recorded single unit response during sinusoidal roll tilt about a fixed axis in the frequency range of 0.01 to 2 Hz with varying amplitude to keep the maximal angular velocity below 31^{o}/sec. Neurons (132) were first characterized by their response to antidromic activation of the LVST or MVST and to electrical stimulation of the labyrinth. The neurons were also classified as having an alpha response (increase in discharge rate to ipsilateral tilts) or a beta response (increase in discharge rate to contralateral tilts). Schor et al.[228] examined the response dynamics of 72 central

vestibular neurons (mainly in DN) during sinusoidal tilts about a fixed axis, and also by using wobble stimuli[227] in the frequency range of 0.01 to 2 Hz. From these studies it was found that the response dynamics of central vestibular neurons fall two major classes. One group of neurons (most of the units with alpha responses) had response dynamics that closely resembled those of otolith afferents[67 10], i.e. slight gain and phase changes over the frequency range tested. The authors proposed that these neurons act as simple relays of otolith afferent signals. The other class of neurons (the majority of units with beta response) exhibited a large gain enhancement and a phase lag as much as 180^{o} as frequency increased. Although the basis of the large gain increases and phase lags observed in these DN cells is largely unknown, it was suggested that some form of neural processing is occurring in these neurons and that DN operates as an integrative canter. In this regard, anatomical and electrophysiological studies show that the vestibular complex receives synaptic input from a variety of sources other than labyrinthine, which include peripheral somatosensory receptors[74 281 181 28], reticular formation[102 259], and the cerebellum[260 120 121 124].

2.41 - Pathways Linking The Vestibular Nuclei To The Spinal Cord.

There is good reason to believe that vestibular influences on lower limb muscle activity are mainly conveyed through the lateral vestibulospinal tract (LVST), the most direct source of vestibulospinal fibers to the lumbosacral spinal cord. Other less direct pathways through the reticular formation and the cerebellum have been identified (for review see 273, 230 199 207)

From anatomically[208 195 194 203] and electrophysiological studies[125 282 5 6 1 213] there is general agreement that LVST is a principle source of vestibulospinal fibers

to the lumbosacral spinal cord, and that this tract arises from neurons located mainly in DN, and also in part from the descending vestibular nucleus. Deiters' nucleus appears to be somatotopically organized such that cells projecting to the lumbar cord are more concentrated in the dorsocaudal aspect and cells projecting to the cervical cord in the rostroventral aspect[208 282 198]. It has also been reported that axons of LVST neurons projecting to the cervical cord give off collateral branches that reach thoracic and in some cases lumbar segments[1 213]. The conduction velocity of LVST fibers has been determined in the rabbit and the cat, and found to range from 20 to 140 m/sec. with a mean value about 90 m/sec.[125 282 6 236].

Early anatomical observations by Nyberg-Hansen and Mascitti1[95], Nyberg-Hansen[194], and Petras[203] have shown that the vestibulospinal fibers originating from DN descend ipsilaterally in the ventral fasciculus of the spinal cord and terminate in the ventromedial aspect of Rexed's laminae VII and VIII, but rarely in lamina IX. A recent study by Shinoda, et al.[236] has examined the terminal distribution (C_5 to T_1) of single LVST axons using intra-axonal staining with horseradish peroxidase (HRP). Axons penetrated in the lower cervical cord of the cat were identified as LVST fibers by their response to vestibular nerve stimulation and to their direct activation by stimulation of the ipsilateral DN. The results reported by Shinoda et al.[236] are in good agreement with the findings of Nyberg-Hansen and Mascitti[195] Petras[203] and Nyberg-Hansen[194]. They also observed that a considerable number of LVST axons cross in the anterior commissure of the spinal cord and terminate in the contralateral lamina VII and VIII, and that LVST axons also terminate in lamina IX. These findings have not been previously reported. The terminal distribution of LVST fibers in the lumber cord has not been investigated in this manner.

As mentioned earlier, the reticular formation (RF) may process activity originating from the vestibular system and relay this information to the spinal cord through the

reticulospinal tract. Physiological studies have shown that reticulospinal neurons respond to vestibular nerve or vestibular nuclei stimulation[200 101 202]. Manzoni et al.[167] have observed that reticulospinal neurons, identified by antidromic activation of the spinal cord between T_12 and L_1, are modulated during sinusoidal rotation of 0.026 Hz, 10^o peak amplitude. The neurons were histologically located in the ventrocaudal and medial aspects of the medullary RF. In this study a comparison was made of the effect of sinusoidal rotation of the animal in the roll axis on the reticulospinal neurons and neurons located in DN. It was found that the predominant response pattern of the reticulospinal neurons (excitation during side-up rotations) was opposite to the predominate response pattern of the DN cells (excitation during side-down tilt).

2.42 - Vestibulospinal Effects On Spinal Neurons.

The majority of studies undertaken to examine vestibulospinal synaptology and the effects of vestibular signals on muscle activity, have concentrated upon electrical stimulation of vestibular nuclei, in particular DN. Other approaches, such as vestibular nerve stimulation and natural labyrinth stimulation, have also contributed to our understanding of vestibulospinal mechanisms in skeletomotor control.

With respect to axial (neck and trunk) motoneurons, postsynaptic potentials have been recorded during stimulation, the vestibular nuclei and, the vestibular nerve or its branches[275 276 7 279]. These studies show that axial motoneurons receive disynaptic EPSPs and IPSPs from the semicircular canals, and short latency excitatory and inhibitory effects from the otolith organs. It was noted that the short-latency effects from the semicircular canals were stronger that those from the utricle or saccule. These studies provide evidence that the vestibular nuclei do serve as relays of the excitatory and inhibitory effects from the vestibular receptors to axial motoneurons.

It has long been known that impulses in vestibulospinal fibers , originating from DN, have a significant influence on the activity of hind limb extensor muscles. Lesions of DN or the LVST markedly reduce or even abolish the extensor tonus present in the decerebrate cat preparation[26 176]. Furthermore, it has long been established that DN stimulation increases the excitability of lumbar motoneurons of the cat[221 233 154 155]. These studies have been followed by detailed investigations of the functional linkages between DN and spinal neurons. Before discussing the effects of DN stimulation on lumbar spinal neurons, the effects of vestibular nerve stimulation on limb motoneurons will be examined.

Work done by Wilson and Yoshida[275 276], recording intracellularlly from various limb motoneurons in the barbiturate-anesthetized cat, found no effects at all during whole vestibular nerve stimulation. In a subsequent study on the decerebrate cat, Maeda et al.[158] reported that stimulation of the whole vestibular nerve evoked bilateral postsynaptic potentials in forelimb motoneurons. Usually, multiple shocks were required to elicit the responses. Depolarizing potentials were mainly observed in extensor motoneurons and hyperpolarizing potentials in the flexor motoneurons. They also showed that selective stimulation of the ampullary nerves evoked postsynaptic potentials in forelimb motoneurons. The pattern of extensor excitation and flexor inhibition predominated. However, the postsynaptic potentials evoked from ampullary nerve stimulation were considerably weaker and more variable than whole vestibular nerve stimulation. This would indicate that the otolith receptors do contribute to the vestibular nerve effects. Similar experiments have not been done on mammalian hindlimb motoneurons.

One of the first detailed studies of the functional linkage between DN and the lumbar spinal cord was done by Lund and Pompeiano[154 155]. The main purpose of this study was to establish the origin of the descending pathway with monosynaptic connection to motoneurons. They reported that stimulation of the ventral quadrant of the

spinal cord (T_{12} level) and DN, evoked monosynaptic EPSPs in hindlimb motoneurons. After chronic lesions of DN (allowing for degeneration of the vestibulospinal tract) no monosynaptic EPSPs were elicited during stimulation of the ventral quadrant. It was concluded from this study that DN had monosynaptic connections with extensor motoneurons.

More extensive investigations of the effects of DN stimulation on various hindlimb motoneurons have been made by Wilson and Yoshida[275] and Grillner et al.[94 95]. These studies were performed on anesthetized cats with intracellular recording of motoneurons. The results show that monosynaptic EPSPs were not the principle effect during DN stimulation. Rather di(poly)synaptic EPSPs and IPSPs were more common. Typically, EPSPs were found in hindlimb extensors (some in pretibial flexors), and IPSPs occurred mainly in flexors (some in hip extensor). The monosynaptic EPSPs were only observed in quadriceps and gastrocnemius-soleus motoneurons and it was reported by Grillner et al.[95] (see also ten Bruggencate and Lunberg[27]) that the monosynaptic EPSPs were not found in all knee or ankle extensor motoneurons, or in all cats.

Monosynaptic EPSPs in hindlimb motoneurons produced by DN stimulation have been reported in the monkey[233 234]. The monosynaptic EPSPs were found mainly in the knee extensor motoneurons and some in the ankle extensor.

Postsynaptic effects in hindlimb motoneurons have also been examined during stimulation of DN, contralateral to the recording side by Aoyama et al.[14] and Hongo et al.[106]. In these experiments on anesthetized cats using intracellular recording techniques, the response of motoneurons to stimulation of the contralateral and/or the ipsilateral DN were examined. To eliminate possible effects passing from one side of DN to the other through commisural fibers, the brain stem was sectioned in the mid-sagittal plane at a level between the inferior colliculus and the obex. Also PSP's were compared when the stimulus was applied to DN and the axonal region of the LVST 5-6

mm. caudal to DN. It was found that stimulation of the contralateral DN evokes effects in motoneurons that were similar to those recorded in the same motoneuron during ipsilateral DN stimulation, typically EPSPs were recorded in extensor motoneurons and IPSPs in flexor motoneurons. The contralateral effects were notably smaller (about half the amplitude) than the ipsilateral effects and the results of latency measurements indicated that the response to contralateral DN stimulation required at least one more synapse than did ipsilateral DN stimulation. Furthermore, during stimulation of the contralateral DN preceded by a conditioning shock to the ipsilateral DN and vice versa, it was determined that effects from contralateral and ipsilateral DN stimulation were transmitted to motoneurons throughout a final common pathway. After hemisection of the contralateral cord (lower thoracic region) disynaptic EPSPs from ipsilateral DN stimulation were no longer facilitated by conditioning stimulation of the contralateral DN. These findings indicate that the convergence underlying the facilitation took place in spinal relay interneurons below the lesion site.

Attempts have been made to identify the interneurons that function as relay cells for the bilateral effects described above. Aoyama et al.[14] examined the effects of contralateral DN stimulation on 76 interneurons (49 intracellular and 27 extracellular recordings) which received short latency excitation from ipsilateral DN stimulation. These interneurons were located in lamina VII and VIII in the L_5-S_1 segments. In thirty-two of the interneurons, contralateral DN stimulation evoked short latency depolarization while hyperpolarization was observed in 32 others. It should be remembered that anatomical studies have shown that axons of the LVST do cross the midline in the spinal cord and terminate in Lamina VII-VIII in the cervical cord (Shinoda et[236]). With intracellular recording techniques in anesthetized cat, others have reported that ipsilateral DN stimulation elicits monosynaptic excitation of interneurons in the lumbar cord. Grillner and Hongo[92] reported that interneurons in lamina VII-VIII (L_5-

L_7) were monosynaptically activated from ipsilateral DN stimulation. These cells were activated by single shocks and could follow very high frequency stimulation (up to 600Hz). Skinner and Remmel[238] have also recorded monosynaptic EPSPs in lamina VII-VIII (L_6-L_7) interneurons. Hultborn et al.[114] have made intracellular recordings of a variety of flexor coupled and extensor coupled 1a inhibitory interneurons (L_5-L_7) in the anesthetized cat during ipsilateral DN stimulation. They observed that DN exerts excitatory monosynaptic effects almost exclusively in extensor-coupled Ia inhibitory interneurons, in particular in quadriceps-coupled Ia inhibitory interneurons. In the flexor- coupled Ia inhibitory interneurons examined, only one (sartorius coupled cell) received a monosynaptic EPSP.

Interactions between vestibulospinal volleys and peripheral afferents in transmission to hindlimb motoneurons has also been investigated using the spatial facilitation technique (see Baldissera et al.[16] for a summary of this technique). These studies showed that di(poly)synaptic DN effects in motoneurons are mediated by segmental interneurons with convergent input from Ia afferents (direct evidence as discussed above) and cutaneous afferents.

Grillner et al.[93] have investigated the inhibitory effects from DN to lumbosacral motoneurons with intracellular motoneuron recordings. They observed that stimulation of DN elicits a short latency IPSP in knee flexor motoneurons. It was found that the effects of stimulation of the quadriceps nerve at group I strength in flexor motoneurons (short latency IPSP) could be facilitated by stimulation of DN. It was suggested that volleys in the vestibulospinal tract evoke monosynaptic EPSPs in the interneurons transmitting the reciprocal Ia IPSP to knee flexor motoneurons. A subsequent study by Hultborn and Udo[112], using similar methods, confirmed these findings. They observed that facilitation of Ia IPSP by volleys in the vestibulospinal tract is seen in flexor motoneurons supplying mainly the knee muscles.

Ten Bruggencate and Lundberg[27] have identified the pattern of excitatory and inhibitory effects from the vestibulospinal tract on cat hindlimb motoneurons and have examined the interaction of these effects with volleys in peripheral afferents, in particular contralateral primary afferents (see also ten Bruggencate et al.[29] and Hongo et al.[105]). These experiments were performed on anesthetized cats. Intracellular recordings were made from motoneurons supplying hindlimb extensor and flexor muscles. The pattern of mono- di- and polysynaptic connections from the vestibulospinal tract described by Wilson and Yoshida[275] and Grillner et al.[94 95] were confirmed in this study. The authors discussed the close resemblance between the pattern of these vestibulospinal effects and the crossed extensor reflex. While recording from motoneurons they observed that the effects from stimulation of contralateral peripheral nerves were facilitated by conditioning stimulation of ipsilateral DN. In order to test the hypothesis that disynaptic vestibulospinal PSP's evoked in motoneurons are mediated by interneurons interposed in polysynaptic spinal pathways transmitting crossed peripheral somatosensory reflex actions, the effects of conditioning volleys in the contralateral peripheral nerves on the disynaptic vestibulospinal PSP's were examined. In this series of experiments test shocks were delivered to DN, preceded by conditioning volleys in a variety of contralateral primary afferents (nerve branches supplying muscle, and cutaneous nerves in particular the sural nerve). It was found that both disynaptic vestibulospinal EPSPs to extensor motoneurons, and disynaptic vestibulospinal IPSPs to flexor motoneurons were facilitated by conditioning volleys in all contralateral nerves stimulated. It was also shown that for the knee flexor motoneurons, conditioning stimuli of the contralateral peripheral nerves gave a parallel facilitation of disynaptic vestibulospinal IPSPs and Ia IPSPs. This was not the case for knee extensor or ankle flexor and extensor motoneurons, rather, only facilitation of disynaptic vestibulospinal IPSPs was observed. The effects of graded stimulation of the peripheral nerves revealed that high stimulus

strengths were needed to produce the facilitation, i.e. for the contralateral hamstring nerve, 8 times threshold was required to observe a clear effect and for sural nerve about 10 times threshold. The time courses (time interval between test and conditioning shocks) of the facilitation of the disynaptic vestibulospinal EPSP and IPSP were similar, ranging from 10 ms. to 70 ms. with a peak facilitation at approximately 20-25 ms. Control experiments were performed to determine if facilitation was evoked segmentally (spatial facilitation) or was the result of activation of cells in DN by ascending pathways from the contralateral peripheral afferents (temporal facilitation). In these control experiments vestibulospinal fibers were stimulated by two electrodes, one located in DN and the other positioned 5mm. caudal to DN in the region of the LVST axons. Virtually identical effects were recorded in motoneurons when shocks were delivered to either of the two electrodes. This was true of the unconditioned and conditioned postsynaptic effects. Furthermore, occlusion of the descending volleys occurred when both sites were stimulated, as recorded with surface electrodes at T_{12}. These findings indicate that the interaction between vestibulospinal effects and volleys in contralateral peripheral afferents is the result of spatial facilitation evoked segmentally. Based on the conditioning- testing order (test stimulus to DN and conditioning stimulus to the peripheral nerves), it was concluded that the convergence occurred on last order interneurons of the coFRA spinal reflex arc. It should be noted that a systematic examination of the convergent effects from the vestibulospinal tract and ipsilateral cutaneous afferents was not performed in this study. In this respect, facilitation of vestibulospinal PSP's to knee flexor motoneurons by volleys in ipsilateral cutaneous afferents has been reported[156].

High frequency, high threshold stimulation of the whole vestibular nerve or vestibular nuclei produces dorsal root potentials (DRP) in the cat lumbar region[37 40 41]. These DRP's are indicative of presynaptic inhibition of primary afferent terminals

(for review see Baldissera et al.[16]). Cook et al.[40] recorded primary afferent depolarization (PAD) in group I muscle afferent from flexor and extensor muscles, and cutaneous afferents during stimulation of the vestibular nerve. In these experiments, due to the nature of the stimulus (500 Hz train of pulses lasting 400 ms), the time course of the PAD could not be precisely determined. Reportedly, the functional consequence of the PAD is largely unknown since it was also found that conditioning stimulation of the vestibular nerve resulted in facilitation of the monosynaptic Ia (gastrocnemius-soleus) reflex, notwithstanding, the PAD of the group Ia afferents to this muscle.

Natural vestibular stimulation has been employed to identify and characterize the spinal neural elements mediating vestibulospinal reflexes, and to examine otolith reflex behaviour of neck and limb muscles.

Wilson et al.278 and Schor et al.[229], with extracellular recording techniques, have identified spinal interneurons in C_4-C_8 segments whose spontaneous activity is modulated sinusoidally during slow sinusoidal tilts and wobble stimuli. These studies were performed on the decerebrate cat which was also paralyzed. Most of the neurons that responded to tilt stimuli were found to be located in lamina VII-VIII. Schor et al.[229] also report that, of the tilt sensitive interneurons examined one-third responded with short latency PSP's during electrical stimulation of the labyrinth.

The response dynamics of 45 tilt sensitive cervical interneurons in the cat with intact canals and plugged canals have been examined by Schor et al.[229]. Once the response vector orientation was determined, the animal was subjected to a series of sinusoidal stimuli (0.02 to 1.0 Hz) in the plane aligned with the polarization vector. In the cat with intact canals, it was found that the tilt-sensitive interneurons could be grouped into two populations. One group had dynamic responses proportional to and in phase with the position of the animal, indicative of otolith stimulation. The second group exhibited a velocity response i.e., modest gain increase and phase leads up to

90^{o} over the frequency range, indicative of semicircular canal stimulation. In the cats with plugged canals, the velocity response was absent; only a position response was observed. It was also reported that with increasing frequency of stimulation a few interneurons exhibited large gain enhancements and phase lags, dynamic responses which have been previously recorded in DN cells[228].

Suzuki et al.[243] have studied the response of interneurons (extracellular recordings) in the L_3-L_6 segment of the spinal cord to natural neck and vestibular stimulation. The experiments were performed on the decerebrate cat with intact canals. Slow sinusoidal tilts or wobble stimuli were used (0.05 or 0.1 Hz) to minimize the activation of semicircular canals. The majority of the interneurons responsive to vestibular or neck stimulation were located in lamina VII or VIII. Twenty-seven lumbar interneurons were responsive to whole body tilt. It was found that the response vectors for these interneurons were widely distributed, except that there was a lack of response vectors at or near nose-down tilt. It was concluded that the origin of the activity responsible for the observed tilt dependent responses in the lumber interneurons was most likely the otolith organs.

Vertical acceleration stimuli (free fall), has been used to investigate otolith-dependent reflexes in the lower limb muscles of the cat[262 263 264] and the baboon[133 134].

In the awake cat, Watt[262] demonstrated the appearance of two bursts of EMG activity in both gastrocnemius and tibialis anterior during sudden unexpected falls. The early burst began about 15 ms. from the onset of the vertical linear acceleration and had a duration of up to 85 ms. A later burst of muscle activity commenced 75-100 ms. after the beginning of the fall. Using similar methods, EMG responses were recorded in previously labyrinthectomized and canal plugged cats. It was found that the first burst was completely and permanently abolished after bilateral labyrinthectomy, but in

the canal plugged cats the first burst still remained.

Work by Lacour et al.[133 134] on the baboon had also demonstrated the appearance of two burst of EMG activity in lower limb flexor and extensor during vertical linear acceleration . They found that after labyrinthectomy, the onset latency of the first burst increased from 32 to 60 ms. (average values) and its amplitude was markedly reduced. In these experiments the effects of vertical linear acceleration was also assessed by H-reflex (soleus) testing in normal , unilateral and bilaterally labyrinthectomized baboons. In the normal baboon, the H-reflex was depressed for the first 100 ms. after release, then increased to levels about 200% of the control values. The early depression was interrupted by a brief period of facilitation with an onset latency of 30 ms. and a duration of about 20-30 ms. In the animals with the unilateral labyrinthectomy, an asymmetry was observed between the H-reflex pattern of the soleus ipsilateral and contralateral to the lesion site. The H-reflex pattern on the contralateral side was almost identical to the pattern recorded in the normal baboon. As for the H-reflex pattern of the ipsilateral limb, the early facilitation phase was absent. This pattern, loss of early facilitation, was observed in both limbs In the animals with bilateral labyrinthectomy.

In the decerebrate cat, Watt[263 264] has also examined the effects of vertical linear acceleration on the H-reflex amplitude before and after bilateral labyrinthectomy. His findings were very similar to those of Lacour et a[132 134]. In the decerebrate cat before labyrinthectomy, a marked suppression of the H-reflex was observed during free fall. The suppression was of rapid onset which gradually declined back to the control value at about 250 ms. The depression of the H-reflex was interrupted by a period of facilitation or reduced suppression with an onset latency of 50 ms. and a duration of approximately 50 ms. This facilitation or disinhibition was not present after bilateral labyrinthectomy.

Lacour et al.[135] have examined the effects of unilateral vestibular neurotomy on the soleus H-reflex recovery curve (H_2/H_1 ratio vs S_1-S_2 delay) in baboons. It was shown that in comparison to pre-operative controls, the H-reflex recovery curve was strongly depressed in the limb ipsilateral to the neurotomy and slightly depressed in the limb contralateral to the neurotomy. This effect was only observed for part of the H-reflex recovery curve, specifically, the H_2/H_1 ratio at S_1-S_2 delays between 250 and 1000 ms.

To further elucidate the role played by the otolith organs in postural control, a number of investigators have examined the dynamic characteristics of the motor output of neck and forelimb muscles in response to sinusoidally varying natural otolith stimulation. It should be noted that this type of study has not been done on the hindlimb muscles.

Anderson et al.[11] have examined the effects of sinusoidal linear acceleration on the EMG response (motor unit firing probability) of the forelimb triceps muscle in the decerebrate cat. In these series of experiments the motor output of the triceps muscle did vary sinusoidal in response to sinusoidal accelerations in the horizontal plane (X- and Y-axis) and vertical plane (Z-axis). For acceleration in the x-axis (fore-aft) the EMG activity of both triceps muscles were in phase. When the acceleration was applied along the Y-axis (left-right) the right and left extensor muscles were 180^o out of phase. The gain and phase relations between the firing probability and the input acceleration were the same for sinusoidal linear acceleration in all three axis. Over the frequency range of 0.1 to 1.0 Hz the gain dropped 14-20dB and the phase showed a lag of up to 60^o at 1.0 HZ. They concluded that the phase lag at the higher frequency could not be explained by the conduction time from the otolith organs to the forelimb motoneurons, and it was suggested that the phase lag is likely the result of processing of the otolith input prior to the generation of motoneuron activity.

The dynamic response of the EMG response of neck and forelimb muscles during sinusoidal tilt stimuli has also been examined in the in the decerebrate cat with intact canals[17 18 176 225 62 283]. Sinusoidal modulation of the muscle activity was observed during sinusoidal tilts . This sinusoidal modulation was absent in bilateral labyrinthectomized animals which indicates that the recorded effects are of vestibular origin. Over the frequency range of 0.01 to 2 Hz a characteristic pattern of modest gain increase and phase leads (relative to position) was observed in both neck and forelimb muscles. A similar experiment by Schor and Miller[225] has been performed on the decerebrate cat with plugged canals. It was found that the gain and phase relationships were the same as those seen in the intact decerebrate cat at frequencies below 0.1 Hz. However at frequencies between 0.1 to 2 Hz the reflex gain decreased and a phase lag of up to 180^{o} developed. It was concluded that the otolith organs are responsible for the low frequency response observed in the neck and forelimb muscle during tilt, with the semicircular canals contributing at the higher frequencies.

Miller et al.[176] have examined the effects of vestibulospinal tract lesions on the dynamic response of forelimb and neck extensor to sinusoidal roll tilt in the decerebrate cat. The LVST was lesioned unilaterally at the C_2-C_3 segments. To test the extent of the lesions, antidromic field potentials were recorded in DN by stimulating the ventral cord at T_{11} segment. Disappearance of the field potentials was taken as evidence that the LVST was sectioned. In this study two main effects were reported. First of all, it was noted that after the lesion the background EMG activity was abolished in the ipsilateral muscles and was partially depressed in the contralateral muscles. As a result it was usually necessary to increase background EMG level with an injection of L-dopa. Secondly, after the LVST lesion a difference in the dynamic response of the muscles was observed in the contralateral limb. Here, a marked phase lag occurred even at low frequency which was in contrast to the modest phase leads observed in the intact

decerebrate cat.

The last part of this section will present the results of human experiments that have investigated the effects of natural vestibular stimulation on the EMG activity of lower limb muscles.

The effects of static tilt on alpha motoneuron excitability in the triceps surae muscle as assessed by the H-reflex method have been investigated in normal human subjects. In the study of Chan and Kearney[38], the stimulus intensity used evoked an H-reflex of between 24 to 54% of the maximum M response. The stimulus strength employed by Aiello et al.[4] evoked both an H-reflex and a small M response. Subject position (recumbent or lying flat) and methods of tilting were similar in both experiments. Head straps were used to maintain head orientation relative to the body during tilts between the horizontal and vertical positions in the pitch axis. A body sling or parachute harness was used to maintain body position relative to the tilt table, and suspended the subjects in the vertical or near vertical positions to a achieve nonweight-bearing status. During each session, the peak to peak amplitude of the H-reflex was recorded at several tilt positions. In the work done by Chan and Kearney[38], subjects were positioned with the head in a number orientations, ranging from 30 degrees (head down 30 degrees or nose-up from the horizontal position) to 150 degrees (head prone or nose-down). They reported that the H-reflex amplitude was minimal when the head was in the vertical position and often increased as a sinusoidal function of tilt. The data analysis in this study consisted of fitting the individual tilt-response curves with the sinusoidal function $k_1 + k_2 * \sin(x + y)$. K_1 was defined as the tonic level of motoneuron excitability, k_2 as the gain of the vestibulospinal input, x = angle of the bed relative to the horizontal, and y = angle between direction of maximum sensitivity of otolith receptors and the bed. For each subjects a non-linear regression was performed to determine the extent to which the change in H-reflex amplitude

during tilt could be described by the sinusoidal function. From this analysis, the magnitude of the tilt effect was described in terms of the ratio k_2/k_1, which represented the change in H-reflex amplitude to be expected from a 90 degrees change in orientation. The calculated values of k_2/k_1 for the individuals had a wide range (0.15 to 0.8), and it surprising that this analysis was not done on the subjects as a group. Since the "normal" individual variation in the H-reflex amplitude at each tilt positions has been presented or incorporated into the evaluation of the tilt effects, statistically, it is difficult to ascribe what are the causes of the deviation in H-reflex amplitude when tested at several tilt positions. Furthermore, the significance of the tilt effects on H-reflex amplitude was not determined. Aiello et al.[4] on the other hand reports that the H-reflex amplitude was minimal when the head was in the horizontal (0 degrees) position and maximal in the vertical (90 degrees) position. However, although the H-reflex amplitude was recorded at seven angles of tilt, i.e., from O degrees to 90 degrees in 15 degree steps, in their statistical analysis (students t-test) only two of the seven angles were compared, the 0 degrees and the 90 degrees positions. Myklebust et al.[186] have examined the effect of whole body position on monosynaptic reflex parameters in humans. H-reflex and M-response recruitment curves were determined for subjects (lying flat) in the prone and vertical position. As with the studies of Chan and Kearney[38] and Aiello et al.[4], a parachute harness was used to suspend the subjects in the vertical position. One subject was tested serially in prone, vertical, and then prone positions. It was found that thresholds and maximal amplitudes of both the H-reflex and M response recruitment curves shifted between the prone and vertical position, which implied a change in the stimulating electrodes relative to the posterior tibial nerve. It was suggested that artifacts due to tilt induced movement of soft tissue at the stimulus electrode site may explain the current disagreement in the literature regarding the tilt dependent effects on the H-reflex amplitude. A study by

Rudell and Eberle[218] also reported orientation induced artifacts in the measurement of the H-reflex and M response in humans. They observed a marked difference in the amplitude of both the H- and M-wave when the subjects were sitting erect or leaning forward. This is probably the result of stretching the sciatic nerve and thus changing its relationship to the stimulating electrode.

Investigations by Melvill-Jones and Watt[173], Greenwood and Hopkins[89], and Watt et al.[265] recorded surface EMG activity in human lower limb extensors and flexors during a step input of vertical linear acceleration(unexpected free falls). In accordance with the findings of similar experiments in the cat[262] and the baboon[133], the observed response consisted of two bursts of EMG activity. It was found that the onset latency of the initial burst of activity (minimal latency of 50 ms.) was fixed relative to the moment of release and was independent of fall height The second burst of activity commenced about 150 to 220 ms. after release. Its timing has been shown to be related to the timing of landing and it was suggested that this is activity concerned with the voluntary control of landing. Greenwood and Hopkins[89] reported that in two labyrinth-defective patients (no response to caloric stimulation and no vestibulo-ocular reflex (VOR) during 40^{o} per second and 60^{o} per second step pulse of angular rotation), the initial burst of EMG activity was absent. However, the initial burst was present in two labyrinth-defective patients, one with a minimal caloric and VOR response and the other with a partial VOR response.

Watt et al.[265] have examined the effects of vertical linear accelerations on the EMG activity of human subjects in weightlessness during a Skylab-1 mission. The accelerations were produced by using a torso harness and elastic (bungee) cords. The results were compared to those obtained during free fall on earth prior to and after the mission. Similar accelerations were used in both terrestrial and microgravity environments. It was found that the EMG response occurring in the first 100-120 ms. of a

fall decreased in amplitude on the first day of the flight (microgravity) as compared to pre- or post-flight values. The EMG amplitude continued to decline throughout the mission. Similar comparisons were made on the second burst of EMG activity (120-160 ms.). The results were variable, increases and decreases in the EMG amplitude were observed.

The H-reflex has been used to asses the excitability of the soleus motoneuron pool during unexpected free falls in human subjects. Matthews and Whitside[169] reported that the amplitude of the H-reflex of subjects seated in a drop chair was depressed about 60-100 ms. after its release. Greenwood and Hopkins[90] observed a potentiation of the H-reflex during the first 30 to 80 ms. after release. Reschke et al.[214] also observed a potentiation of the H-reflex during drops , commencing at about 30 ms. The potentiation peaked at 80 ms. and was present at 100 ms., the last delay to drop time tested. These same experiments were performed in microgravity (Spacelab-1 mission) and compared to results obtained under similar vertical accelerations per- and post-flight. No difference was found in the H-reflex amplitude potentiation after drops on the first mission day as compared to the pre-flight values. However, by mission day 7 no potentiation of the H-reflex was observed during drops.

A number of investigators have examined the role various sensory inputs play !n generating sway stabilizing responses in human lower limb muscles[188 190 191 192 51 19 49 50 51 9]. Automatic postural responses are evoked in standing humans when subjected to unexpected translation or rotation perturbations. These sway stabilizing response have been described as stereotyped in terms of their timing and synergic organization, and are context dependent as they can differ depending on the weight bearing status and support surface characteristics (for review see Nashner and McCollum[193]. In human subjects, Nashner[188 189] has postulated that the delayed (200-300 ms.) sway stabilizing responses observed during stance perturbations in the

absence of ankle joint cues are primarily of vestibular origin. In these experiments the platform on which the subjects stood was translated in an A-P direction, while at the same time the platform base was rotated in direct proportion to the induced A-P sway. thus preventing ankle joint movement. Using a similar movable platform device Black et al.[19] have examined the sway stabilizing responses of normal subjects and labyrinth-defective patients (assessed by the presence of spontaneous nystagmus and/or VOR testing) under a variety of altered somatosensory and visual conditions. In response to translation perturbations, body sway amplitude and onset latency of EMG activity in lower limb muscles were recorded under normal conditions and eyes closed conditions. The subjects were also tested under stabilized somatosensory and/or visual conditions. The "stabilized somatosensory" condition (S_S) was achieved by rotating the platform surface support in direct proportion to the A-P body sway of the subject. In a similar manner the "stabilized visual" condition (V_S) was achieved by moving a visual surround in direct proportion to and in phase with the body sway of the subject Under normal test conditions no significant increase in sway amplitude or onset latency of the EMG activity (about 100 ms.) was observed in the labyrinth-defective patients during translation perturbations as compared to subjects with no know history of vestibular disease. The most difficult test condition was that in which the subjects were concurrently deprived of normal somatosensory inapt (S_S) and visual input (V_S). In these test situations normal subjects could maintain their balance, but the majority of the patients could not maintain an upright position . Albeit to a lesser degree, similar results were found in the S_S condition with eyes closed, i.e patients had much more difficulty keeping upright than normal subjects. For the labyrinth-defective patients, the increase in body sway and the inability to maintain balance was correlated with a marked increase in the onset latency of the EMG activity, from 101 ms (normal conditions) to 200-400 ms. (stabilized conditions). It was concluded that under certain conditions vestibular

orientation information is required by the postural control system, although the relative contribution of the semicircular canals and/or otolith organs remains to be determined.

In summary, electrophysiological observation have demonstrated that activity originating from the vestibular end organs is conveyed, via the vestibular nuclei, to all levels of the spinal cord. These findings conform with the pathways identified by anatomical tracing techniques.

The available evidence supports the view that the principle pathway linking the vestibular system to the lumbosacral spinal cord is the LVST, which arises from cells located mainly in Deiters' nucleus. It is well established that stimulation of Deiters' nucleus will elicit short latency excitatory and inhibitory effects in lumbosacral spinal motoneurons and interneurons. In this respect, interneurons interposed in segmental reflex pathways from the Flexion Reflex Afferents (FRA) to most lower limb muscles, and the extensor coupled Ia inhibitory interneuron supplying the knee flexor motoneurons, have been reported to transmit vestibulospinal PSP's to lumbosacral motoneurons.

Animal studies have demonstrated labyrinthine reflexes which are usually considered to aid in maintaining postural equilibrium in the face of external perturbations. Furthermore, studies which have examined the effects of natural otolith stimulation on muscle activity suggest that otolith stimulation does produce a net excitatory or inhibitory effect on lower limb motoneurons.

Studies in the decerebrate cat have examined the dynamic behaviour of spinal interneurons, and neck and forelimb muscles activity during sinusoidally varying natural vestibular stimulation in an effort to determine how head (and body) position are coded at different stages of the reflex pathway. It does appear that otolith receptor activity is relayed to the spinal cord and that the otolith organs are responsible for at least the low frequency response observed in neck and forelimb muscle during natural

vestibular stimulation.

In an effort to identify and describe a functional connection between the otolith organs and the lower limb muscles in human subjects, a number of investigators have examined the effects of natural vestibular stimulation on motoneuron excitability . In terms of the activation of otolith receptors by static tilt stimulation opposing results have been reported. Dynamic vestibular effects have been reported although the contribution of otolith organs is not known.

2.5 - PHYSIOLOGICAL MECHANISMS UNDERLYING MYOTATIC AND CUTANEOMUS CULAR REFLEXES IN HUMANS.

This section will provide a concise overview of the salient physiological effects evoked in central neurons and muscle by electrical stimulation of peripheral afferents.

The myotatic reflex and the pattern of excitation of alpha motoneurons during group Ia afferents stimulation has been extensively studied in the cat[142 143 144 53 54 31 174 175] and also examined in the baboon[197]. From these investigations it is generally agreed that activation of Ia afferents by electrical or natural means will produce a characteristic monosynaptic depolarization of homonyms and heteronomous motoneurons.

When the posterior tibial nerve is stimulated in man, two distinct compound muscle potentials can be recorded from the soleus muscle. An H-wave first appears with weak stimuli, and as the intensity of the stimulus is increased an M-wave (direct motor response) will also occur. This reflex, known as the H-reflex, has been extensively examined in human subjects[160 161 159 170 248 110 42 30]. From the characteristics of the human H-reflex described by these studies, it has been concluded that the H-wave is the peripheral manifestation of the monosynaptic activation of motoneurons by stimulation of the group Ia afferents. In this regards Magladery et al.[161] have studied the effects of posterior tibial nerve stimulation by recording electrical potentials in soleus muscle, spinal roots, and dorsal spinal cord of humans. To record electrical potentials from the spinal roots and spinal cord, long needle electrodes were inserted throughout the back into the thecal space at various spinal levels (L_5 to T_10). The location of the electrode tips were verified at the conclusion of the experiment by roentgenogram. It was thus possible to determine if the electrodes lay dorsal or ventral

to the spinal cord. However it could not be determined if the needle tip lay anterior or posterior to the spinal roots. In this experiment, from the spinal root recordings it was possible to identify: 1) dorsal root potentials which corresponded to the afferent volley; 2) ventral root potentials which correspond to the H-wave; 3) antidromic volley along the motor axons which corresponded to the M-wave. The characteristic changes observed in the muscle potentials, recorded during graded stimulation of the posterior tibial nerve and ischemic block of the Ia afferents proximal to the stimulating site, were also evident in the spinal root recordings. The dorsal root potentials were separated from the ventral root potentials by only 1.5 ms. Allowing for central conduction time, it was concluded that the human H-reflex arc is monosynaptic.

The H-reflex is considered a measure of the net level of excitability of the motoneuron pool and the H-reflex amplitude has been employed as a means of studying stimulus-induced, and task-related changes in the human motoneuron excitability[248 33 111 204 205 45 46 74].

The excitability cycle or recovery cycle of the H-reflex, first described by Magladery et al.[162 163], has also been used to study motoneuron excitability in humans. This method involves stimulating the posterior tibial nerve with paired electrical impulses (S1 and S_2) separated by varying intervals. The S_1 stimulus need not evoke an H-reflex. The H-reflex recovery curve is the H-response amplitude (H_2) of the test reflex corresponding to S_2 as a ratio of its amplitude in the unconditioned situation. In humans, a characteristic recovery pattern of H_2 as a function of S_1-S_2 delay is observed[163 251 285 249 82 204 42]. The H_2 reflex is largely suppressed at S_1-S_2 intervals between 10 ms. to 100 - 150 ms. Superimposed on the recovery of the conditioned H_2 reflex (which reaches its unconditioned value at S_1-S_2 delays of 1 to 2 seconds) is a period of late depression at S_1-S_2 delays between 250 to 800 ms. A mechanism that could contribute to the early H_2 suppression is presynaptic inhibition[55 182 117].

The physiological mechanism underlying the late depression phase in the recovery of the H_2 reflex is largely unknown. A series of studies by Magladery and colleagues[163 251 164] have examined the H-reflex recovery curves in: 1) normal subjects; 2) patients with upper motor neurone lesions lesion in the cerebral hemispheres, brain stem, or upper spinal cord, 3) chronic paraplegic patients with lesions within two or three segments of the lumber cord or diffuse disseminated sclerosis throughout the cord. The early suppression of test H_2 reflex was present in all groups. However, the late depression of the H-reflex recovery curve between S_1-S_2 delays of 300 to 600 ms. was absent only in the chronic paraplegic patients with lesions situated within a few segments of the tested spinal segment. It was concluded that the lower spinal cord damage may interrupt some propriospinal integrative mechanism which normally suppresses the monosynaptic discharge of the motoneuron and which is activated by low threshold afferent volleys. It should also be noted that stimulation of the posterior tibial nerve at strengths just sufficient to produce a H-wave will result in activation of a variety of low threshold afferents other than the Ia afferents, which may include low threshold cutaneous and possibly group II afferents[161 30]. It is possible that volleys in these fibers may contribute to the recovery pattern of the H2 reflex.

It has long been known that flexion of the limb can be evoked by stimulating the skin of the limb or cutaneous nerves This flexion reflex was first systematically studied by Sherrington[235]. Since this time a large number of animal[96 126 127 43 229 222 39 223] and human[132 82 232 63 109 270 206 171 45 46] investigations have examined the short and long latency effects evoked in central neurons or muscle during stimulation of low and high threshold somatosensory afferents.

In the spinalized cat, Lloyd[143 145], Hagbrath[96], Eccles and Lundberg[52], and Holmquist and Lundberg[104] have found that group II and III muscle afferents, cutaneous afferents, and joint afferents have widespread reflex actions in the lower limbs. Some

common ground has been established and a unified hypothesis concerning the reflex action of the Flexion Reflex Afferents (FRA) - cutaneous afferents, joint afferents, and group II and III muscle afferents - has been proposed by Lundberg[156] and extended by Lundberg et al.[157]. In brief, of significance are the findings that: 1) as a group, the FRA can evoke common widespread central actions i.e. ipsilateral excitation of flexor and contralateral excitation of extensors; 2) depending on the preparation, alternative pathways from the same FRA to extensor and flexor motoneurons do exist which can produce long lasting responses; 3) there is a multisensory convergence of the FRA on spinal interneurons interposed in reflex pathways to motoneurons and those ascending to supraspinal centers, notably the cerebellum; 4) there is a conjoint action of the FRA and descending tracts on spinal interneurons and thus integration of descending motor commands with peripheral afferent signals will occur at a pre-motoneuronal level. The functional significance of the FRA system, as suggested by Lundberg and colleagues[156 157] is that the FRA functions as a segmental, multisensory, positive feedback mechanism common for a number of pathways or restricted to one pathway by virtue of descending control.

In human subjects at rest, a cutaneomuscular reflex can be evoked in lower limb muscles by electrical stimulation of the skin or peripheral nerves. These reflexes are characterized by an EMG discharge (onset latency about 55-70 ms.) consisting of several components which are separated by periods of EMG silence[132 232 63 109 271]. This response can last for several hundred milliseconds. Similar cutaneomuscular reflexes are evoked in muscle under tonic voluntary contraction[132 82 109 206 171 15].

The effects of conditioning volleys in cutaneous nerve on: 1) the human soleus and tibialis anterior H-reflex[45 46]; 2) the monosynaptic test reflex of hindlimb flexor and extensor muscles in the decerebrate and spinalized cat[96 43], have been examined.

In human and cat, a complex pattern of alternating depression and facilitation of the test H-reflex was observed for both soleus and tibialis anterior when conditioned by ipsilateral or contralateral sural nerve stimulation.

In spinalized cats injected with L-dopa, electrical stimulation of cutaneous nerves has been shown to elicit long latency and long lasting discharges in flexor and extensor motoneurons[126 127]. Also, during sural nerve stimulation long lasting responses in soleus and tibialis anterior have been observed in spinalized cats not treated with L-dopa[43]. It has been reported that cutaneomuscular reflexes with the same characteristics as those obtained in normal human subjects occur in patients with partial or complete transection of the spinal cord[132 109 232]. Taken together, these findings indicate that the spinal cord contains the necessary elements capable of supporting long duration cutaneomuscular reflexes.

Willer[270] and Willer et al.[271] have examined the contribution of different populations of peripheral cutaneous afferents to cutaneomuscular reflexes in humans. Orthodromic sensory action potentials (SAP) and cutaneomuscular reflexes in the biceps femoris were recorded during stimulation of the sural nerve. To obtain records of sural SAP needle electrodes were inserted through the skin directly to contact the nerve. During graded sural nerve stimulation the first SAP to appear had a conduction velocity of 51 m/sec (range 45-62 m/sec). It was concluded that this would be the A-alpha wave. With much stronger stimuli a second small SAP was observed and was designated the A-delta wave. Its conduction velocity was determined to be 22 m/sec (range 17-27 m/sec). Single sural shocks just sufficient to evoke an A-alpha wave did not elicit a cutaneomuscular reflex in the biceps femoris. Single shocks to the sural nerve which produced both A-alpha and A-delta waves did elicit a strong reflex discharge in the biceps muscle with an onset latency of about 80 ms. It was further observed that a reflex discharge with a minimal onset latency of 50 ms. would occur when

trains of impulse (only A-alpha waves) were evoked in the sural afferents. It was conclude that both low threshold and high threshold cutaneous afferents can activate human muscle and a special note was made of temporal summation.

CHAPTER 3

STATEMENT OF WORKING HYPOTHESIS

The purpose of this study was to examine the effects of static tilt, a practical form of natural otolith stimulation on the reflex excitability of human lower limb muscles. In animal studies several investigators have identified a functional linkage between otolith end organs and lumbosacral alpha motoneurons. At least for the ankle and knee extensors in the lower limb of the cat and monkey, a monosynaptic linkage between Deiters' nucleus (DN) neurons and alpha motoneuron has been reported. In the decerebrate cat, it has also been observed that vestibulospinal signals (originating from DN) exert di- and poly-synaptic PSP's in extensor and flexor alpha motoneurons through interneurons which also mediate FRA reflex actions.

The first series of experiments, addressed the effects of natural otolith stimulation on connections to ankle extensor motoneurons from Deiters' nucleus (DN), the site of second order neurons of the primary otolith afferents. The hypothesis underlying the first series of experiments was that alterations in the excitability of soleus motoneurons, as assessed by H-reflex testing, accompany changes in the orientation of the head relative to the gravity vector. By stimulating the posterior tibial nerve with paired (S_1-S_2) shocks, both the monosynaptic pattern of excitability of the soleus motoneuron pool and the H-reflex recovery curve was examined during whole body tilts in the pitch axis.

The outcome of the first study revealed no dependence between tilt position and the magnitude of the H-reflex. However a highly significant effect was observed between tilt position and the recovery of a test H-reflex preceded by a conditioning H-reflex. It was concluded that changes in whole body orientation modulate motoneuron

excitability through an indirect pathway, rather than directly affecting the excitability of the motoneuron.

These results were followed up with a second series of experiments designed to test for an interaction between the central effects of static tilt and the reflex action of cutaneous nerve stimulation. The hypothesis underlying this study was that tilt dependent effects in lower limb muscles involve a pathway which is shared by primary cutaneous afferents. The latency and magnitude of cutaneomuscular reflex effects in lower limb flexors and extensors evoked by sural nerve stimulation were examined during whole body tilt in the pitch axis.

CHAPTER 4

EXPERIMENTAL DESIGN AND METHODS

4.1 - Experiment 1: The Effects Of Natural Otolith Stimulation On Spinally Mediated Myotatic Reflexes Assessed By H-reflex Testing.

Subjects were 14 male and female male volunteers (22-35 years of age) with no known history of vestibular disease. H-reflexes were measured according to the method described by Hugon[110] and Crayton and King[42]. The general experimental arrangement is illustrated in Fig. 11.

An adjustable knee brace was constructed to fix and maintain the knee at 20 degrees of flexion. Built into the brace on the posterior aspect was an apparatus to which the cathode stimulating electrode (1 cm. metal electrode with a mushroom shaped head) was attached. This device permitted movement of the electrode with 3 degrees of freedom and firmly secured the electrode in place into the popliteal fossa. The anode component (flexible lead plate electrode 3 cm. by 3 cm.) was secured to the anterior aspect of the thigh immediately above the patella.

The recording electrodes (silver disc electrodes) were carefully positioned 2 cm apart over the soleus under the lateral distal head of the gastrocnemius.

Before applying the stimulating and recording electrodes, the skin was thoroughly decreased and abraided.

Grass S88, and S44 simulators were used to deliver single, and paired pulses (S_1, S_2 of equal intensity) through the stimulating electrodes to the posterior tibial nerve. Rectangular pulses of 0.5 ms. duration were used. The evoked muscle potentials were amplified and displayed on the screen of a Teca-TD20A electromyograph

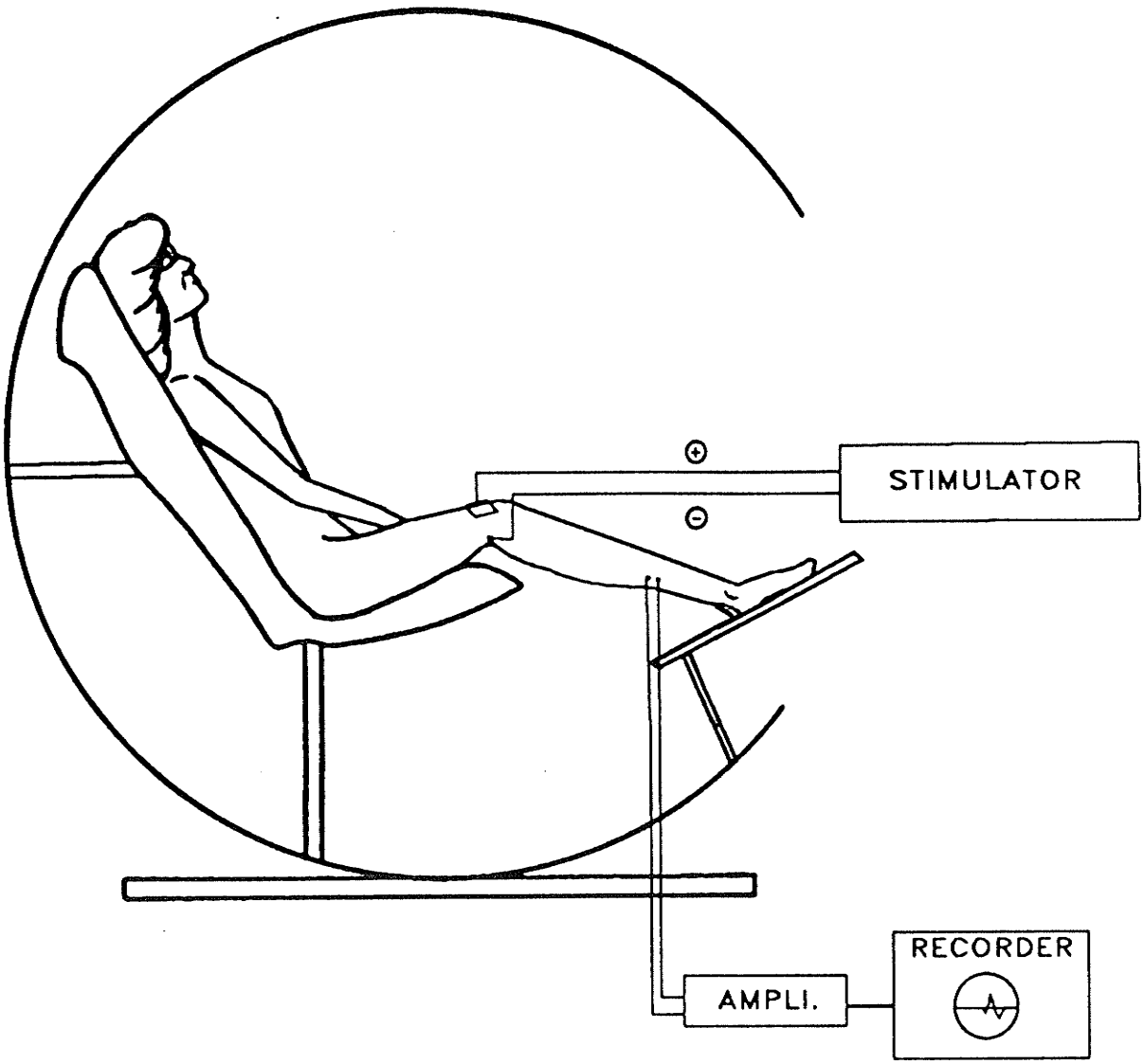

FIG 11. Experimental Set up for eliciting and recording H-reflexes during one tilt position in the pitch axis. The supports immobilizing head, trunk, and extremities are not shown, nor is the device used to secure stimulating electrodes.

and recorded on chart paper. From the Grass stimulator SYNC. output, the Teca was triggered to record a 200 ms., 500 ms., or a 1000 ms. sweep of the soleus EMG signal. The sweep time depended on the S_1-S_2 delay interval. The recorded EMG input signal was band pass filtered with a low cut-off frequency of 2 Hz and a high cut-off frequency of 10 KHz, with the Teca filter settings.

The precise position of the cathode was carefully adjusted so that: 1) weak stimuli produced a painless muscle twitch in the triceps surae, and a triphasic H-wave without the appearance of an M-wave; 2) when increasing the stimulus strength a maximal triphasic H-wave with a minimal M-wave in the soleus was produced with no radiating paraesthesia.

Each subject was placed in a reclining chair apparatus within the frame of a circular electric bed. Care was taken to ensure comfortable and maintained body and extremity position. A splint was used to fix and maintain the ankle joint in the neutral anatomical position. The head was fixed relative to the trunk and secured within the confines of an adjustable head rest apparatus built onto the bed frame.

Each subject was tested on 4 separate occasions at 4 tilt positions in the pitch axis. The test positions varied from trunk vertical (90 degrees) to supine (0 degrees) in 30 degree intervals. For the group of subjects, the sequence of the tilt positions tested was arranged such that any possible order effect was eliminated. Subjects were usually tested once a week on the same day and at the same time of the day. Crayton and King[42], testing 55 normal human subjects, reported that H-reflex parameters derived from recruitment curves and recovery curves show large inter-subject variability. On the other hand, it was observed that the same H-reflex parameters show small test-retest variability, a finding which is supported by Tardieu et al.[250].

In the present study, each subject was tested using two stimulus intensities: 1)

MT; 2) 0.8MT, which was defined as M-wave threshold intensity (MT) minus 20% of the difference in stimulus intensity (volts) between MT and H-wave threshold (HT). HT and MT were determined with the subject in the 60 degrees position (30 degrees pitched backward from the trunk vertical position). To this end, a series of single shocks were delivered, at three second intervals, to the posterior tibial nerve while the stimulus strength was slowly adjusted. The critical intensity, below which no H-wave response was observed and above which each stimulus elicited a response, was defined as HT. In a similar fashion MT was determined.

The stimulus intensity MT was chosen because a small M-wave is present which was used: 1) as an index of stimulus electrode stability relative to the posterior tibial nerve within each session,; 2) as a criteria for electrode placement between sessions. However, there were some concerns with the intensity of this stimulus. Besides the central effects of alpha motoneuron volleys and activation of large diameter cutaneous afferent[30], the degree of Ia stimulation at MT may obscure relatively small effects of static tilt. For these reasons a lower stimulus intensity, 0.8MT, was also chosen. In this regard, to ensure consistent electrode placement between sessions both HT and MT were used to define this stimulus intensity, as it has been shown that the ratio HT/MT is stable between session[44].

For each stimulus intensity (MT and 0.8MT), with the subject placed at the appropriate test position, the posterior tibial nerve was stimulated with paired (S_1-S_2) shocks of equal intensity. The time interval or delay between shocks varied from 115 ms. to 465 ms. in 50 ms.steps. At each delay, chosen at random, the stimulus pair was given 7 times with a 12 second intervals between paired shocks. The responses were displayed on the Teca and recorded on chart paper. At no time during the tests was there any evidence of tonic EMG activity as assessed with surface EMG recording.

The peak-to-peak amplitude of the H-wave for each record was determined by

hand analysis, Thus estimates of H_1 amplitude, which corresponds to S_1,and H_2 amplitude which corresponds to S_2 were obtained.

The mean H_1 amplitude, which corresponds to the S_1 stimulus of the paired shocks was calculated from the 7 replicates. Thus each mean H_1 amplitude value represents the amplitude of the H-wave averaged over an 84 second time period (TP). At each test position 8 values of mean H_1 amplitude were obtained, representing the TP (increments of 84 seconds) from the beginning of the test.

The H_2/H_1 ratio for each of the 7 replicates at each of the 8 S_1-S_2 delays was calculated. From these values the mean H_2/H_1 ratio for each delay was obtained.

In this study and for Experiment 2 (Section 4.2), a statistical analysis approach was chosen to determine and evaluate the effects of static tilt on the recorded parameters. In this regard, when only two samples or groups are involved the students t-test is traditionally used to test significant difference between the means. However the analysis of variance (ANOVA) is the preferred procedure when testing more than two groups as is the case in the present study. i.e., four static tilt positions and thus four groups. The experimental design for Experiment 1 and Experiment 2 was prearranged with the ANOVA in mind. Strictly speaking the purpose of the ANOVA is to estimate the true differences among the groups means by testing for the presence of an added component due to a fixed treatment (static tilt) or due to chance alone. The critical calculation in the ANOVA is the F ratio or F value, which is analogous to the t statistic of the students t-test. In the calculation of the F value one compares the variation of the means between the groups (due to the treatment and/or chance) to the difference within the groups (individual variation within the groups). The outcome of the F-test, i.e., test of significance or the probability that the group means are different as a result of the treatment effect, is dependent on the magnitude of the F value.

For both stimulus intensities, a repeated measures ANOVA (two-way) was used

for the statistical analysis of: 1) the effect of angle of tilt and TP on the mean H_1 amplitudes (8 estimates for each tilt position), 2) the effect of angle of tilt and S_1-S_2 delay on the mean H_1/H_2 ratios. The BMDP statistical package was used for all ANOVA procedures.

A repeated measures ANOVA (one-way) was employed to analyze the effects of tilt angle on the mean H_2/H_1 ratio at the individual S_1-S_2 delays. In this regards it has been established that the H_2 to H_1 ratio is dependent on delay period between the paired shocks, and reportedly (see literature review chapter 2 section 2.4), various physiological mechanisms are operating at different delays.

4.2 - Experiment 2: Effects Of Natural Otolith Stimulation On Lower Limb Cutaneomuscular Reflexes

This series of experiments were carried out on 12 subjects (11 male and 1 female, 23-35 years of age) with no known history of vestibular disease. Reflex effects in lower limb muscles elicited by peripheral nerve stimulation were produced and assessed according to the method described by Gassel and Ott[82], Piesiur-Strehlow and Meinck[206], and Meinck et al.[171] which allows for the quantitative analysis of latency and magnitude of inhibitory and excitatory responses. The general experimental arrangement is illustrated in Fig. 12.

Stimulation of the left (L) sural nerve was performed using a pair of metal electrodes with a mushroom shaped head (0.5 cm. in diameter). The electrode pair was fixed (1.5 cm. apart) in a small, thin plastic device to facilitate positioning and securing of the stimulating electrodes over the lateral retro-malleolar pathway of the sural nerve. The precise position of the stimulating electrodes (cathode proximal) was carefully adjusted so that weak stimuli produced; 1) a radiating paraesthesia along the distal distribution of the sural nerve, in particular the lateral aspect of the foot towards the little toe and not down the heel, 2) no sensation of burning or sharpness. Once these criteria were met the electrode pair was secured in place with surgical tape.

Two silver disc surface electrodes (0.75 cm. in diameter) were used for recording surface EMG activity. These electrodes were positioned and secured 2 cm. apart over the belly of the muscle to be tested. The EMG activity was amplified and displayed on the screen of a Teca-TD20A 2-channel electromyograph and recorded on chart paper. The recorded EMG input signal was band pass filtered with a low cut-off frequency of 2 Hz and a high cut-off frequency of 10 KHz, with the Teca filter settings. This signal,

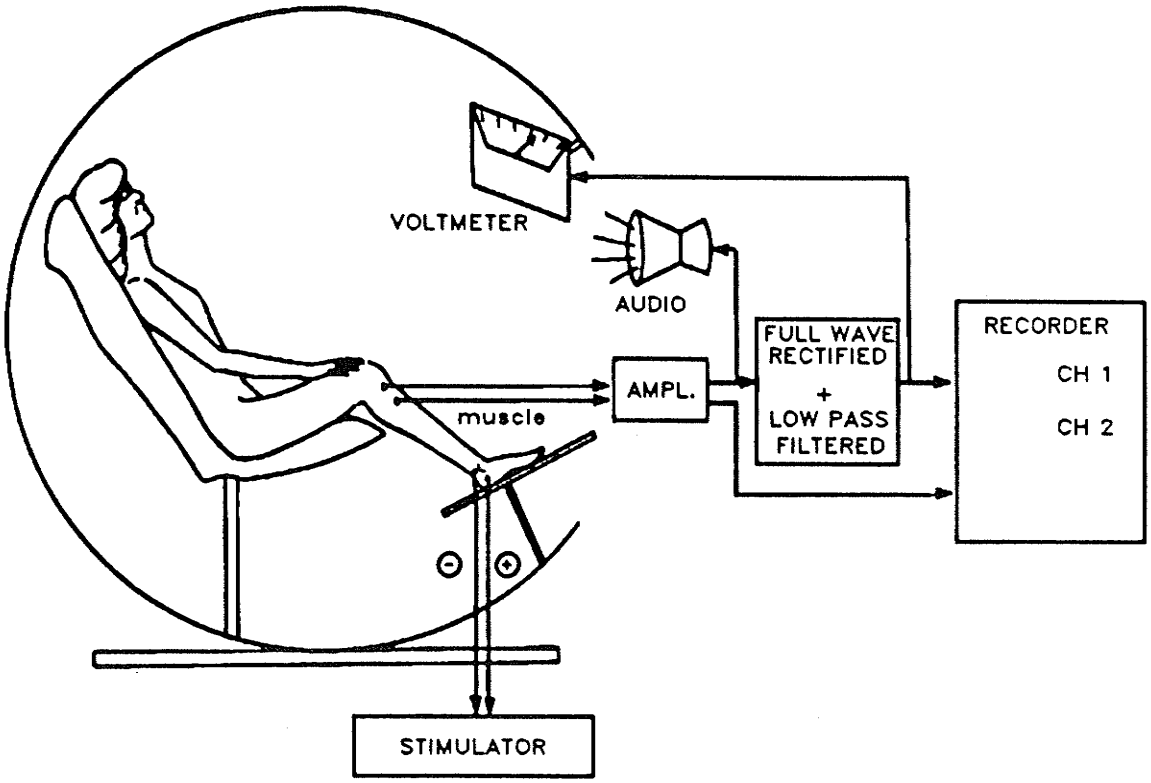

FIG 12. Experimental setup for eliciting and recording cutaneomuscular reflexes during one tilt position in the pitch axis. The supports immobilizing head, trunk, and extremity position are not shown, nor is the setup used for producing isometric contraction.

designated the raw EMG signal, was then full wave rectified and integrated. The integrator consisted of an active RC low pass filter with a time constant of 24 ms.

Before applying the stimulating and recording electrodes, the skin was thoroughly decreased and abraided.

As in Experiment 1, a reclining chair apparatus within the confines of a circular electric bed was used for tilting the subjects. Appropriate measures were taken to ensure comfortable and maintained body and extremity position. The head was secured in an adjustable head rest apparatus built onto the bed frame to immobilize it relative to the trunk.

The test reflex employed in this study was evoked by stimulation of the left (L) sural nerve while the subject maintained a voluntary contraction of the muscle. A Grass S88 stimulator was used to deliver, once every five seconds, a train (3 at 500 Hz.) of rectangular pulses of 0.5 ms. duration. The stimulus intensity was subjectively determined as pain threshold, which was determined to be about 3 times the stimulus intensity of the minimal perceived tactile response (range 2.8 to 3.5 for all subjects). In this manner, test reflexes were evoked in eight muscles; contralateral soleus (coSol), contralateral tibialis anterior (coTA), ipsilateral soleus (iSol), ipsilateral tibialis anterior (iTA), contralateral quadriceps (coQ), contralateral lateral hamstrings (coH), ipsilateral quadriceps (iQ), and ipsilateral lateral hamstrings (iH). Subjects were instructed to performed and maintain a voluntary muscle contraction throughout the test. Isometric contraction of about 10% of the maximum voluntary contraction were used. To produce an isometric contraction the subjects flexed or extended against an immovable stop. Care was taken to ensure that the mean EMG level of the contracting muscle did not vary during the session, i.e. between tilt positions. In this respect the full wave rectified and integrated surface EMG signals were displayed on a voltmeter and monitored by experimenter and subject. Also, auditory feedback of the

raw EMG signals was available to the subject and experimenter.

During each session, the test reflex of one contralateral muscle or two ipsilateral muscles was investigated at four tilt positions in the pitch axis, i.e., trunk vertical (90 degrees), trunk horizontal (0 degrees), and at two angles in between which were 60 degrees and 30 degrees. For the group of subjects, the sequence of the tilt positions tested was arranged such that any possible order effect was eliminated.

At each tilt position, the Teca electromyograph triggered by the sural nerve stimulus, was set to record and store consecutive one second sweeps (270 ms. prestimulus and 730 ms. poststimulus) of the raw and integrated EMG signal. Each test reflex response, the average of 90 integrated EMG sweeps for the contralateral muscles and 50 integrated EMG sweeps for the ipsilateral muscles was recorded on chart paper for hand and computer analysis.

The multiphasic cutaneomuscular reflex responses obtained by this method are shown in Fig. 13 (soleus and tibialis anterior muscles from one subject) and Fig. 14 (quadriceps and lateral hamstrings from one subject). Both the averaged raw EMG records and averaged rectified and integrated EMG records are presented.

For each averaged rectified and integrated EMG record, the latency to peak amplitude of the various phases of the test reflex response, and the magnitude of the excitatory or inhibitory phases at this latency were determined by hand analysis. The magnitude values were measured from the base line voltage which had a fixed relationship to the output integrated EMG signal. In Fig. 13 and 14, the dots adjacent to the peaks of the averaged integrated EMG responses denote the peaks that were measured. The magnitude values were expressed in arbitrary units which , in any one session, were the same for all test positions. Also each record was digitized with a Houston Hipad graphics tablet and stored using a Hewit-Packard HP9836 computer which provided a grand average of the digitized test reflex response for each muscle.

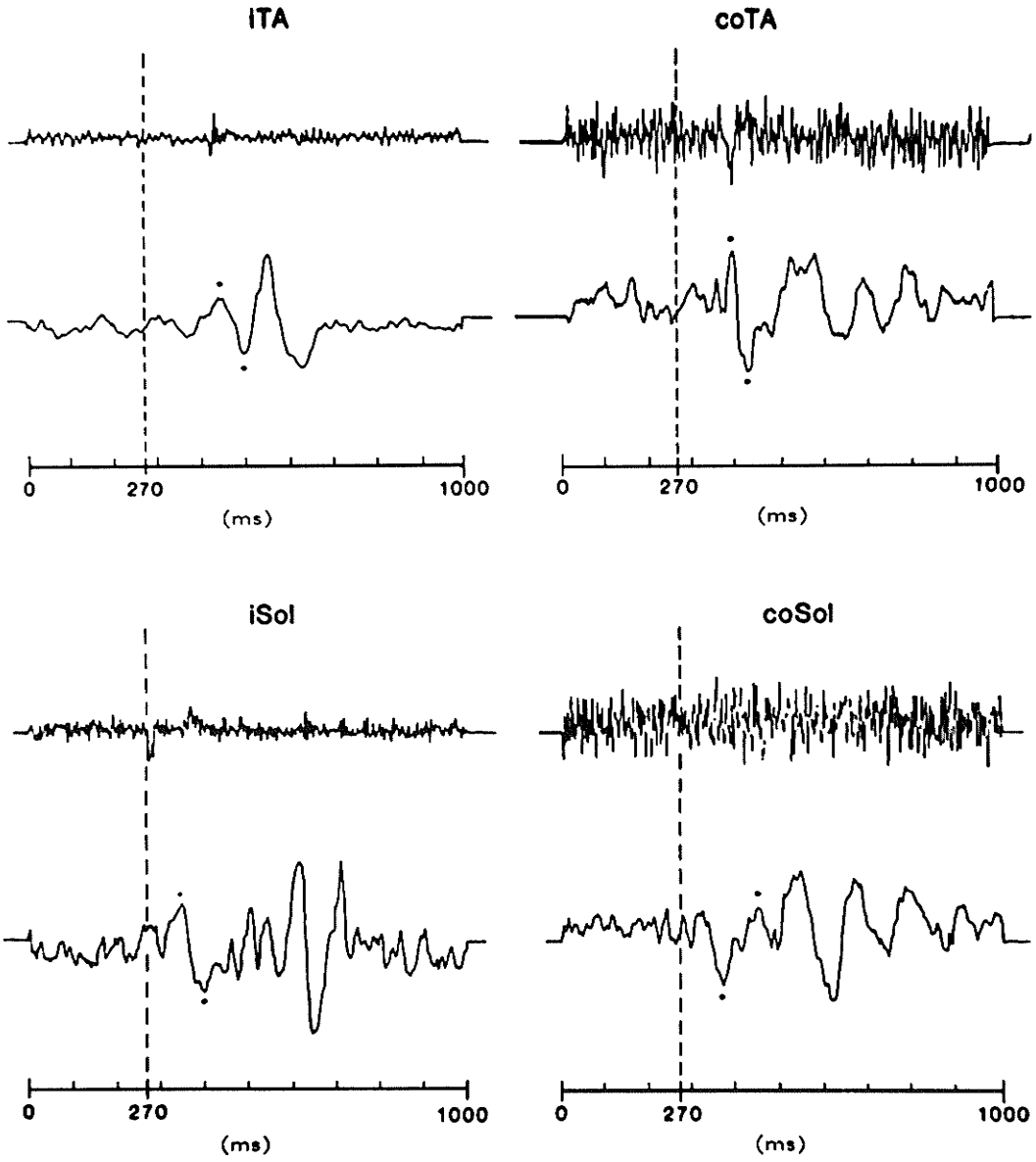

FIG 13. Cutaneomuscular reflex response to sural nerve stimulation for one subject at the 60° tilt position. in ipsilateral tibialis anterior (iTA), contralateral tibialis anterior (coTA), ipsilateral soleus (iSol), and contralateral soleus (coSol). Upper traces: raw EMG; lower traces: identical but full wave rectified and low pass filtered EMG. For the ipsilateral muscles each record was the average of 50 consecutive sweeps, and for the contralateral muscles of 90 consecutive sweeps. Dots represent the peaks measured. Time scale at the bottom applies to all records. Onset of stimulus occurred at 270 ms. (vertical dashed line), the prestimulus interval representing the background activity level.

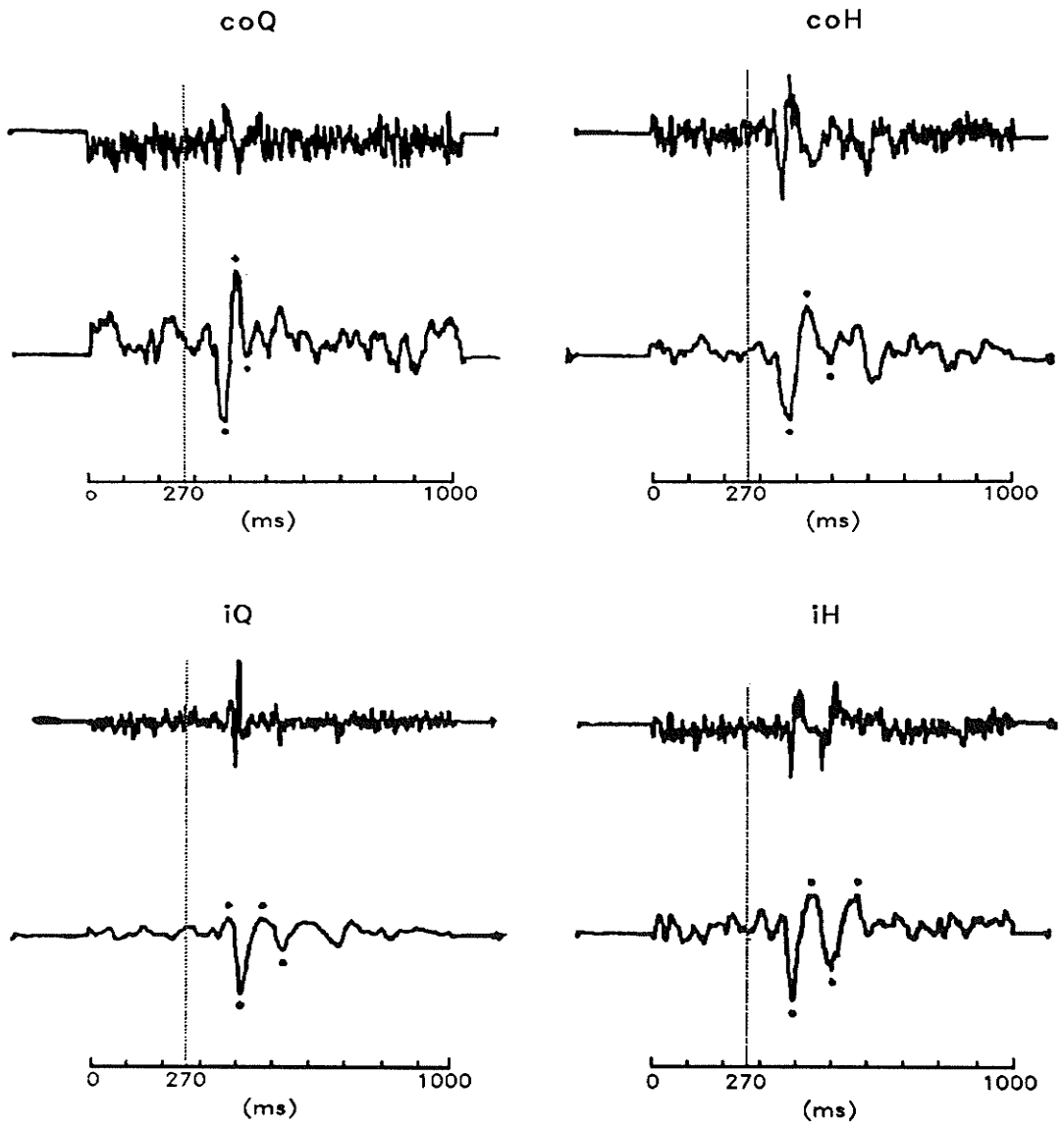

FIG 14. Same as FIG 13 except cutaneomuscular reflex response in contralateral quadriceps (coQ), ipsilateral quadriceps (iQ), contralateral hamstrings (coH), and ipsilateral hamstrings (iH).

As discussed in SECTION 4.1, an ANOVA with repeated measures was used to examine the effect of angle of tilt on the magnitude (peak amplitude) of; 1) the first two components of the multiphasic test reflex for the contralateral and ipsilateral fig soleus and tibialis anterior muscles; 2) the first three components of the multiphasic test reflex for the contralateral and ipsilateral quadriceps and lateral hamstring muscle. The BMDP statistical package was used for this purpose. A similar statistical analysis was not performed on the latency to peak amplitude measurements as it became evident that for each subject the latency values remained extremely stable over the four tilt positions.

CHAPTER 5

RESULTS

5.1 - Experiment 1; The Effects Of Natural Otolith Stimulation On Spinally Mediated Myotatic Reflexes Assessed By H-reflex Testing

H1 AMPLITUDE

The results of the 2-way ANOVA which examined the effects of pitch angle (A) and time period (TP) on the H_1 amplitude at MT and 0.8MT are presented in Table 1. This analysis reveals that, at either stimulus intensity, angle of tilt had no significant effect on the magnitude of the H_1-reflex . Furthermore, since the effect of TP was not significant, the mean H_1 amplitude did not vary during the experiment. This would indicate that test conditions remained stable throughout each experiment.

H2 TO HI RATIO

The second comparison made between tilt position and pattern motoneuron pool excitability involves the examination of H_2/H_1 ratio during changes in subject orientation relative to the gravity vector.

The H-reflex recovery curves (H_2/H_1 vs S_1-S_2 delay) at the 60 degree tilt position for all subjects are presented in Figure 15 which illustrates the variability in the degree of H_2 recovery among the individuals. It also evident from Figure 15 that the pattern of recovery was similar at both stimulus intensities.

For four subjects the H-reflex recovery curves at each angle of tilt are shown in Fig.16a (0.8MT) and Fig 16b (MT). The mean H-reflex recovery curve (average records of all subjects) at each angle of tilt are presented in Fig. 17 (0.8MT) and Fig.

TABLE 1 **Main effects of repeated measures ANOVA of data from 14 subjects. Variable is H1 amplitude.**

A) INTENSITY = MT

	df	F VALUE	SIGNIFICANCE
ANGLE (A)	3	0.69	NS
TIME PERIOD (TP)	7	1.22	NS
INTERACTION (A*TP)	21	1.69	NS

B) INTENSITY = 0.8MT

	df	F VALUE	SIGNIFICANCE
ANGLE (A)	3	0.73	NS
TIME PERIOD (TP)	7	0.73	NS
INTERACTION (A*TP)	21	1.65	NS

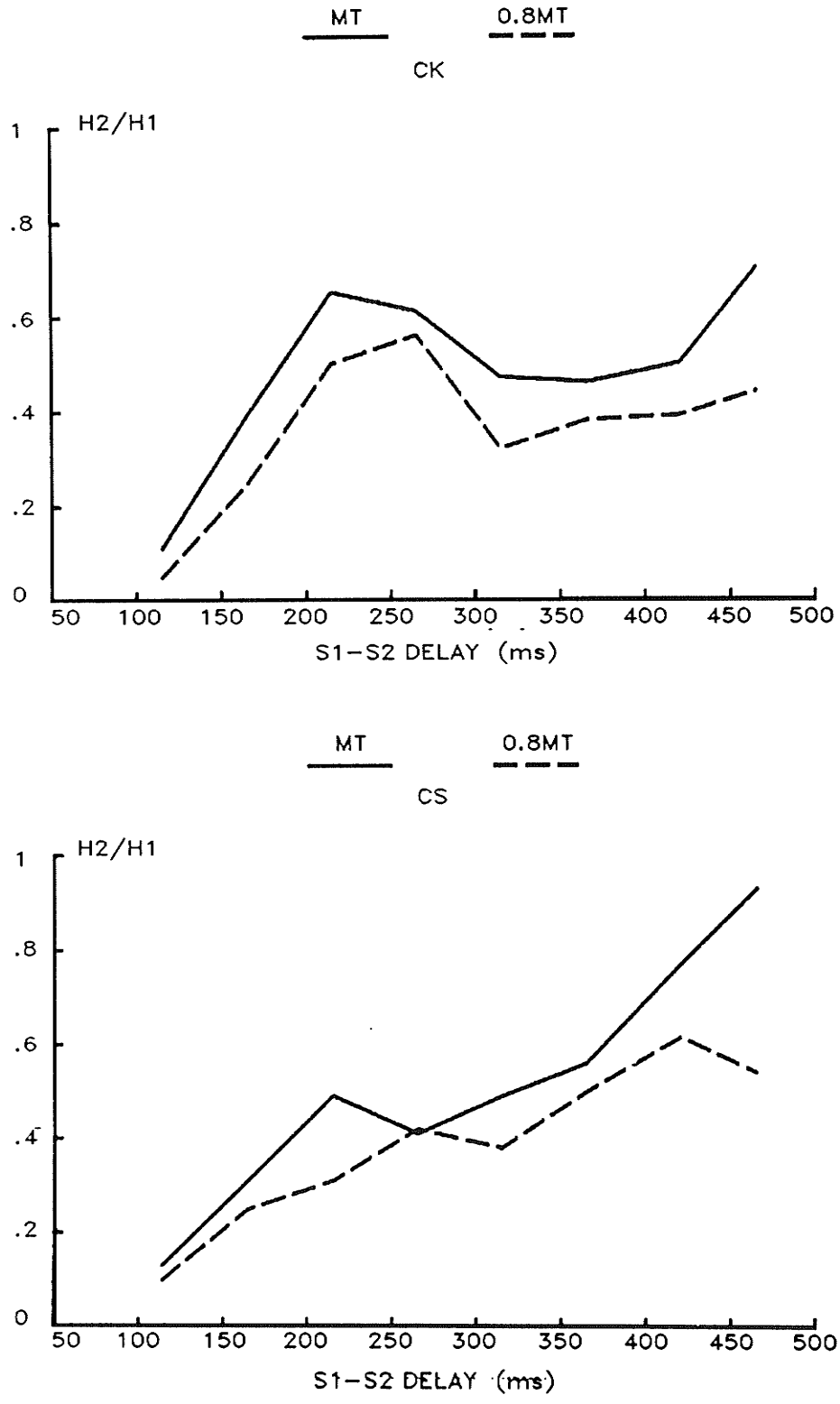

FIG 15a. H-reflex recovery curves for subjects CK and CS recorded at MT and 0.8MT stimulus intensities. Test position is 60 degrees.

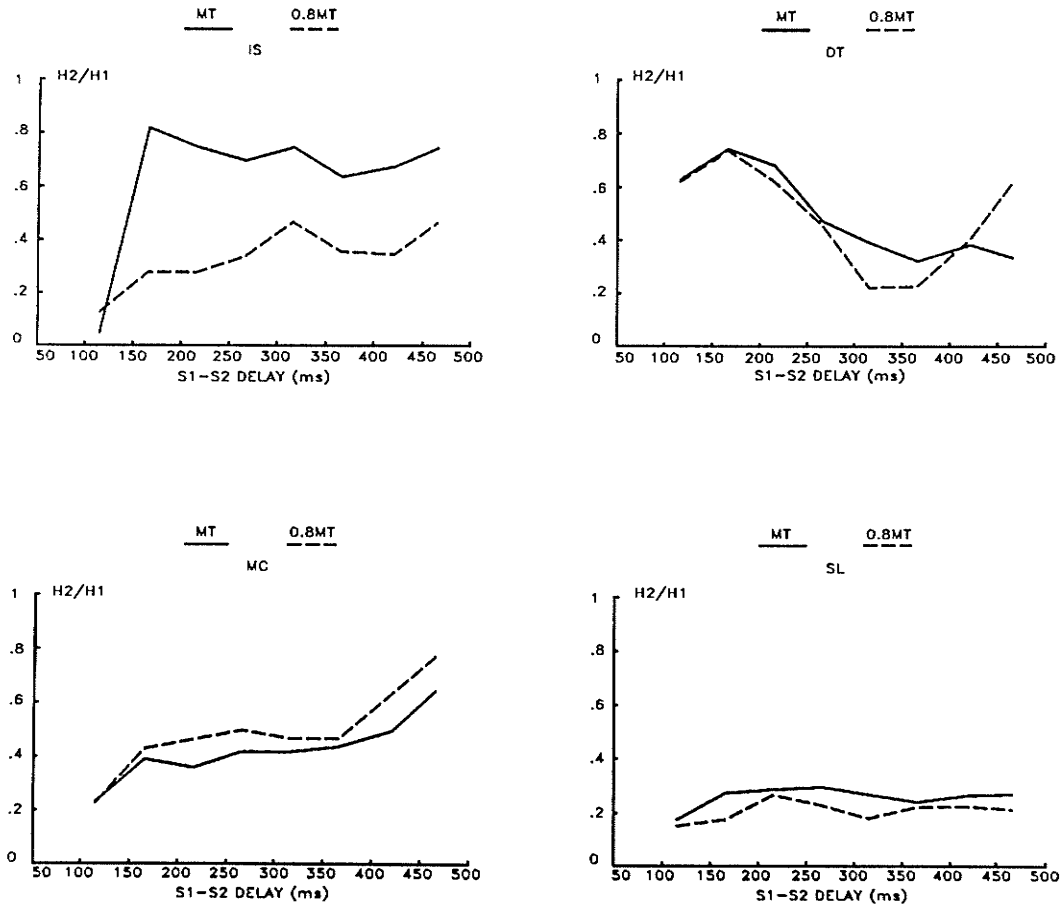

FIG 15 b. Same as FIG 15a except subjects are IS, DT, MC, and SL.

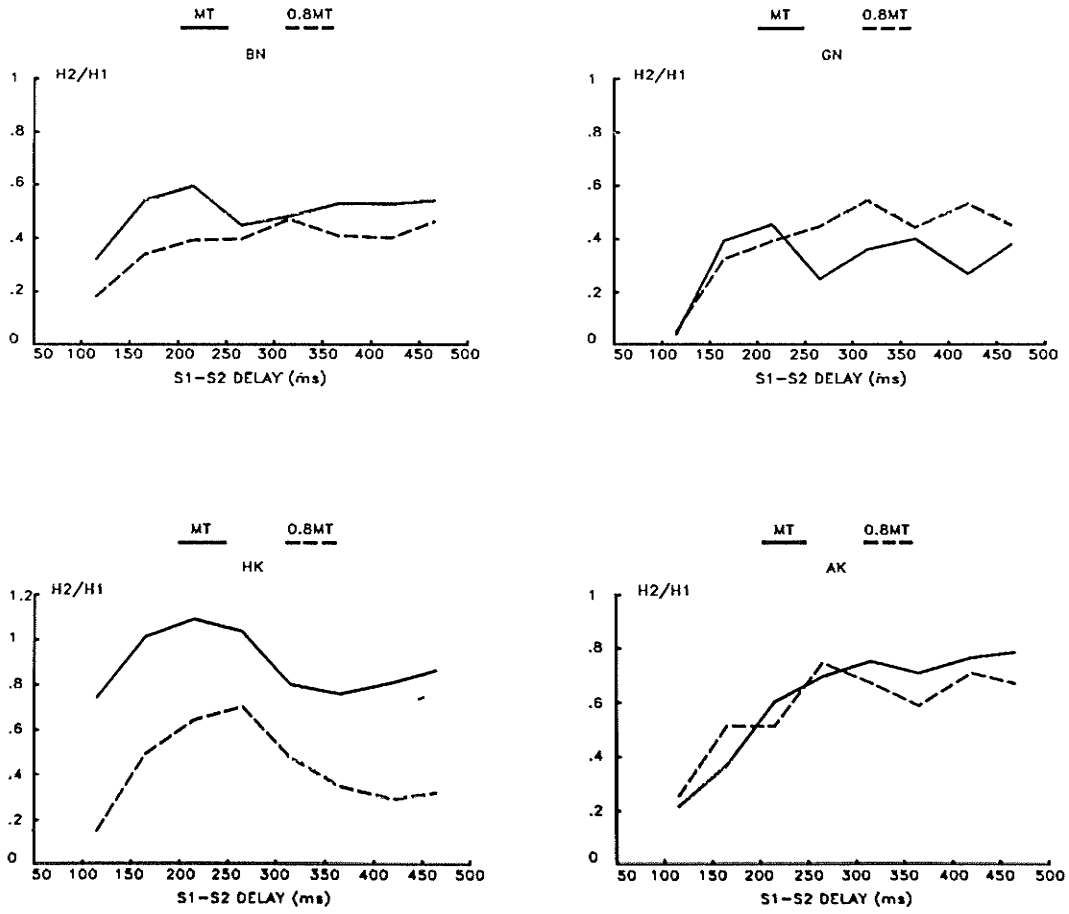

FIG 15c. Same as FIG 15a except subjects are BN, GN, HK, and AK.

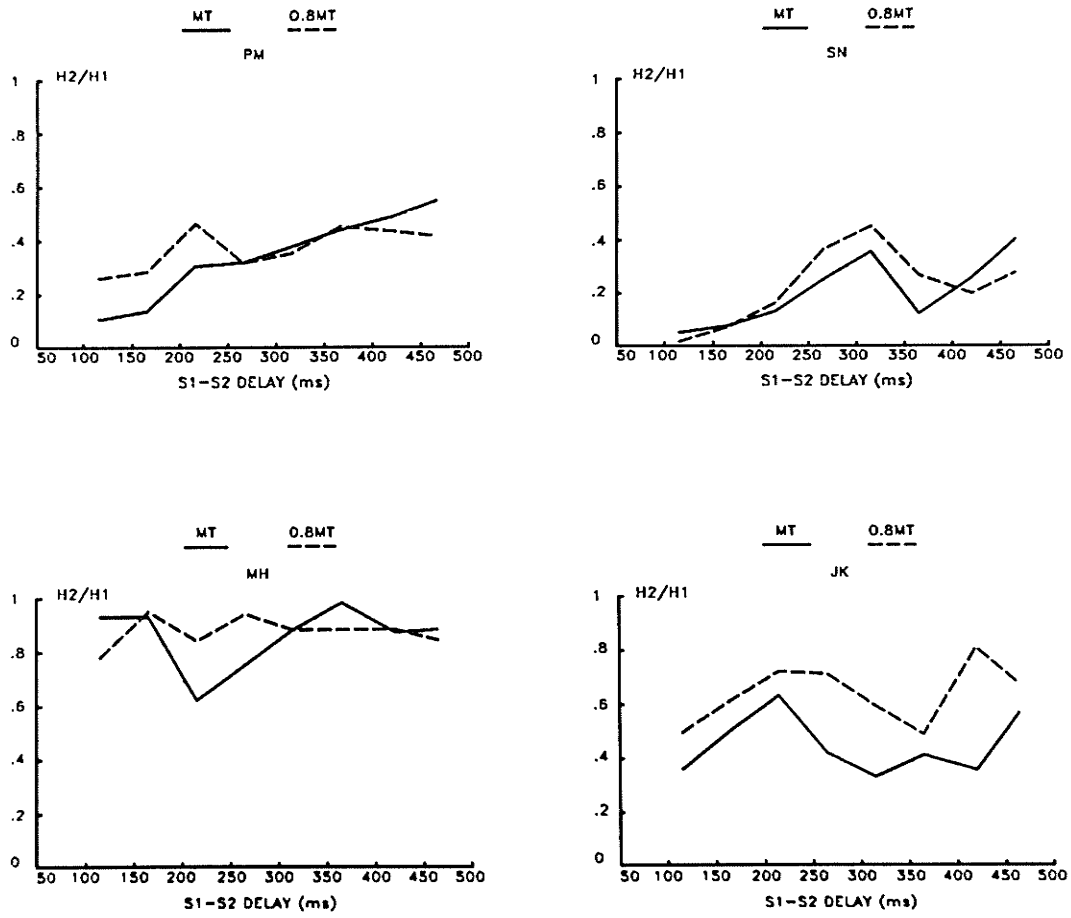

FIG 15 d. Same as FIG 15a except subjects are PM, SN, MH, and JK.

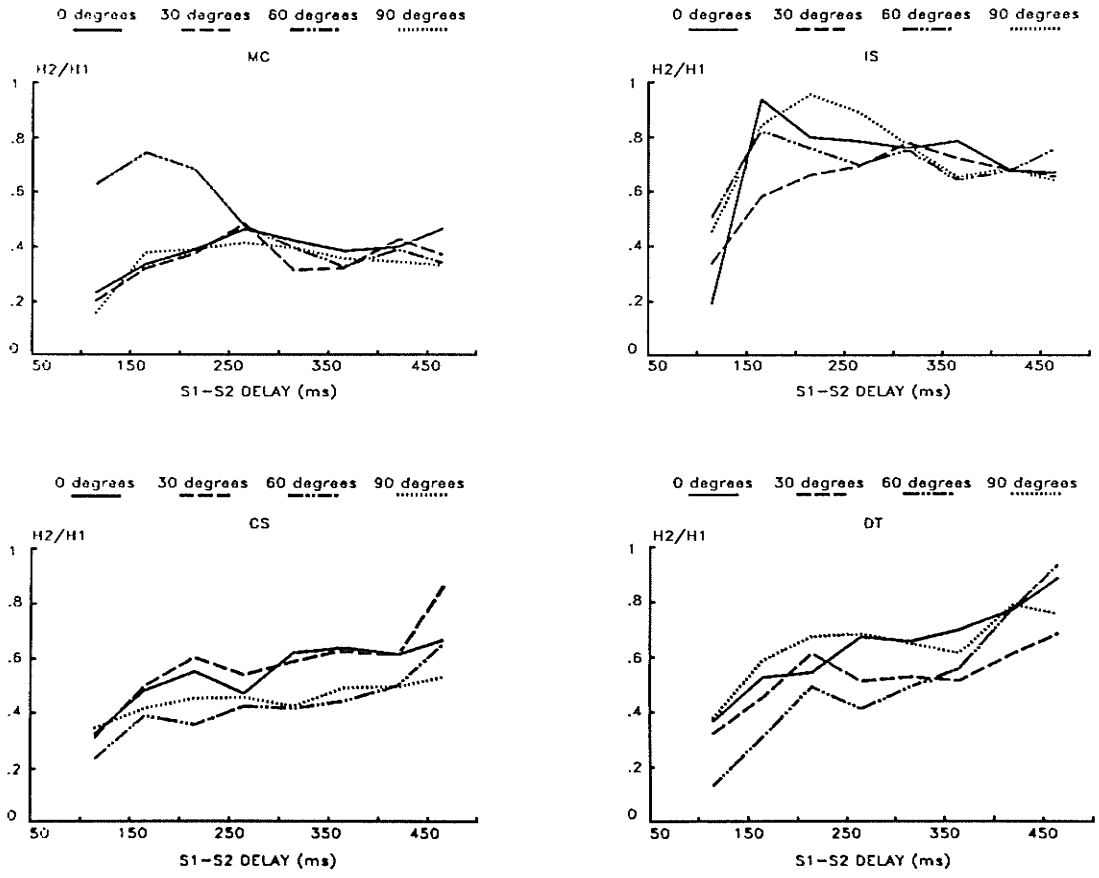

FIG 16a. H-reflex recovery curves for subjects MC, IS, CS, and DT at the four test positions. Stimulus intensity is MT.

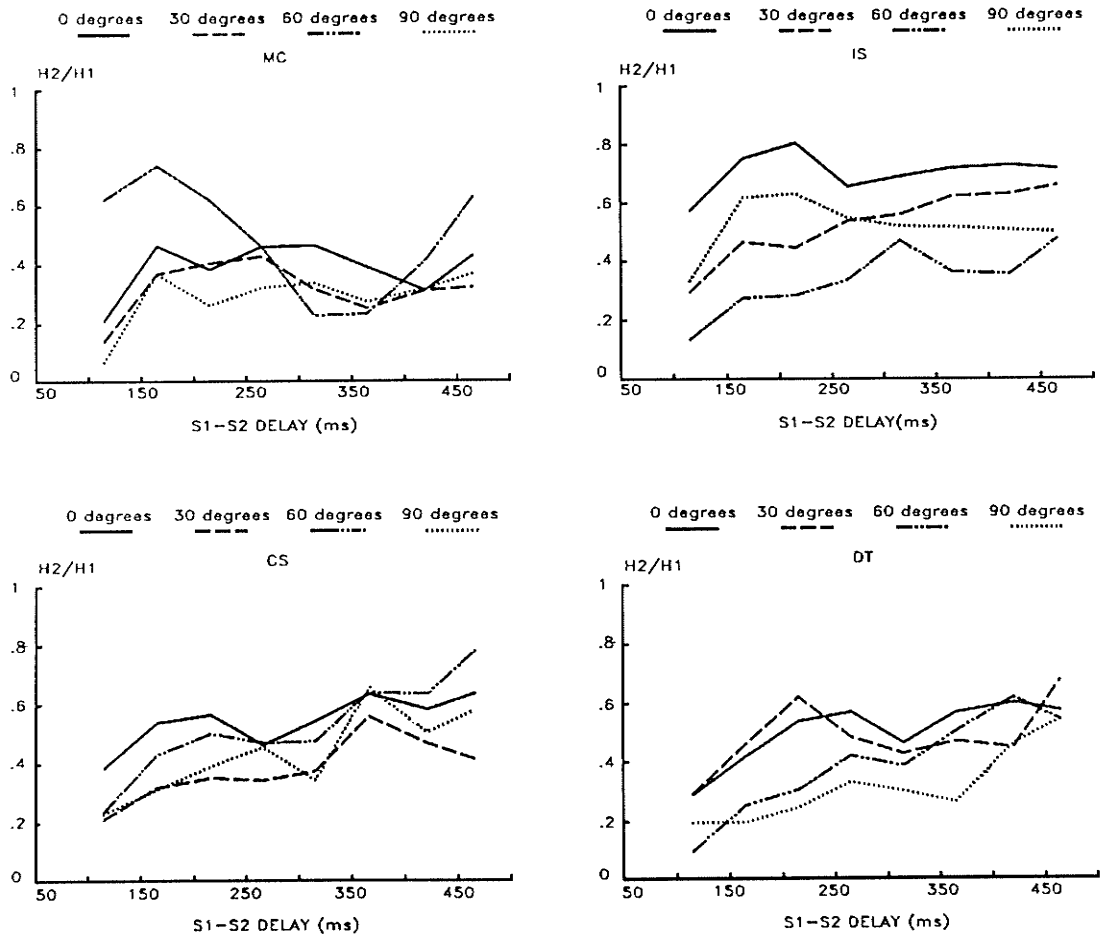

FIG 16b. Same as FIG 16a except stimulus intensity is 0.8MT.

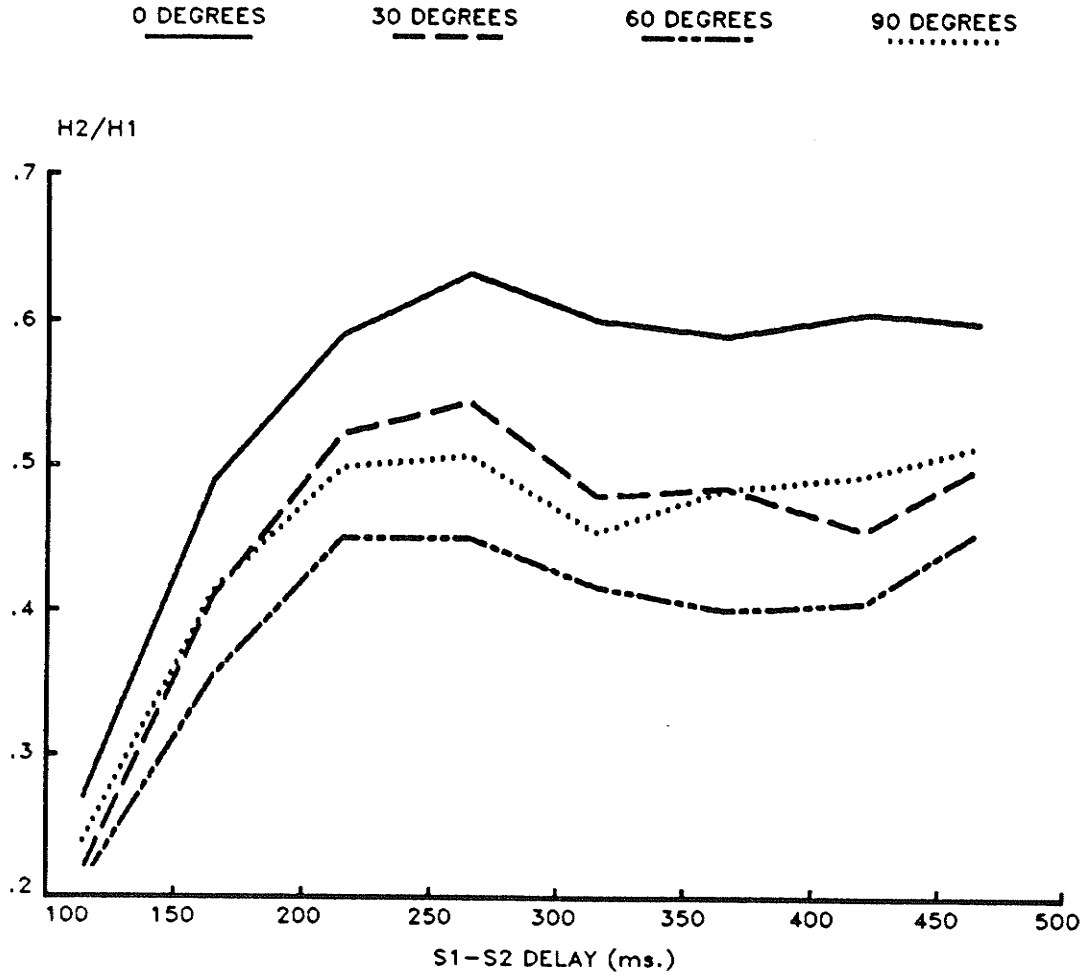

FIG 17. Mean H-reflex recovery curve at the four tset positions. Each point represents the mean response of 14 subjects with 7 observations of the H2/H1 ratio taken at each delay for every subject. Stimulus intensity is 0.8MT.

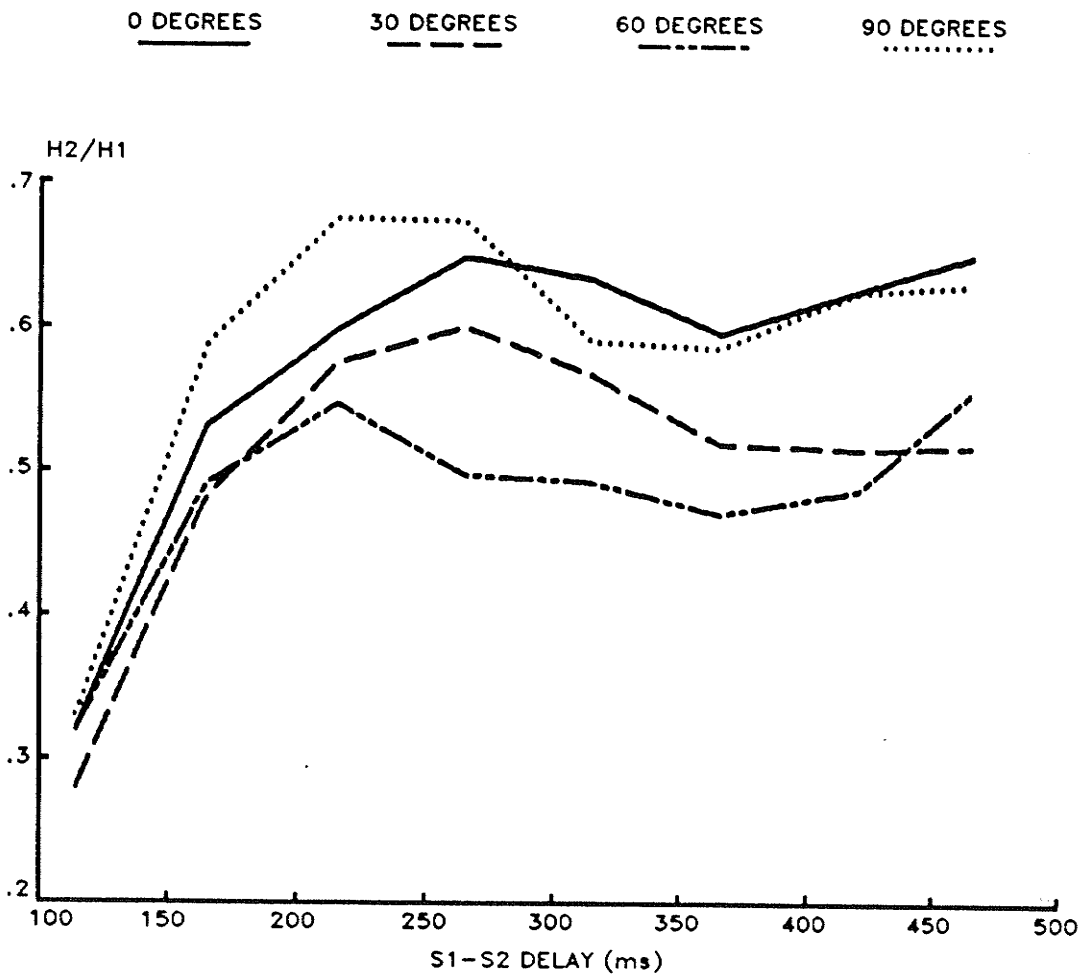

FIG 18. Same as FIG 17 execpt stimulus intensity is MT.

18 (MT). All curves exhibit a similar pattern. At the initial S_1-S_2 delays, an early depression period is evident where the H_2 reflex is generally suppressed. This is followed by a rapid rise in recovery to a peak value below an H_2/H_1 ratio of about 0.7. Superimposed on the recovery is a period of late depression or a plateau in H_2 recovery. The pattern of excitability represented by the mean recovery curves obtained in this investigation, such as degree of recovery at the various phases, the time to initial peak , the onset and duration of the late depression period are in good agreement with the findings of similar human studies by Magladery et al.[163] Yap[285] Taborikova and Sax[249] Crayton and King[42]. In general, the recovery of H_2 was greater at the MT stimulus intensity. This is consistent with the findings of Magladery et al.[163] and Crayton and King[42]. The results of the 2-way ANOVA, which are presented in Table 2, show the main effects of angle of tilt (A), S_1-S_2 delay (D) and their interaction (A*D) on the H2/Hl ratio. It is clear that the magnitude of H_2 recovery is highly dependent upon Sl-S2 delay at both stimulus intensities. Also the table reveals that the magnitude of recovery is highly dependent ($p < 0.006$) upon angle of tilt at the stimulus intensity 0.8MT, with a possible dependance at MT ($p < 0.08$). In the ANOVA, no significant interaction between angle of tilt and delay (A*D) was found. Thus, with respect to H_2/H_1 ratio, the main effect due to angle occurs independently of the delay effect.

The results of the one-way ANOVA which compares the effect of angle of tilt (A) on the H_2/H_1 ratio for the individual S_1-S_2 delays are presented in Table 3 (MT) and Table 4 (0.8MT). The analysis reveals that H2/Hl ratio is dependent on tilt angle only at S_1-S_2 delays of 265 ms. to 420 ms. (D4 to D7) . This is true for both stimulus intensities, although the significance was greater at 0.8MT.

In Fig. 19, the mean H_2/H_1 ratios at the S_1-S_2 delays of 265-420 ms. for all subjects were pooled and plotted against angle of tilt. The relationship between angle

TABLE 2 **Main effects of repeated measures ANOVA of data from 14 subjects. Variable is H2/H1 amplitude.**

A) INTENSITY = MT

	df	F VALUE	SIGNIFICANCE
ANGLE (A)	3	2.57	.08
DELAY (D)	7	21.5	.0001
INTERACTION (A*D)	21	1.48	NS

B) INTENSITY = 0.8MT

	df	F VALUE	SIGNIFICANCE
ANGLE (A)	3	5.07	.006
DELAY (D)	7	26.4	.0001
INTERACTION (A*D)	21	1.16	NS

TABLE 3 **Main effects of repeated measures ANOVA of data from 14 subjects. Variable is H2/H1. Here the analysis was performed at each delay. Stimulus intensity is MT.**

INTENSITY = MT and DELAY (D) = Di

SOURCE OF VARIATION	SIGNIFICANCE
ANGLE (D = 1 115 msec.)	NS
ANGLE (D = 2 165 msec.)	NS
ANGLE (D = 3 215 msec.)	NS
ANGLE (D = 4 265 msec.)	.02
ANGLE (D = 5 315 msec.)	.05
ANGLE (D = 6 365 msec.)	.03
ANGLE (D = 7 420 msec.)	.04
ANGLE (D = 8 465 msec.)	NS

TABLE 4 **Main effects of repeated measures ANOVA of data from 14 subjects. Variable is H2/H1. Here the analysis was performed at each delay. Stimulus intensity is 0.8MT.**

INTENSITY = 0.8MT and DELAY (D) = Di

SOURCE OF VARIATION	SIGNIFICANCE
ANGLE (D = 1 115 msec.)	NS
ANGLE (D = 2 165 msec.)	NS
ANGLE (D = 3 215 msec.)	NS
ANGLE (D = 4 265 msec.)	.01
ANGLE (D = 5 315 msec.)	.0001
ANGLE (D = 6 365 msec.)	.005
ANGLE (D = 7 420 msec.)	.003
ANGLE (D = 8 465 msec.)	.09

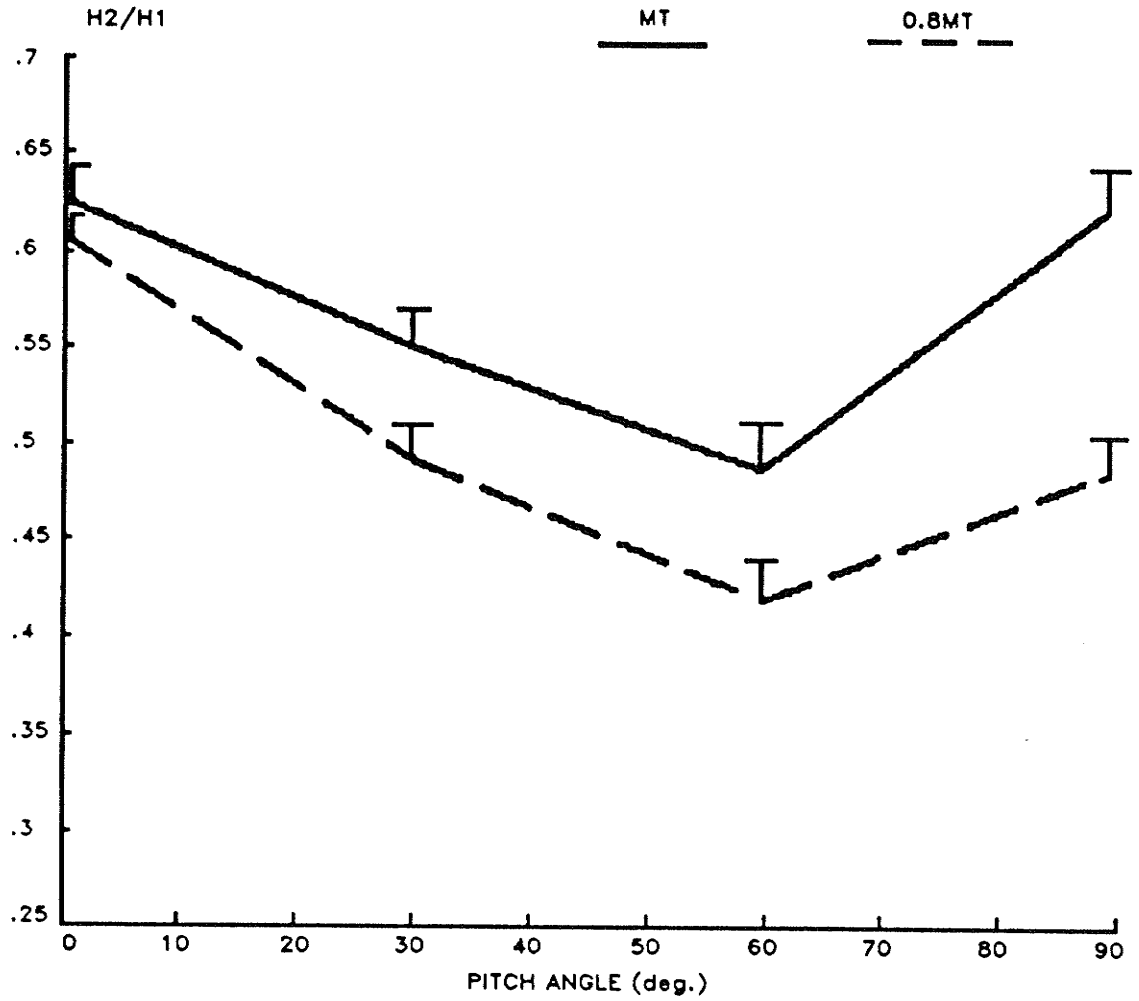

FIG 19. Plot of H2/H1 ratio versus pitch angle. Each point represents the mean H2/H1 value for 14 subjects taken from delays 265 to 420 ms. Bars = 1 SEM.

of tilt and H_2/H_1 ratio is similar at both stimulus intensities. It is shown that the conditioned H_2 response was maximal at 0 degrees of tilt, decreased until 60 degrees of tilt, and then increased from the 60 degrees tilt position to the 90 degrees tilt position.

5.2 - Experiment 2: Effects Of Natural Otolith Stimulation On Lower Limb Cutaneomuscular Reflexes

ANKLE MUSCLES (tibialis anterior and soleus)

The test reflex responses evoked in the four ankle muscles by sural nerve stimulation for one subject at one tilt position are presented in Fig. 13. These records are representative of the records of all 12 subjects so examined. The analysis of reflex latency and magnitude was determined from the full wave rectified and low passed filtered test reflex records (bottom traces of Fig. 13 A-D). By our convention, upward deflections of the test reflex represent inhibitory phases or silent period, and downward deflections represent excitatory phases with respect to the prestimulus tonic contraction level. For each muscle a characteristic reflex pattern was revealed which consisted of alternating sequences of excitation and inhibition. The reflex pattern of each muscle could be defined by the sign of its initial phase and by latency measurements. Computer averages of the digitized test reflex records from all subjects are presented in Fig. 20a (TA) and Fig. 20b (Sol) to illustrate the mean reflex patterns of the four muscle. The initial phase for coSol is excitatory while for the remaining muscles, coTA, iSol, and iTA, the initial phase was inhibitory. The records shown in Fig. 13 and Fig. 20a,b are consistent with the results of similar studies by Gassel and Ott[82], Piesiur-Strehlow and Meinck[294], and Meinck et al.[171].

The test reflex evoked at the four tilt positions during one session for one representative subject is presented in Fig. 21a,b. The magnitude of the test reflex, measured at peak amplitude, did vary between positions. However, the latency of the different phases, measured from stimulus onset to peak amplitude, did not vary with angle of tilt. The latency to peak amplitude remained extremely stable during each session (over the four test positions). This was the case for all subjects and for

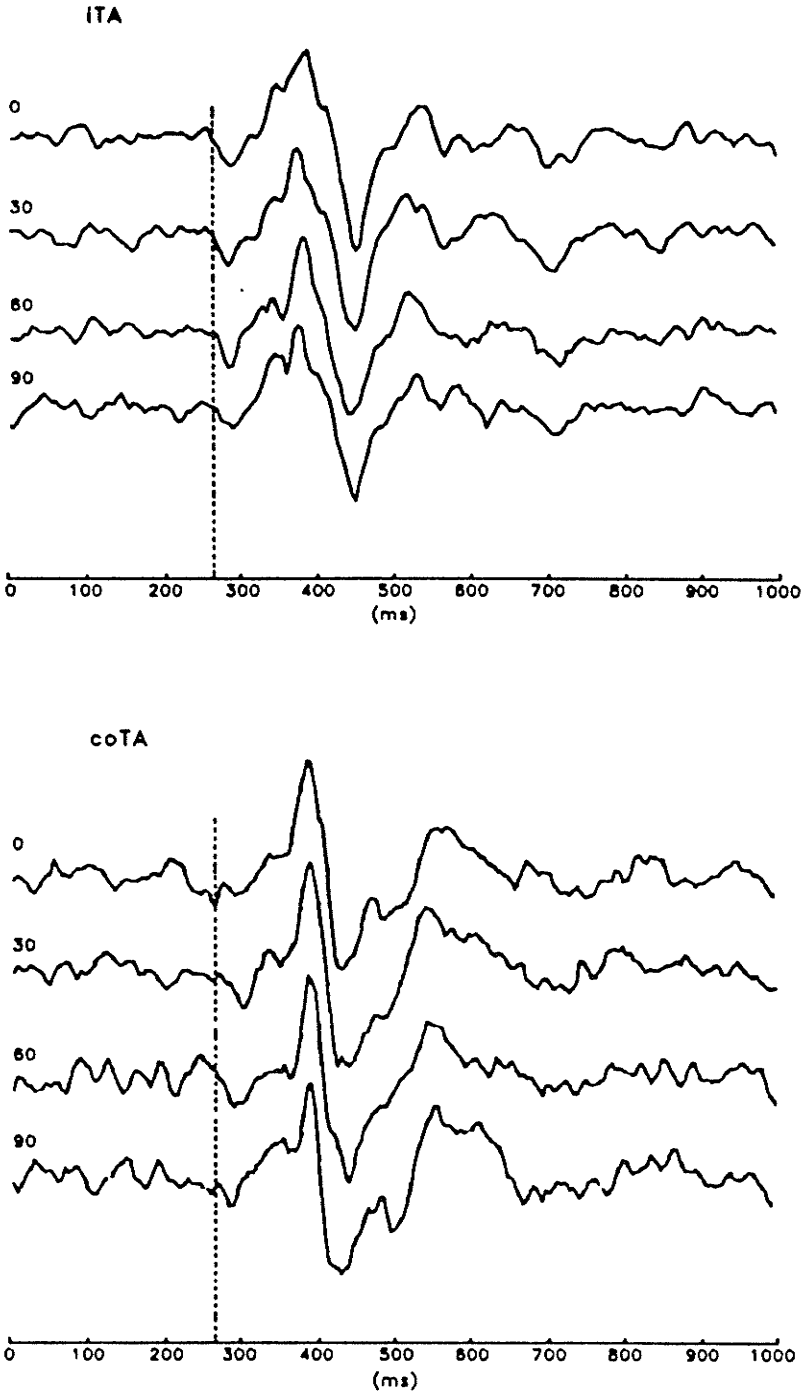

FIG 20a. Average reflex pattern in ITA and coTA at the four test positions. Each trace represents the computer average of the digitized records of the rectified and low pass filtered EMG response of all subjects (individual subject records are presented in FIG 13 and FIG 21a,b). Time scale at the bottom applies to all traces. Onset of stimulus is indicated by vertical dashed line.

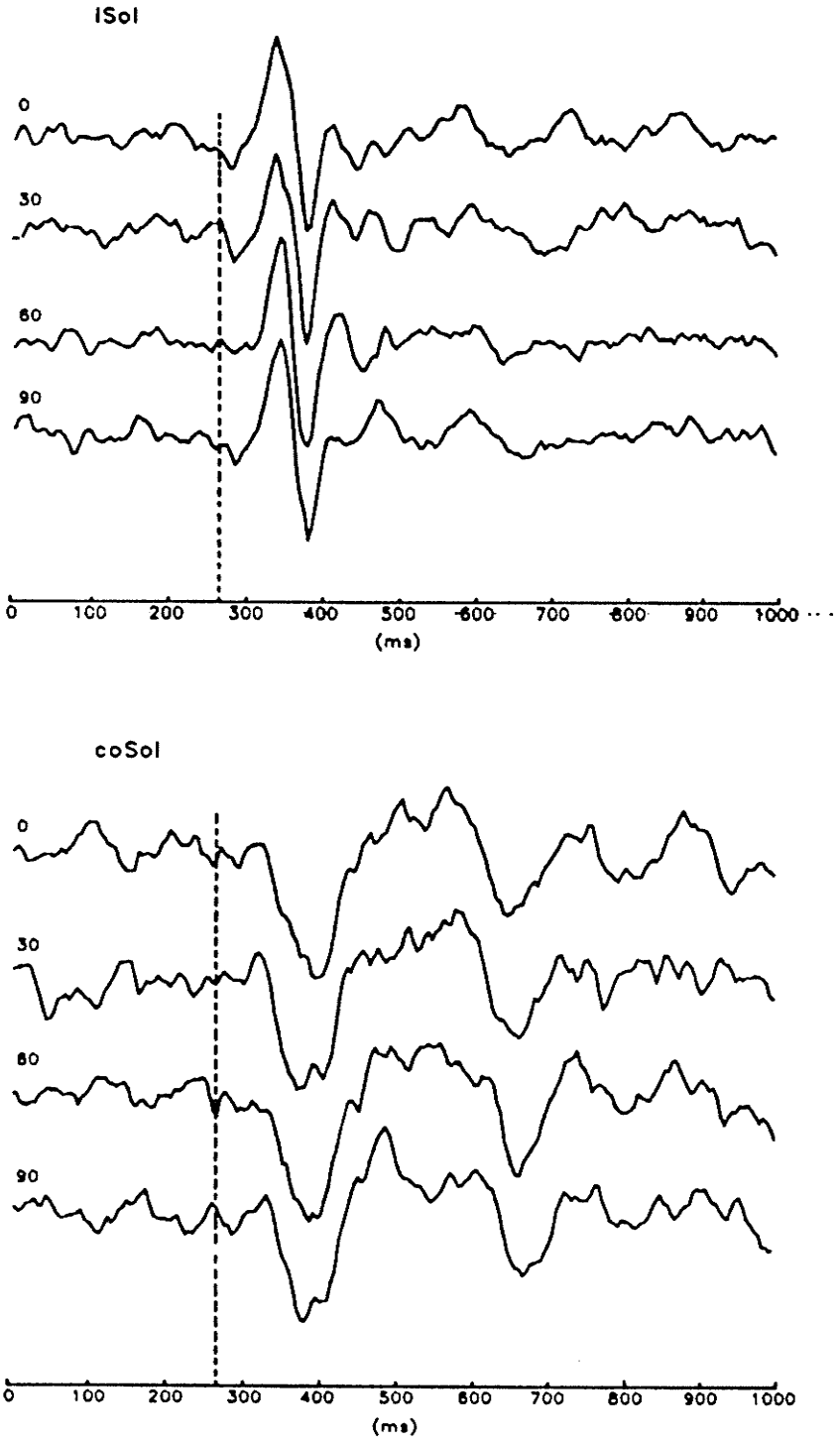

Fig 20b. Same as FIG 20a except average reflex pattern for iSol and coSo

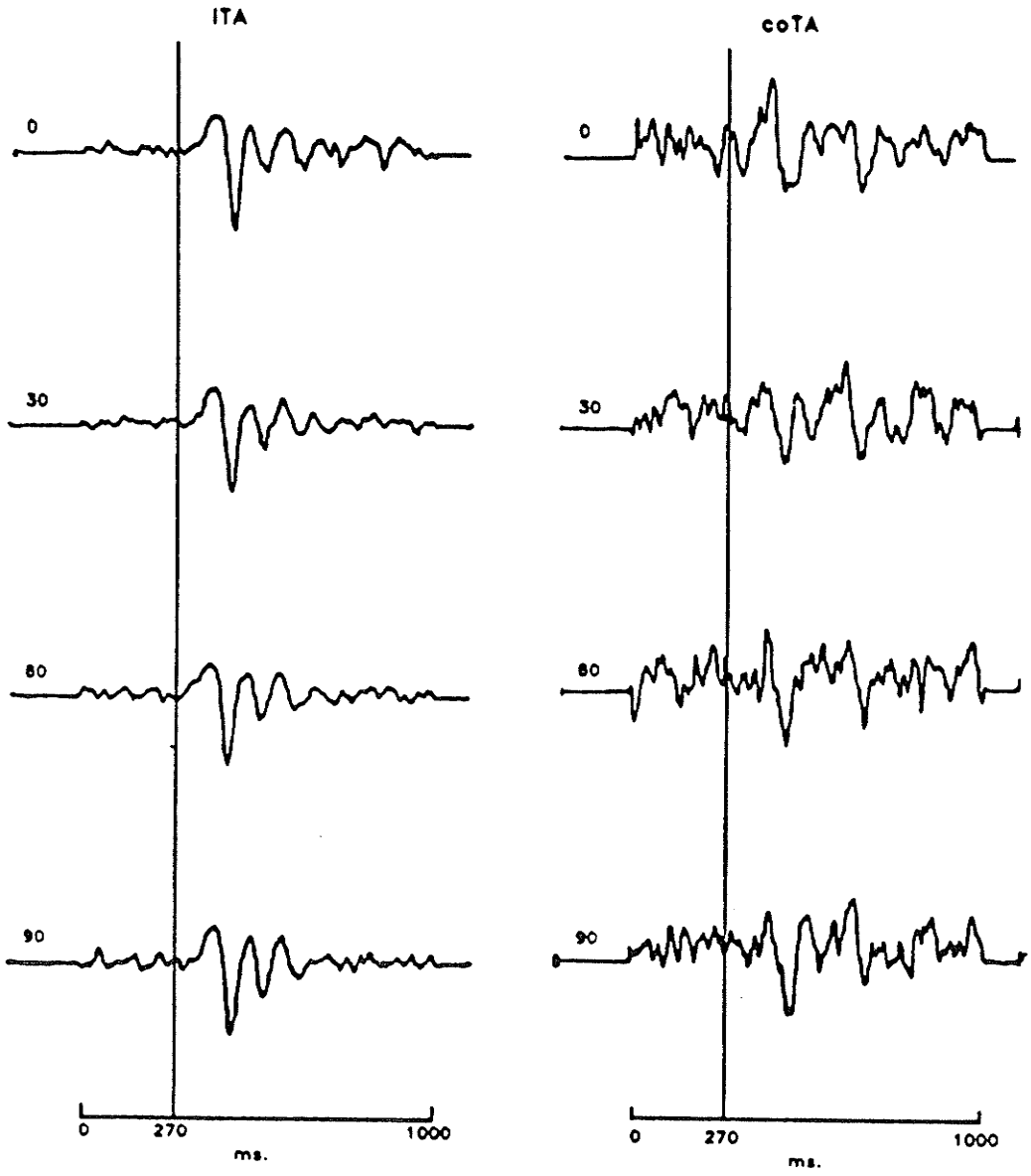

FIG 21a. Cutaneomuscular reflexes elicited in one subject in iTA and coTA at the four tilt positions. Time scale at the bottom applies to all records. Onset of stimulus ocurred at 270 ms. (vertical line).

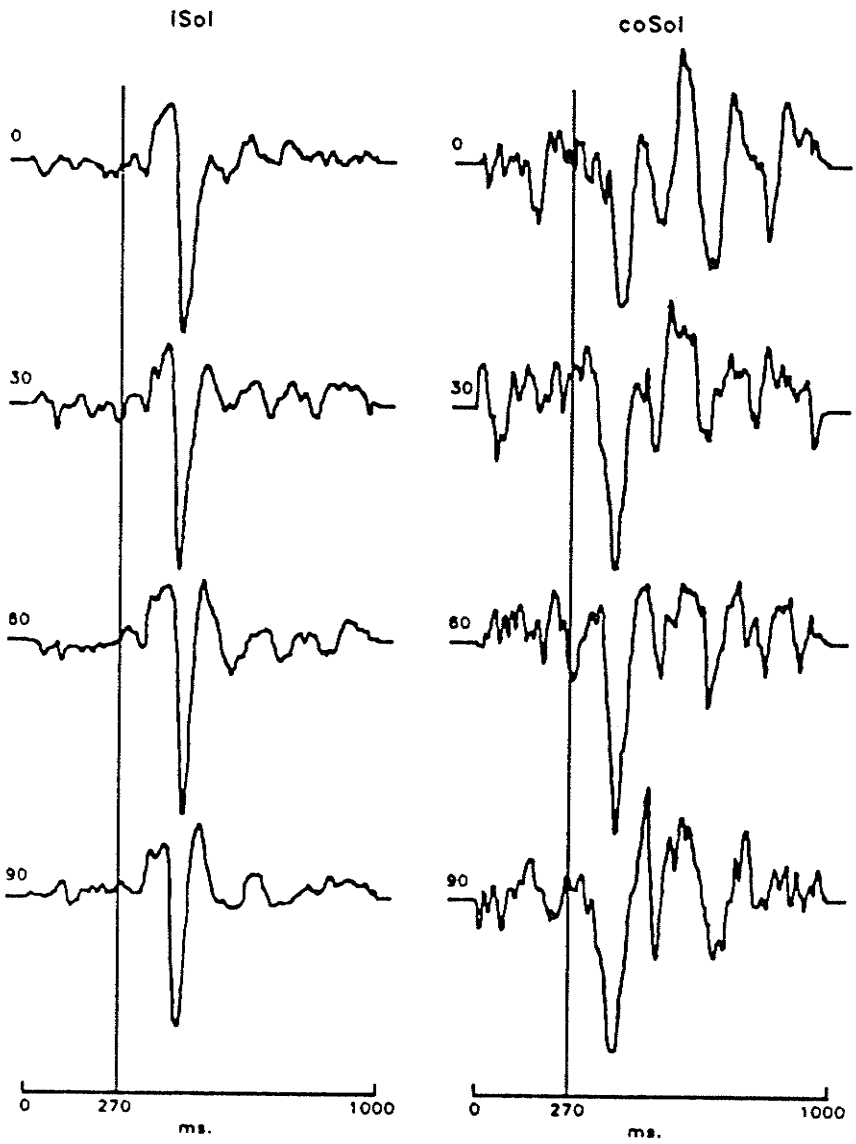

FIG 21b. Same as FIG 21a except cutaneomuscular reflexes elicited in the lSol and the coSol.

each muscle. The average latency to peak amplitude (calculated from the records of all subjects) of the first two phase of the test reflexes for coTA, iTA, coSol, and iSol is presented in Table 5. On the average the latencies for iSol were less than coSol (for the first phase 102 ms., 112 ms. respectively and the second phase 150 ms., 201 ms., respectively) while the latencies for iTA and coTA were similar (for the first phase 113 ms., 115 ms. respectively and the second phase 176 ms., 169 ms. respectively). The onset latency of the initial phase of the test reflex was not precisely determined because it was sometimes difficult to distinguish the onset of the first phase from the background EMG. However it can be seen from Fig. 20a,b that the onset latency of the initial phase of the four muscles is between 50-70 ms. These latency measures are consistent with those reported by Gassel and Ctt[82], Piesiur-Strehlow and Meinck[206], and Meinck et al.[171].

The results of the ANOVA, which are presented in Table 6 (first peak) and Table 7 (second peak), show the main effects of tilt angle on the magnitude (peak) of the first two phases of the test reflex for coTA, iTA, coSOL, and iSol. A highly significant (p 0.005) tilt dependent modulation of the magnitude of the initial inhibitory phase is demonstrated for the coTA test reflex. The amount of inhibition was greatest at 0 degrees (trunk/head horizontal) and progressively decreased as the angle of tilt was changed to 90 degrees (trunk/head vertical). No dependence between tilt position and magnitude of the excitatory (second) phase for coTA or the two phases of the test reflex for iTA, coSol, and iSol was observed.

PROXIMAL LEG MUSCLES (quadriceps and lateral hamstrings)

The test reflex responses evoked in coQ, iQ, coH, and coH by sural nerve stimulation for one subject at one tilt position are presented in Fig. 14. These records are representative of the records of all 12 subjects so examined. The analysis of

TABLE 5 **Mean and standard deviation (S.D.) in msec. of latency to peak amplitude of the first two phases of the test reflex calculated from the records of all subjects.**

	coTA	coSOL	iTA	iSOL
PEAK 1	115	123	113	102
S.D.	9	23	15	28
PEAK 2	169	201	176	150
S.D.	18	44	18	52

TABLE 6 **Results of ANOVA of the values representing the magnitude of the initial peak from the records of all subjects. For each muscle the mean peak amplitude at four angles of tilt and significance level are presented.**

ANGLE (deg.)	MEAN AMPLITUDE coTA	coSol	iTA	iSol
0	19.3	12.4	17.0	14.4
30	17.3	12.2	15.9	14.1
60	15.8	11.3	15.2	16.0
90	12.9	10.9	14.9	14.9
SIGNIFICANCE LEVEL				
p	< 0.005	NS	NS	NS

TABLE 7 **Results of ANOVA of the values representing the magnitude of the second peak from the records of all subjects. For each muscle the mean peak amplitude at four angles of tilt and significance level are presented.**

ANGLE (deg.)	MEAN AMPLITUDE coTA	coSol	iTA	iSol
0	10.5	15.3	15.0	16.5
30	10.5	14.2	12.8	16.3
60	11.0	12.9	14.1	17.9
90	9.9	14.5	13.3	14.0
SIGNIFICANCE LEVEL				
p	NS	NS	NS	NS

reflex latency and magnitude was determined from the full wave rectified and integrated records (bottom records in A-D). As with the records of the ankle muscles, upward deflections in the test reflex records for the proximal leg muscles represent inhibitory phases or silent periods, and downward deflections represent excitatory phases with respect to the prestimulus tonic contraction level. For all subjects the test reflex consisted of oscillating sequences of excitation and inhibition, each muscle exhibiting a characteristic pattern defined by the latency of the various phases and sign of the initial phase.

In Fig 22a, b, the traces (computer average of digitized records from all subjects) illustrate the various reflex patterns observed in iQ, iH, coQ, and coH. This general pattern of reflex activity was evident in the ankle muscles and is consistent with the observations of Piesiur-Strehlow and Meinck[206] and Meinck et al.[171]. The sign of the initial phase of the test reflex patterns for coQ (Fig. 22a and coH (Fig. 22b) are the same. On the other hand, the reflex patterns for iQ (Fig. 22a) and iH (Fig. 22b) are opposite, the initial phase for iQ is inhibitory while the initial phase for iH is excitatory.

Within one session, the test reflex evoked at the four tilt positions for one representative subject is presented in Fig. 23. The magnitude of the test reflex (measured at peak amplitude) did vary with tilt position, but the latency of the different phases, measured from stimulus onset to peak amplitude, did not vary with angle of tilt. As with the ankle muscles, the latency to peak amplitude of the proximal muscles remained extremely stable during each sessions (over the four test positions). This was the case for all subjects and for each muscle. The average latency to peak amplitude (calculated from the records of all subjects) of the first three phase of the test reflexes for coQ, iQ, coH, and iH are presented in Table 8. The latencies to peak amplitude for quadriceps were less than those of hamstrings. The onset latency for the initial fig 22a

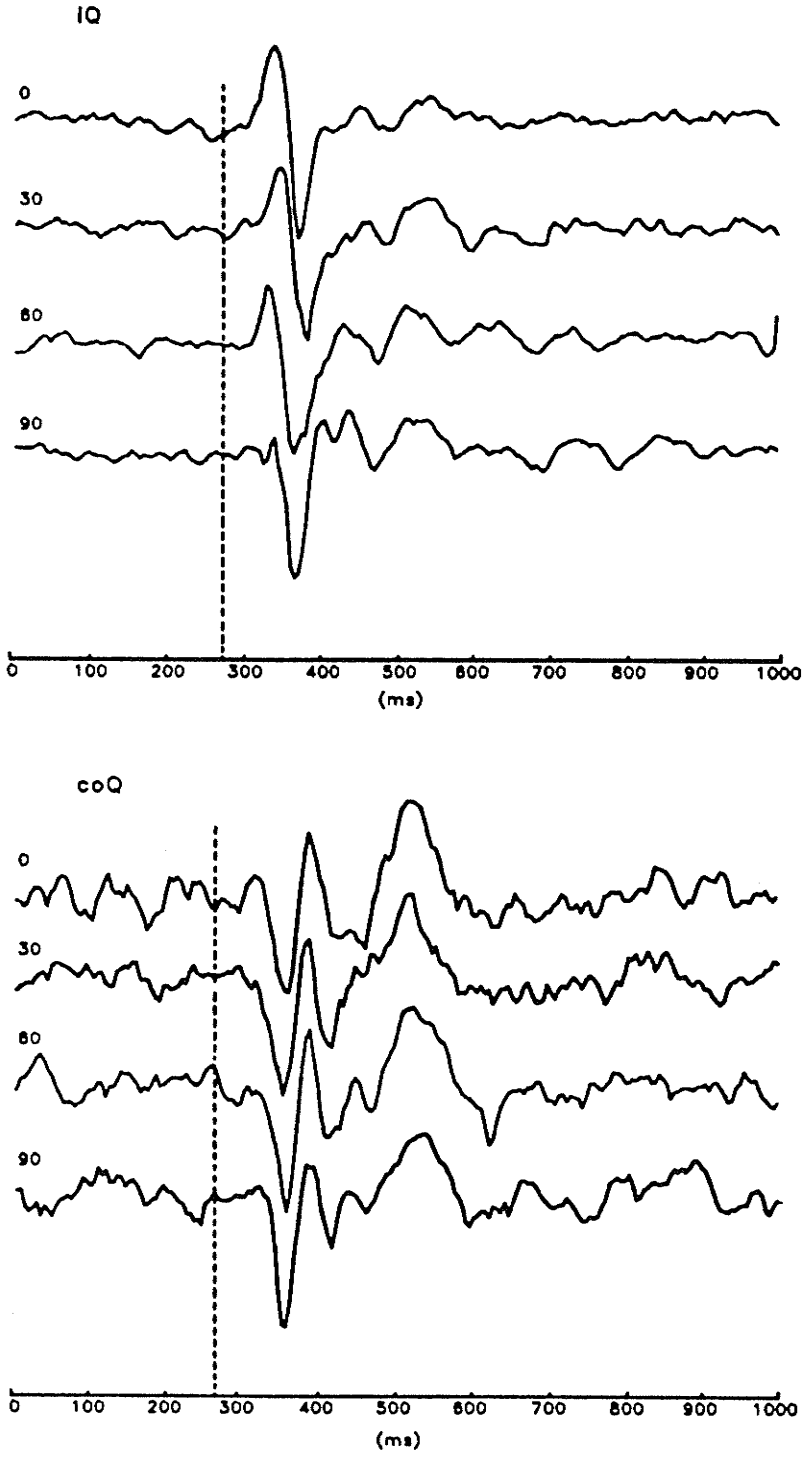

FIG 22a. Average reflex pattern in coQ and IQ at the four test positions. Each trace represents the computer average of the digitized records of the rectified and low pass filtered EMG response of all subjects (individual subject records are presented in FIG 14 and FIG 23). Time scale at the bottom applies to all traces. Onset of stimulus is indicated by vertical dashed line.

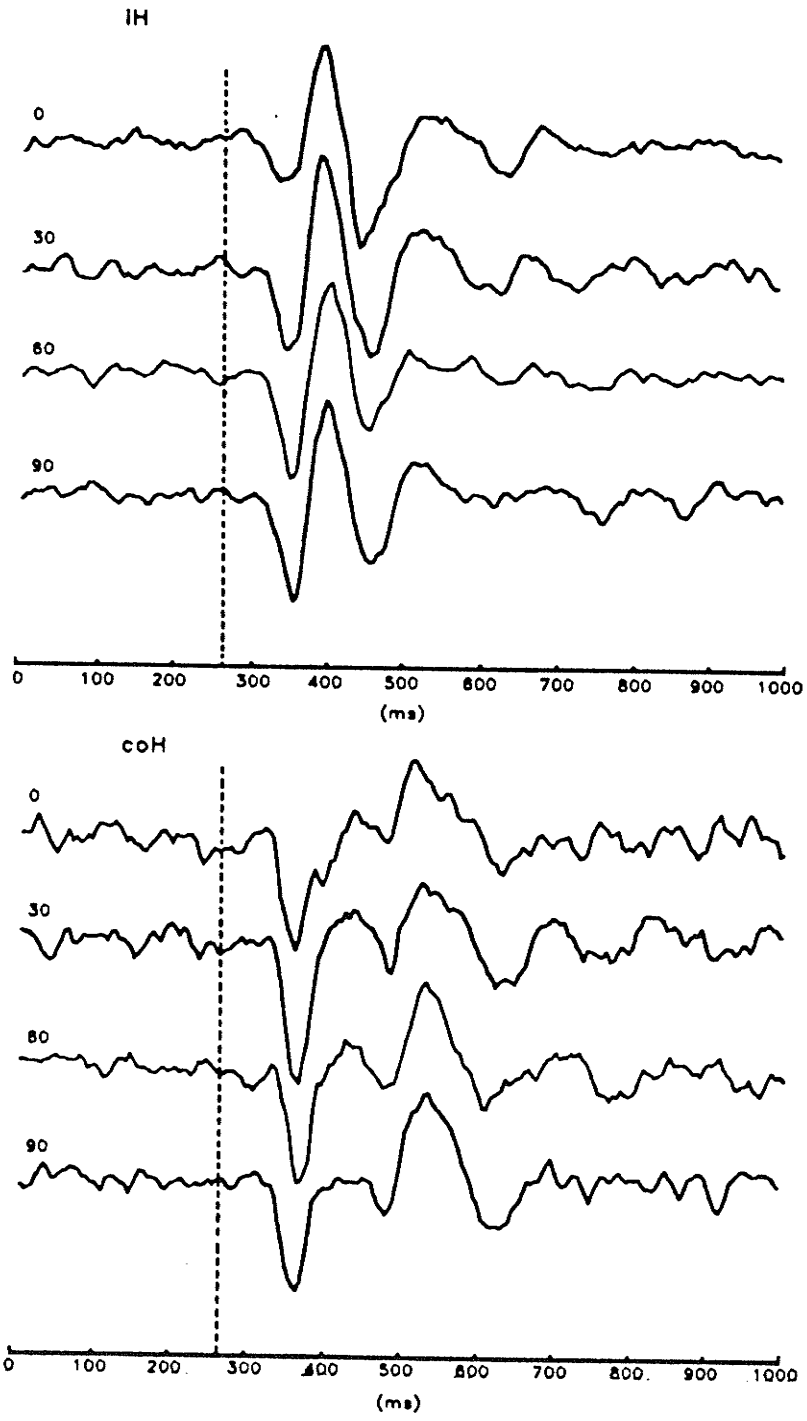

FIG 22b. Same as FIG 22a except average reflex pattern for IH and coH.

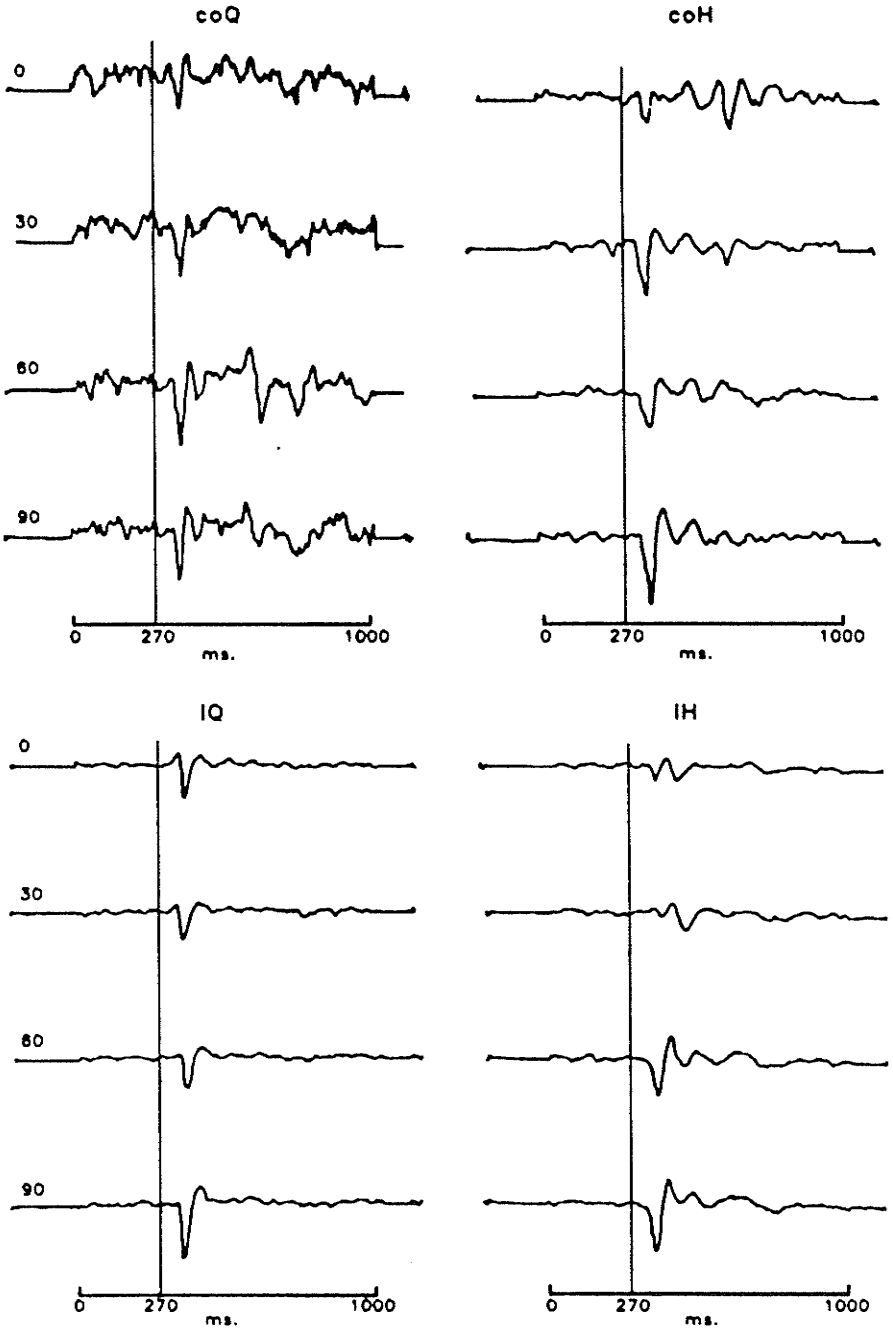

FIG 23. Cutaneomuscular reflexes elicited in one subject in the coQ, coH, lQ, and lH at the four test positions. Time scale at the bottom applies to all records. Onset of stimulus occurred at 270 ms. (vertical line).

TABLE 8 **Mean and standard deviation (S.D.) in msec. of latency to peak amplitude of the various phases of the test reflex calculated from the records of all subjects.**

	coQ	coH	iQ	iH
PEAK 1	81	94	78	87
S.D.	8	16	12	14
PEAK 2	114	138	104	133
S.D.	18	22	16	14
PEAK 3	163	192	163	190
S.D.	27	25	21	20

phase of the test reflex for the four muscles could not be precisely defined for the same reasons discussed for the ankle muscles. The onset latency as approximated from Fig. 22a,b ranged from 50 to 60 ms.

For the proximal muscles, the results of the ANOVA with repeated measures are presented in Tables 9-11. These results demonstrate a highly significant, tilt dependent modulation of the magnitude of the initial peak of the test reflex for iQ ($p < 0.0005$), and iH ($p < 0.001$). Also, there is a tilt dependent modulation of the magnitude of the second peak of the test reflex for iH ($p < 0.05$). No dependence between tilt position and magnitude of the remaining peaks for iQ and iH was observed. There was no dependence between tilt position and magnitude of the three peaks of the test reflex for coQ or coH. It is evident from the results of the ANOVA (see Tables 8-10) that there is a step wise change in the magnitude of the initial phase for iQ and iH. As the angle of tilt varies from 90 to 0 degrees one sees an increase in the inhibitory peak of iQ and a decrease in the excitatory peak of iH. In other words as the orientation of the body changes from vertical to horizontal a greater amount of inhibition arises in s both muscles which is evident in only the initial phase of the reflex.

TABLE 9 **Results of ANOVA of the values representing the magnitude of the initial peak from the records of all subjects. For each muscle the mean peak amplitude at four angles of tilt and significance level are presented.**

ANGLE (deg.)	MEAN AMPLITUDE coQ	coH	iQ	iH
0	7.9	14.5	12.2	6.8
30	9.1	12.3	9.1	10.5
60	10.3	13.2	7.1	16.6
90	10.1	12.5	3.3	17.6
SIGNIFICANCE LEVEL p	NS	NS	< 0.0004	< 0.002

TABLE 10 **Results of ANOVA of the values representing the magnitude of the second peak from the records of all subjects. For each muscle the mean peak amplitude at four angles of tilt and significance level are presented.**

ANGLE (deg.)	MEAN AMPLITUDE coQ	coH	iQ	iH
0	16.6	12.0	12.6	12.7
30	15.2	10.0	12.5	12.5
60	14.2	10.8	13.8	16.4
90	13.8	10.7	11.5	16.0
SIGNIFICANCE LEVEL p	NS	NS	NS	< 0.05

TABLE 11 **Results of ANOVA of the values representing the magnitude of the third peak from the records of all subjects. For each muscle the mean peak amplitude at four angles of tilt and significance level are presented.**

ANGLE (deg.)	MEAN AMPLITUDE coQ	coH	iQ	iH
0	7.5	3.5	8.7	11.4
30	6.3	2.0	7.5	9.8
60	5.6	3.0	8.7	8.6
90	6.2	2.9	8.9	8.9
SIGNIFICANCE LEVEL				
p	NS	NS	NS	NS

CHAPTER 6

DISCUSSION

The main results of the first series of experiments have shown that there was no dependence of motoneuron excitability on angle of tilt as assessed by the monosynaptic myotatic reflex method. However, a significant relationship was revealed between angle of tilt and the recovery of a test H-reflex preceded by a conditioning H-reflex.

Contrary to the present findings (results summarized in Table 1), Chan and Kearney[38] and Aiello et al.[4], claim that static tilt in the pitch axis does modulate the amplitude of the H-reflex. However, in these similar studies, conflicting results were reported. As discussed in SECTION 2.42, because of the weaknesses and deficiencies in the statistical analysis procedures, their conclusion are questionable. In the present study, a balanced, repeated measures ANOVA was designed to examine the effect of angle of tilt (four static positions) on the H-reflex amplitude among all subjects. Furthermore, in the present study, subjects were seated in a chair apparatus rather than positioned supine. With this procedure, the subjects were fully supported and a comfortable resting position was easily maintained during tilts. There was no need to suspend the subjects in the vertical or near vertical tilt positions which may result in a change in the baseline EMG level and a significant differential activation of somatosensory receptors, including neck, static length, joint, and cutaneous receptors. In this regard, it has been reported that the magnitude of the H-reflex is dependent on the pre-existing level of EMG activity[161 257]. These analysis and methodological considerations may account for the differences between the present findings and those of Chan and Kearney[38] and Aiello et al.[4].

As indicated in the results and summarized in Tables 2-3, a significant influence

of angle of tilt on H_2/H_1 ratio has been revealed, in particular at S_1-S_2 delays of 265 to 420 ms. This was true at both stimulus intensities. With respect to the directional selectivity, a similar relationship was observed (Fig. 19) between angle of tilt and the degree of H_2 recovery at 0.8 MT and MT. It was also determined that the effect of angle of tilt on the H_2/H_1 ratio occurs independently of the S_1-S_2 delay effect, i.e., with respect to the H_2/H_1 parameter, no interaction between angle of tilt and S_1-S_2 delay was observed. This is evidence of a tonic effect of tilt angle on H_2 recovery.

The segment of H_2 recovery between S_1-S_2 delays of 265 to 420 ms. coincides with the late depression or plateau phase of the recovery curve1[62 249 42]. The neural mechanisms which underlie the various phases of the H-reflex recovery curve are not clear. Due to its long time course (in the order of 100 to 200 ms.)[55 182 117], presynaptic inhibition of the Ia terminals produced by the activation of muscle spindle afferents during the S_1 volley could account for the early depression of the H_2 test reflex which occurs in the first 100 to 150 ms. after the conditioning S_1 volley[162 249 81 42]. With respect to the late depression phase, based on the time course involved (test-condition interval in the order of 250 to 500 ms.) the participation of supraspinal centers can not be excluded. In this respect, a long loop pathway which includes the cerebellum (group I activation of spinocerebellar tract cells) and a descending route through the vestibular complex or the reticular formation may produce the delayed depression of the conditioned H_2 response[249]. On the other hand, from the observations of Magladery and colleagues[163 251 164], as discussed in SECTION 2.5, it has been proposed that a spinal integrative mechanism activated by the S_1 conditioning volley could give rise to the late depression phase of the H-reflex recovery curve. The information about the receptor origin of the afferents that contribute to the late depression phase is incomplete. The activation of group I muscle afferents, low threshold cutaneous afferents, and possible group II muscle afferents by the S_1 conditioning volley[161 30 81] are all

possible candidates. Also, the conditioning reflex contraction in the soleus will excite spindle afferents and cutaneous afferents, although it has been shown that a late depression phase in the H-reflex recovery curve persists when a subliminal conditioning S_1 volley (subthreshold for an H-reflex) is used[248].

A point that needs further discussion is that in the investigation of the effect of static tilt on H_1 amplitude and H_2/H_1 ratio, only one of the four test positions was examined per session. This procedure could introduced a source of variability that may account for any effects observed in the study. The following considerations have some bearing on this matter. Test-retest studies by Crayton and King[42] show that H-reflex parameters derived from recruitment and recovery curves curve are highly stable within subjects. A similar finding for the H-reflex recovery curve has also been reported by Tardieu et al.[250]. In the present study test position sequence and S_1-S_2 delay sequence were randomized which should eliminate any systematic order effect. Furthermore, any source of variability introduced by testing on separate occasions should occur to the same extent in both H_1 and H_2, and thus is an unlikely factor when using the H_2/H_1 parameter for comparison. This argument is strengthened by the finding that the H_1 amplitude (conditioned reflex contraction) did not vary with angle of tilt. For these reasons it is believed that the present results are a manifestation of a change in body position relative to the gravity vector and it can be concluded that the origin of the tilt dependent response most likely arises from activation of the otolith end organs and/or nonadapting somatosensory receptors (neck, static length, joint, and cutaneous receptors).

There is little question that the otolith end organs are excited by changes in head position relative to the gravity vector, discussed in detail in CHAPTER 2. The morphological nature of the otolith end organs[153 241 139 140] leads one to believe that an adequate stimulus of the otolith receptors would result from bending of the

hair fibers due to the shearing of the statoconial membrane relative to the sensory epithelium. This has been substantiated with electrophysiological studies[66 108 136]. In mammals, the sensitivity and direction selectivity to head tilt of otolith afferents and vestibular neurons including vestibulospinal neurons, is well documented[198 146 86 65 10 226 227]. Fernandez and Goldberg[65], recording from primary afferent, have shown that many otolith units did respond in a sustained manner (nonadapting) to maintained linear forces. Furthermore, in the animal literature it is generally agreed that when stimulated, the otolith system contributes a significant fraction of PSP's to spinal neurons involved in the control of lower limb activity. The present data (Fig.19), describes the relationship between angle of tilt and H_2/H_1 ratio. From a tilt angle of 0 degrees (head horizontal) to 90 degrees (head vertical) the mode of utricular stimulation would change from shear to compression while the saccule would remain in a state of shear but through a rotated gravity vector. A prediction of the net change in reflex excitability of otolith stimulation during tilt in pitch seems unwise for the following reasons: 1) it would be difficult to determine the net outflow from the utricular and saccular maculae based on the details of morphological and functional polarization vectors in the otolith system; 2) little information is available on the directional selectivity of the spinal elements in the otolith reflex pathway to lower limb muscles.

In support of an otolith contribution to the tilt-dependent effect on the H-reflex recovery curve, the present results are highly consistent with the findings of Lacour et al.[135] whom recorded soleus H-reflex recovery curves before and after unilateral vestibular neurotomy in the baboon. They show that in comparison to pre-operative controls, the H-reflex recovery curve was strongly depressed in the limb ipsilateral to the neurotomy and slightly depressed in the limb contralateral to the neurotomy. Furthermore, the modifications observed after surgery affected only part

of the H-reflex recovery curve (S_1-S_2 delays between 250 and 1000 ms.), which coincides with that section the which we have demonstrated to be sensitive to tilt angle. Thus, we believe that the otolith end organs are the primary candidates accountable for the tilt dependent modulation of the H-reflex recovery curve.

From the findings of Experiment 1 it can be concluded that static tilt in pitch modulates the H-reflex recovery curve, and does not directly affecting the excitability of the motoneuron pool. Thus, regardless of the sensory structures involved the results support the view that, with surface EMG recordings, the soleus H-reflex does not provided us with a sensitive measures of the central effects of static tilt. Since the H-reflex is a measure of the amount of current produced by the depolarization of muscle fibers and not the number of motoneurons recruited and since it is probable that a motoneuron or a motoneuron pool may receive more EPSPs without discharging or recruiting more motor units, it follows that central effects of tilt if relatively small would not be observed. With respect to the tilt-dependent effects on the H-reflex recovery curve (late depression phase in the conditioned H_2 response), unfortunately little information is available as to the neural elements involved. As to the sensory structures accountable for the tilt dependent response the otolith end organs are primary candidates. However, even though no movement occurred during testing and joint position changes were minimal between tilt positions, it is possible that the differential activation of somatosensory receptors (neck, static length, joint, and cutaneous receptors) at the different positions may also contributed to the tilt dependent modulation of H_2 recovery.

In the second series of experiments a test for a convergent effect in lower limb muscles of static tilt and the reflex action of sural nerve stimulation was performed. The main finding in this investigation was that transmission in the early component of a cutaneomuscular reflex to coTA, iQ, and iH was modulated during static tilts in

pitch. It was also evident that the latency to peak amplitude of the various components of the multiphasic test reflex was unaffected by static tilt.

The present study has not demonstrated an interaction of the central effects of static tilt and the reflex actions of sural nerve stimulation to iSol, coSol, ITA, coQ, or coH. For these muscle, this nay be due to factors other than the absence of an infraction. First, only one direction of tilt in the pitch axis was examined i.e. from the normal head position to a nose up tilt position, and if the nose down direction was tested then possibly an affect may have emerged. Second, It is possible that a central interaction does occur but for the following reasons the present testing method, like any indirect method of examining spatial facilitation, is unable to detect it: 1) if the central effects of static tilt are small it is possible that no difference in firing level was achieved during summation with the postsynaptic effect evoked from the sural nerve stimulation; 2) the central effects of static tilt may explore only the subliminal fringe of the neuronal pool excited by the sural nerve volleys[145 204].

The organization of the spinal elements involved in reflex pathways from the cutaneous afferents has received much attention and it has been shown that inter-neurons of the "FRA" reflex pathways are shared with descending tracts[27 156]. Indeed, integration at the interneuronal level of supraspinal motor commands and afferent activity from the periphery appears to be the rule rather than the exception [for review see Baldissera et al.[16]. Although the FRA concept is far from being established in humans, cutaneomuscular reflexes evoked in human lower limb muscles do share some of the features of the FRA system described by Lundberg and colleges[156 157]. It is well documented that at rest stimulation of the sural nerve or the skin of the foot will produce widespread EMG discharges[132 232 109 63 270 271]. These reflex responses (onset latency of about 60-80 ms.) can last for several hundred milliseconds, and consist of several burst of activity separated by periods of EMG silence. With

EMG integration and averaging techniques, comparable cutaneomuscular reflexes (onset latency of 50-60 ms.) have been recorded in a variety of human muscles under tonic voluntary contractions[82 109 206 171 15]. These studies, as with the present results (Fig. 20a,b and Fig. 22a,b), reveal that the cutaneomuscular reflexes consist of a sequence of alternating excitation and inhibition in ipsilateral and contralateral flexor and extensor muscles. The complex pattern of these reflexes and presumably the organization of the neural elements involved are little affected by stimulus parameters[109 271 171], i.e. stimulus trains at low threshold or single shocks at pain threshold will elicit a similar reflex pattern varying only in magnitude. This has also been observed in the course of the present investigation (unpublished observations).

As discussed in SECTION 2.5, Willer et al.[271] have reported that a train of sural nerve volleys (tactile or low threshold stimulus intensity) conducting at 50 m/sec. or single sural nerve volleys (pain threshold stimulus intensity) conducting at 22 m/sec. could evoke a reflex discharge in the knee flexor of human subjects with an onset latency about 80 ms. It would be reasonable to assume, based on these findings, and the stimulus parameters used in the present study, that at least for the initial component (onset latency of 50-60 ms.), the test reflex here most probably is a spinal reflex. As for the late components of the test reflex, little information is available that would help determine the neural elements involved, although it should be noted that comparable long duration cutaneomuscular response have been reported in humans with spinal transections[132 109 232], and spinal cat[126 43].

There are reasons to believe that the tilt dependent effects on the cutaneomuscular reflex response observed in this investigation originate from activity in the otolith receptors. The following discussion will focus on the evidence which supports this view.

As indicated in the results (Table 6 and 9), from the 90 degrees or vertical

position to the 0 degrees or horizontal position an increase in the magnitude of the initial inhibitory phase for coTA and iQ, and a decrease in the magnitude of the initial excitatory phase for IH was observed. The organization of sway stabilizing postural reflexes in standing human subjects has been examined during translation perturbations which induce body accelerations in the anterior-posterior (A-P) direction[188 189 190 191 19]. These studies have shown that induced body sway about the ankle joints in the posterior direction results in activation of muscles on the anterior aspect of the leg, i.e. tibialis anterior and quadriceps. Conversely, during anterior body accelerations a reflex contraction occurs in the muscles on the posterior aspect of the leg (soleus-gastrocnemius and hamstring). In such experiments, when ankle motion cues are eliminated190, it has been postulated that the delayed reflex muscle contraction which commences about 200-300 msec after the beginning of induced body sway is primarily of vestibular origin. This view has gained experimental support from an examination of patients with vestibular deficits19 as discussed in SECTION 2.42. In these investigations it is most likely that the effective force acting on the vestibular end organs during the initial period of body sway was largely linear acceleration (see Fig 2 Nashner[190]). Although it has been reported that otolith units activated by tilt in one direction invariably respond to linear acceleration stimuli in the opposite direction3, it would be highly speculative to compare the present findings to the organization of muscle contractions obtained from human perturbation studies which involve linear accelerations, mainly because of the difference in weight bearing status.

In animal studies, a functional linkage between the otolith receptors and alpha motoneurons of the spinal cord has been identified using natural otolith stimulation in the form of roll tilt[17 225 176 283] and linear acceleration[262 11 133 134 263].

As discussed in detail in SECTION 2.41 and 2.42, for the most part, our knowledge of otolith-spinal synaptology has been derived from: 1) electrophysiological studies

which have employed DN stimulation; 2) anatomical studies which have lesioned or labelled fibers of the LVST. In this regard, on anatomical[208 195 184 242 203 77] and electrophysiological[125 282 198 219 115 226] grounds, it is generally believed that the central vestibular neurons (second order neurons) subserving otolith-spinal function are located primarily in DN. During DN stimulation, monosynaptic EPSPs in ankle and knee extensor motoneurons have been reported in the cat[155 94] and the monkey[233]. However, as pointed out by ten Bruggencate and Lundberg[27] (see also Grillner et al.[94]) this monosynaptic linkage is not seen in all motoneurons or in all cats; rather di(poly)synaptic linkages are more common.

Anatomical observations[195 203 194 236] have revealed that the vestibulospinal fibers originating from DN terminate extensively in lamina VII-VIII of the spinal cord and it has been reported that stimulation of DN evokes monosynaptic EPSPs (intracellular recordings) in lamina VII-VIII interneurons of the lumber spinal cord of the cat[14 92 238]. Using extracellular and intracellular recordings techniques, Harrison et al.[99] have examined the sources of peripheral afferent input to lamina VIII interneurons of the L_6 lumbar segment. Although group I PSP's were evoked, it was determined that cutaneous afferrents and high threshold muscle afferents constitute the main input to these interneurons. It was also observed that many of the lamina VIII interneurons were antidromically activated during stimulation of the contralateral motor nuclei. As discussed in SECTION 2.42, a number of investigators have examined the convergent effects of DN and FRA stimulation on flexor and extensor motoneurons in the hindlimb of the decerebrate cat. Ten Bruggencate and Lundberg[27] have shown that for both flexor and extensor motoneurons, vestibulospinal impulses facilitate transmission of PSP's from contralateral cutaneous afferents and high threshold muscle afferents. In this study however a systematic examination of the convergent effects from the vestibulospinal tract and iFRA was not performed. In fact, it has been reported by Lund-

berg[156] that disynaptic EPSPs evoked in an extensor motoneuron during DN stimulation are facilitated by conditioning volleys in ipsilateral or contralateral FRA. Furthermore, lamina VII-VIII interneurons (L_5-L_7) monosynaptically excited from DN have been found to receive convergence of excitatory effects from the iFRA[92]. Given the above findings, it can be concluded that activity arising from DN evokes excitatory actions on late order interneurons of FRA reflex pathways to lumber motoneurons. One may therefore expect that some lamina VII-VIII interneurons, with convergent input from the a variety of somatosensory afferents mediate otolith-spinal reflexes to lower limb muscles. This view has gain experimental support from the findings of Suzuki et al.[243] who have examined the response of lamina VII-VIII interneurons (L_3-L_6) during natural otolith stimulation. The results show that these interneurons are modulated during whole body tilts and it was concluded that otolith receptors are the most likely candidates contributing to the tilt dependent response.

Based on the above considerations it would be reasonable to suggest that, in the present study, activity arising from the otolith end organs is responsible for the modulation of the cutaneomuscular reflex response during static tilt.

As in the previous study, no control experiments have been performed that would exclude the possibility that receptors other than the otolith end organs participate in the modulation of the cutaneomuscular reflex during static tilts. However, unlike Experiment 1, in the second series of experiments a step toward an identification of the neural elements involved in the central effects of static tilt and perhaps natural otolith stimulation has been made. The next stage in the development of a human model of otolith spinal function will be to examine the cutaneomuscular reflex response in patients with surgically removed labyrinths during static tilts. These control experiments, with the otolith input eliminated, will allow an analysis of the tonic effects of the somatosensory receptors on the cutaneomuscular test reflex at the various tilt

positions in pitch. For this purpose, patients with non-functioning labyrinths, bilaterally, would be preferred. However, such patients are rare. and given the clinical tests of vestibular function that are available today, a positive diagnosis of non-fuctioning labyrinths, bilateral, would be difficult to confirm. A similar examination of patients with unilateral labyrinthectomies may also provide a suitable control, when a comparison of the effect of tilt angle on the cutaneomuscular reflex response elicited with left and right sural nerve stimulation is made. But, as discussed in SECTION 2.4, is must be kept in mind that activity arising from DN and descending in the LVST will terminate[236] and influence contralateral spinal neurons in a manner similar to the ipsilateral effects, albeit to a lesser extent[14 106]. This information must be taken into consideration in a control study involving compensated unilateral labyrinthectomized subjects,

CHAPTER 7

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