44894

NAME OF AUTHOR/*NOM DE L'AUTEUR* EKE-OKORO, Sunday Theophilus

TITLE OF THESIS/*TITRE DE LA THÈSE* THE EFFECTS OF FORCE, FATIGUE, ALCOHOL, ASPIRIN AND CAFFEINE ON THE HOFFMANN REFLEX

UNIVERSITY/*UNIVERSITÉ* SIMON FRASER UNIVERSITY, BURNABY B.C.

DEGREE FOR WHICH THESIS WAS PRESENTED/ *GRADE POUR LEQUEL CETTE THÈSE FUT PRÉSENTÉE* M.Sc. (Kinesiology)

YEAR THIS DEGREE CONFERRED/*ANNÉE D'OBTENTION DE CE GRADE* 1979

NAME OF SUPERVISOR/*NOM DU DIRECTEUR DE THÈSE* Prof. T. W. CALVERT

DATED/*DATÉ* 13 - 7 - 79 SIGNED/*SIGNÉ*

PERMANENT ADDRESS/*RÉSIDENCE FIXE* [redacted]

THE EFFECTS OF FORCE, FATIGUE, ALCOHOL, ASPIRIN AND CAFFEINE ON THE HOFFMANN REFLEX

by

Sunday Theophilus Eke-Okoro
B.Sc. (Physiotherapy), University of Ibadan, Nigeria, 1975

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF
MASTER OF SCIENCE (KINESIOLOGY)
in the Department
of
Kinesiology

SIMON FRASER UNIVERSITY
June 1979

PARTIAL COPYRIGHT LICENSE

Title of Thesis/D~~issertation~~:

the effects of force, fatigue, alcohol, aspirin and caffeine on the Hoffmann reflex

Author:

(signature)

EKE-OKORO S.T

(name)

13 - 7 - 79

(date)

APPROVAL

Name: Sunday Theophilus Eke-Okoro

Degree: Master of Science (Kinesiology)

Title of thesis: The effects of force, fatigue, alcohol, aspirin and caffeine on the Hoffmann reflex

Examining Committee:

Chairman: M.V. Savage

T.W. Calvert
Senior Supervisor

C.M. Davis
Psychology Department

P.N. Bawa
Kinesiology Department

G.L. Diewert
External Examiner
Department of Kinesiology
Simon Fraser University

Date Approved: 20 August 1979

ABSTRACT

The Hoffmann reflex represents a relatively unexplored phenomenon in neurology and neurophysiology. Its production by electrical stimulus and its prominent responses make it not only easily elicitable but also readily quantifiable. The reflex was first produced in the calf by Hoffmann in 1918, and its presence in the quadriceps femoris and human masseter has been confirmed more recently. The purpose of this study is to use the H-reflex to observe the effects on the nervous system of agents which have a widespread effect (alcohol, aspirin, and caffeine) and agents which have a local effect (force and fatigue), to determine how sensitive the reflex is for use as a model of the nervous system and to examine the possibility of quantification in reflex testing.

Five paid undergraduate students of different disciplines were used as subjects. The subject lay prone on a table with pillow supports for the head and ankle. A ground electrode was strapped on the calf and surface electrodes were placed just below the calf. The stimulating electrode was a small cathode placed in the popliteal fossa while the indifferent electrode was large and placed just below the patella. Control recordings were made just before the test conditions were applied, care

being taken to ensure that subjects did not alter their position.

From the experiments it was observed that force, alcohol, aspirin, caffeine and fatigue had significant effects on the Hoffmann reflex.

It is suggested that the facilitatory effects of alcohol and caffeine can be a measure of the excitability of the nervous system. It is implied that quantities of alcohol and caffeine greater than those used in this study may not have facilitatory effects and may have other non-beneficial effects on the body. The effect of coffee which was due to its caffeine content (100-150 mg) was marked potentiation of the reflex and the direct muscle (M) response. This suggests an increased arousal of the nervous system.

The depressant effect of aspirin on the reflex indicated a depression of the nervous system. It is known that aspirin kills pain by depressing pain receptors and suppressing the release of bradykinin-like polypeptides which produce pain.

Facilitation of the Hoffmann reflex during fatigue was projected to be due to increased feedback to the higher centers which facilitate the spinal centers to compensate for loss of force. Other observations in the fatigue study were the gradual rise in integrated EMG (IEMG) and a marked depression of the M-response. Fatigue produced by the method used in this study was blamed more on ischemia than on neuromuscular junction malfunction.

The reflex is projected as a diagnostic tool for a number of pathological conditions and as a sensitive measure of the effects of drugs on the nervous system.

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to Dr. T. W. Calvert, my Senior Supervisor, for his advice and support during this study. My thanks also go to the other members of the Thesis Committee for their guidance and ability to meet even when it was impromptu, and to the Audio Visual Department for making it possible for me to produce acceptable figures. I would also like to thank my senior borther, Mr. Herbert Eke-Okoro, for being a true guardian.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

I. INTRODUCTION

A reflex is an automatic response to a specific stimulus and may be mediated by monosynaptic, disynaptic or polysynaptic pathways. Reflexes may be deep or superficial. Deep reflexes are elicited by stretching muscles, (e.g. the muscle stretch reflex) and superficial reflexes are produced by stimulating the body surface, (e.g. the flexor reflex caused by noxious stimuli). Pathological reflexes accompany disease conditions; examples include the Babinski response and the grasp reflex. Many reflexes are easy to test and are used to monitor the physiological state of the neuromuscular system. Although the characteristics of a reflex are not complete confirmation of a pathological condition they may suggest it, while giving way to more elaborate methods of examination.

Stretch reflexes are important in the control of movement and posture. For these deep reflexes the receptors are muscle spindles and the gains are controlled by the higher centers of the central nervous system (Matthews, 1968). Thus in upper motor neurone lesions (pyramidal tract lesions) such as hemiplegia, the stretch reflexes are freed from inhibition by higher centers. These deep reflexes are therefore increased, and this increase is often characterized by clonus. Usually the testing of reflexes involves comparison with the opposite body segments to determine deviation from the normal, but these comparisons are hardly quantitative and cannot be fully relied upon when estimating the severity of a pathological condition. Thus the need to quantify spinal reflex tests cannot be overemphasized. It is for the purpose of quantification in diagnostic reflexology and for the evaluation of treatment that the Hoffmann reflex has become an important topic of recent research. Unquestionably the reflex has desirable characteristics for clinical use, and this research is therefore directed towards determining how these characteristics can be beneficially utilized.

The Hoffmann reflex is a monosynaptic reflex and it is the electrical equivalent of the tendon jerk. It was first described by Hoffmann, (1918) and was named the Hoffmann reflex by Magladery and McDougal, (1950). Its short form description is the H-reflex.

The sciatic nerve (Fig. 1) from which the tibial nerve branches is the major nerve of the lumbosacral plexus (Fig. 2) with widespread roots of origin in the spinal cord (L4,5, S1,2,3). It is the largest nerve in the human body and the central motorneurone pool of innervated muscles is extensive. In view of this large motoneurone pool, nearly anything that affects the lumbar and sacral regions will affect some roots of the nerve. The primary mediator of the gastrocsoleus H-reflex is the tibial nerve which is the largest branch of the sciatic nerve, having contribution from all its roots. The H-reflex is obtainable in the soleus because the Ia afferents are larger than the alpha motoneurone axons in the tibial nerve. The several roots of the tibial nerve and its extensive central neurone pool make the H-reflex a diagnostic tool for monitoring the neural state of the lumbosacral region and to some extent the state of the higher centers.

The method used to produce the H-reflex is shown in (Fig. 3). Electrical percutaneous stimulation of the tibial nerve takes place in the popliteal fossa. The stimulus (S) depolarizes the alpha motoneurone axons resulting in the development of electrical action in the extrafusal fibers. The M-wave indicating direct stimulation of the muscle therefore appears.

The stimulus also causes a synchronous stimulation of the large primary Ia afferents generating an impulse to the spinal cord and to higher centers. When this impulse completes the monosynaptic reflex arc, the H- reflex is produced and is represented by the H-wave recorded from the muscle.

The application of the electrical stimulus also produces an antidromic volley along the large alpha motoneurone axons in the spinal cord. When the stimulus is submaximal for the alpha motoneurone axons, the antidromic volley will not be strong enough to block the reflex by collision or by activating several Renshaw cells. When the stimulus is maximal, the antidromic volley (Fig. 3) will eliminate the reflex by these dual actions.

Characteristics of the Reflex

The H-reflex is a monosynaptic reflex which is elicited with moderate electrical stimulation but eliminated by maximal stimulation. The reflex is due solely to low threshold Ia afferents, mostly from the tibial branch of the sciatic nerve. It can be blocked by antidromic volleys and depressed by presynaptic inhibition. The latency range is approximately 25 to 30 milliseconds and amplitude range is approximately 0.44 to 1.1 millivolts. The Hmax/Mmax ratio is in the range 0.22 to 0.69 (where Hmax and Mmax are maximum possible reflex and muscle responses obtainable during experiment).

Clinical Importance

Owing to the projected importance of the H-reflex in the field of neurology, it has become one of the most studied human reflexes. Most workers are in agreement that the reflex from the soleus and quadriceps femoris can be of use in the following areas: measurement and assessment of spasticity in a variety of medical conditions, determination of the effectiveness of drugs, e.g. Levo-Dopa (L-Dopa), Nembutal and Diazepam, evaluation of the presence of S1 radiculopathy, studying early events in spinal shock, determination of maturation in the nervous system of infants, and the assessment of proximal nerve conduction in lumbar and sacral disease conditions. Thus there is a general need to better understand the mechanism of spinal cord reflexes and in order to do this, it was decided to investigate the effects of a variety of common agents which are known to affect both the peripheral system and the nervous system as a whole. The present research will investigate the effects of force, fatigue,alcohol, aspirin, and caffeine on the H-reflex. The potential benefits of this work include a determination of how useful the reflex is for use as a model of the nervous system and examination of the possibility of quantification in the testing of the reflex. The work should also provide an indication of which nerves in the body have Ia fibers bigger than the alpha motoneurone fibers. In the normal adults only the tibial nerve, femoral nerve and nerve to the masseter muscle have some Ia fibers bigger than all alpha motoneurones. In infants many other nerves could have larger Ia fibers, but as development takes place, the alpha motoneurones grow bigger than Ia fibers and the reflex disappears. Also in pathological conditions, if the H-reflex can be elicited in conditions where it is not usually present, there is an indication that alpha motoneurones have been affected.

In Chapter 2, the history of the H-reflex is reviewed and the literature on its clinical and research applications is discussed. The literature on the effects of force, fatigue, alcohol, aspirin, and caffeine on the nervous system are reviewed. Chapter 3 deals with experimental objectives, hypotheses, equipment and methods including experimental procedure. In Chapter 4, the methods of data analysis are discussed and the results obtained from the different experiments are reported, while Chapter 5 contains discussion and conclusions.

Figure 1 The Course of the Sciatic Nerve

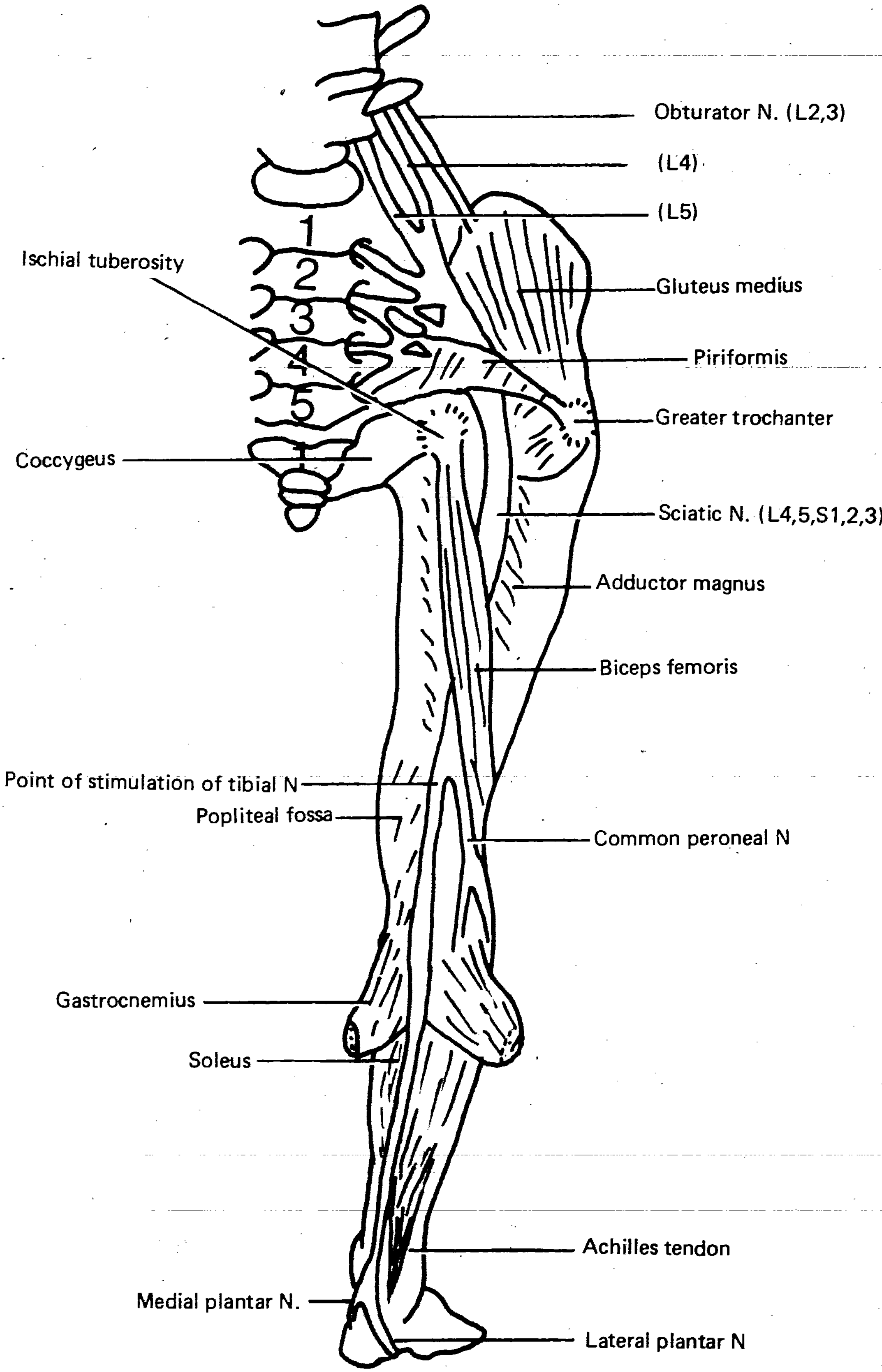

Obturator N. (L2,3)
(L4)
(L5)
Ischial tuberosity
1
2
3
4
5
Gluteus medius
Piriformis
Greater trochanter
Coccygeus
Sciatic N. (L4,5,S1,2,3)
Adductor magnus
Biceps femoris
Point of stimulation of tibial N
Popliteal fossa
Common peroneal N
Gastrocnemius
Soleus
Achilles tendon
Medial plantar N.
Lateral plantar N

Figure 2 The Lumbosacral Plexus

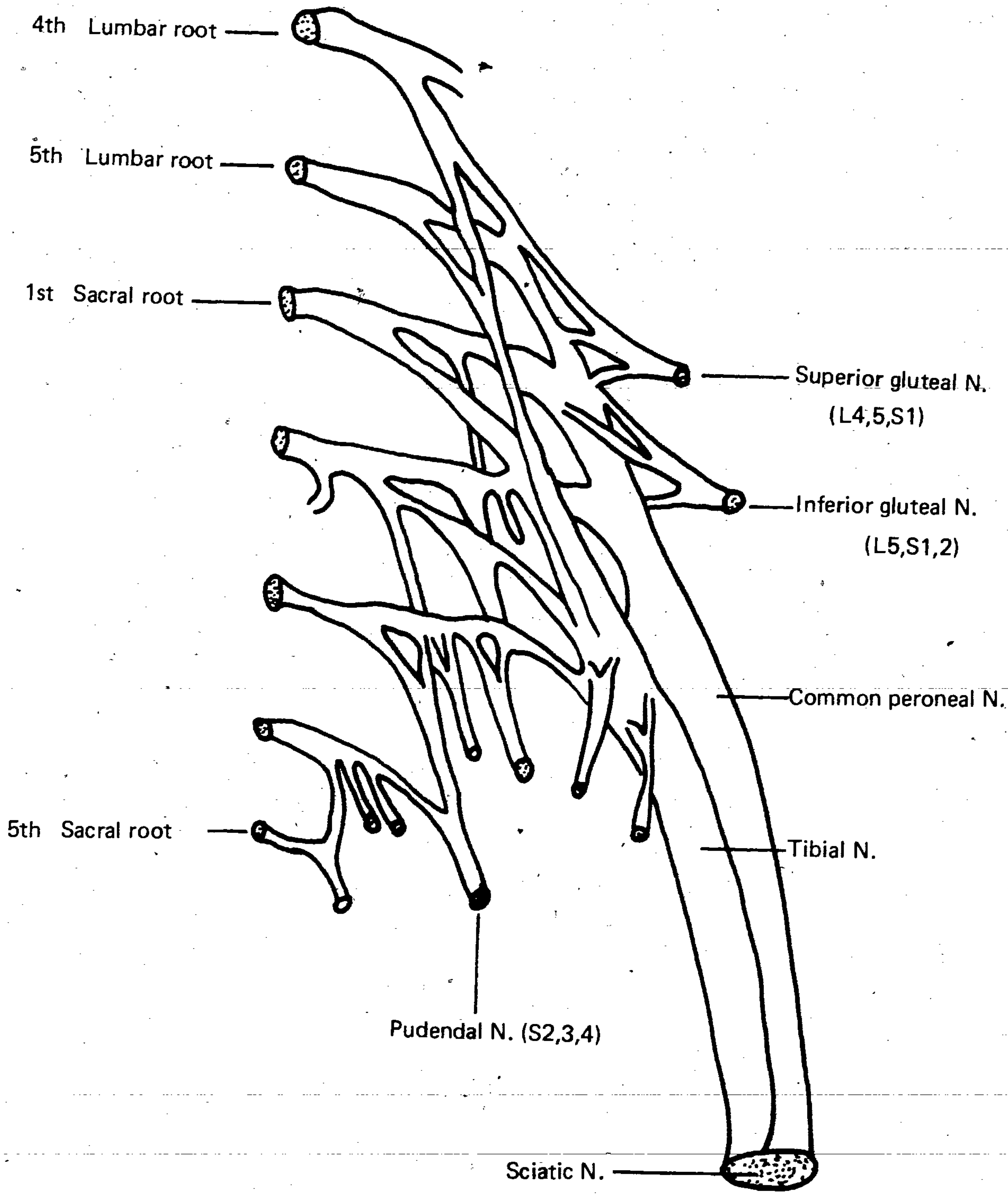
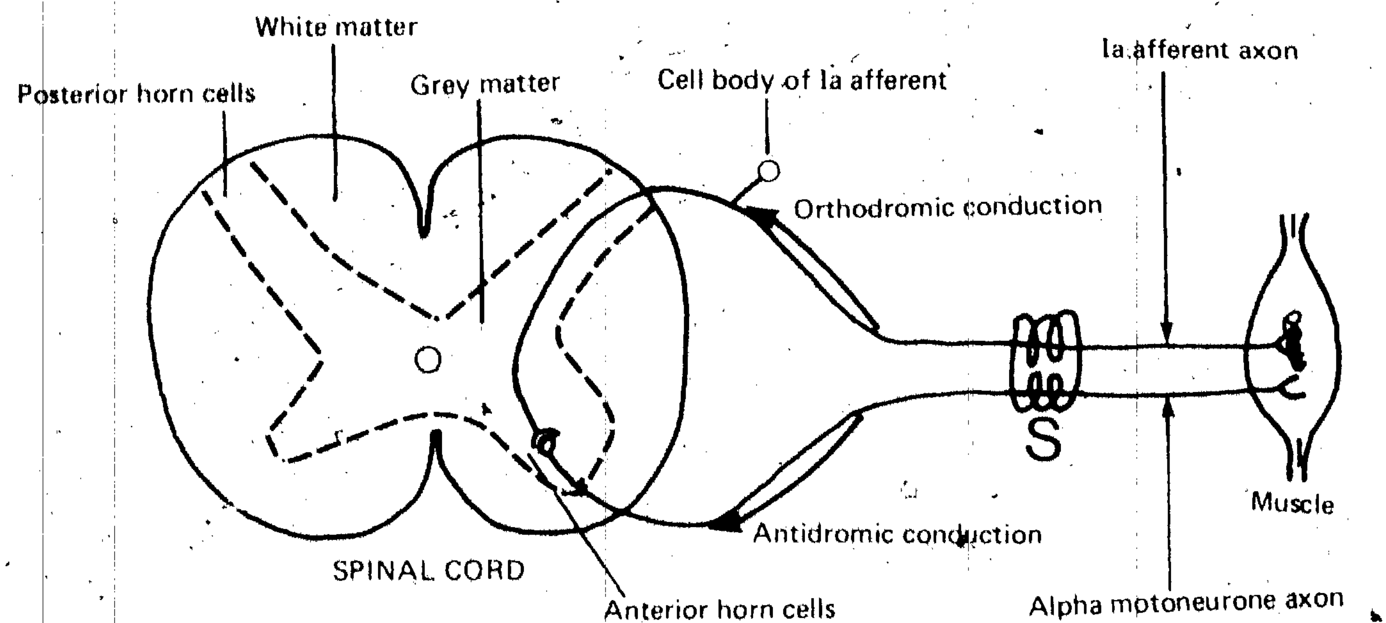
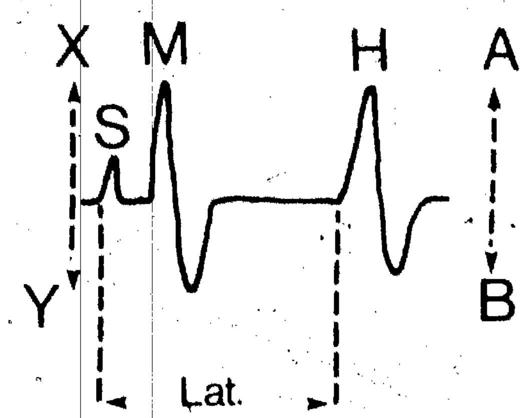

4th Lumbar root
5th Lumbar root
1st Sacral root
5th Sacral root
Superior gluteal N.
(L4,5,S1)
Inferior gluteal N.
(L5,S1,2)
Common peroneal N.
Tibial N.
Pudendal N. (S2,3,4)
Sciatic N.

Figure 3 Method Used in the Production of the Hoffmann Reflex





S	Stimulus
M	Muscle response (M-wave)
XY	M-amplitude
AB	H-amplitude
H	Reflex (H - Wave)

II. REVIEW OF THE LITERATURE

The description of the Hoffmann reflex by Hoffmann in 1918 marked a new era in reflexology. A detailed study of the reflex was made by Magladery and McDougal (1950). They repeated Hoffmann's experiment by stimulating the tibial nerve in the popliteal fossa and obtaining the reflex from calf muscles. They gave it the name 'Hoffmann reflex,' and used the term H-reflex as a short form description (Fig. 3).

H-Reflex in Other Muscels

Although the reflex was originally obtained from the calf muscles (gastrocsoleus), other workers have searched for the reflex in other muscles of the body. It has been obtained from the quadriceps femoris by stimulating the femoral nerve in the femoral triangle just below the inguinal ligament (Mongia, 1972; Guiheneuc and Ginet, 1974). The reflex has been obtained from human masseter by Godaux and Desmedt (1975) who stimulated the masseter branch of the mandibular nerve, and from hand muscles by percutaneous stimulation of the ulnar nerve of newborns and infants (Thomas and Lambert, 1960). After the age of one, the reflex is unobtainable from the child's ulnar nerve as it is suppressed with age (Thomas and Lambert, 1960). It has also been obtained from hands of spastic patients (Teasdall, et al.

1952).

Physiological Mechanisms Influencing the H-Reflex

Having identified the reflex in man it became necessary to identify the factors which contribute to the reflex and how it can be beneficial to clinical neurology. The relationship between motoneurone pools in the spinal cord and the H-reflex has been studied. Jefferson and Benson (1953) determined that between 12.5 to 26.5 percent of the motoneurone pool in the spinal cord fire in the production of the H-reflex. Angel and Hoffmann (1963) showed that the fraction of motoneurone pool involved is represented by the H/M fraction (where H and M are H- and M-wave amplitudes). Taborikova (1966) initially reported that in man 100 percent of the motoneurone pool is involved. When Taborikova and Sax (1968) repeated the earlier investigations they concluded that as small as 24 percent, usually 50 percent and sometimes virtually 100 percent of motoneurone pool could be involved in the elicitation of the reflex. The fraction of motoneurone pool firing depends on the background facilitation during the experiment and can therefore always fall within the ranges postulated by both groups of workers. The inference is that the strength of the reflex depends on the general arousal of the nervous system.

The control of the H-reflex from the higher centers has been the subject of controversy. Accumulating evidence is in favour of at least some supraspinal control. Jendrassik's manoeuvre (after Ernest Jendrassik, a Physician in Hungary, 1858-1921) is a technique by which a subject hooks the fingers of two hands together and forcibly pulls one against the other. The manoeuvre was originally used for testing of the knee jerk reflex but now it is being used in testing other reflexes also. The effect of this manoeuvre on the H-reflex is that of facilitation (Mark, 1963; Ferrari, et al. 1966; and Bussel, et al. 1978). The mechanism by which Jendrassik's manoeuvre facilitates the H-reflex is not completely clear. Burg, et al. (1974) reported that potentiation of the reflex is due to fusimotor drive. Spindle activation is often accompanied by some contraction of the extrafusal fibers meaning indirect alpha motoneurone activation. Bussel, et al. (1978) emphasized that facilitation of the Hoffmann reflex is not solely due to gamma motoneurone activation but that direct alpha motoneurone activation could be an important contributing factor.

Though potentiation of the H-reflex by Jendrassik's manoeuvre has to a large extent been attributed to fusimotor activation, Procaine block of fusimotor fibers is unable to end potentiation (Taborikova, 1973). It is therefore postulated that the supraspinal influences apart from acting on gamma motoneurones also act on alpha motoneurones increasing their excitability (Taborikova, 1973). In acute spinal shock, areflexia is due to the cessation of supraspinal influences. It has been suggested that stimulation of the anterior cerebellum reduces the excitability of motoneurones and could depress or even eliminate the H-reflex through presynaptic inhibition (Morris and Penn, 1978).

Taborikova (1973) has surmised that the following tracts are the routes for supraspinal influences on the Hoffmann reflex: Corticospinal tract (CST) to the motoneurones and spinal interneurones; the reticulospinal tract (ReST) to the spinal motor center and to the motoneurones. The vestibulospinal tract (VST) appears to influence the motoneurones either via the interneurones or directly.

The influence of the vestibular system on proprioceptive reflexes of human lower limbs has been investigated (Delwaide and Delbecq, 1973). They reported potentiation of tendon reflexes but not the H-reflex. Probably this would indicate a pathological condition.

Visual Influences

Evidence of visual influence on the reflex is available in the literature. Using blindfolded and eyes-open subjects, Shashami(1977) studied visual influence on the Hoffmann reflex. In this study, reflex amplitude was depressed with blindfolded and enhanced with eyes-open subjects. Potentiation in eyes-open subjects could be due to increased stimulation of the eyes compared to the decreased stimulation of blindfolded subjects. This implies that the firing rate of the central nervous system in eyes-open subjects is greater than for blindfolded subjects.

Head Positions

The effect of tonic neck reflexes on the H-reflex was studied by Isaacs, et al. (1968). They reported inconsistent reflex changes associated with positions of the head and its movements. Hayes and Sullivan (1976) reported greater H-reflex amplitude when the right leg was tested with subject looking to the right than in any other head position.

Respiratory Effects

Forced inspiration causes facilitation of the Hoffmann reflex but normal respiration produces no visible effects (Bishops, et al. 1970). Facilitation of the reflex in forced inspiration is likely due to the strong muscular contraction as seen in Jendrassik's manoeuvre. Although the gamma motoneurones are the primary recipients of facilitation (Bishops, et al. 1970) the alpha motoneurones also contribute to reflex facilitation.

Sleep

Hodes and Dement (1964) investigated the reflex in man during low voltage electroencephalograph (EEG) sleep and noticed that the reflex was depressed in rapid eye movement (REM) sleep and enhanced in relaxed wakefulness. A similar result was earlier reported in infants (Hodes and Gribetz, 1963). The pathways involved in the depression of the reflex in (REM) sleep have been studied (Shimizu, et al. 1966).

Clinical Applications

Parkinson's Disease

Changes in the H-reflex in Parkinsonian syndrome patients have been studied. While doing electromyographic studies of monosynaptic reflexes in these patients Ioku, et al. (1965) noticed abnormal facilitation of the reflexes. Increase in alpha motoneurone excitability in Parkinsonism was reported by McLeod, (1972).

Parkinson's disease is generally treated with L-Dopa, and the effect of this drug on the H-reflex has been investigated in patients (McLeod and Vander Muelen, 1972; Herbinson, 1973). The fact that L-Dopa depresses the amplitude of the H-reflex was obtained by both groups of workers. In his own study of the effect of L-Dopa on the reflex, Sax, et al. (1976) suggested that the rate of recovery of depressed reflex curve could be used to determine the effect of medication on reflex activity.

Detection and Assessment of Central Nervous System (CNS) Lesions

Measurement of the Hoffmann reflex appears to be a sensitive method of detecting and assessing upper motoneurone lesions (Upton, et al. 1972). Increased motoneurone excitability and hyperreflexia in patients with upper motoneurone lesions have been reported by Magladery, et al (1952). Diamantopoulos and Zaner (1967) observed an initial decrease in spinal motoneurone excitability followed by increased motoneurone excitability. Garcia-Mullin, and Mayer (1972) studied all grades of vascular hemiplegia and observed a decrease in motoneurone excitability within the first two days compared to the unaffected limb. In some hemiplegics whose cases had become purely chronic, an increase in motoneurone excitability was obtained. The reflex was also obtained from the arm muscles of the chronic hemiplegics.

With the production of the H-wave, a temporary depression of the anterior horn cell excitability occurs, causing an interval of 100 to 200 milliseconds to elapse before another H-wave can be produced (Magladery, et al. 1952). Campbell, and Green (1964) have shown that the interval between two successive H-waves decreases in cases of upper motoneurone lesions. The reduction in interval they claimed is due to facilitatory impulses arriving at the anterior horn cells.

In clinical absences (seizures), it has been shown that initial facilitation is almost always followed by inhibition of the H-reflex (Rabending, 1967). The marked succeeding inhibition may be an attempt by the body to end the seizure by reducing the excessive sudden discharge of the grey matter.

Graphospasm is a disease characterized by difficulty in writing. Kaneko, et al. (1966) studied the H-reflex in patients with this condition. They obtained calf H-reflexes from the subjects while writing that did not differ markedly from resting normal subjects; in the patient group the H-wave amplitude obtained while writing was twice the value in resting state. In normal subjects there are little or no alteration in H-wave amplitudes during sonic, photic stimulation, mental arithmetic and hyperventilation (Sobue, cited in Kaneko, et al. 1966).

The relationship between ankle jerk and Hoffmann reflexes in muscle dystrophy has been studied by Singh, et al. (1971). They studied the following types: Duchenne, Limbgirdle and Facioscapulohumeral. In the Duchenne type they reported H-reflex being absent in 7 of 11 cases with bilateral ankle jerks. This would mean that only 4 had H-reflexes. In three cases with unilateral ankle jerk, the H-reflex was absent on both sides. It was absent in two cases where ankle jerks were absent.

In the Limbgirdle type, H-reflex of small amplitudes was present in 2 of the 5 cases studied where ankle jerks were present. In the remaining 3 cases there were no H-reflexes. In the Facioscapulohumeral type, of the two cases studied the H-reflex was absent in one in which ankle jerk was absent. In the other case the ankle jerk was normal and an H-reflex of small size was produced (it is possible that the Ia afferent had been affected by the disease). They concluded their tests with the observation that the H-reflex is a more sensitive index than the ankle jerk.

Determination of Motoneurone Excitability

Studies have been done on how the H-reflex could be used to determine the excitability of motoneurones (Yap, 1967; Tobin, 1969). Gottlieb and Agarwal (1972) studying the role of the myotatic reflex in voluntary control of movement (voluntary isometric plantarflexions and dorsiflexions of the foot at the ankle), suggested that the peak-to-peak amplitude of the H-wave is proportional to the sensitivity of the spinal reflex arc. They also observed enhancement of reflexes during spasticity.

Widely Accepted Diagnostic Areas

The eventual prominence of the H-reflex as a diagnostic tool is the result of its ingenious study by several workers

(Angel and Hoffmann, 1963; Weaver, et al. 1963; Diamantopoulos and Gassel, 1965; Guiheneuc and Ginet, 1973, 1974; Braddom and Johnson, 1974; Notermans and Vingerhoets, 1974; and Schuchmann, 1976, 1978). The use of the H-reflex as a diagnostic tool in root compression of L5 and S1 has been suggested by Notermans and Vingerhoets (1974); and Schuchmann (1976, 1978). They have shown that latency will increase in root compression. The use of the reflex as a diagnostic tool in S1 root compression was emphasized by Braddom and Johnson (1974) who enumerated several workers' suggestions for clinical applications as follows: anterior tibial muscle H-reflexes are diagnostic (except for infants) of central nervous system lesions from the brainstem rostralwards, in proximal neuropathy and S1 radiculopathy the H-reflex may be absent or show a delayed latency when present, the presence of the H-reflex in the arm of infants after the age of one is diagnostic of central nervous system immaturity or dysfunction.

Agents Under Study

Apart from localized fatigue and force, none of the agents to be studied has been studied via the H-reflex. The effects of localized fatigue on the H-reflex have been reported by Hayes (1975), and Dietz (1978). Both workers reported potentiation of the reflex in fatigue. Other related experiments on fatigue include, Romanul (1965); Stephens and Taylor (1972); and

Stephens, et al. (1973) who showed a depression of the EMG amplitude in fatigue.

Gottlieb and Agarwal (1972) demonstrated potentiation of the H-reflex with plantarflexion and depression with dorsiflexion. During plantarflexion, as the force in the calf muscles increased, the H-reflex increased reflecting increased facilitation of the triceps motoneurone pool. During dorsiflexion, when the tibialis muscle is contracting, triceps alpha motoneurones receive reciprocal inhibition and hence the H-reflex is depressed.

III. MATERIALS AND METHODS

Experimental Objectives and Hypotheses

One purpose of this study is to explore the effects of some agents which have a widespread influence on the nervous system (alcohol, aspirin, caffeine) on the H-reflex. A second purpose was to study the effects of localized phenomena (force and fatigue). The intent was to verify how sensitive the reflex is for use as a model of the nervous system, to examine the possibility of quantification in reflex testing and to see how it could be beneficial in understanding spinal motor control.

It was hypothesized that alcohol of the quantity to be used in this study would potentiate the H-reflex. Low, et al. (1962) have shown that low concentrations of alcohol facilitate human neuromuscular junctions. Aspirin may depress the H-reflex since it is able to suppress pain and headache which are of nervous origin. Caffeine would be expected to potentiate the H-reflex since it is a central nervous system stimulant (Topliss, 1970). Force is known to either potentiate or depress the H-reflex (Gottlieb and Agarwal, 1972). In this study sustained force would be applied and as such a depression of the H-reflex would be expected. Fatigue may potentiate the reflex, as such an effect was reported by Hayes in 1975.

Methods and Equipment

Five normal male undergraduate students between the ages of 19 and 28 were chosen as subjects. They were selected on the basis that their H-reflex was easily elicitable from their calf muscles and that they had accepted the conditions of the experiments by signing the subject consent forms (see Appendix A). They were all paid for their services.

Subjects lay prone on a table with pillow support for the head and ankles. They were completely relaxed and were not allowed to move from the correct position. The neck remained straight such that the head was not turned to any side during the period of the experiment. The pillow support for the ankle served a dual purpose. Firstly, it contributed with another arrangement below it to maintain the ankle and knee at the required angles. Secondly, it improved the subject's relaxation by releasing tension in the hamstrings. The angle between the posterior surfaces of the thigh and the leg was approximately 120 degrees, while the ankle was at the mid-range of plantar-flexion (Fig. 4).

The ground electrode (16x2 cm) was placed on the middle of the calf such that it fitted the circumference of the leg, and was connected to the EMG preamplifier. The recording surface electrodes were placed 3 cm. apart at the lower border of the calf along the midline. These electrodes were then connected to the EMG preamplifier. The stimulating electrodes consisted of a large anode (6x4 cm.) placed just below the patella and a small cathode of diameter 3.2 cm. The cathode was placed on the popliteal surface, care being taken that the tibial nerve was directly below it.

The stimulating current was drawn from an Ortec 4710 Dual Channel Stimulator. The current passed through an SIU 4678 Grass isolation unit to which the electrodes were connected. Rectangular wave pulses of 0.7 to 1.0 milliseconds duration were used in all experiments. Stimulus was also fed to the TECA EMG Unit to produce a stimulus channel on the output display for comparison with the EMG channels.

Connections from the stimulator and TECA EMG Unit to the oscilloscope in front of the subject made it possible for the output to be displayed. This arrangement made it possible for the subject to attempt to alter the reflex and also for the experimenter to determine when the reflex response had been obtained. For the purpose of this research, both the H- and M-waves were required.

In addition to the tests in a relaxed state, the reflex was also studied with muscular effort. In this case the subject's test foot was comfortably strapped onto a force tranducer that was connected to an amplifier which formed a channel of the TECA EMG Unit. The amount of force exerted by the foot of the subject was displayed on the oscilloscope and voluntary force regulation was possible as the subject could see the display in front of him. The reflex was recorded with different force values to help determine how different force levels affected the reflex response. Force values were measured with the force transducer which was calibrated with a known force value before each experiment (Fig. 5).

Experimental Procedure

The following experimental measurements were made:

1. a. H- and M-waves in the normal relaxed subjects (stimulus

only).

b. H- and M-wave changes with force in the normal relaxed subjects.

2. H- and M-wave changes with alcohol in the relaxed subjects.

3. H- and M-wave changes with aspirin in the relaxed subjects.

4. H- and M-wave changes with caffeine in relaxed subjects.

5. H- and M-wave in localized fatigue of the calf muscles.

The experiments were done in the same order for all subjects. There was an interval of at least one day between one test and another. Subjects were advised before the day of each test not to take any of the agents as food before reporting for experiment. When subjects reported for the experiment they were again asked by the experimenter what they had taken for a meal just before reporting for the tests.

Force

This involved application of sustained and regulated force, the force transducer having been previously calibrated with a known force. The subject exerted a regulated force on the force transducer and recordings of the reflex were made as soon as the required force value was seen on the oscilloscope.

Alcohol

A 6 oz. glass of Labatt's Blue beer (5% alcohol) was given to each subject and after waiting for one hour for the alcohol to enter the circulation, the reflex was monitored (blood alcohol concentration reaches peak value one hour after intake (Wallgreen and Barry, 1970). For the average subject this would give a blood alcohol concentration of 0.012 percent (6 oz. of whiskey for average sized man is about 0.12%, Cohen, 1966).

Aspirin

A dose of two aspirin tablets (10 gr.) was given in each case. Aspirin content of the blood reaches its peak between 1.5 to 2 hours after it has been taken (Wilson, et al. 1975). Thus H-responses were recorded 1.5 hours after aspirin had been taken.

Caffeine

Subjects were given a teacup full of Nescafe brand instant coffee (1.3 g). It was a normal light coffee (caffeine content about 100-150 mg.). Recordings were made after one hour when much of the coffee was expected to have been digested and passed into the general circulation.

Localized Fatigue

The subject stood on his toes on one leg with the weight on the front of the foot (Fig. 6); the hands were used to maintain balance. The position of the foot remained unchanged throughout the period of the experiment. The reflex was monitored every minute until the subject could not continue; each time a recording was made the position of the heel above the wooden platform was checked. This was done by placing a small carton below the heel such that the heel just felt it during the recording period.

For all the agents tested, the stimulation voltages depended on the ability of the subject to endure it. The stimulus pulse amplitude ranged between 24 and 104 volts.

The EMG amplifier sensitivity was between 100 and 500 microvolts per division with a sweep duration of 100 milliseconds per division. The paper speed was usually 50 centimeters per second and the low and high cut off frequencies of the EMG amplifiers were set at 50 hz to 5 Khz respectively. The frequency of stimulation was one stimulus per five seconds.

Figure 4 Experimental Design for Relaxed Measurements

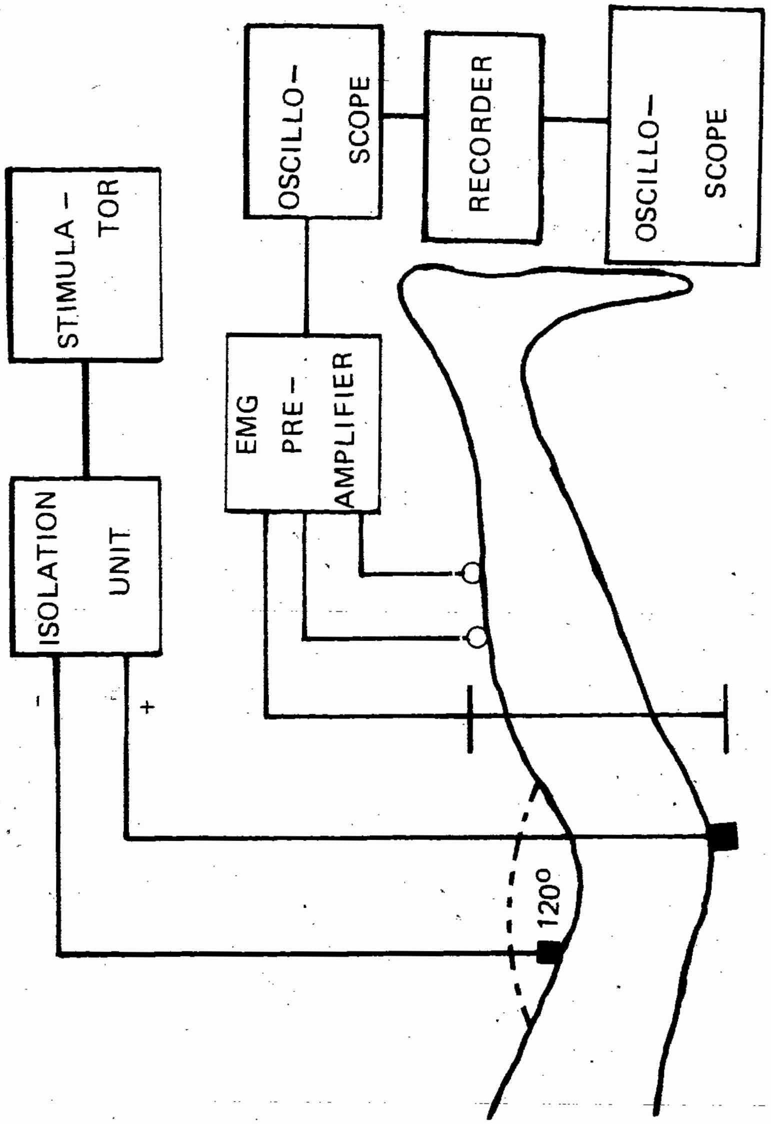

STIMULA - TOR
ISOLATION UNIT
-
+
OSCILLO- SCOPE
RECORDER
OSCILLO- SCOPE
EMG PRE - AMPLIFIER
120°

Figure 5 Experimental Design for the Force Test

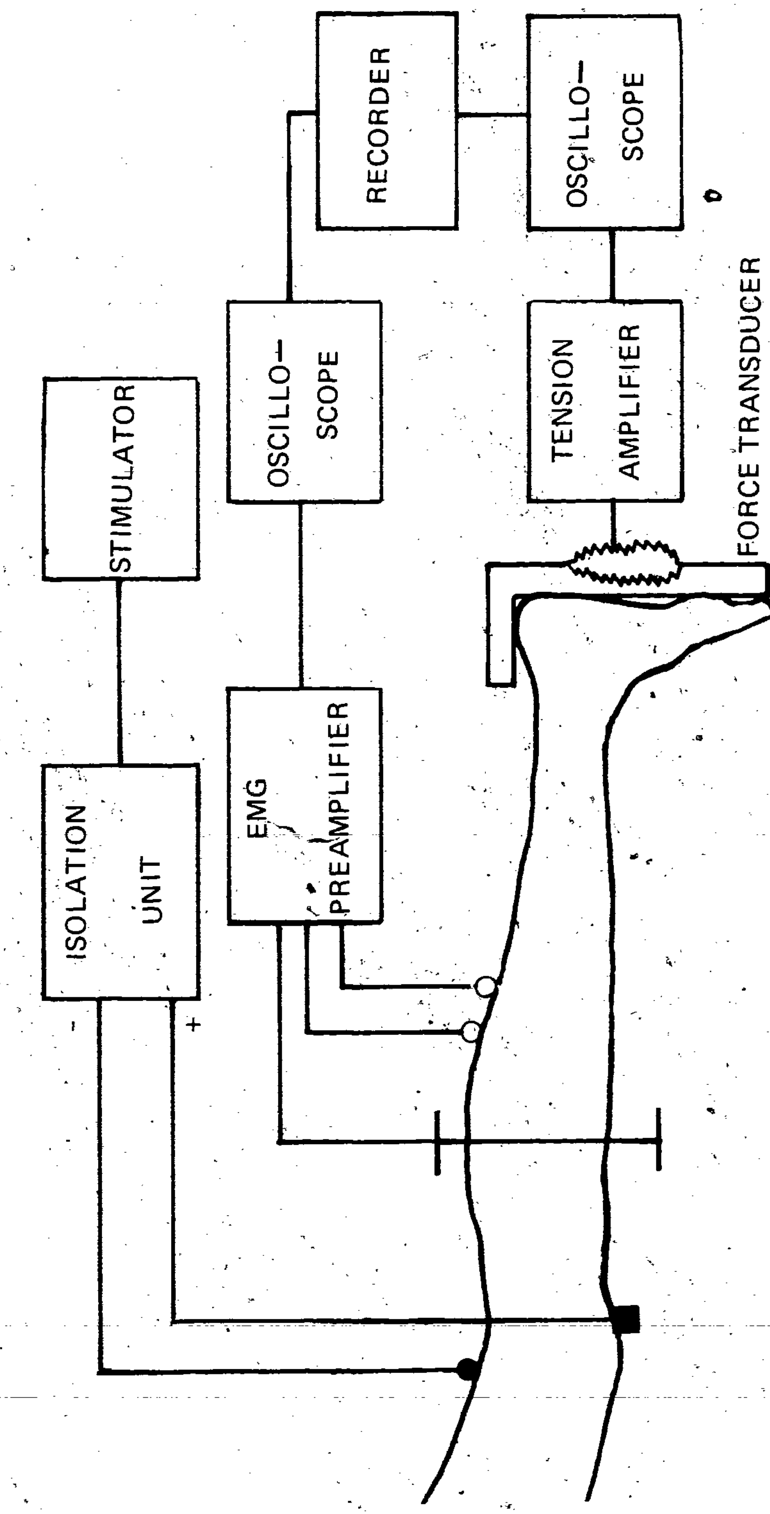
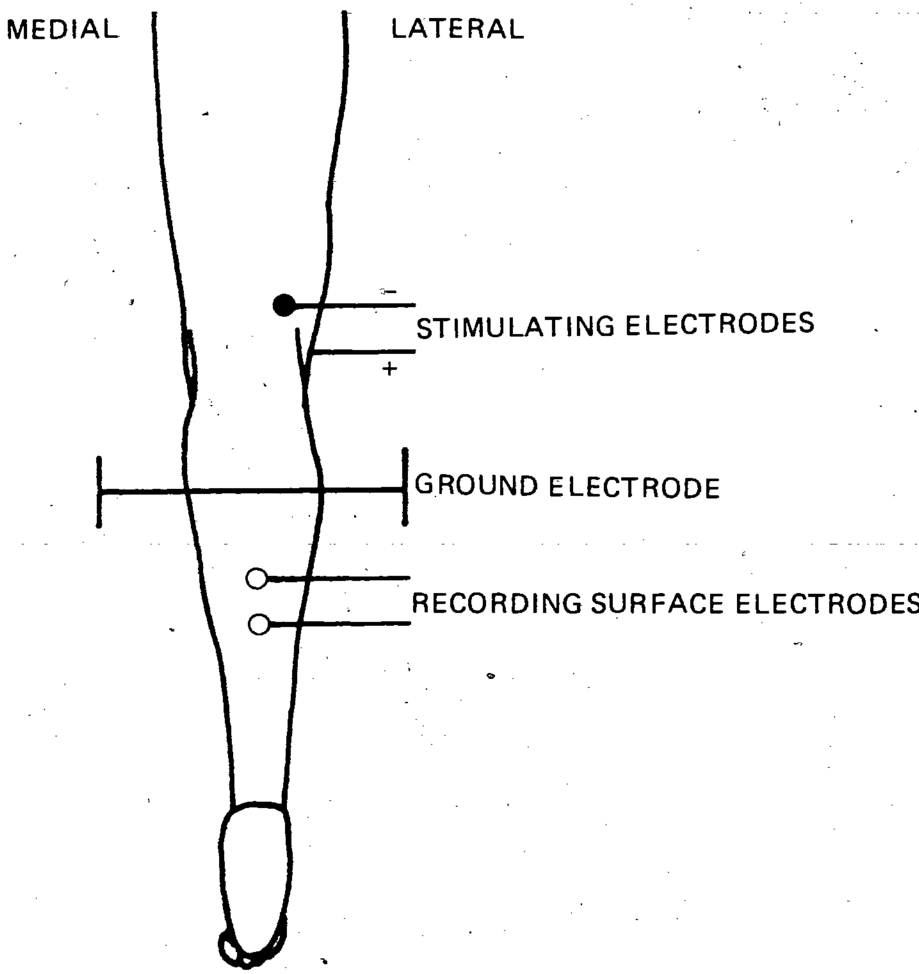

STIMULATOR
ISOLATION UNIT
-
+
OSCILLO-SCOPE
EMG PREAMPLIFIER
RECORDER
OSCILLO-SCOPE
TENSION AMPLIFIER
FORCE TRANSDUCER

Figure 6 Method used to study the effect of fatigue on the Hoffmann reflex


MEDIAL
LATERAL
−
STIMULATING ELECTRODES
+
GROUND ELECTRODE
RECORDING SURFACE ELECTRODES

IV. RESULTS

In order to obtain useful information from the experimental data, it was necessary to control, wherever possible, for systematic and random variations introduced by a number of factors. This is best understood with the aid of diagrams showing typical data collected in an experiment (Fig. 7 and 8).

These figures are typical of the variations of H- and M-wave amplitudes with stimulus voltage for most experimental situations and data were collected to allow such curves to be drawn for all experiments except those involving fatigue. The curves labelled H(c) and M(c) represent data collected under a normal or control situation and H(s) and M(s) represent data collected under an experimental situation (e.g. with alcohol).

The following points summarize the difficulties in analyzing data in this study.

1. For a given subject in a given experiment, the response curves will vary with time. This can be due to changes at the skin electrode interface for both stimulating and recording electrodes and to changes in the internal state of the subject. These changes can be controlled for by running repeated control (normal)

Figure 7 H and M recruitment curves for a typical normal subject

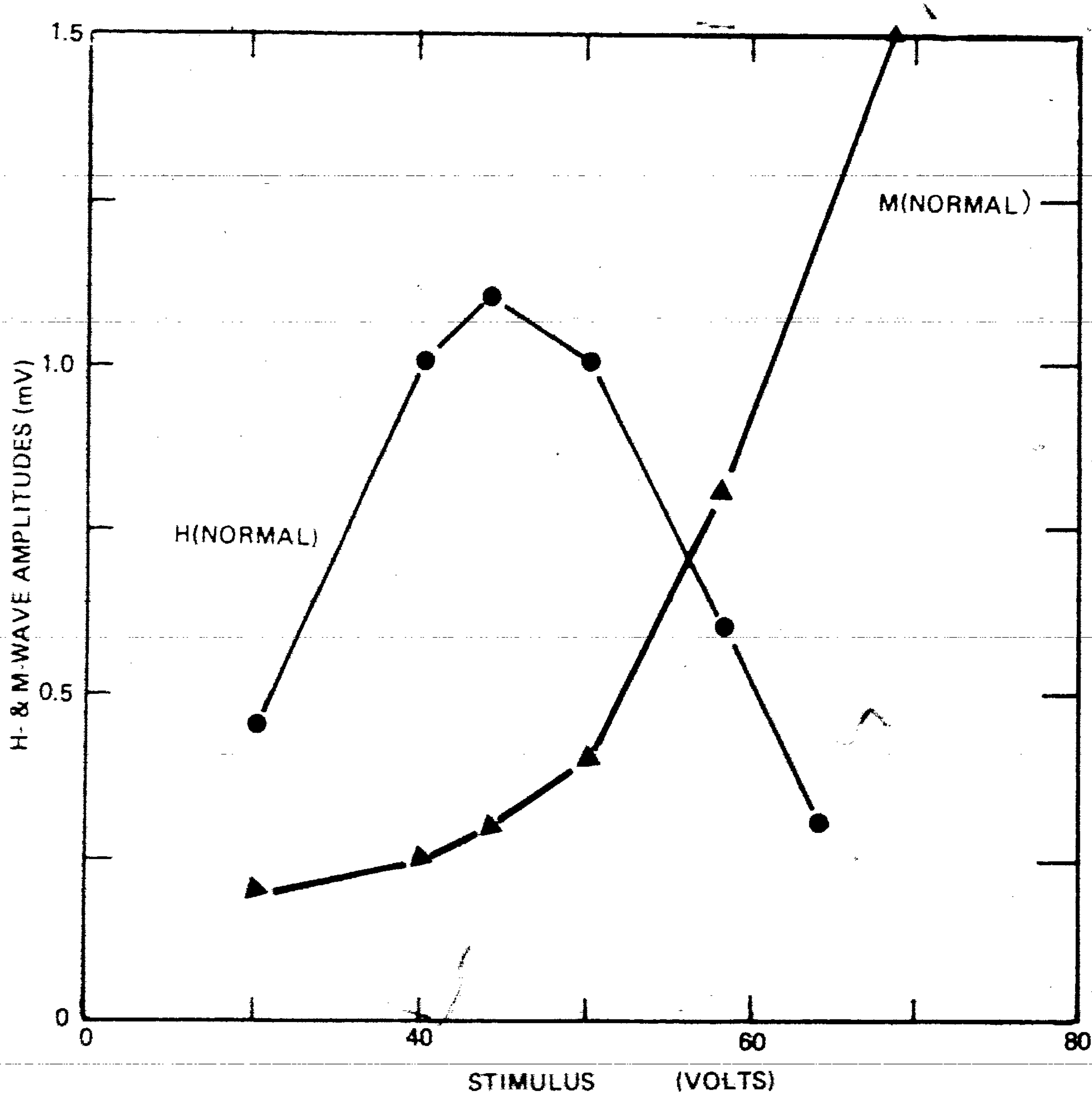
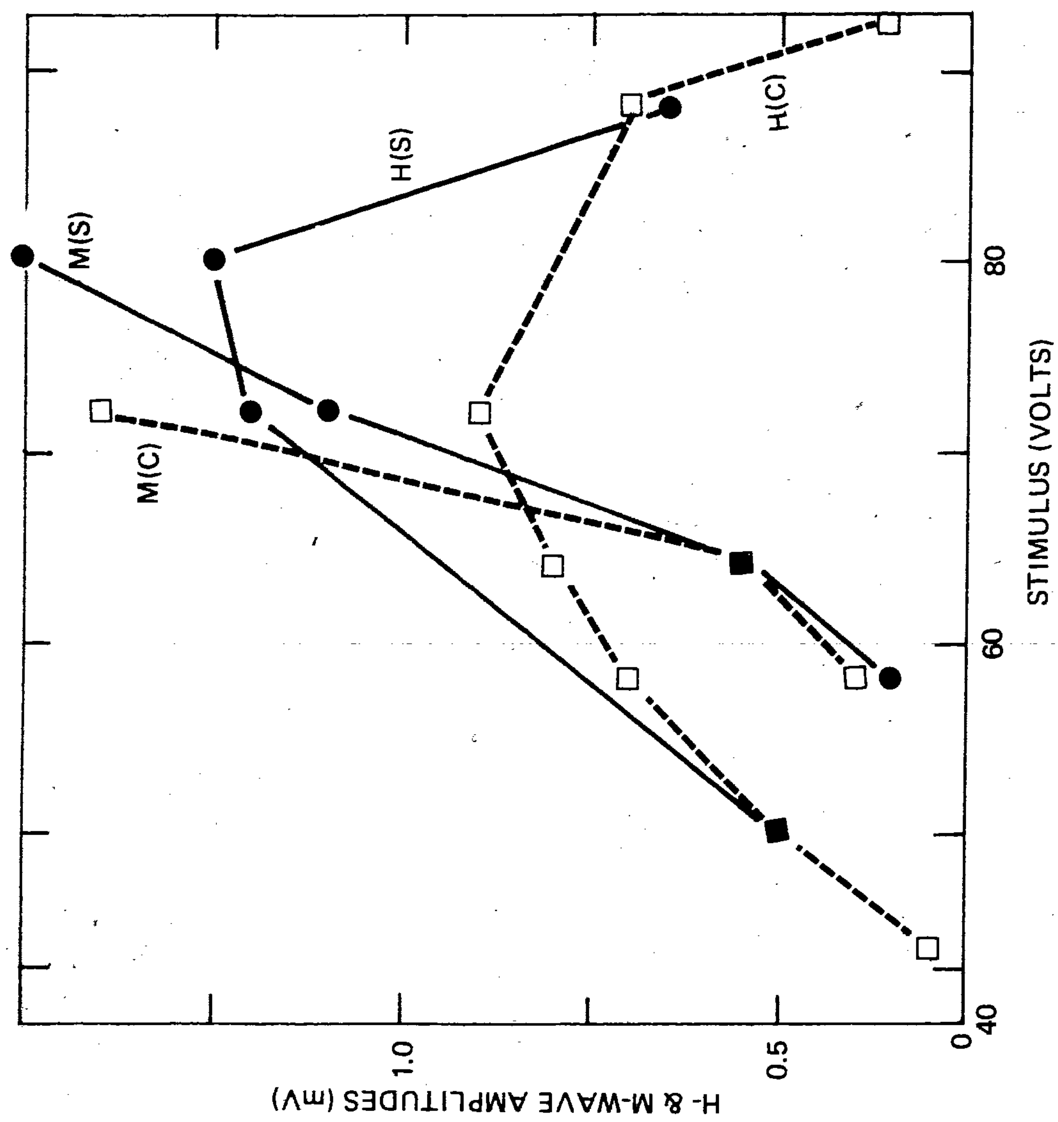

1.5
1.0
0.5
0
0
40
60
80
H- & M-WAVE AMPLITUDES (mV)
STIMULUS (VOLTS)
H(NORMAL)
M(NORMAL)

Figure 8 H and M recruitment curves for test and control experiments with a typical subject to show the graphical method of data analysis



H- & M-WAVE AMPLITUDES (mV)
STIMULUS (VOLTS)
0
0.5
1.0
40
60
80
M(S)
H(S)
H(C)
M(C)

response/stimulus curves or, where this is not possible (e.g. after alcohol has been administered), by using the M-wave amplitude as a control for the H-wave.

2. For a given subject, when different experiments are conducted on different days, the response curves may vary due to small errors in electrode placement. The stimulating electrode is particularly difficult to replace with accuracy since very small changes cause different motor and sensory fibers in the nerve to be stimulated. This is controlled for by running new normal response curves for each experiment.
3. For different subjects, there will be different response curves for the reasons stated above and because of differences between the subjects. The only control is to run normal response curves. The M-wave is not a useful inter-subject control.

Having established controls for each experiment, it is necessary to choose comparable features on the response curves. The most prominent feature is the maximum of the H-wave response (Hmax) and this is selected for measurement. The data is then analyzed either by comparing values of Hmax directly, Hmax(s)/Hmax(c) or by first normalizing by dividing the Hmax by the corresponding value of M,

i.e. $\dfrac{Hmax(s)/M(s)}{Hmax(c)/M(c)}$

where M(s) and M(c) are M-wave amplitudes obtained with Hmax(s) and Hmax(c) respectively.

The question to be answered is whether in the experimental situation Hmax(s) is significantly different from the relevant control Hmax(c). Since each experiment must be compared with its own control, the data is normalized by dividing by the control value Hmax(c) (see Appendix B).

Data Analysis

The methods used in data anlysis include the graphical method employed by Dietz (1978), the percentage method used by Fisher, et al (1979), maximum H-amplitudes, Hmax/M ratios, and histograms.

1. Graphical method: H- and M-amplitudes were plotted against voltage on the same scale for test and control. For the fatigue experiment, a graph of H- and M-amplitudes, integrated EMG (IEMG) and H/M ratios were plotted on the same scale against time.
2. Percentage method

$$\text{Potentiation} = \frac{(H(s) - H(c))}{H(c)} \times 100$$

$$\text{Depression} = \frac{(H(c) - H(s))}{H(c)} \times 100$$

where H(s) is maximum H-amplitude for condition under test H(c) is control maximum H-amplitude.

3. H-amplitudes: This method involved obtaining the highest three values of H-amplitudes for the test and comparing them with the highest three H-amplitudes for the control. The three value method was believed to be more reliable than the peak value alone. Potentiation or depression was determined by H(s)max/H(c)max (when it is observed that the three peak values were greater than 1, then there was potentiation; if equal to 1, no change in reflex was reported; and if less than 1, a depression of reflex was noted.)

4. Hmax/M ratio: In this method potentiation or depression was determined by considering the H/M ratio for both control and test conditions thus

$$\text{Potentiation or depression} = \frac{(Hmax/M(s))}{(Hmax/M(c))}$$

where (s) indicates test condition

(c) indicates control.

5. Histograms: The H-amplitude values obtained in (3) for each experiment with each subject were normalized by dividing by the corresponding control values. These were then averaged and plotted as a histogram in Figure 17, where the bars indicate the standard deviations for each test.

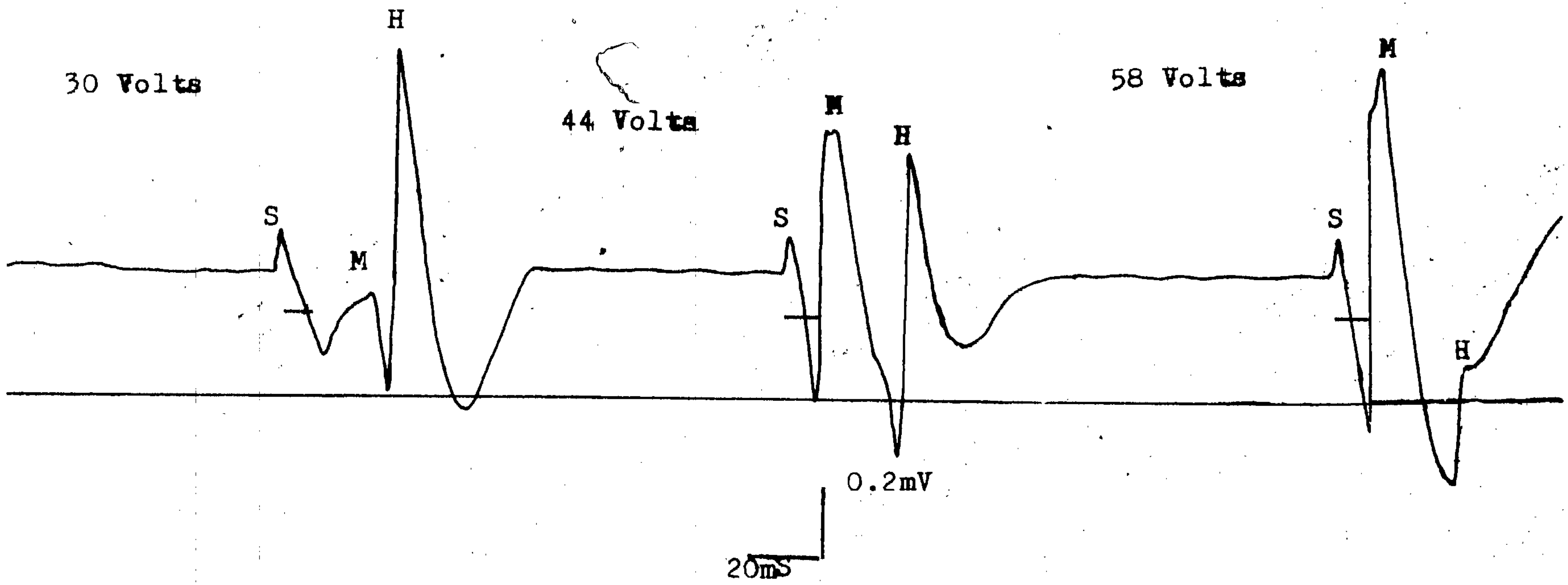
Measurements

H- and M-waves amplitudes were measured from the peak of the wave to its lowest point irrespective of the position of the baseline (Fig. 3 and 9). The measured values were in millimeters but were later converted to millivolts by making use of the EMG sensitivity used.

The interval latency period was measured from the beginning of the stimulus to the beginning of the H-wave. This value was obtained in millimeters and converted to milliseconds by making use of the EMG paper speed (Fig. 3 and 9).

The H-reflex was obtained with submaximal stimulus for the alpha motoneurone, and it appeared before the muscle response. In all but one subject the H-wave did not appear below 40 volts of the stimulus. In one subject it occurred as low as 24 volts of stimulus strength (Fig. 9).

Figure 9 Printout showing the effect on stimulus intensity on the H and M responses


30 Volts
S
M
H
44 Volts
S
M
H
0.2mV
20mS
58 Volts
S
M
H

The characteristics of the H-wave depended on the following factors: condition under test, stimulus voltage and subject's sensitivity, electrode placement, EMG sensitivity, whether subject was relaxed or tensed up, angle between the posterior surfaces of the thigh and leg (the best angle range used was 115 to 125 degrees), and the ankle angle (midplantarflexion range).

Normal

The ranges of H-wave amplitudes were between 0.2 and 1.5 millivolts with the mean range between 0.4 and 1.0 millivolts (Tables 1 and 4). The Hmax/M ratio range was 0.46 to 3.80. The mean value of this ratio was 2.24 for all subjects (Table 2). The Hmax/Mmax ratio had a range of 0.22 to 0.69 and a mean value of 0.46 for all subjects (Table 3). The response curves for the H-reflex and the M-wave of a subject are shown in Figure 7.

Force

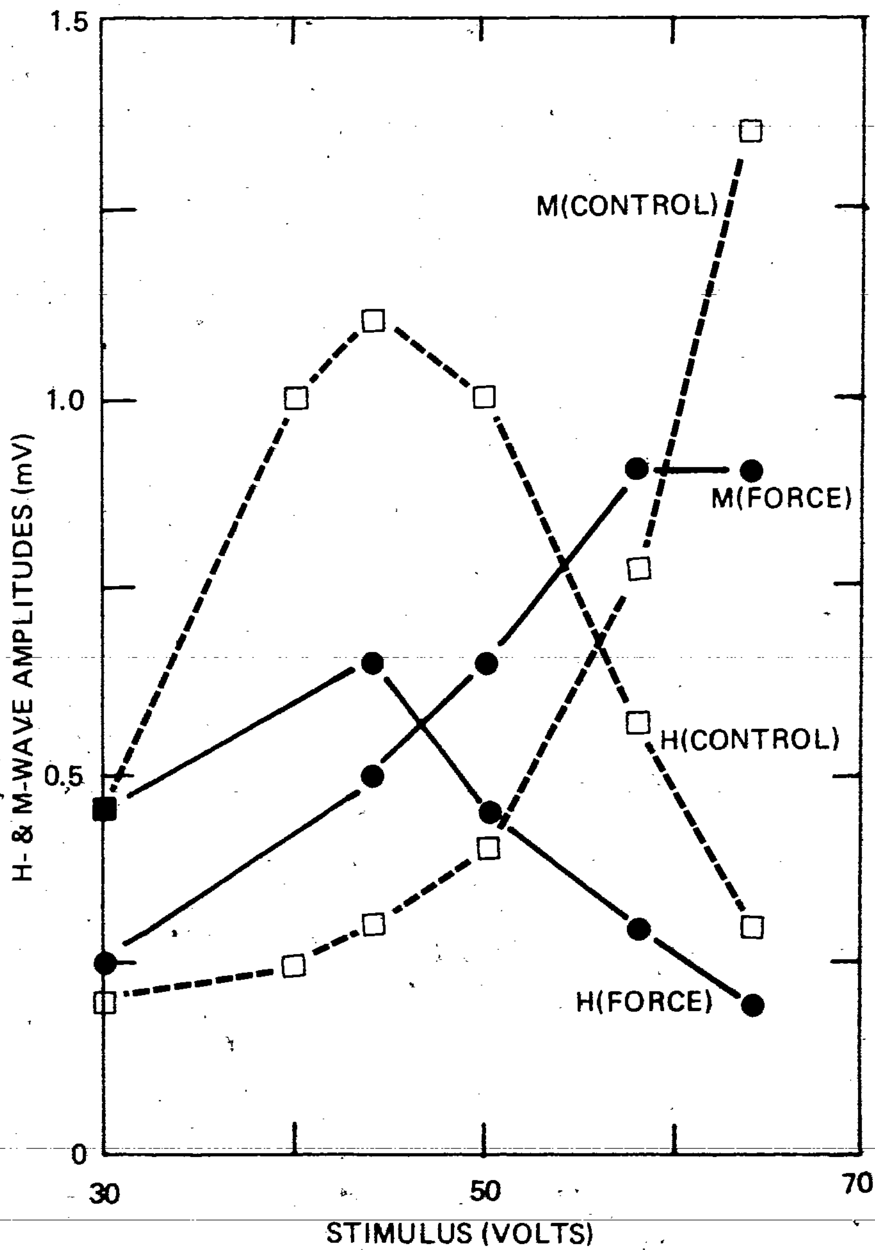
Submaximal phasic forces potentiated the H-reflex but maximal sustained forces depressed the reflex. The overall effects of force on the H-reflex and the M-wave are shown in Figure 10 for a typical subject.

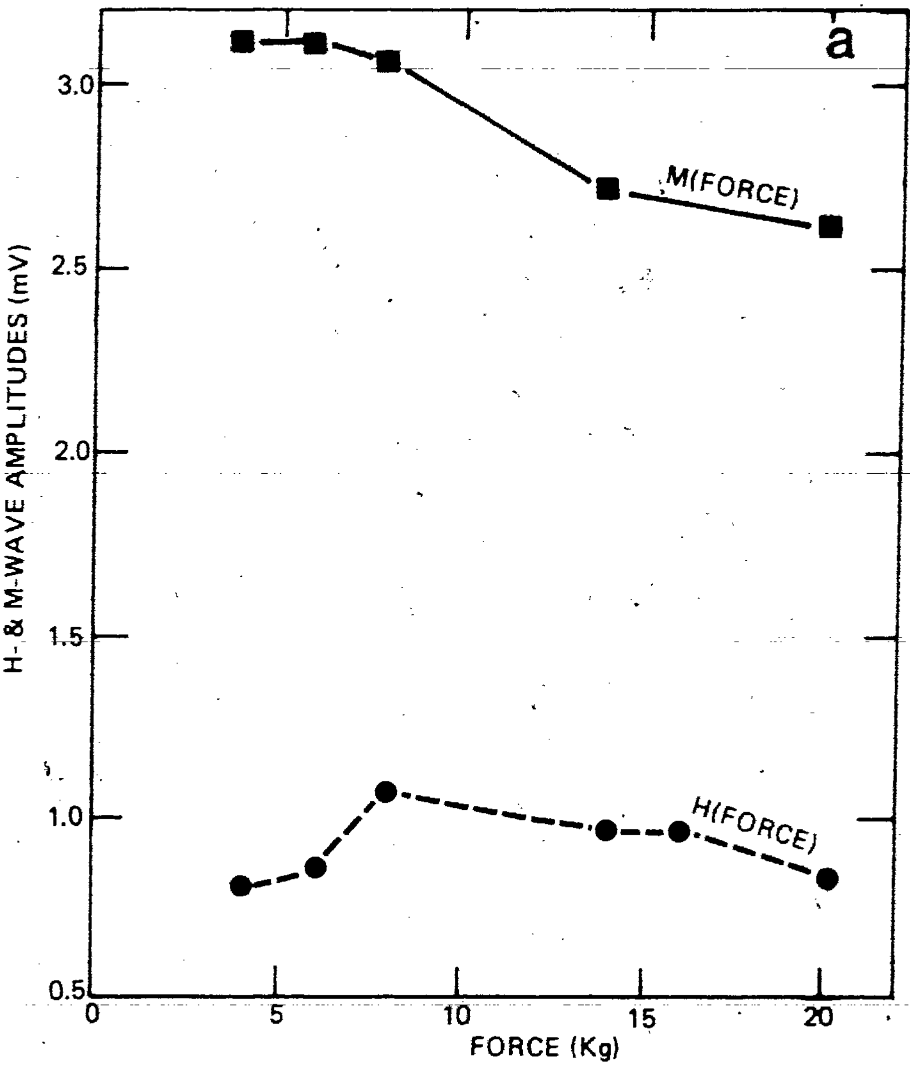
Alcohol

The H-amplitude range was 0.17 to 1.57 millivolts with a mean range of 0.44 to 1.34 millivolts (Tables 1 and 4). The mean potentiation of the H-reflex was 10.6% for all subjects. A typical response curve with alcohol is shown in Figure 11. The Hmax/M range for alcohol for all subjects was 0.71 to 5.0 with a mean of 2.42 (Table 2). The Hmax/Mmax ratio was 0.63 to 0.87 with a mean of 0.77 for all subjects (Table 3).

Figure 10 H and M recruitment curves with force

1. considered with control,
2. graded force


1.5
1.0
0.5
0
30
50
70
H- & M-WAVE AMPLITUDES (mV)
STIMULUS (VOLTS)
M(CONTROL)
M(FORCE)
H(CONTROL)
H(FORCE)


a
M(FORCE)
H(FORCE)
H- & M-WAVE AMPLITUDES (mV)
3.0
2.5
2.0
1.5
1.0
0.5
0
5
10
15
20
FORCE (Kg)

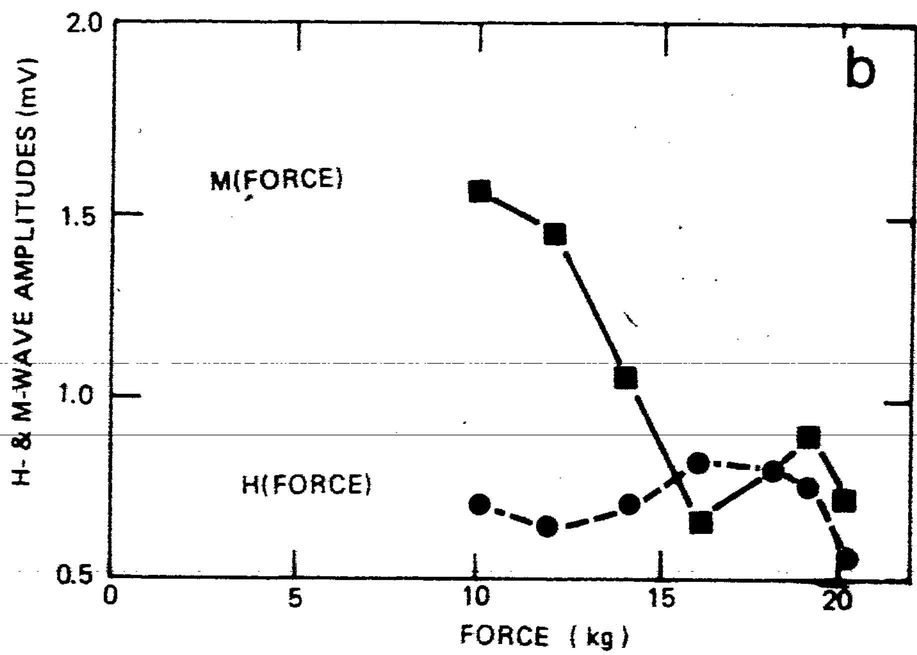
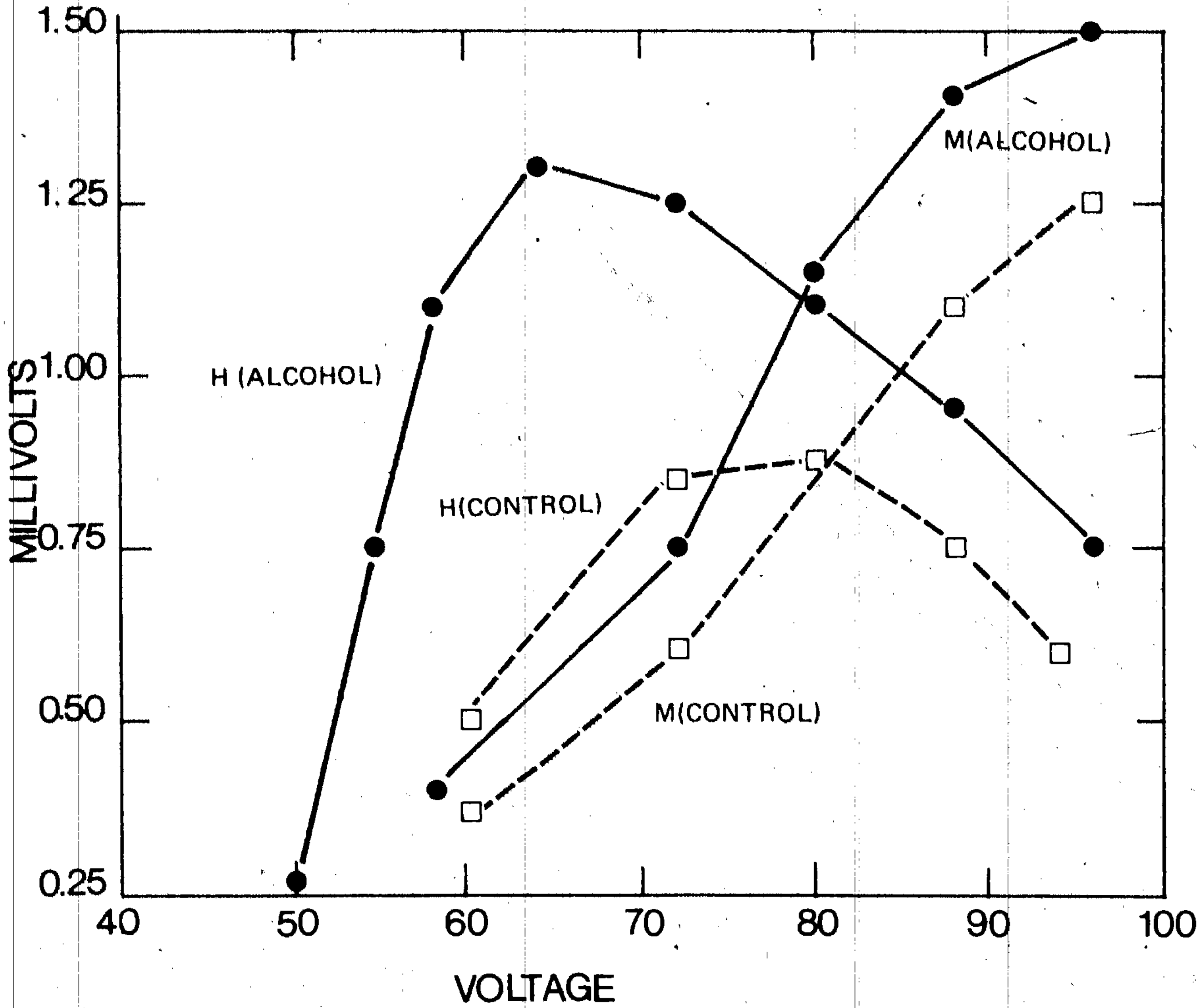

b
M(FORCE)
H(FORCE)
H- & M-WAVE AMPLITUDES (mV)
2.0
1.5
1.0
0.5
0
5
10
15
20
FORCE (kg)

Figure 11 H and M recruitment curves with alcohol compared with the control


1.50
1.25
1.00
0.75
0.50
0.25
MILLIVOLTS
40
50
60
70
80
90
100
VOLTAGE
H (ALCOHOL)
H(CONTROL)
M(ALCOHOL)
M(CONTROL)

Aspirin

In all but one subject aspirin depressed the H-reflex as shown by the response curves of a typical subject in Figure 12. The mean depression of the reflex for all subjects was 13.7%. H-amplitude range (Tables 1 and 4), was 0.25 to 1.25 millivolts with a mean range of 0.32 to 0.93 millivolts for all subjects. The Hmax/M range for aspirin was 0.65 to 5.0 and a mean value of 1.80 (Table 2). Aspirin showed a range of 0.42 to 1.6 with a mean value of 0.83 for all subjects (Table 3).

Caffeine

Caffeine lowered the stimulus threshold for the elicitation of the H-reflex in all subjects and is illustrated for a typical subject in Figure 13. The mean potentiation of the reflex was 18%. The H-wave amplitude range for caffeine (Tables 1 and 4) was 0.25 to 1.75 millivolts with a mean range of 0.54 to 1.33 millivolts for all subjects. The Hmax/M ratio range for caffeine was 1.0 to 3.0 and a mean of 1.94 for all subjects (Table 2). The Hmax/Mmax ratio range was 0.32 to 0.94 with a mean of 0.63 for all subjects (Table 3).

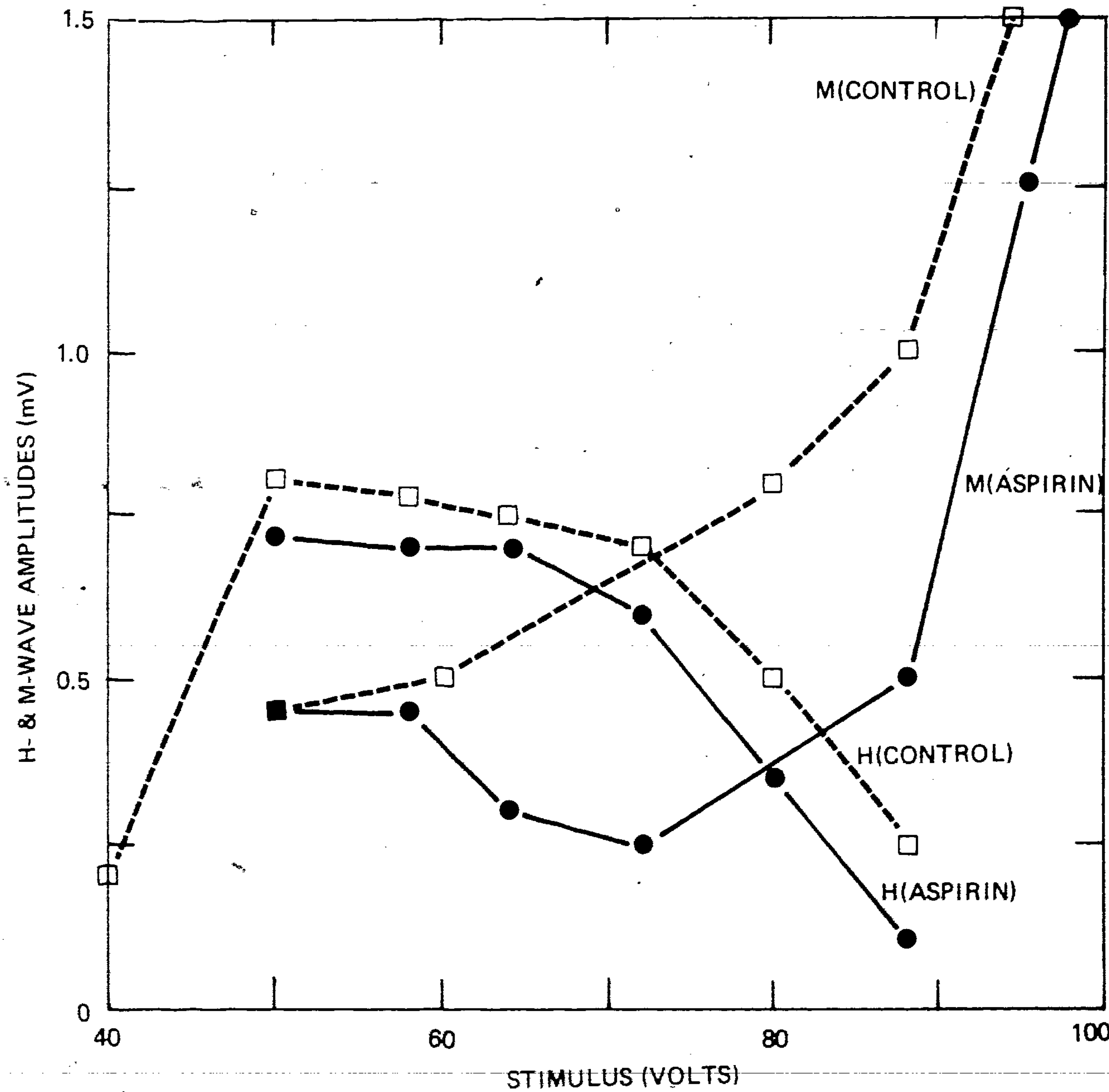
Localized Fatigue

Localized fatigue of the calf muscles resulted in a potentiation of the H-reflex and a depression of the M-wave (Figs. 14, 15, 16). A potentiation of 9.3% was recorded as a mean for all subjects. The H-wave amplitude range was 0.18 to 1.27 millivolts with a mean range of 0.54 to 1.2 millivolts for all subjects (Tables 1 and 4). The Hmax/M range was 0.53 to 3.9 and a mean of 1.81 for all subjects (Table 2). A range of 0.51 to 2.07 was obtained for Hmax/Mmax ratio (Table 3). The histograms (Fig. 17) show the magnitude of the effects of all the tested agents on the H-reflex and their standard deviations (see Appendix C).

H-Latency

Interval latency time was measured at supramaximal voltages when H-wave depression was high. Measurement was taken in this condition because latency values were consistent for the subject and measurement points were well defined. There was a latency range of 27 to 32 milliseconds with a mean value for all subjects of 29.71 milliseconds. H-latency was not affected by any of the conditions tested.

Figure 12 H and M recruitment curves for aspirin



1.5
1.0
0.5
0
H- & M-WAVE AMPLITUDES (mV)
M(CONTROL)
M(ASPIRIN)
H(CONTROL)
H(ASPIRIN)
40
60
80
100
STIMULUS (VOLTS)

Figure 13 H and M recruitment curves for caffeine plotted with the control

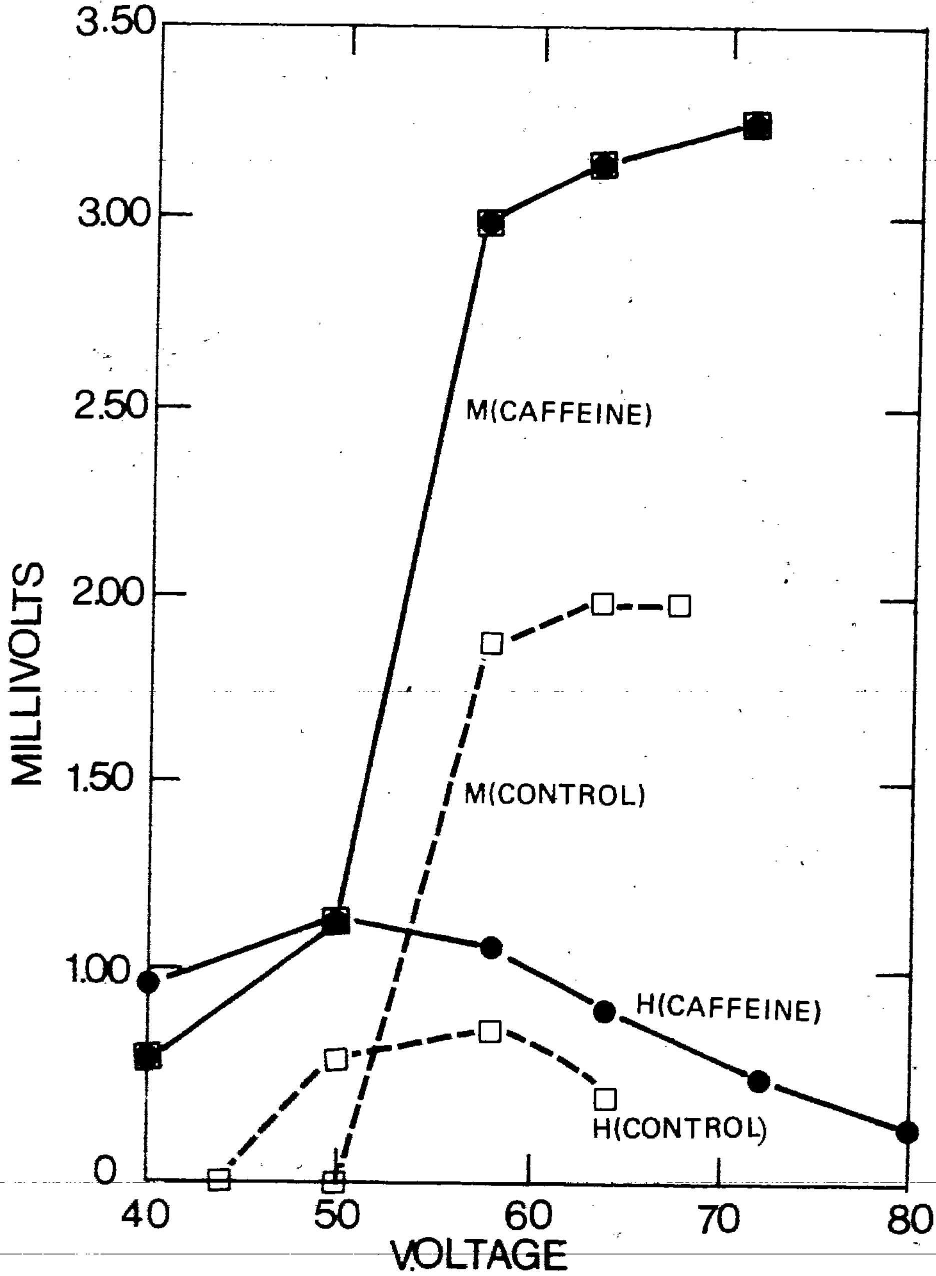
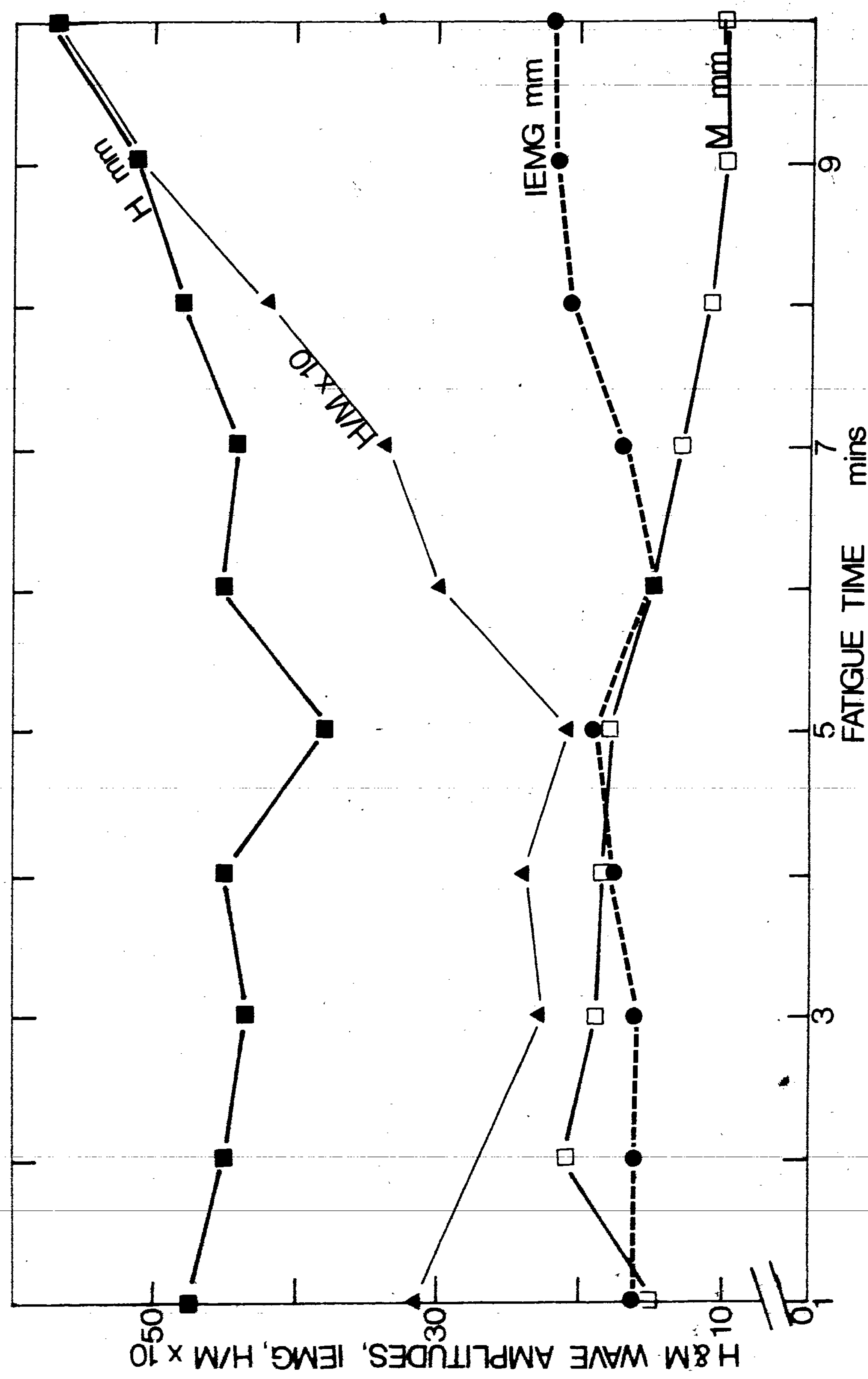

3.50
3.00
2.50
2.00
1.50
1.00
0
MILLIVOLTS
M(CAFFEINE)
M(CONTROL)
H(CAFFEINE)
H(CONTROL)
40
50
60
70
80
VOLTAGE

Figure 14 Hoffmann reflex changes in fatigue: H and M wave response curves, IEMG, and H/M ratio



H & M WAVE AMPLITUDES, IEMG, H/M x 10
50
30
10
0
FATIGUE TIME mins
1
3
5
7
9
H mm
H/M x 10
IEMG mm
M mm

Figure 15 Hoffmann reflex changes in fatigue: the experiment illustrated in Figure 14 was repeated with the same subject

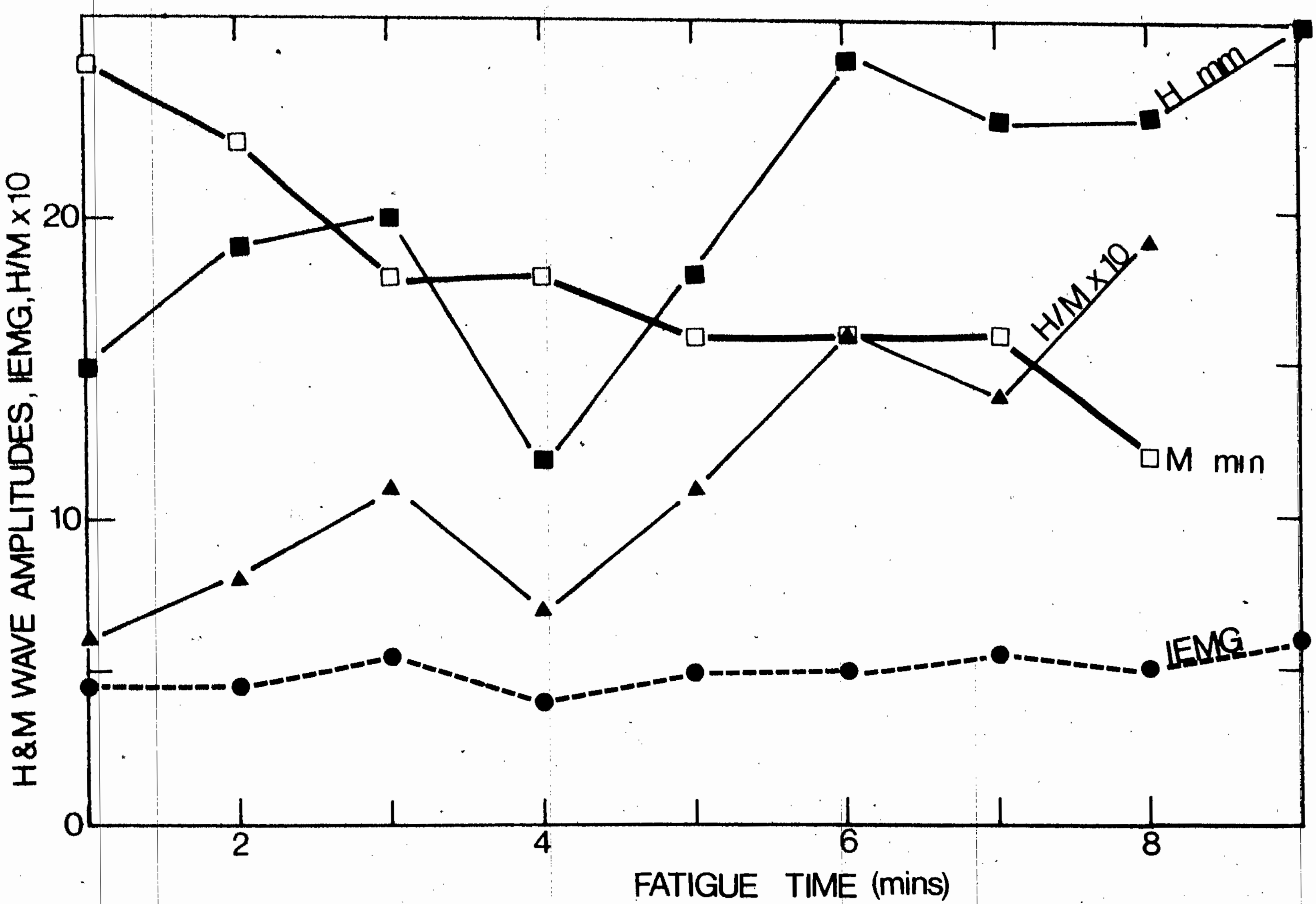

H mm
H/M x 10
M mm
IEMG
H&M WAVE AMPLITUDES, IEMG, H/M x 10
20
10
0
2
4
6
8
FATIGUE TIME (mins)

Figure 16 Printout showing the nature of response in fatigue

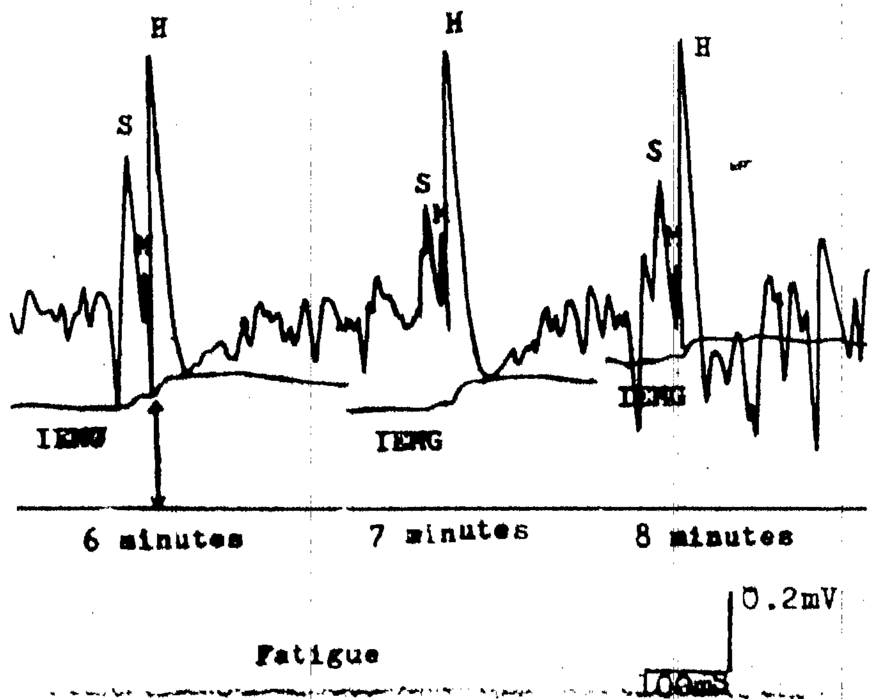

H
S
H
S
H
S
IEMG
IEMG
IEMG
6 minutes
7 minutes
8 minutes
0.2mV
100mS
Fatigue

Figure 17 Histogram showing the effects of tested agents on the Hoffmann reflex

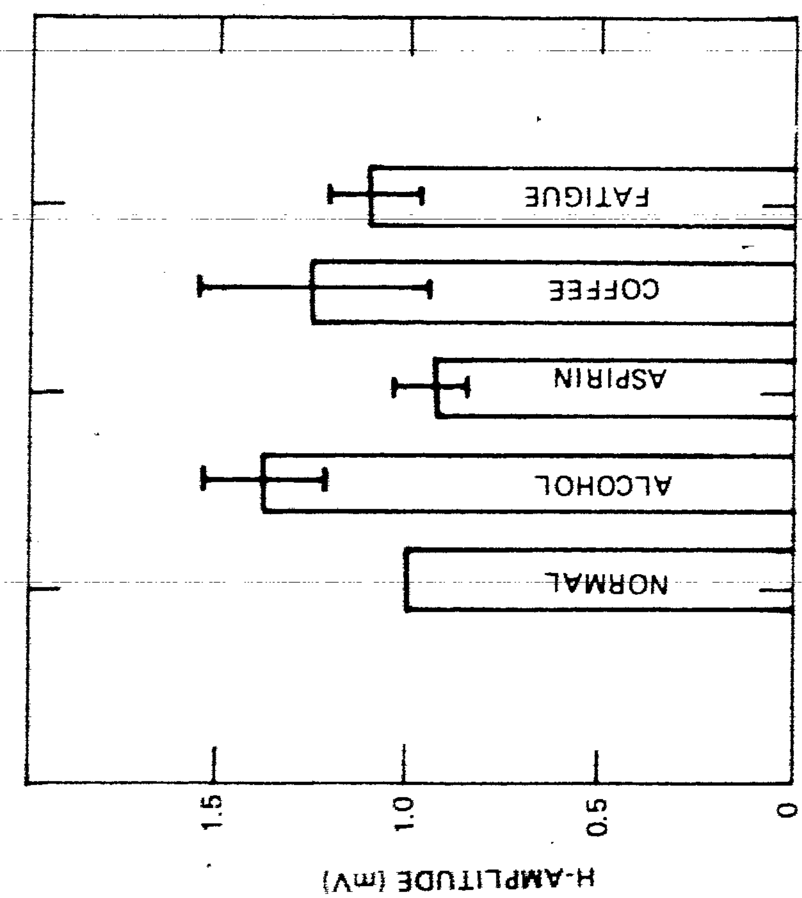

H-AMPLITUDE (mV)
0
0.5
1.0
1.5
NORMAL
ALCOHOL
ASPIRIN
COFFEE
FATIGUE

TABLE 1 Hmax RANGES

CONDITION	RANGE	MEAN
Normal	0.8-1.15	1.0
Alcohol	1.25-1.57	1.34
Aspirin	0.8-1.25	0.93
Caffeine	0.75-1.65	1.33
Fatigue	0.88-1.70	1.27

TABLE 2 Hmax/M RATIO

CONDITION	RANGE	MEAN
Normal	0.46-3.80	2.24
Alcohol	0.71-5.0	2.42
Aspirin	0.65-5.0	1.80
Caffeine	1.00-3.0	1.94
Fatigue	0.53-3.9	1.81

TABLE 3 Hmax/Mmax RATIO

CONDITION	RANGE	MEAN
Normal	0.22-0.69	0.46
Alcohol	0.63-0.87	0.77
Aspirin	0.42-1.60	0.83
Caffeine	0.32-0.94	0.63
Fatigue	0.51-2.07	0.92

TABLE 4 H-AMPLITUDE RANGE

CONDITION	RANGE	MEAN RANGE
Normal	0.20-1.5	0.40-1.00
Alcohol	0.17-1.57	0.40- 1.34
Aspirin	0.25-1.25	0.32-0.93
Caffeine	0.25-1.75	0.54-1.33
Fatigue	0.18-1.27	0.54-1.20

TABLE 5 FATIGUE

PARAMETER	RANGE OF PERCENTAGE CHANGE	TYPE OF CHANGE
H-AMPLITUDE	20-116	Increase
H/M ratio	90-216	Increase
M-amplitude	50-60	Decrease
IEMG	38-55	Increase

V. DISCUSSION

The Effects of Agents with Widespread Influence on the Nervous System

General

The experiments indicate that the H-reflex is a sensitive and quantifiable indicator of the effects of three common but quite different agents on the nervous system. Because of this, there is reason to expect that this reflex can serve as an easily accessible model for testing the general effects of drugs on the CNS. Of course its use with each new agent will have to be considered separately. Further study is necessary to investigate the effects of different doses with the agents tested here.

Alcohol

There was marked potentiation of the Hoffmann reflex and the M-response one hour after subjects drank a 6 oz. glass of Labatt's beer (5% alcohol, about 0.012 percent blood concentration). The potentiation was revealed in all the methods used for analysis. This finding has support in the literature. Low concentrations of alcohol have been shown to excite frog nerve-muscle preparations (Knutsson, 1961). Curare-blocked neuromuscular junctions of a frog's skeletal muscle have been treated with alcohol and an increase in the amplitude of endplate potential observed (Okada, and Adachi, 1962). Low, et al (1962) have shown that low concentrations of alcohol facilitate human neuromuscular junctions. In cholinergic nerve-muscle preparations, alcohol was shown by Sachdev, et al (1964) to potentiate muscle twitches. This report is similar to the increase in M-wave obtained with alcohol in the present study.

In a similar way to calcium, alcohol causes the release of acetylcholine from synaptic vesicles (Wallgren, and Barry, 1970). Cholinergic interactions of alcohol will invariably affect sodium and potassium movements across cell membranes, causing generation of spikes. This therefore means that alcohol will contribute in postsynaptic membrane depolarization. Hence the increase in the H-reflex may be attributed not only to the spinal cord excitability but also to a neuromuscular phenomenon.

Aspirin

Aspirin (acetylsalicylic acid) depressed the H-reflex and the M-wave in all but one subject. This effect was revealed by the graphical and H-amplitude methods of data analysis. The Hmax, Hmax/M and Hmax/Mmax ranges and means for all subjects, when compared with values for the normal subject revealed depression but the mean of Hmax/Mmax indicated potentiation of the H-reflex. This analgetic drug is not only antipyretic, but also a potent pain killer. It eliminates pain by depressing the pain fibers and suppressing the production of polypeptides (e.g. bradykinin) which actually cause the pain (Mountcastle, 1968). Aspirin may produce depression of the H-reflex by inhibiting prostaglandin synthesis and release (Vane, 1973). Probably it depresses the central nervous system by prostaglandin inhibition. Again, since the M-wave decreases, the decrease of the H-wave could be due to a neuromuscular phenomenon.

Caffeine

Caffeine caused marked potentiation of the H-reflex and the M-response amplitude was markedly increased in all subjects. These effects were revealed in all methods used for data analysis except the mean of Hmax/M ratio. The Hmax and Hmax/Mmax ranges and means for all subjects indicated potentiation of the H-reflex but the Hmax/M range and mean showed a depression of the reflex when compared with the normal. This effect was obtained by taking coffee (caffeine content about 100-150 mg).

Caffeine stimulates the central nervous system (Topliss, 1970) and thus causes potentiation of the H-reflex. Caffeine inhibits the hydrolysis of cAMP, has lipolytic actions and potentiates the effects of epinephrine (Triggle, 1970). All of these effects of caffeine constitute important factors in the central action of coffee on the H-reflex. Again, as with alcohol, it is seen that the H-reflex provides a sensitive indicator of CNS stimulation.

The Effects of Agents with Local Influence

General

The experiments with force and fatigue show that the H-reflex can serve as an indicator of the gain of the specific sensory-motor reflex arc involved. Thus it should be a useful tool for fundamental investigations of motor control and for clinical evaluation of lower motorneurone lesions.

Force

The effect of force on the H-reflex was similar to the effect of voltage on the reflex (Fig. 10). In most subjects phasic application of force produced potentiation of the reflex but as force became sustained a pronounced fall in the H-wave amplitude resulted. The M-response, though unchanged in one of the subjects, was generally affected in the same way as the H-wave (Fig. 10). These changes were revealed in the graphical and amplitude methods of data analysis.

These observations on the effects of force are not easy to explain. One explanation is that the decrease in the H-wave could be caused reflexively by the decrease in the M-wave.

Fatigue

It has been suggested in the literature that there are two phases to the buildup of fatigue during a sustained isometric contraction (Stephens and Taylor, 1972). In the first phase the decrease in force is accompanied by a proportional decrease in the synchronous muscle action potential (M-wave) whereas in the second phase the force falls more quickly than the action potential. The results reported here are not completely consistent with this. In our experiment the total force was maintained constant; presumably the build up of fatigue in the initially recruited units results in decreasing force and additional motor units are recruited. This accounts for the observed increase in the H-reflex. The decrease in amplitude of the M-wave is particularly marked in the later phase of fatigue. These results show that the decrease in M-amplitude is roughly parallel to the increase in H-amplitude. This is an indirect indication that in our experiment there is parallel decrease in force and synchronous action potential, i.e. the two phases observed by other workers cannot be seen in our data.

It has been hypothesized by others (Merton 1954; Edwards and Lippold 1956) that the principal mechanism of fatigue is the impairment of the contractile mechanism of the muscle, possibly due to ischemia. This would probably result in force declining more rapidly than the action potential and accounts for the second phase identified by Stephens and Taylor (1972). Our data suggests a rather large decrease in the action potential (M-wave) throughout the development of fatigue and this suggests that other mechanisms may be involved. Other suggestions include, cessation in central excitatory activity (Bigland-Ritchie: cited in Dietz 1978), impairment of neuromuscular transmission (Stephens and Taylor, 1972) and a drop in spinal motoneurone firing rate (Dietz, 1978). The H-reflex may be a useful tool to investigate these suggestions.

Limitations and Future Work

This series of experiments was exploratory in nature and the experimental design had definite limitations: a) there was no real control of the subjects' diet before each experiment,

b) the experiments were performed in the same order for each subject so a learning effect cannot be excluded; however the series was repeated for one subject and essentially identical results were obtained, c) the fatigue experiments were conducted with only one subject d) only one dose level was investigated for each agent tested, e) the possible psychological effect of knowing the nature of the experimental agents (alcohol, aspirin and coffee) was not investigated by repeating the experiments with a placebo, f) the H-reflex experiments are necessarily sensitive to many factors--limb angles, general arousal of subjects, diet of subjects, electrodes etc. Consequently more reliable data would result if more subjects had been used since random variations would tend to cancel out. In spite of these reservations we are quite confident in the general conclusions we have drawn and in the direction of the effects of specific agents.

In further work, a more elaborate experimental design could be used to investigate the results of these experiments and to use a wide range of doses for each agent. Probably the most interesting direction for further work is in the use of this tool to investigate neuromuscular fatigue in sustained alternating contractions.

VI. CONCLUSIONS

The H-reflex changes obtained by the use of the drugs in this study indicate that the reflex can not only be an effective tool in testing the excitability of the nervous system but can also determine the action and effectiveness of some drugs. Quantification is possible in the H-reflex studies and this would be an asset in its diagnostic use. In addition to these general conclusions, this study has also given new or confirmatory evidence of the action of certain agents on spinal reflexes. Specifically, alcohol (0.012 percent blood concentration) potentiated the H-reflex and increased the size of the muscle response, caffeine (1.3 g coffee) potentiated the reflex and the direct muscle response while aspirin (10 gr) depressed both the reflex and muscle response. It was also suggested that earlier explanations of fatigue in sustained contractions need to be re-examined.

APPENDIX A

INFORMED CONSENT

Subject's Name: Age:

I hereby authorize (name of person(s) who will perform procedure(s) or investigation(s) and/or such assistants as may be selected by him/her to perform the following procedure(s) and investigation(s):

on (subject)

The procedure(s) and investigation(s) have been fully explained to me by (name). I understand that the procedure(s) and investigation(s) involve the following possible risks and discomforts:

and that the potential benefits of the investigation are as follows:

I have had ample opportunity to ask questions regarding the above described procedures, risks, and benefits, and I have had all such questions answered to my satisfaction. Furthermore, I understand that I may withdraw my consent and terminate my participation in the study at any time.

Date: Subject's signature:

Time: Signature of parent or guardian:(if necessary)

Witness;

MEDICAL HISTORY

Name: Age:

Weight: Height:

Date:

Check (x) if answer is yes:

Past History:	Present Symptons:
Have you ever had?	Have you recently had?
Rheumatic fever	Chest pains
Heart murmur	Shortness of breath
High blood pressure	Heart palpitations
Any heart trouble	Cough on exertion
Diseases of arteries	Coughing of blood
Varicose veins	Back pain
Lung disease	Swollen, stiff, or
Operations	painful joints
Injuries to back, etc.	Muscle or tendon injury
Epilepsy	
Spells of severe dizziness	

Explain:

Is there a good physical reason not mentioned here why you should not participate in certain types of physical activity, even if you wanted to?

Do you engage in sports? What? How often?

Subject's signature:

APPENDIX B

<u>Peak H-Amplitudes</u>

Subject No.	Alcohol (A)	Aspirin (As)	Caffeine (Ca)
1	A 1.25	As 0.85	Ca 0.95
	C 0.90	C 0.95	C 0.91
	A/C 1.38	As/C 0.89	Ca/C 1.04
2	A 1.57	As 0.85	Ca 1.65
	C 0.97	C 0.95	C 0.90
	A/C 1.60	As/C 0.89	Ca/C 1.83
3	A 1.30	As 0.80	Ca 0.75
	C 0.85	C 0.80	C 0.72
	A/C 1.50	As/C 1.00	Ca/C 1.04
4	A 1.35	As 0.92	Ca 1.15
	C 1.10	C 1.12	C 0.88
	A/C 1.20	As/C 0.82	Ca/C 1.30
5	A 1.25	As 1.25	Ca 1.15
	C 1.10	C 1.13	C 1.10
	A/C 1.19	As/C 1.10	Ca/C 1.04
Mean Ratios	A/C 1.37	As/C 0.94	Ca/C 1.25

Second to the Peak H-Amplitude

Subject No.	Alcohol(A)	Aspirin(As)	Caffeine(Ca)
1	A 1.20	As 0.90	Ca 0.85
	C 0.70	C 0.90	C 0.65
	A/C 1.70	As/C 1.00	Ca/C 1.30
2	A 1.40	As 0.82	Ca 1.45
	C 0.95	C 0.90	C 0.85
	A/C 1.50	As/C 0.91	Ca/C 1.70
3	A 1.25	As 0.77	Ca 0.70
	C 0.75	C 0.77	C 0.66
	A/C 1.70	As/C 1.00	Ca/C 1.06
4	A 1.30	As 0.90	Ca 1.10
	C 1.05	C 1.05	C 0.84
	A/C 1.24	As/C 0.86	Ca/C 1.30
5	A 1.15	As 1.05	Ca 1.10
	C 0.95	C 1.08	C 1.07
	A/C 1.20	As/C 0.97	Ca/C 1.02
Mean Ratios	A/C 1.47	As/C 0.95	Ca/C 1.28

Third to the Peak H-Amplitude

Subject No.	Alcohol(A)	Aspirin(As)	Caffeine(Ca)
1	A 0.70	As 0.60	Ca 0.70
	C 0.65	C 0.85	C 0.63
	A/C 1.10	As/C 0.70	Ca/C 1.10
2	A 1.16	As 0.75	Ca 1.30
	C 0.94	C 0.75	C 0.80

	A/C 1.20	As/C 1.00	Ca/C 1.60
3	A 1.10	As 0.72	Ca 0.55
	C 0.71	C 0.72	C 0.47
	A/C 1.60	As/C 1.00	Ca/C 1.10
4	A 1.20	As 0.75	Ca 0.92
	C 1.00	C 0.95	C 0.81
	A/C 1.20	As/C 0.79	Ca/C 1.13
5	A 0.85	As 0.67	Ca 0.95
	C 0.55	C 1.05	C 0.60
	A/C 1.54	As/C 0.64	Ca/C 1.60
Mean Ratios	A/C 1.40	As/C 0.91	Ca/C 1.30

<u>Mean Ratios (X,Y,Z)</u>

Category	Alcohol	Aspirin	Caffeine
X	1.37	0.94	1.25
Y	1.47	0.95	1.28
Z	1.40	0.91	1.30
Total	4.24	2.80	3.83
Mean	1.41	0.93	1.28

APPENDIX C

Standard Deviation

Subject No.	Alcohol
1	1.38
2	1.60
3	1.50
4	1.20
5	1.19
Mean	1.37

Deviations (d)

1	0.01
2	0.23
3	0.13
4	-0.17
5	-0.18

d squared

1	0.0001
2	0.0529
3	0.0169
4	0.0289
5	0.0324
Sum	0.1312

Variance = Sum/5 = 0.026

Standard deviation = Square Root of Variance = 0.16

BIBLIOGRAPHY

Abe K. (1978): A study of sensory projection from jaw muscles to the cerebral cortex in the rat. Jap. J. Physiol. 28:309-322.

Angel R.W. and Hoffmann W.W. (1963): H reflex in normal, spastic and rigid subjects. Arch. Neurol. 8:591-596.

Asmussen E. and Mazin B. (1978): A central nervous component in local muscular fatigue. Europ. J. Appl. Physiol. 38:9-15.

Bishop B., Machova S., Johnston R., and Anderson M., (1968): A quantitative assessment of gamma motoneuron contribution to the Achilles tendon reflex in normal subjects. Arch. Phys. Med. 49:145-154.

Bishop B., Machova S., Johnston R., Wash W., and Anderson M. (1968): Role of the gamma motor system in the Achilles tendon reflex of hemiplegic patients. Arch. Phys. Med. Rehab. 49:698-707.

Bishop B., Johnston R.M. and Wash W. (1970): Changes in alpha and gamma motoneuron excitability with respirations. Arch. Phys. Med. Rehabil. 51: 383-390.

Blackstock E., Rushwort G. and Gath D. (1972): Electrophysiological studies in alcoholism. J. Neurol. Neurosurg. Psychiat. 35:326-334.

Blom S., Hagbarth K.E. and Skoglund S. (1964): Post tetanic potentiation of H-reflexes in human infants. Exp. Neurol. 9:198-211.

Braddom R.L. and Johnson E.W. (1974): Standardization of H reflex and diagnostic use of S1 radiculopathy. Arch. Phys. Med. Rehabil. 55:161166.

Braddom R.L. and Johnson E.W. (1974): H reflex: review and classification with suggested clinical uses. Arch. Phys. Med. Rehabil. 55:412-417.

Braddom R.L. (1976): H reflex. Arch. Phys. Med. Rehabil. 57:407.

Brooks C. McC. and Eccles J.C. (1947): A study of the effects of anaesthesia and asphyxia on the monosynaptic pathway through the spinal cord. J. Neurophysiol. 10:349-360.

Broughton R., Vera C., Meir-Ewert K., Ebe M. and Andermann F. (1968): H reflex studies and the effects of iv. diazepam (valium) in subacute sclerosing leucoencephalitis. Electroenceph. Clin. Neurophysiol. 24:288.

Buchthal F. and Schmalbruch H. (1970): Contraction times of twitches evoked by H reflexes. Acta. Physiologica Scandinavica. 80:378-382.

Burg D., Szumski A., Struppler A. and Velho F. (1974): Assessment of fusimotor contribution to reflex reinforcement in humans. J. Neurol. Neurosurg. and Psychiatry. 37:1012-1021.

Burger A. (1970): Medicinal Chemistry, Third Edition, Part II. Edited by Burger A., Wiley-Interscience New York. p. 1273.

Burke D., Andrews C.J. and Lance J.W. (1972): Tonic vibration reflex in spasticity, Parkinson's disease and normal subjects. J. Neurol. Neurosurg. Psychiat. 35:477-486.

Burke E.R., Levine D.N., Zajac E.F., Tsairis P. and Engel K.W. (1971): Mammalian motor units: Physiological histochemical correlation in three types in cat gastrocnemius. Science. 174:709-712.

Bussel B., Morin C. and Pierrot-Deseilligny E. (1978): Mechanisms of monosynaptic reflex reinforcement during Jendrassik manoeuvre in man. J. Neurol. Neurosur. and Psychiat. 41:40-44.

Cadilhac J., Georgesco M., Benezech J., Duday H. and Dapres G. (1977): Somatosensory cerebral potential and H reflex after acute spinal cord lesions. Electroenceph. Clin. Neurophysiol. 43:160-167.

Campbell E.D. and Green E. (1964): An attempt to measure muscle spasticity by H wave changes and the effect on these measurements of a skeletal muscle relaxant (carisoprodol). Electroenceph. Clin. Neurophysiol. 17:705-706.

Casey, E.B., LeQuesne P.M. (1972): Electrophysiological evidence for a distal lesion in alcoholic neuropathy. J. Neurol. Neurosurg. Psychiat. 35:624-630.

Chu N., Squires K. and Starr (1978): Auditory brainstem potentials in chronic alcohol intoxication and alcohol withdrawal. Arch. Neurol. 35:596-602.

Cianchetti C. (1975): Soleus H reflex and afferent discharges from antagonistic muscles. An electrophysiological method of evaluation. Electroenceph. Clin. Neurophysiol. 39:425-427.

Cohen S. (1966): Metabolism and pharmacology. Alcoholism. Edited by Max Hayman. Charles C. Thomas Publisher 1966. p 17-25.

Cook W.A. Jnr. (1968): Effects of low frequency stimulation on monosynaptic reflex (H reflex) in man. Neurology (Minneap). 18:47-51.

Cooper S. (1966): Muscle spindles and motor units. In Andrew control and Innervation of skeletal muscle. University of St. Andrews Press. Aberdeen 1966. p. 15.

Corrie W.S. and Hardin W.B. (1974): Post-tetanic potentiation of H reflex in normal man. Quantitative study. Arch. Neurol. (Chic) 11:317-323.

Decandia M., Provini L. and Taborikova H. (1967b): Presynaptic inhibition of the monosynaptic reflex following the stimulation of nerve to extensor muscles of the ankle. Exp. Brain Res. 4:34-42.

del Castillo J. and Katz B. (1954): Statistical factors involved in neuromuscular facilitation and depression. J. Physiol. 124:574-585.

Delwaide P. and Delbecq P. (1973): Vestibular influences on proprioceptive reflexes of the lower limb in normal man. New Dev. in EMG and Clin. Neurophysiol. Edited by Desmedt J. 3:336-341 (Karger Basel 1973).

Delwaide P.J., Cordonnier M. and Charlier M. (1976): Functional relationships between myotatic reflex arcs of the lower limbs in man: Investigation by excitability curves. J. Neurol. Neurosurg. and Psychiat. 39:545-554.

Delwaide P., Cordonnier M. and Gadeaciria M. (1978): Excitability relationship between lower limb myotatic arcs in spasticity. J. Neurol. Neurosurg. and Psychiat. 41:636-641.

Denny-Brown D. (1960): Cited in: Taborikova H. and Sax D.S. (1969): Conditioning of H reflexes by a preceding subthreshold H reflex stimulus. Brain. 92:203-212.

De Gail P., Lance J.W. and Neilson P.D. (1966): Differential effects on tonic and phasic reflex mechanisms produced by vibration of muscles in man. J. Neurol. Neurosurg. Psychiat. 29:1-10.

Deschuytere J. and Rossell N. (1973): Diagnostic use of monosynaptic reflexes in L5 and S1 root compression. In: New Dev. in EMG and Clin. Neurophysiol. Edited by Desmedt J.E. (Basel Karger) 1973. 3:360-366.

Deschuytere J. and Rosselle N. (19[illegible]): Identification of certain EMG patterns of spinal cord reflexive activity in man. Electrophysiological study of discharges from spinal origin in forearm flexors in normal adults. Electromyograph. Clin. Neurophysiol. 14:497-511.

Diamantopoulos E. and Gassel M. (1965): Electrically induced monosynaptic reflexes in man. J. Neurol. Neurosurg. Psychiat. 28:495-502.

Diamantopoulos E. and Zander Olsen O. (1967): Excitability of motorneurons in spinal shock in man. J. Neurol. Neurosurg. Psychiat. 30:427-431.

Dietz V. (1978): Analysis of the electrical muscle activity during maximal contraction and influence of ischaemia. J. Neurological Sciences. 37:187-197.

Drechsler B., Lastovka M. and Kalvodova E. (1966): Electrophysiological study of patients with herniated intervertebral disc. Electromyography. 6:187.

Edwards R. and Lippold C. (1956): The relation between force and integrated EMG in fatigued muscle. J. Physiol. 132:677-681.

Ekholm J. and Skoglund S. (1964): Possible factors influencing the demonstration of post-tetanic potentiation of the H reflex as studied in the cat. Exp. Neurol. 9:183-197.

Erokhina L.G., Rekhtman M.B. and Chekneva N.S. (1976): Interaction between peripheral motoneurons of antagonist muscles in normal subjects and spastic hemiparesis studied by the H reflex method. Neuroscience and Behavioral Physiology. 7:232-235.

Ferrari E., Sanna G. and Bravaccio F. (1966): Effects of Jendrassik's manoeuvre on tendon jerk and H reflex in subjects with functional and pyramidal hyperreflexia. Electroenceph. Clin. Neurophysiol. 21:90.

Fisher M. and Penn R. (1978): Evidence for changes in segmental motoneurone pools by chronic cerebellar stimulation and its clinical significance. J. Neurol. Neurosurg. and Psychiat. 41:630-635.

Fisher M., Shashani B. and Young R. (1979): Electrophysiologic analysis of the motor system after stroke: The 'suppressive' effects of vibration. Arch. Phys. Med. Rehabil. 60:11-13.

Fra L. and Briognolio F. (1968): F and H responses elicited from muscle of lower limb in normal subjects. J. Neurol. Science. 7:251-261.

Fujita S. and Cooper I.S. (1971): Effects of L-dopa on H reflex in Parkinsonism. J. Am. Geriatric Soc. 19:289-295.

Gage P. W. (1965b): The effect of methyl, ethyl and n-propyl alcohol on neuromuscular transmission in the rat. J. Pharmacol. Exptl. Ther. 150: 236-243.

Gassel M. (1970): A critical review of evidence concerning long loop reflexes excited by muscle afferents in man. J. Neurol. Neurosurg. Psychiat. 33:358-362.

Gassel M. M. (1973): An objective technique for the analysis of the clinical effectiveness and physiology of action of drugs in man. In: New Developments in EMG and Clinical Neurophysiology, Edited by J.E. Desmedt. Vol. 3 (Karger Basel 1973). p. 342-359.

Garcia-Mullin R. and Mayer R. F. (1972): H reflexes in acute and chronic hemiplegia. Bran. 95:559-572.

Gerilovsky L., Radichera N., Gydikov A. (1977): The shape of the Achilles tendon reflex potentials. Electromyogra. Clin. Neurophysiol. 17:143-153.

Gillies J. D., Lance J. W., Neilson P. D. and Tassinari C. A. (1969): Presynaptic inhibition of the monosynaptic reflex by vibration. J. Physiol. (Lond). 205: 329-339.

Glass A. and Smolen A. (1976): H reflex recovery curves in the evaluation of dantrolene sodium and Diazepam. Arch. Phys. Med. Rehabil. 57:598.

Glylys J. A. and Tilson H. A. (1975): Pharmacological approaches to maintaining and improving walking function. Annual Rep. Med. Chem. Vol. 10. Academic Press. New York.

1975. p. 21-26.

Godaux E. and Desmedt J. E. (1975): Human masseter muscle: H and tendon reflexes. Arch. Neurol. 32:229-234.

Goodgold J. and Eberstein A. (1971): Electrodiagnosis of Neuromuscular diseases. Baltimore, Williams and Wilkins P. p. 170-171.

Goodwill C. J. and O'Tuama L. (1968): The normal jaw reflex: Measurement of the action potential in the masseter muscles. Ann. Phys. Med. 9:183-188.

Gottlieb G. L., Agarwal G. C. and Stark L. (1970): Interactions between voluntary and postural mechanisms of the human motor system. J. Neurophysiol. 33:365-381.

Gottlieb G. L. and Agarwal G. C. (1976): Extinction of the Hoffmann reflex by antidromic conduction. Electroenceph. Clin. Neurophysiol. 41:19-24.

Gottlieb G. L. and Agarwal C. G. (1971): Effects of initial conditions on Hoffmann reflex. J. Neurol. Neurosurg. Psychiat. 34:226-230.

Gottlieb G. L. and Agarwal G. C. (1972): The role of the myotatic reflex in the voluntary control of movements. Brain Res. 40:139-143.

Granit R. and Burke R. E. (1973): Control of movement and posture. Brain Res. 53:1-28.

Guiheneuc P. and Ginet J. (1973): The Hoffmann reflex in lumbosacral root inuries. Electroenceph. Clin. Neurophysiol. 34:814.

Guiheneuc P. and Ginet J. (1974): Etude reflexe de Hoffmann obtenu au niveau du muscle quadriceps de sujets humains normaux. Electroenceph. Clin. Neurophysiol. 36:225-231.

Guiheneuc P. and Bathien N. (1976): Two patterns of results in polyneurophathies investigated with the H reflex. J. Neurol. Science. 30:83-94.

Gydikov A., Gerilovsky L. and Dimitorv G. V. (1976): Dependence of the H reflex potential shape on extraterritorial potentials of triceps surae motor units. Electromyograph Clin. Neurophysiol. 16:555-567.

Grylys J. and and Tilson H. A. (1975): Pharmacological approaches to maintaining and improving walking functions. In: Ann. Reports in Med. Chem. Vol. 10. Edited by Heinzelman R. V., Academic Press, N.Y., Lond. 1975. pp. 21-26.

Hagbath K. (1962): Post-tetanic potentiation of myotatic reflexes in man. J. Neurology Neurosurg. and Psychiat. 25:1-10.

Hayes K. C. (1972): Jendrassik's manoeuvre facilitation and fractioned patella reflex times. J. Applied Physiol. 32:290-295.

Hayes K. C. (1975): Effects of fatiguing isometric exercise upon Achilles tendon reflex and plantarflexion reaction time components in man. Europ. J. Appl. Physiol. 34: 69-79.

Hayes K. C. and Sullivan J. (1976): Tonic neck reflex influence on tendon and Hoffmann reflexes in man. Electromyogr. Clin. Neurophysiol. 16:251-261.

Herbison G. J. (1973): H reflex in patients with Parkinsonism: Effect of L-Dopa. Arch. Phys. Med. Rehabil. 54:291-295.

Herman R. (1969): Relationship between the H reflex and the tendon jerk response. Electromyogr. 9:359-370.

Hodes R. and Gribetz I. (1963): Normal electrically induced reflexes ('H reflexes') in a 2-week-old infant with acrania and cerebral dysgenesis. Electroenceph. Clin. Neurophysiol. 15:1033-1036.

Hodes R. and Dement W. (1964): Depression of electrically induced reflexes ('H-reflexes') in man during low voltage EEG 'sleep.' Electrenceph. Clin. Neurophysiol. 17:617-629.

Hoffmann P. (1918): Uber die Beziehungen der Sehneneflexe zur Willkurlichen Bewegung und zum Tonus. Z. Biol. 68:351.

Hoffmann P. (1922): Cited in: Gottlieb G. L. and Agarwal G. C. (1976): Extinction of the Hoffman reflex by antidromic conduction. Electroenceph. Clin. Neurophysiol. 41:19-24.

Hoffmann Von P. (1952): Kurzer Uberblick Uber die Beziehungen de reflexversuche mit der elektrischen methodik bei mensch und tier, Experientia. 8:371-375.

Homma S. and Kano M. (1962): Electrical properties of the tonic reflex arc in the human proprioceptive reflex. Symposium on Muscle Receptors. Edited by David Barker. Hong Kong University Press. 1962. pp. 167-174.

Hugon M. (1973): Methodology of the Hoffmann reflex in man. New Dev. in EMG & Clin. Neurophysiol. 3:277-293.

Ioku M., Ribera V. A., Cooper I. S. and Matsuoka S. (1965): Parkinsonism: Electromyographic studies of monosynaptic reflex. Science. 150:1472-1475.

Ioku M. (1968): H reflex elicited by tetanization in hand muscle. Electromyogr. 8:305-310.

Ioku M., Nakatani S. and Oku Y. (1969): H reflex study with high frequency stimulation. Electromyogr. 9:219-227.

Ioku M., Ogawa M. and Jinnai D. (1971): Studies on facilitation of the H reflex in spasticity and rigidity. Electromyography. 11:11-23.

Isaacs E. R., Szumski A. J. and Suter C. (1968): Central and peripheral influences on the H reflex in normal man. Neurology (Minneap). 18:907-914.

Ishikawa K., Ott K., Porter R. W. and Stuart D. (1966): Low frequency depression of the H-wave in normal and spinal man. Exp. Neurology. 15:140-156.

Jefferson A. and Benson A. (1953): Some effects of post-tetanic potentiation of monosynaptic response of spinal cord of cat. J. Neurophysiol. 16:381-396.

Johns R., Grob D. and harvey M. (1957): Electromyographic study of a spinal cord reflex in the normal human arm. Bull. Johns Hopkins Hosp. 101:232-239.

Johnson E.W., Burkhart J. A. and Earl W. C. (1972): Electromyography in post laminectomy patients. Arch. Phys. Med. Rehabil. 53:407-409.

Johnson, E. W., Radecki P. L. and Paulson G. W. (1977): Huntington Disease: Early identification by H reflex testing. Arch. Phys. Med. Rehabil. 58:162-166.

Johnson T. L., Sax D. S. and Feldham R. G. (1974): A technique for feature extraction and interpatient comparison of H reflex conditioning curves. Electro-enceph. Clin. Neurophysiol. 37:188-190.

Jun Tanji and Kotaro T. (1976): Presetting of excitability of the spinal la inhibitory pathway in relation to the direction of an intended movement. Neurosciences Letters. 3:321-327.

Kalow W. (1973): Genes controlling drug action in man: Pharmacology and the future of man. Proc. 5th Int. Cong. Pharmacology, San Francisco, 1972, 1972. 3:2-16. (Karger and Basel 1973).

Kaneko Z., Matsumoto K., Shimizu A. and Sumitsuji N. (1966): H reflex study on graphospasm. Electromyogr. 6:45-53.

Katz R., Morin C., Pierrot-Deseilligny E. and Hibino R. (1977): Conditioning of H reflex by a preceding sub-threshold tendon reflex stimulus. J. Neurol. Neurosurg. and Psychiatr. 40:575-580.

Kidokoro Y., Kubota K. and Shuto S. (1968): Reflex organization of cat masticatory muscles. J. Neurophysiol. 31:695-708.

Knutsson E. (1961): Effects of ethanol on the membrane potential and membrane resistance of frog muscle fibers. Acta Physiol. Scan. 52:242-253.

Krnjevic K. and Miledi R. (1958): Failure of neuromuscular propagation in rats. J. Physiol. 140:440-461.

Kurihara T. and Brooks J. (1975): The mechanism of neuro-muscular fatigue. Arch. Neurol. 32:168.

Landau W. M. (1953): Automatic responses medicated via the corticospinal tract. J. Neurophysiol. 16:299-311.

Landau W. and Clare M. (1964): Fusimotor function vi: H reflex, tendon jerk and reinforcement in hemiplegia. Arch. Neurol. (Chic.) 10:128-134.

Languth H. W., Teasdall R. D. and Magladery J. W. (1952): Electrophysiological studies of reflex activity in patients with lesions of the nervous system: Motoneurone excitability following afferent nerve volleys in patient with rostrally adjacent spinal cord damage. Bull. Johns Hopkins Hosp. 91:257-266.

Liberson W. T. (1962): Monosynaptic reflexes and their clinical significance. Electroenceph. Clin. Neurophysiol. Suppl. 22:79-89.

---------(1965): Experiment concerning receiprocal inhibition of antagonists excited by electrical-stimulation of agonists in a normal individual. Am. J. Phys. Med. 44:306-308.

---------, Chen L. Y., Fok S. K., Patel K. K., Yu G. H. and Fried P. (1975): H reflexes and F waves in hemiplegics. Arch. Phys. Med. Rehabil. 56:551.

Lloyd P. C., Hunt C. C. and Mcintyre A. K. (1955): Transmission in fractionated monosynaptic spinal reflex systems. J. Gen. Physiol. 38:307-317.

Low M. D., Basmajian J. V. and Lyons G. M. (1962): Conduction velocity and residual latency in human ulnar nerve and effects on them of ethyl alcohol. Am. J. Med. Sci. 244:720-730.

Lundberg A. (1975): Control of spinal mechanisms from the brain. 'The Nervous System' - Donald B. Tower. Vol. 1: The Basic Neurosciences. Raven Press 1975. p. 253-265.

Luttgau C. H. (1965): The effect of metabolic inhibitors on the fatigue of the action potential of single muscle fibers. J. Physiol. 178:45-67.

Madkour O. and Jacobsen W. (1967): H and F reflexes in man. Electroenceph. Clin. Neurophysiol. 23:391.

Magladery J., Teasdall R., Park A. and Languth H. (1952): Electrophysiological studies of reflex activity in patients with lesions of the nervous system. 1. A comparison of spinal motoneurone excitability following afferent nerve volleys in normal person and patients with upper motoneurone lesion. Bull. Johns Hopk. Hosp. 91:219-244.

--------- and McDougal D. B. (1950): Electrophysiological studies of nerve reflex activity in normal man. 1. Identification of certain reflexes in electromyogram and conduction velocity of peripheral nerve fibers. Bull. Johns Hopkins Hosp. 86:265-290.

Magladery J. W. (1955): Some observations on spinal reflexes in man. Pflugers Arch. Ges. Physiol. 261:302-321.

Malcolm D. S. (1951): A method of measuring reflex time applied in sciatica and other conditions due to nerve root compression. J. Neurol. Neurosurg. Psychiatr. 14:15.

Malouin F. and Simard T. (1978): Vibration influence on control of single motor unit activity. Arch. Phys. Med. Rehabil. 59:144-151.

Mark R. F. (1963): Tonic stretch reflexes in the calf muscles of normal human subjects. Nature (Lond). 199:50-52.

Marinacci A. (1966): Electromyogram in the elevation of lumbar herniated disc. Electromyogram. 6:25.

Martinez A. C., Conde P. and Ferrer M. T. (1977): Motor conduction velocity and H reflex in infancy and childhood - study in newborns, twins and small-for-dates. Electromyogr. Clin. Neurophysiol. 17:493-505.

Masland W. S. and Tucson A. (1972): Facilitation during the H reflex recovery cycle. Arch. Neurol. (Chic.) 26:313-319.

Matsuoka S., Waltz J. M., Terada C., Ikeda T. and Cooper I. S. (1966): A computer technique for evaluation of recovery cycle of the H reflex in the abnormal movement disorders. Electroenceph. Clin. Neurophysiol. 21:496-500.

Matthews P. B. and Rushworth G. (1957a): The selective effect of procaine on the stretch reflex and tendon jerk of soleus muscle when applied to its nerve. J. Physiol. (Lond). 135:245-262.

Matthews W. B. (1966): Ratio of maximum H reflex to maximum M response as a measure of spasticity. J. Neurol. Neurosurg. Psychiat. 29:201-204.

Matthews W. B. (1968): Introduction to clinical Neurology. The Williams and Wilkins Company, Baltimore. 1968.

--------(1970): Clinical implications of H reflex and of other electrically induced reflexes. In: Modern Trends in Neurology - 5th Ed. D. Williams Lond. Butterworths.

Mawdsley C. and Mayer R. F. (1965): Nerve conduction in alcoholic neuropathy. Brain. 88:335-356.

Mayer R. (1963): Nerve conduction studies in man. Neurology (Minneap) 13:1021-1030.

----------and Mawdsley C. (1965): Studies in man and cat of the significance of the H wave. J. Neurol. Neurosurg. Psychiat. 28:201-211.

----------and Feldman R. G. (1967): Observations on nature of F wave in man. Neurology. 17:147-156.

----------and Mosser R. S. (1973): Maturation of human reflexes. New Developments Edited by Desmedt J. E. 3:294-307. (Karger, Basel 1973).

McIntyre A. K. and Robinson R. G. (1959): Pathway for the jaw-jerk in man. Brain. 82:468-474.

McLeod J. G. and Van der Meulen J. P. (1967): Effect of cerebellar ablation on the H reflex in the cat. Arch. Neurol. 16:421-432.

----------(1969): H reflex studies in patients with cerebellar disorders. J. Neurol. Neurosurg. Psychiatr. 32:21-27.

----------(1972): H reflex studies in patients with Parkinson's disease. J. Neurol. Neurosurg. Psychiat. 35:77-80.

Meinck H. M. (1976): Occurrence of the H reflex and F wave in the rat. Electroenceph. Clin. Neurophysiol. 41:530-533.

Merton P. (1954): Voluntary strength and fatigue. J. Physiol. 123:553-564.

Mongia S. K. (1972): Significance of certain evoked responses in neurogenic disorders, Electroenceph. Clin. Neurophysiol. 33:236.

-----------(1972): H reflex from quadriceps and gastocnemius muscles. Electromyography. 12:179-190.

Morin C. and Pierrot-Deseilligny E. (1977): Role of la afferents in the soleus motoneurones inhibition during tibialis anterior voluntary contractions in man. Exp. Brain Res. 27:509-522.

Morris F., Penn R. D. (1978): Evidence for changes in segmental motoneurone pools by chronic cerebellar stimulation and its clinical significance. J. Neurol. Neurosurg. Psychiatr. 41:630-633.

Mountcastle V. B. (1968): Pain and temperature sensibilities. In: Medical Physiology Vol. II. 12th Edition. Edited by Mountcastle V. B. The C. V. Mosby Company. p. 1424-1460.

Murakami M. (1971): Evoked EMG (M and H wave) in rat. Cited In: Meinck H. M. (1976): Occurrence of the H reflex and the F wave in the rat. Electroenceph. Clin. Neurophysiol. 41:530-533.

Nathanson J. A. (1977): Cyclic nucleotides and nervous system function. Physiol. Reviews. 57:157-265.

Notermans S. L. and Vingerhoets H. M. (1974): The importance of the Hoffmann reflex in the diagnosis of the lumbar root lesions. Clin. Neurol. and Neurosurg. 77:54-65.

Okada K. and Adachi M. (1962): Effects of ethyl alcohol on the endplate potential. J. Physiol. Soc. Japan. 23:255-664.

Oku Y. (1973): Studies on the H reflex induced from human hand muscles. Electromyogr. Clin. Neurophysiol. 13:403-431.

Otsuka M., Endo M. and Monomura Y. (1962): Presynaptic nature of neuromuscular depression. Jap. J. Physiol. 12:573-584.

Paillard J. (1955): Cited In: Rossignol S. and Jones, M. G. (1976). Electroenceph. Clin. Neurophysiol. 41:83-92.

----------(1959): Functional organization of afferent innervation of muscle studied in man by monosynaptic testing. Amer. J. Phys. Med. 38:239-247.

Peiris O. A., Miles D. W. and Anderson W. N. (1966): The action of ethyl alcohol on the peripheral nerves. Am. J. Med. Sci. 251:207-210.

Pierrot-Deseilligny E., Bussel B., Held J. P. and Katz R. (1976): Excitability of human motoneurones after discharge in a conditioning reflex. Electroenceph. Clin. Neurophysiol. 40:279-287.

Rabending G. and Koch R. D. (1962): Influence of amplitude of monosynaptic reflexes on the duration of the silent period. In: Progress in EMG Electroenceph. and Clin. Neurophysiol. Suppl No. 22:120-121.

Rabending G. (1967): Variations of proprioceptive reflex excitability during clinical absences (seizures) and at the beginning of photosensitive centrencephalic grand mal. Electroenceph. Clin. Neurophysiol. 23:387-388.

Renshaw (1941): Cited In: Gottlieb G. L. and Agarwal G. C. (1976): Extinction of the Hoffmann reflex by antidromic conduction. Electroenceph. Clin. Neurophysiol. 41:19-24.

Romanul F. C. (1965): Capillary supply and metabolism of muscle fibers. Arch. Neurol. 12:497-509.

Rossignol S. and Jones G. M. (1976): Audiospinal influence in man studied by the H reflex and its possible role on rhythmic movements synchronised to sound. Electroenceph. Clin. Neurophysiol. 41:83-92.

Roth G. and Baer S. (1975): Reflex H Heteronyme et unidirectionnel Thenarien Chez L'Homme. Electromyogr. Clin. Neurophysiol. 15:503-521.

Sachdev K. S., Rana P. K., Dave K. C. and Joseph A. D. (1964): A study of the mechanism of action of the potentiation by aliphatic alcohols of the acetyl-choline response on the frog's rectus abdominis. Arch. Intern. Pharmacodyn. Therap. 152:408-415.

Sax D. S., Johnson T. L. and Feldman R. G. (1976): Computerized study of H reflex recovery curves in Parkinson's disease: Effect of L-Dopa. Arch. Phys. Med. Rehabil. 57:604.

Schuchmann J. A. (1976): H reflex latency in the evaluation of radiculopathy. Arch. Phys. Med. Rehabil. 57:560.

Schuchmann J. A. (1978): H reflex latency in radiculopathy. Arch. Phys. Med. Rehabil. 59:185-187.

Siça, R. E., Comas A. J. and Upton A. R. (1971): Impaired potentiation of H reflexes in patients with upper motoneurone lesions. J. Neurol. Neurosurg. Psychiat. 34:712-717.

Simoyama M. and Tanaka R. (1974): Reciprocal la inhibition at the onset of voluntary movements in man. Brain Res. 82:334-337.

Singh N., Bhatia H. and Singh B. (1971): Study of H reflex in muscular dystrophy. Electromyography. 11:379-387.

Shashami Manik (1977): Influence of visual input on monosynaptic reflex. Electromyogr. Clin. Neurophysiol. 17:3-11.

Shea P. A., Woods W. W. and Werden D. H. (1950): Electromyography in diagnosis of nerve root compression syndrome. Arch. Neurol. Psychiat. 64:93.

Shimizu A., Yamada Y., Yamoto J., Fujiki A. and Kaneko Z. (1966): Pathways of descending influence on H reflex during sleep. Electroenceph. Clin. Neurophysiol. 20:337-347.

Sobue I: Cited In: Kaneko Z., Matsumoto K., Shimizu A. and Sumitsuji N. (1966): H reflex study in graphospasm. Electromyography. 6:45:45-53.

Somerville J. and Ashby P. (1978): Hemiplegic spasticity: Neurophysiologic studies. Arch. Phys. Med. Rehabil. 59:592-596.

Stephens J. A. and Taylor A. (1972): Fatigue maintained voluntary contraction in man. J. Physiol. (Lond). 220:1-18.

Stephens J. A., Gerlach R. L., Reinking R. M. and Stuart D. G. (1973): Fatigability of medial gastrocnemius motor units in the cat. In: Control of Posture and Locomotion Vol. 7 Edited by Stein R. B., Pearson K. G., Smith R. S. and Redford J. B. Plenum Press. N.Y. 1973. p. 179-185.

Stoupel N. and Monseu G. (1967): Hoffman's reflex in children with cerebral palsy. Electroenceph. Clin. Neurophysiol. 22:391.

Szentagothai J. (1948): Anatomical considerations of monosynaptic reflex arcs. J. Neurophysiol. 11:445-454.

Taborikova H. (1966): Fraction of the motoneurone pool activated in the monosynaptic H reflexes in man. Nature (Lond). 209:206-207.

----------, Provini L. and Decandia M. (1966): Evidence that muscle stretch evokes long-loop reflexes from higher centers. Brain Res. 2:192-194.

------------and Sax D. S. (1968): Motoneurone pool of the H reflex. J. Neurol. Neurosurg. Psychiat. 31:354-361.

------------(1969): Conditioning of H reflexes by a preceding subthreshold H reflex stimulus. Brain. 92:203-212.

------------(1973): Supraspinal influences on H reflex. New Dev. in EMG and Clin. Neurophysiol. 3:328-335. Edited by Desmedt J. (Karger Basel 1973).

Takamori M. (1967): H reflex study in upper motoneurone diseases. Neurology. 17:32-40.

Teasdall R. D., Park A. M., Languth H. W. and Magladery W. (1952): Electrophysiological studies of reflex activity in patients with lesions of the nervous system. Bull. Johns Hopk. Hosp. 91:245-256.

Thomas J. E. and Lambert E. W. (1960): Ulnar nerve conduction velocity and H reflex in infants and children. J. Appl. Physiol. 15:1-9.

Tobin W. (1969): Monosynaptic reflexes (H reflex) and motoneurone excitability in man. Dev. Med. Child Neurol. 11:193-197.

Topliss J. G. (1970): Xanthines: In: Medical Chemistry. Third Edition, Part II. Edited by Alfred Burger. Wiley Interscience, New York. 1970. p. 892.

Triggle D. J. (1970): Adrenergic hormones and drugs. In: Medical Chemistry. Third Edition, Part II. Edited by Alfred Burger. Wiley Interscience, New York. 1970. p. 1273.

Trontel J. V. (1968): H reflex of single motoneurone in man. Nature (Lond). 220:1043-1044.

-------------(1973): A study of the H reflex by single fibre EMG J. Neurol. Neurosurg. Psychiat. 36:951-595.

Upton A. R., Sica R. E. and McComas A. J. (1972): Potentiated H reflexes in healthy and hemiplegic subjects. Electromyography. 12:63-70.

Van Der Meulen J. P. and Gilman S. (1965): Recovery of muscle spindle activity in cats after cerebellar ablation. J. Neurophysiol. 28:943-957.

Vane J. R. (1972): Prostaglandins and aspirin-like drugs: Pharmacology and the future of man. Proc. 5th International Congr. Pharmacology, San Francisco. 5:352-378. (Karger Basel 1973).

Veale J. L. and Rees S. (1973): Renshaw cell activity in man. J. Neurol. Neurosurg. Psychiatr. 36:674-683.

Wallgren H. and Barry H. III (1970): Actions of alcohol. Vol. I. Elsevier Publishing Company, New York. p. 209-273.

Walsh J. and McLeod J. (1970): Alcoholic neuropathy - An electrophysiological and histological study. J. Neurol. Science. 10:457-469.

Weber R. J. and Piero D. L. (1978): F wave evaluation of thoracic outlet syndrome: Multiple regression derived F wave latency predicting technique. Arch. Phys. Med. Rehabil. 59:464-469.

Weaver R., Landau W. and Higgins J. (1963): Fusimotor function. Part 2: Evidence of fusimotor depression in human spinal shock. Arch. Neurol. (Chic). 9:127-132.

Willer J. C. and Dehen H. (1977): The H reflex in the extensor digitorum brevis muscle: A study in latent alcoholic neuropathy. Electroenceph. Clin. Neurophysiol. 42:205-212.

Wilson A., Schild H., Modell W. (1975): Applied pharmacology. 11th edition. churchill Livingstone 1975. pp. 336-337.

-------------(1977): Respective importance of different electrophysiological parameters in alcoholic neuropathy. J. Neurological Sciences. 33:387-396.

Yap C. B. (1967): Spinal segmental and long loop reflexes on spinal motoneurone excitability in spasticity and rigidity. Brain. 90:887-895.

Zander Olsen P. and Diamantopoulos E. (1967): Excitability of ~~spinal motor neurones in normal subjects and patients with~~ spasticity, Parkinsonian rigidity, and cerebellar hypotonia. J. Neurol. Neurosurg. Psychiat. 30:325-331.