Study of the efficacy of the Distribution of F-latency (DFL) in the diagnosis of cervical spondylosis

A dissertation submitted as a partial fulfilment of the requirements of the degree of M.Phil in Biomedical Physics & Technology under the University of Dhaka

Ehsan Alam Chowdhury

Registration no. 257
Session: 2009- 2010
Department of Biomedical Physics & Technology
University of Dhaka Bangladesh
August 2013

DECLARATION

This thesis entitled ***"Study of the efficacy of the Distribution of F-latency (DFL) in the diagnosis of cervical spondylosis"*** is an original work carried out by me under the supervision of Professor K Siddique-e Rabbani of the Department of Biomedical Physics & Technology, University of Dhaka, Bangladesh. I further declare that this thesis has been completed by myself and no part of it has been submitted anywhere else in any form for any academic degree.

Ehsan Alam Chowdhury

Candidate for M.Phil.

Registration No. 257

Session 2009 -10

Department of Biomedical Physics & Technology

University of Dhaka, Bangladesh

August 2013

DECLARATION

I hereby certify that the present work entitled *"**Study of the efficacy of the Distribution of F-latency (DFL) in the diagnosis of cervical spondylosis***" is an original research work being submitted by Ehsan Alam Chowdhury as a thesis for the award of the degree of Master of Philosophy. He conducted these studies under my close supervision at the Department of Biomedical Physics & Technology, University of Dhaka, Bangladesh.

To the best of my knowledge the work embodied in this thesis or any part thereof has not been submitted anywhere in any form for any academic degree.

Dr. Khondkar Siddique–e Rabbani

(Supervisor)

Professor and Chairperson

Department of Biomedical Physics & Technology

University of Dhaka, Bangladesh

August 2013

ACKNOWLEDGEMENT

I express my heartiest gratitude and indebtedness to my supervisor Dr. Khondkar Siddique-e-Rabbani, Professor and Chairperson of Department of Biomedical Physics,and Technology University of Dhaka. The new method of DFL was his conception. His constant encouragement is the foundation of this study.

I express my sincere gratitude to Dr Md Zakir Husain of Square Hospital, Dhaka who painstakingly studied and compiled all the MRI results, which was vital to this study.

I would also like to thank Mr. Abdus Salam, Technical Assistant, BIBEAT, for his sincere help in carrying out the DFL tests on the subjects.

I would like to convey thanks to my junior colleagues and all the members of my Department all of whom had volunteered to become subjects of this study.

Above all, I remember and thank Almighty Allah for His Grace, without which I could not have completed this thesis work successfully.

ABSTRACT

Distribution of F-Latency (DFL) is a new parameter in peripheral nerve conduction measurement initiated by our extended group in Dhaka University which has been established to give a Distribution of Conduction Velocity (DCV) of motor nerve fibres in a peripheral nerve trunk as its approximate mirror image. An important application of this new technique, developed by the same group, is the detection of Cervical Spondylotic Neuropathy at an early stage through an evaluation of the pattern of DFL. Typically a single sharp peak corresponds to normalcy while double peak or a broad peak represents pathology. The definition of a broad peak was formalised through an earlier study by the extended group in collaboration with a group in Singapore. The current study is an exercise in validating DFL as a screening tool for CSN by comparing the data obtained from an extended pool of subjects (62 median nerves of 31 persons) against corresponding MRI findings through a double blind study. Subject selection was done randomly to fall under two age groups: 20 to 50 yrs, and above 50 yrs. A 1.5 Tesla MRI scanner and a home built Computerised EMG equipment were used for this study.

The data were analysed with two slightly different approaches. In one, a mild compression of the spinal cord or a nerve root, as assessed through MRI, was counted as negative for CSN. In the other, the same was counted as positive. The sensitivities thus calculated for both the age groups combined (62 nerves) were 82% and 78% respectively while the specificities were 28% and 50% respectively. This suggested the consideration of abnormality for mild compression. Based on this, analyses for the lower age group (20-50 yrs, 44 nerves of 22 subjects) gave a sensitivity of 73% and a specificity of 50% while for the higher age group (>50 yrs, 18 nerves of 9 subjects), the sensitivity was 89%. The specificity could not be determined for this group as none came out as true negative and false positive.

A surprising find of this study was the high prevalence (91%) of CSN in the younger age group, based on the MRI results, which needs further epidemiologic study.

The present study establishes DFL on a stronger footing for assessment of cervical spondylotic neuropathy, whether due to spinal cord or nerve root compression. With further development, the performance is expected to improve making it more effective. . Being a non-invasive technique requiring virtually zero expenditure in consumables, it promises greater access to patients, and could be used for extensive prevalence study. The capability of DFL in detecting subclinical stages of CSN holds a promise as an awareness development tool alongside screening for prevalence of neuropathy. Those individuals who are diagnosed as positive for CSN and are still asymptomatic could be persuaded to make changes of lifestyle to lessen the chance of progression of their health condition. The main conclusion of the work is that DFL can not only be a cost effective screening test for CSN but also be instrumental in building awareness about preventive lifestyles in the general population (both young and old). The favourable results obtained here inspire confidence that this technique would prove its robustness and over time gain widespread acceptance.

Contents

CHAPTER 1

INTRODUCTION

Distribution of F-Latency (DFL) is a new parameter in peripheral nerve conduction measurement initiated by our extended group in Dhaka University which has been established to give a distribution of Conduction Velocity(DCV) of motor nerve fibres in a peripheral nerve trunkas its approximate mirror image (Rabbani et al 2007).To determine DCV experimentally an alternative method and its few variations exist which are based on collisions of two nerve action potentials generated through two stimulators with varying time delay. However, these methods (Hopf 1962, Ingram 1987, Haryama et al 1991) are complex and conceptually prone to error (Rabbani et al 2007). Through earlier work it was indicated that DFL obtained from the median nerve has a single peak for normal subjects while a double or a triple peak is demonstrated for subjects having cervical spondylosis (Alam and Rabbani 2010). Hypotheses were put forward in terms of segmental lesions in a nerve trunk, caused by both radiculopathy and myelopathy (Rabbani 2011). Broad peaks were hypothesized to represent early cervical spondylosis. Of course, partial nerve injuries also appeared to cause double peaks, therefore, in the assessment of cervical spondylosis, cases with injuries near the nerve were avoided.

Extensive laboratory and clinical testing of DFL has firmly established that the test results are very consistent and repeatable on the same subjects (Rabbani et al 2007). This indicates that it is potentially very suitable as a clinical test. Ithas been possible to detect subclinical cases of cervical spondylosiswhere the patients did not have any complain or symptoms to suggest the clinical condition but after a suggestion from DFL, X-ray or MRI revealed the presence of neuropathy (Hossain et al 2011). This justifies the expectation that DFL could be very useful as a screening test for cervical spondylotic neuropathy (CSN) without any history of nerve injury.

In the diagnosis of cervical spondylosis MRI is the standard investigation carried out. So we decided to do MRI investigation of the cervical spine of both symptomatic and asymptomatic subjects and then performed DFL investigation on the same subjects to draw a comparison.

DFL is muchless expensive and easier to perform than MRI. So the aim of the present work is to establish the efficacy of DFL as a screening test for CSN. In order to do so we have attempted to compare and correlate MRI of the cervical region with the DFL obtained from the Median nerve of many subjects.

In the present study we carried out a double blind trial where 60 median nerves on both sides of 30 subjects, chosen from two age groups: 25-50 yrs and 50 upwards, were assessed for CSN by both MRI and DFL separately; the results of each being kept hidden from the other. Some of the subjects had symptoms of neck pains and some had none. At the end of the study the results were combined to compare the agreement between the two methods. This study willallow us determine the quality of diagnosis or detection of CSN using this new method of DFL.We also plan to assess the cost effectiveness of this technique through ROC analysis in terms of sensitivity and specificity.The results will indicate whether DFL may be used as a screening test for cervical spondylotic neuropathy.

Chapter 2

NEURO-MUSCULAR SYSTEM

2.1 OVERVIEW

The Neuro-muscularsystem comprises of two slightly different systems – the nervous system and the muscular system.

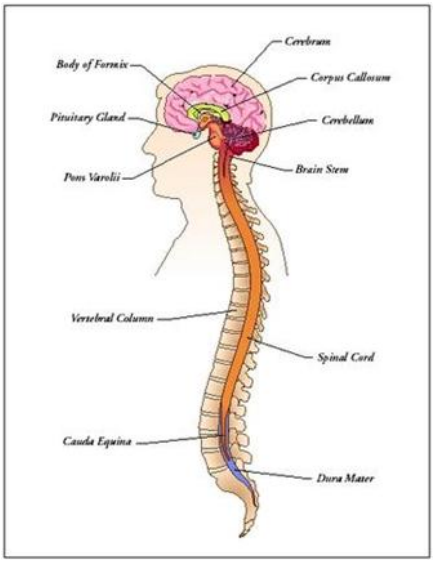

Fig 2.1: The central nervous system

The nervous system is the part of the information management of the human body. It coordinates the many systems which make up a complex organism into a functional unit. This system forms the interface of an organism with its external environment allowing it to receive information and interpret it and then instruct the body to respond in an appropriate manner.At the same time it also continuously monitors the internal environment of the body and sends appropriate signals which maintain a state of dynamic equilibrium called homeostasis. The internal and external aspect of this control system is integrated to create a state of seamless coordination. The responses in the form of movement of some organs or limbs are performed by the muscular system.

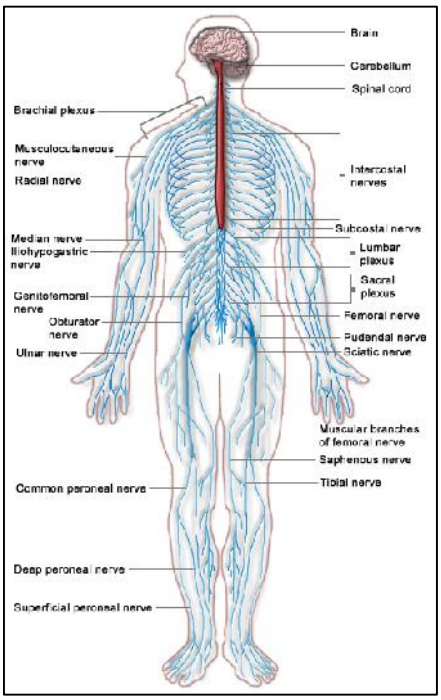

Fig 2.2: The peripheral nervous system

The nervous system is divided into two parts - the central nervous system and the peripheral nervous system. The central nervous system consists of the brain and the spinal cordas shown in Fig 2.1while the peripheral nervous system is composed of the cranial and spinal nerves and their associated ganglia as indicated in Fig 2.2.

The central and peripheral parts each have somatic and autonomic components. The somatic nerves mainly deal with structures which are under

conscious voluntary control, for example the skeletal muscles. While the autonomic nerves mainly are concerned with processes which are beyond the consciousness such as the various internal organs. Thesomatic components are concerned with the transmission of sensory information along afferent pathways(or sensory nerves) and the innervation of skeletal muscles along efferent pathways(or motor nerves). The autonomic components are concerned with the control of cardiac muscle, smooth muscle and glands (also involving afferent and efferent pathways). The brain receives signals from all parts of the body through the sensory nerves and integrates them and then sends out responses through appropriate motor signals to appropriate muscles and internal organs.

The three basic functions performed by the nervous systemsmay be summarized as follows.

1. Receive sensory input from internal and external environments
2. Integrate the input
3. Respond to stimuli by giving out appropriate signals through the motor nerves

2.2 CENTRAL NERVOUS SYSTEM: BRAIN AND SPINAL CORD

The central nervous system (CNS) is the largest part of the nervous system, which comprises of the brain and the spinal cord. The brain is encapsulated within the skull and the spinal cord is at the center of the vertebral column. Developmentally the brain consists of the forebrain, midbrain and hindbrain (Fig 2.3). The forebrain is composed of the cerebrum and diencephalon. Cerebrum is the largest part of the brain, which is divided into left and right hemispheres connected to each other by the corpus callosum. The cerebral hemispheres are covered by a thin layer of gray matter, known as the cerebral cortex, each with a cavity named lateral ventricle. The deeper central portion of the forebrain is the diencephalon, whose main parts are the thalamus and hypothalamus and whose cavity is the third ventricle. The thalamus acts

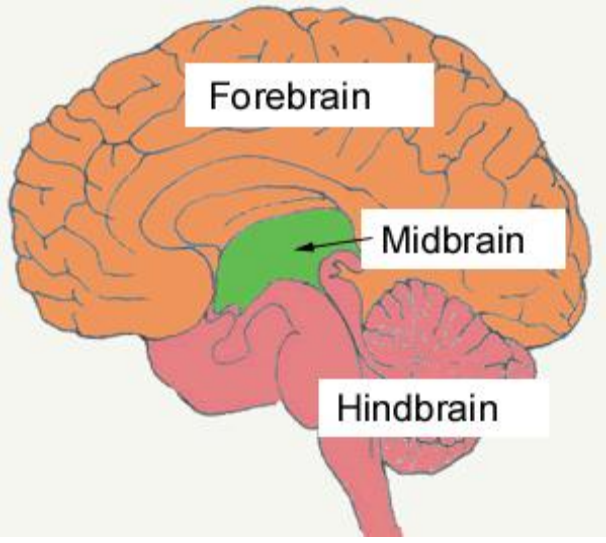

Figure 2.3.The parts of the Brain

as a central relay point for incoming nervous messages. The hypothalamus is a major homeostatic center having both nervous and endocrine functions. It has regulatory areas for thirst, hunger, body temperature, water balance and blood pressure.

The midbrain is a small region whose cavity is the aqueduct and which connects the forebrain with the hindbrain, consisting of the pons, medulla oblongata and cerebellum and whose cavity is the fourth ventricle. The midbrain, pons and medulla collectively form the brainstem, which is the oldest and most primitive part of the brain. The brainstem is continuous with the spinal cord, and is composed of the parts of the hindbrain and midbrain. The medulla oblongata and pons control heart rates, constriction of blood vessels, digestion and respiration. The cerebellum is the second largest part of the brain, after the cerebrum, which functions for motor coordination and body movement, posture and balance.

All parts of the brain are contained within the cranial cavity; the medulla passes through the foramen magnum of the skull and changes its name to spinal cord where the first cervical nerve roots emerge. Cerebrospinal fluid is produced by the choroid plexuses within the ventricles, which it fills; it exits through the midline and lateral apertures of the fourth ventricle to cover the surface of the brain and spinal cord.

The spinal cord and the nerve rootstraverse the spinal canal. The spinal cord is approximately 40- to 45-cm long in the adult and usually terminates at the L1-2 vertebral level. The dura matter, the pia matter and the arachnoid are the three membranes that cover the spinal cord. The spinal cord is suspended in the spinal canal by the dentate ligaments. These arise from the pia and are attached to the dura. Usually the spinal cord terminates approximately at the caudal aspect of the Lumbar 1 vertebral body. Anatomically, the spinal cord is divided into five sections: 8 cervical (C), 12 thoracic (T), 5 lumber (L), 5 sacral (S) and 1 coccygeal Figure: 2.4 shows a schematic of the spinal cord, indicating the relationship among spinal segments, nerves and vertebral bodies. .With the exception of the C1 and C2 contributions to the spinal accessory nerve, nerve roots leave the spinal canal via the neural foramina(opening), formed by bony processes of the vertebral segments. The caudaequinaat the lower part of the spinal canal consists of the nerve roots, which have not yet exited through their neural foramina.

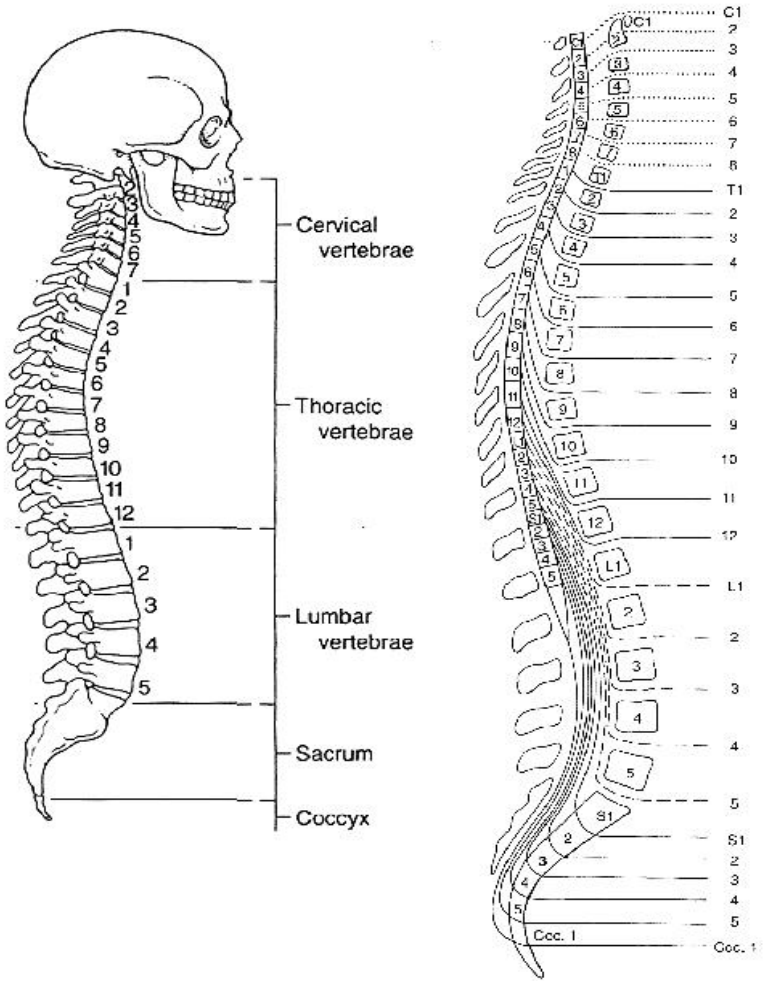

Fig 2.4: Schematic of the spinal cord, indicating the relationship among spinal segments, nerves and vertebral bodies.

2.3 PERIPHERAL NERVOUS SYSTEM

The peripheral nervous system (PNS) consists of the nerves emerging from the brain (called cranial nerves) and from the spinal cord (called spinal nerves) that exit the different vertebral levels. Spinal nerves are composed of a dorsal (backside) sensory root and a ventral (front side) motor rootwhich then mix up in certain ways to form the peripheral nerves. Throughout most of their length, many peripheral nerves are mixed, in that they contain both afferent and efferent fibers.

Two main components of the PNS are:

1. Sensory (afferent) pathwaysthat convey sensory information from the sense organs and sensory receptors in the organism inward to the CNS.
2. Motor (efferent) pathways that carry signals from the CNS outward to the muscles and glands of the body.

Most sensory input carried in the PNS remains below the level of conscious awareness. Input that does reach the conscious level contributes to perception of our external environment. Peripheral nerves leave the spinal cord at different levels, and the nerves that innervate a given level of body structures come from the same level of the spinal cord.

There are two major subdivisions of peripheral nervous system: somatic nervous system and autonomic nervous system. The somatic nervous system consists of those neural structures of the CNS and PNS responsible for 1) conveying and processing conscious and unconscious sensory (afferent) information, vision, pain, touch, and proprioceptive (positional) sense from the head, body wall, and extremities to the CNS and 2) motor (efferent) control of the voluntary (striated) muscles. Visual pathways carry sensory information from the eyes to the brain, whereas the auditory nervous system carries information from auditory sensors in the ears to the brain.

The autonomic nervous system is composed of the neural structures responsible for 1) conveying and processing sensory input from the visceral organs (e.g., digestive system and cardiovascular system) and 2) motor control of the involuntary (smooth) and cardiac musculature, and of glands of the viscera.The autonomic nervous system is composed of two main subsystems that appear to be somewhat antagonistic to each other. These are 1) sympathetic nervous system, which is involved in the fight or flight response and 2) parasympathetic nervous system, which is involved in relaxation. Both systems innervate the same organs and act in opposition to maintain homeostasis. For example, sympathetic nervous system speeds up the heart, causes secretion of some glands and the parasympathetic nervous system tends to slow the heart and controls contraction and secretion of stomach. In general the sympathetic nervous system tends to mobilize the body for emergencies, whereas the parasympathetic nervous system tends to conserve and store bodily resources.

2.3.1 Spinal Nerves

There are 31 pairs of spinal nerves: 8 cervical(C1 –C8), 12 thoracic(T1-T12), 5 lumbar(L1-L5), 5 sacral(S1-S5) and 1 coccygeal(CO1) as shown in Fig 2.4. Each spinal nerve is formed by the union of an anterior (ventral) and posterior (dorsal) root, which, in turn, are attached to the side of the spinal cord by little rootlets. The union takes place within the intervertebral foramen of the appropriate nerve, immediately distal to the swelling on the posterior root, the posterior root ganglion, which is also within the foramen. The anterior root of every spinal nerve contains motor (efferent) fibers for skeletal muscle; those from T1 to L2 inclusive and from S2 to S4 also contain autonomic fibers. The anterior root also contains a small number of unmyelinated afferent pain fibers which have 'doubled back' from their cells of origin in the posterior root ganglion to enter the spinal cord by the anterior root instead of by the posterior root. The posterior root of every nerve contains sensory (afferent) fibers whose cell bodies are in the posterior root ganglion. Immediately after its formation the spinal nerve divides into an anterior (front side) and a posterior (backside) ramus. The great nerve plexuses- cervical, brachial, lumbar and sacral-are formed from anterior rami; posterior rami do not form plexuses.

2.4BASIC STRUCTURAL UNIT OF NERVE SYSTEM

2.4.1 THE NEURON

2.4.1.1 Sensory neuron

The neuron is the functional unit of the nervous system;it can generate, send and receive electrochemical impulses. In other words it is excitable. The neuron has three parts – the cell body, dendritesand the axon (Fig: 2.5).

Cell body: It is the main part of a neuron which contains the nucleus.

Dendrites:These are processes(protrusions)of the cell body whichreceives information from other neurons or sensory endings. There may be

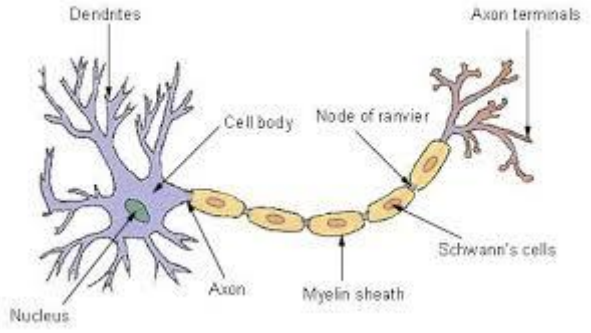

Figure 2.5 Diagram of a neuron

several dendrites from a cell body. Nervefibers are of two types depending on the direction in which the impulse is conducted with respect to the cell body. The axons conduct impulse away from the cell body and the dendrites conduct impulse towards the cell body. Sensory neurons have long dendrites and short axons and carry information from the sensory receptors to the central nervous system. Motor neurons conduct impulse to the muscles or glands and have long axons and short dendrites.

The axon: It is a single process which is variable in length, and conducts impulses away from the cell body. It terminates on other nerve cell bodies or target cells of different organs of the body like muscle cells

2.4.1.2 Motor neuron

With adequate stimulation the nerve cell body generates a signal or action potential which usually spreads outward along the axon to the target which may be muscle cells, glands or other neurons. The impulse usually originates in the cell bodyfor motor neurons. It may also be generated by stimulating axons and dendrites too,typicallythrough artificial means, and in such cases the signal can spread in both directions from the point of origin of the stimulus.

The nerve cell body contains the nucleus and all the usual organelles such as mitochondria Golgi apparatus endoplasmic reticulum and secretory vesicles etc. An axon is connected to the nerve cell body at the axon hillock, which has a role in the generation of the nerve impulses.

The axons and dendrites have specialized endings called synapseswhich serve to transmit the nerve impulse from one nerve to another or from the nerve to target organ through the release of neurotransmitters. These neurotransmitters transmit the signal by affecting the ion channels present on the membrane of the recipient structure. The axons of motor nerves end on muscle fibres in a similar structure called the motor end plate.

Neurons are embedded in a support structure of fibers and ground substance. There are also some cells which provide support nutrition and immune protection to the nerve cells though these cells (called glial cells) do not conduct nerve impulse.

Peripheral nerves (or nerve trunks) are composed of multiple nerve processes (both axons and Dendrites bundled together fascicles and bundles Some axons may be covered by a fatty

substance called Myelinin multiple segments, with gaps in between called nodes of Ranvier.When a nerve fiber has a myelin sheath, it conducts impulses much faster than non-myelinatedfibers.Myelinis generated by Schwann cells in the peripheral nervous system and Oligodendrocytes in the central nervous system,

2.4.1.3 Interneuron, Reflex arc

Interneurons connect adjacent neurons and typically form part of the reflex arc. An interneuron typically connects a sensory neuron to a peripheral motor neuron in the spinal cord. The reflex arc acts as a fast response mechanism by which the body rapidly responds to simple danger signals like sharp pain or loud sound or bright flash of light etc, which are generally interpreted as danger signals requiring the fastest possible response. The pathway of the reflex arc is shown in figure 2.6

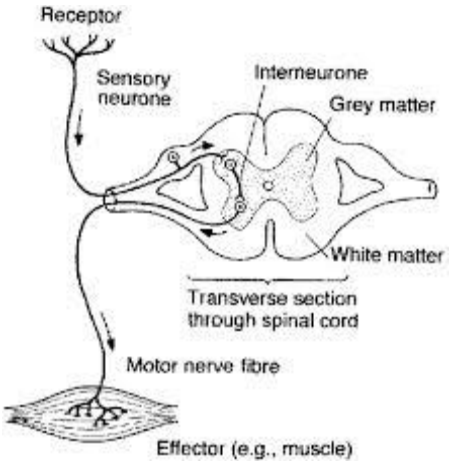

Figure 1.6 Cross section of spinal cord showing reflex arc

2.4.1.4Pathway from the Brain to the Periphery

Because our work involves only the peripheral nervous system we are not going to describe the central part of the nervous system in any detail and limit ourselvesto a general outline.

The motor pathway (Fig:2.7) consists of a relay of nerves comprising the upper motor neuron and the lower motor neuron. The upper motor neurons reside in the cortex of the brain from there the axons of these neurons converge on the brain stem and pass down the spinal cord to synapse with lower motor neurons in the anterior horns of the cord. The nerve cells in the anterior horns are the lower motor neurons which send axons to the various end organs

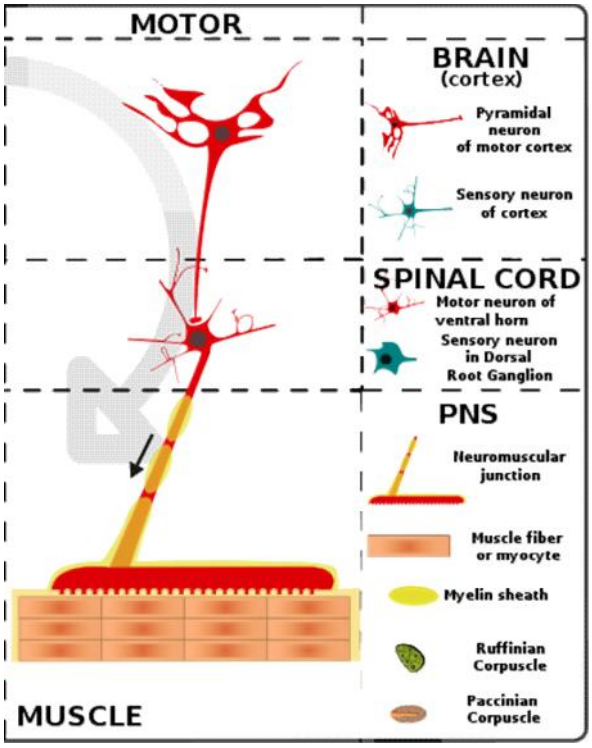

Figure 2.7 The motor pathway (outline)

and muscles. Near the end organs and muscles the axons branch into smaller processes. These processes innervate individual muscle cells via the motor end plate, the fibres innervated in this way collectively form the motor unit of the innervating nerve.

2.4.1.5NEUROMUSCULAR JUNCTION

As the axon supplying a skeletal muscle fiber approaches its termination, it loses its myelin sheath and divides into a number of terminal buttons or end-feet. The end-feet contain many small, clear vesicles that contain acetylcholine, the transmitter at these junctions. The endings fit into depressions in the motor end plate, the thickened portion of the muscle membrane of the junction. Underneath the nerve ending, the muscle membrane of the endplate is thrown into junctional folds. The space between the thickened muscle membrane is comparable to the synaptic cleft at synapses. The whole structure is known as the neuromuscular junction.

Thus the neuromuscular junction (fig 2.8) consists of the motor nerve ending, Schwann cell and muscle end plate. At the junction region between the nerve ending and end plate, Schwann cells are absent. Here the nerve ending forms a flattened plate lying within a surface depression of the end plate. This indentation of the muscle fiber, called synaptic gutter or a primary synaptic cleft, is about 20 to 50 nm deep. The thickened post synaptic membrane in this region has narrow infoldings called junctional folds or secondary clefts. A large number of mitochondria, nuclei and small granules accumulate close to the secondary clefts. Many mitochondria and synaptic vesicles also lie in the axon terminals, just proximal to the presynaptic membrane.

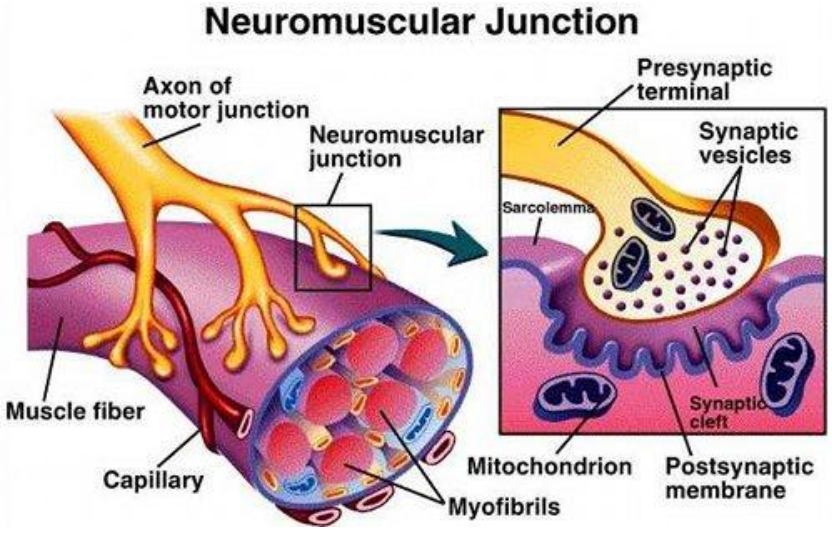

Figure 2.8The Neuromuscular junction

Only one nerve fiber ends on each endplate, with no convergence of multiple inputs. The transmission of signal from unmyelinatedmotor nerve end to muscle is electro-chemical in nature. The junction is approximately at the midpoint of the muscle fiber, so that the action potential in the muscle fiber travels in both directions.

As mentioned before, the motor nerve fiber loses the myelin sheath at the nerve terminals. Distal to the myelin sheath, therefore, only the Schwann cells separate the nerve terminals from the surrounding tissue.

2.5MUSCLE

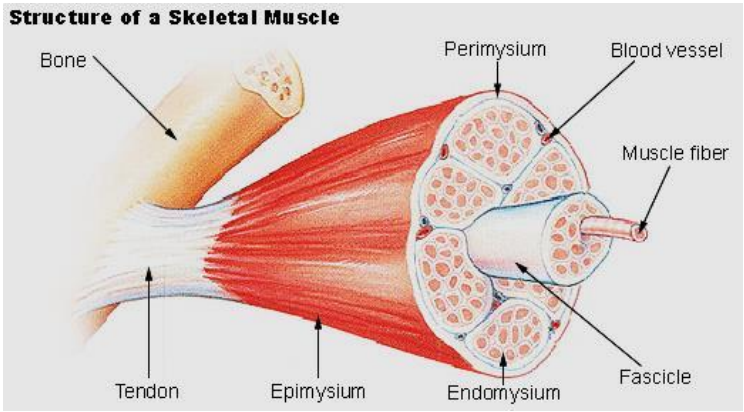

Figure 2.9 Cross section of muscle tissue

Muscle cells, like neurons, can be excited chemically, electrically, and mechanically to provide an action potential that is transmitted along their cell membrane. Unlike neurons, they have a contractile mechanism that is activated by the action potential. The contractile proteins actin and myosin are abundant in muscle, using whichthey bring about contraction.Muscle is generally divided into three types- skeletal, cardiac and smooth muscle. Skeletal muscle makes up the great mass of the somatic musculature. It has well-developed cross-striations, does not normally contract in the absence of nervous stimulation, lacks anatomic and functional connections between individual muscle fibers, and is generally under voluntary control. Cardiac muscle also has cross-striations, but it is functionally syncytial and contracts rhythmically in the absence of external innervation owing to the presence in the myocardium of pacemaker cells that discharge spontaneously. Smooth muscle lacks cross-striations, which are found in most hollow viscera and contains pacemakers that discharge irregularly.

A connective tissue called epimysium covers the surface of each muscle. Inside this sheath are many fascicles bound by the course sleeves of the connective tissue perimysium. Individual fascicles contain many muscle fibers, each surrounded by a delicate network of fine connective tissue, called endomysium(fig: 2.9). A muscle fiberhas a typical diameter of 10 μm in a newborn and 50 μm in an adult. Individual muscle fibers range from 2 to 12 cm in length, some extending entire length of the muscle and others only through a short segment of the total length.

The sarcolemma on the surface membrane of a muscle fiber contains multiple nuclei distributed beneath the thin sheath. The membrane has functional properties of excitability and conductivity similar to those of an axon. A myoelectric signal, originating from a neuromuscular junction, propagates in both the proximal and distal directions of a muscle fiber. The muscle fibers conduct considerably more slowly than nerve axons, with an estimated rate of 3 to 5 m/s.

2.6 THE SENSORY MOTOR REFLEX

The reflex mechanism(fig:2.10) is an involuntary and unconscious response which allows a person withdraw from the source of a painful stimulus very fast. The pathway involved in reflex mechanism bypasses the brain and starts at sensory nerve endings. The endings pick up the stimulus and send the signal to the spinal cord along sensory afferent nerves to the dorsal root of the spinal cord. Here the afferent nerve synapses with interneurons which relay the signal to adjacent lower motor neurons. These motor neurons pass the signal to muscles which contract and cause the body to withdraw from the source of the stimulus. There is no involvement of the brain in the action loop alerting signals pass to the conscious part of the brain after the action has already occurred.

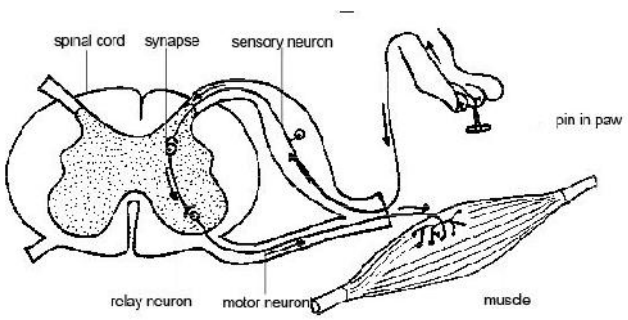

Figure 2.10: The reflex arc

2.7 ELECTRIAL PROPERTIES OF NERVE AND MUSCLE

The neuro-muscular system is used for all fast control functions of the body. The electrical potentials that the brain, nerves and muscles generate are not the result of activity but the cause of it. If we make the analogy between the brain and a computer then we have to consider the brain as a digital computer and not an analogue computer. The signals which travels down nerves are pulses of electricity whose repetition frequency changes but whose amplitude is constant. For example, if we wish to inform the brain that a more intense pain has been received, then it is not the amplitude of the electrical pulse which changes but it is the frequency. Similarly, in order to increase the contraction of a muscle, it is the frequency of impulses travelling down the efferent nerve, which is increased. Thus in carrying out the special functions of the body, many electrical signals are generated, which are the result of the electrochemical action of certain type of cells. Superficially it seems unlikely that the control of our muscles is digital because we make smooth graded actions rather than the twitches which would result from a digital system. However this smooth movement is achieved through branching out of each motor axon near the termination, where each branch connects to an individual muscle fibre, and through random delays at each of these neuromuscular junctions. Thus the contractions of individual muscle fibers overlap in time giving a smooth movement.

2.8 RESTING POTENTIAL

The origin of almost every electrical potential which arises within the body is a semipermeable membrane. A single nerve fibre or axon consists of a cylindrical semipermeable membrane surrounding an electrically conducting centre or axon. The membrane is called semipermeable because it is partially permeable to ions such as potassium (K^+) and sodium (Na^+), which can pass more freely in one direction through the membrane than the other. Due to such properties of the membrane the axoplasm inside the axon has a high concentration of potassium (K^+) ions and a low concentration of sodium (Na^+) ions, in contrast to the fluid outside

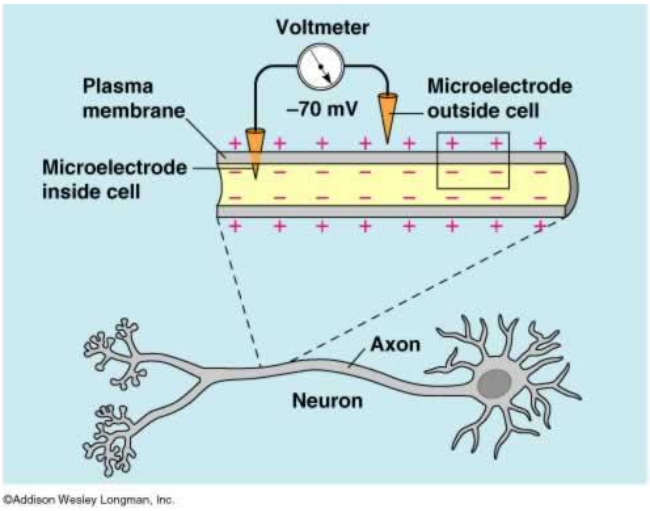

Figure 2.11 Resting membrane potential

the axon which has a low concentration of (K^+) ions and a high concentration of (Na^+)ions.Thisresults in a potential of about -100 mV between the inside and the outside of the fiber as shown in Fig. 2.11. The nerve is said to be polarized. This membrane potential in the polarized state is called the resting potential. The resting potential of most mammalian neurons is constant as long as the cell remains inactive due to lack of stimulation. The distribution of ions inside and outside a nerve axon is listed in Table 2.1. Although there are different ions present, Na^+ and K^+ contribute the most to the electrical action potentials.

Table 2.1: Ionic concentrations of extracellular and intracellular fluids in squid axon.
(Values given are approximations in mmol/kg H_2O, data from Hodgkin, 1958)

Ion	Extracellular Concentration(mmol)	Intracellular Concentration (mmol)
K^+	20	400
Na^+	460	50
Cl^-	560	100
A^-	0	370

Analyses of the intracellular fluid of the axon and the extracellular water bathing the axon showed that ionic electrochemical gradients exist. These electrochemical gradients are maintained by the active transport of ions against their electrochemical gradients in specific regions of the membrane by a sodium-potassium pump, which transports sodium ion out of the cell to the exterior and at the same time pumpspotassium ions from the outside to the inside. Here two K^+ ions are transferred for each three Na^+ ions by a carrier protein. The carrier protein has three receptor sites for binding sodium ions inside the cell and two receptor sites for potassium ions on the outside. When 3 Na^+ ions bind on the inside of the carrier protein and two K^+ ions on the outside, one molecule of ATP is released. The active transport of ions is opposed by the passive diffusion of ions, which constantly pass down their electrochemical gradients at a rate determined by the permeability of the axon membrane to the ion. K^+ ion has an ionic mobility and membrane permeability which is 20 times greater than that of Na^+ ion. This leads to a net loss of K^+ ions from the axon and the production of negative charge within the axon. The value of resting potential is largely determined by the K^+ electrochemical gradient. Changes in the permeability of the membrane of excitable cells to K^+ and Na^+ ions lead to changes in the

potential difference across the membrane and the formation of action potentials, which propagates along the axon.

2.9 ORIGIN OF ACTION POTENTIAL

Normally the membranes of the nerve cells are polarized in their resting state as mentioned above. Thesemembranes have a low threshold for excitation. The stimulus may be electrical, chemical, or mechanical.When stimulated electrically or by other means, the cell membrane undergoes an intensity-dependent depolarization. If the change reaches a critical thresholdlevel, it results in generation of an action potential, which then propagates across the membrane. This happens within the cell body as well as along any dendrites or axons.

When a section of the cell membrane is excited beyond the critical threshold, either by the flow of ionic current or by an externally supplied stimulus, the membrane characteristics change and begin to allow sodium ions to enter and potassium ions to leave the nerve axon. This causes the transmembrane potential to change, which in turn causes further changes in the properties of the membrane, accelerating this ion movement across the membrane. We can make an analogy by saying that the membrane resistance depends upon the voltage across it, while the voltage again depends on the membrane resistance, both acting in the same direction.

The movement of Na^+ ions into the cell constitutes an ionic current flow that further reduces the barrier of the membrane to Na^+ ions. The net result is an avalanche effect (rather like the effect of positive-feedback in an electronic circuit) in which Na^+ ions literally rush into the cell to try to reach a balance with the ions outside. At the same time K^+ ions, which were in higher concentration inside the cell during the resting state, try to leave the cell but are unable to move as rapidly as the Na^+ ions. As a result, the cell has a slightly positive potential on the inside due to the imbalance of K^+ ions.

When this potential is reversed it is known as the action potential and is approximately +60 mV. The cell, which has been excited and generates an action potential, is said to be depolarized, and the process of changing from the resting potential state to the action potential state, is called depolarization.

Depolarization is not a permanent state, because the properties of the semipermeable membrane change with time, so that, after a short time, the nerve fiber reverts to the polarized state. Once the rush of Na^+ ions through the cell membrane has stopped, a new state of equilibrium is reached. The ionic currents that lowered the barrier to Na^+ ions are no longer present and the membrane reverts back to its original selectively permeable state, in which the passage of Na^+ ions from the outside to the inside of the cell is again blocked. By an active process, called a sodium pump, the Na^+ ions are quickly transported to the outside of the cell, and the cell again becomes polarized and assumes its resting potential. The process is called repolarization. Although little is known about the exact chemical steps involved in the sodium pump, it is quite generally believed that sodium is withdrawn against both charge and concentration gradients supported by some form of high-energy phosphate compound derived from Adenosine Tri-Phosphate (ATP). This compound is composed of three phosphate compounds bound to adenosine and it breaks down into adenosine diphosphate and sometimes into adenosine monophosphate. This releases the energy needed to power the needed chemical reactions

The rate of pumping is directly proportional to the sodium concentration in the cell. The operation of the pump is also believed to be linked with the influx of potassium into the cell, as if a cyclic process involving an exchange of sodium for potassium existed. Regardless of the method by which a cell is excited or the intensity of the stimulus (provided it is sufficient to activate the cell), the action potential is always the same for any given cell. This is known as the all-or -nothing law. The net height of the action potential is defined as the difference between the potential of the depolarized membrane at the peak of action potential and the resting potential.

Following the generation of an action potential, there is a brief period of time, during which the cell cannot respond to any new stimulus. This period, called the absolute refractory period, lasts about 1 msec in nerve cells. Following the absolute refractory period, there occurs a relative refractory period, during which another action potential can be triggered, but a much stronger stimulation is required. In nerve cells, the relative refractory period lasts several milliseconds. These refractory periods are believed to be the result of after-potentials that follow an action potential.

2.10 PROPAGATION OF NERVE ACTION POTENTIAL

The mechanism for the propagation of a nerve action potential (NAP) is briefly described below. Because a nerve fiber is immersed in conducting fluids, ionic currents will flow around it from the polarized to the depolarized parts. Intracellular current flows from the positively charged active area to the adjacent negatively charged inactive region. An opposing current flows through the extracellular fluid from the inactive to the active region. This local current depolarizes the inactive regions on both sides of the active area. When it attains the critical level, an action potential generated there initiates a new local current further distally or proximally. These external currents are very important because they are the only external evidence that the action potential is present, which give rise to most of bioelectric signals, which can be recorded.

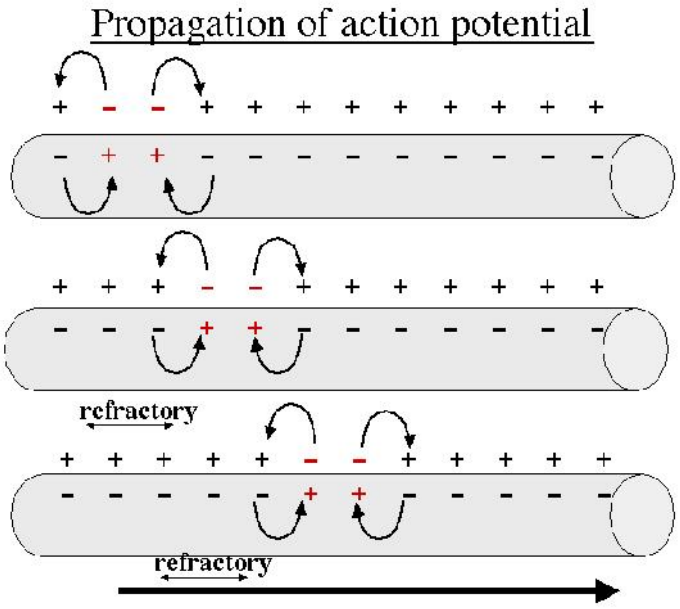

Figure 2.12 Sequence showing propagation of action potential

External current flow around a nerve fiber is also responsible for the transmission of an action potential along the nerve. The external current flow at the point of depolarization disturbs the transmembrane potential further along the fiber and this causes depolarization to spread (fig :2.12). An action potential is transmitted along a fiber with a speed of a few meters each second. It can be shown experimentally that external current flow is essential to the

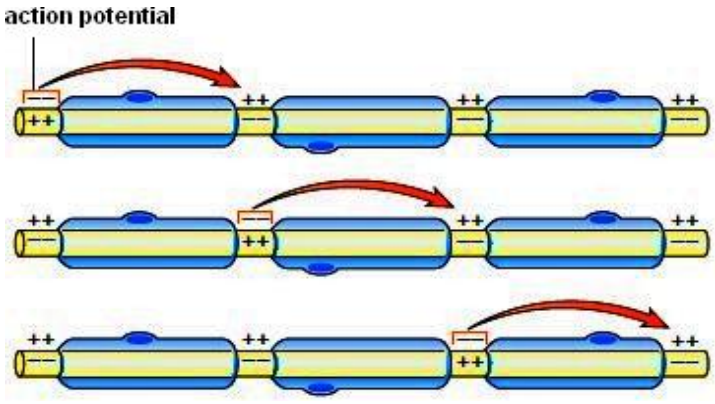

Figure 2.13 Saltatory conduction

transmission of action potentials by removing a single nerve fiber from the surrounding extracellular fluid; under these conditions an action potential does not propagate.

The nerve fiber is surrounded bya fatty insulating layer, called Myelin, which prevents current flowing from the nerve axon into the extracellular fluid, and if it were continuous along the nerve, then no action potentials would be possible. However, the myelin sheath is interrupted at regular intervals, called the nodes of Ranvier. External current can flow from the nodes of Ranvier and the effect of the myelin is to speed up the transmission of NAP which jumps from one node to the next as shown in figure 2.13. This process is called saltatory conduction and it allows action potentials to be transmitted at about ten times the speed at which the unmyelinatedfiber would conduct. For example, the fast nerve fibers which supply our muscles are myelinatedfiber, whereas the slow fibers used to transmit pain sensation are slow non-myelinatedfibers. The speed of transmission,or the conduction velocity (CV) of nerve impulse is actually determined by the capacitance of the membrane and myelin which separate the axon from the external fluid, and the resistance of the axon. Any resistance and capacitance has a time constant, which controls the rate at which the potential across the capacitor can change.

As mentioned above the nerve comes in two forms unmyelinated and myelinated. The myelin sheath acts as an insulator and has gaps called nodes of Ranvier where the gap is unmyelinated. In the myelinated segment the action potential gets attenuated but upon reaching the next gap the action potential gets restored to its original voltage. This process is repeated along the myelinated nerve and thus the signal appears to jump from one node to the next.

Two factors affect the propagation speed of a signal: the resistance within the core of the membrane and the capacitance across the membrane. A decrease in resistance or the capacitance will both increase the speed of conduction. The increase of the diameter of the nerve fibre decreases the resistance, so the axon with a larger diameter will have a higher speed of conduction than that of an axon with a smaller diameter.

The greater the charge stored in a membrane the longer it takes to depolarize it thus leading to a slower propagation speed. Because the capacitance of the myelinatedfiber is much smaller

compared to that on an ummyelinatedfiber of same diameter and length, the conduction speed of a myelinatedfiber is much faster. So the myelin sheath allows the nerve to conduct signals fast and at the same time be of a small diameter at the same time

2.10 CERVICAL AND BRACHIAL PLEXUSES

The anterior rami of the upper four cervical nerves, C-1 through C-4, form the cervical plexus. It innervates the lateral and anterior flexors of the head, which consist of the rectus capitislateralis, anterior longuscapitis, and anterior longuscolli. The brachial plexus, formed by the anterior rami of C-5 through T-1 spinal nerves, supply the muscles of the upper limbOccasional variations of innervation include the prefixed brachial plexus, with main contributions from C-4 through C-8, and the postfixed brachial plexus, derived primarily from C-6 through T-2. Topographic

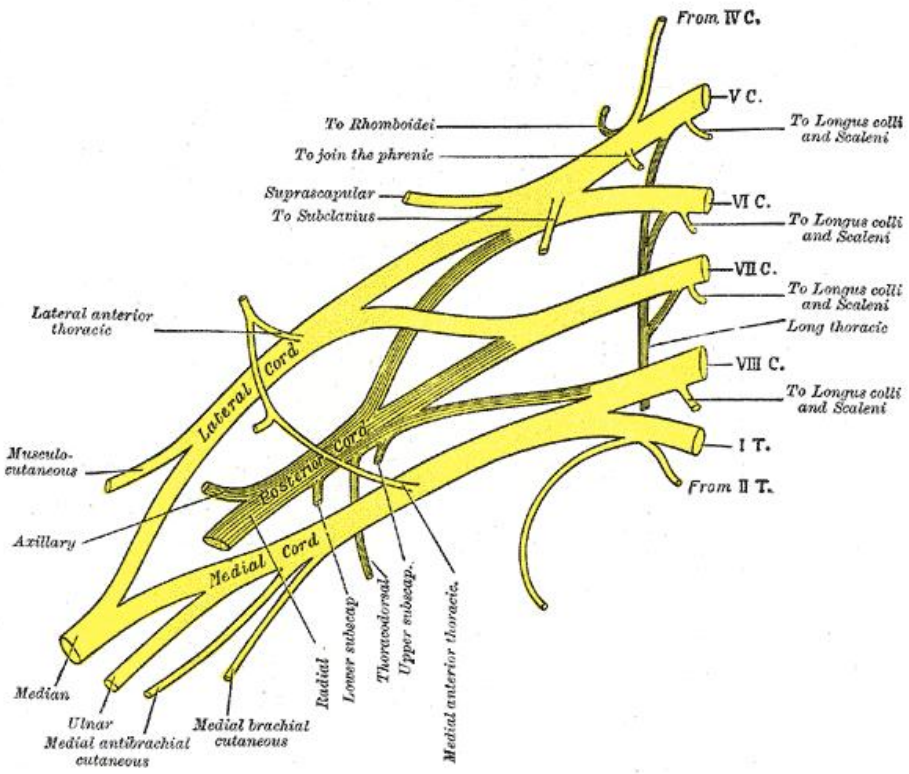

Figure 2.14 The Brachial Plezus

divisions of the brachial plexus include root, trunk, cord, and peripheral nervesandare shown in Fig:2.14. The roots combine to form three trunks, the union of C-5 and C-6 forms the upper trunk, and that of C-8 and T-1 roots, the lower trunks; whereas the C-7 root alone continues as

the middle trunk. Each of the three trunks divides into anterior and posterior divisions. The posterior cord,formed by the union of all three posterior divisions, gives off the axillary nerve at the axilla and continues as the radial nerve. The anterior divisions of the upper and middle trunks form the lateral cord, which gives rise to the musculocutaneous nerve and the outer branch of the median nerve. The anterior division of the lower trunk, forming the medial cord, gives off the ulnar nerve, the inner branch of the median nerve, and the cutaneous nerves. (Kimura 1989)

2.11MAJOR NERVES IN THE UPPER LIMB

2.11.1Median nerve

The median nerve runs relatively superficially in its entire course from the axilla to the palm (Fig: 2.15). The median nerve arises from the lateral and median cords of the brachial plexus as a mixed nerve derived from the C6 and T1 roots (Fig: 2.14). It supplies most forearm flexors and the muscles of the thenar eminence. It also subserves sensation to the skin over the lateral aspect

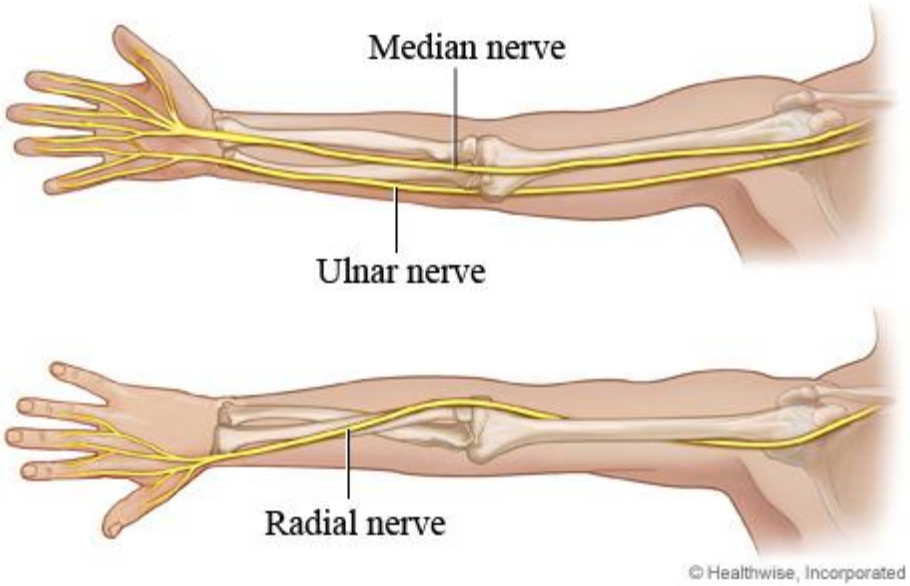

Figure 2.15 Median Ulnar and Radial nerves (HealthwiseInc)

of the palm and the dorsal surfaces of the terminal phalanges, along with the volar surfaces of the thumb, the index, and middle fingers, and half of the ring finger. The sensory fibers of the middle finger enter the C-7 root through the lateral cord and middle trunk, whereas the skin of the thumb and the index finger receives fibers from the C-6 or C-7 root through the lateral cord and upper or middle trunk. The median nerve innervates no muscles in the upper arm. It enters

the forearm between the two heads of the pronator teres, which it supplies along with the flexor carpi radialis, palmarislongus, and flexor digitorumsuperficialis. It then gives rise to a puremuscle branch called the anterior interosseous nerve, which innervates the flexor pollicislongus, pronator quadratus and flexor digitorumprofundus I and II.

The main nerve descends the forearm and passes through the carpal tunnel between the wrist and palm.It supplies lumbricals I and II after giving off the recurrent thenar nerve at the distal edge of the carpal ligaments (Kimura 1989).

2.11.2 Ulnar nerve

Like the median nerve, the ulnar nerve takes a relatively superficial course along its entire length. Common sites of stimulation include Erb's point, the axilla, the elbow, the wrist, and the palm. The ulnar nerve, as a continuation of the medial cord of the brachial plexus, derives its fibers from the C-8 and T-1 roots (Fig: 2.14). It lies in close proximity to the median nerve and brachial artery at the axilla. In this position the ulnar nerve passes between the biceps and triceps, then deviates posteriorly at the midportion of the upper arm and becomes superficial behind the medial epicondyle. After entering the forearm, it supplies the flexor carpi ulnaris and flexor digitorumprofundus III and IV. It passes along the medial aspect of the wrist to enter the hand, where it gives off two branches. The superficial sensory branch supplies the skin over the medial aspect of the hand from the wrist distally, including the hypothenar eminence, the fifth digit, and half of the fourth digit.

2.11.3 Radial nerve

The radial nerve, as a continuation of the posterior cord, derives its axons from the C-5 through T-1, or all the spinal roots contributing to the brachial plexus (Fig: 2.14).The nerve give off its supply to the three heads of the triceps and the anconeus, which originates from the lateral epicondyle of the humerus as an extension of the medial head. The radial nerve then enters the spiral groove, winding around the humerus posteriorly from the medial to the lateral side.

2.12 ORGANISATION OF NERVE FIBERS WITHIN NERVE TRUNKS

A peripheral nerve consists of thousands of nerve fibers with different conduction velocities these fibres are of two types – motor and sensory. The fibres are organized into larger groups called fascicles. The fascicles are organized into larger units called bundles. And the bundles in their turn finally form the nerve trunks as shown in Fig. 2.15.1

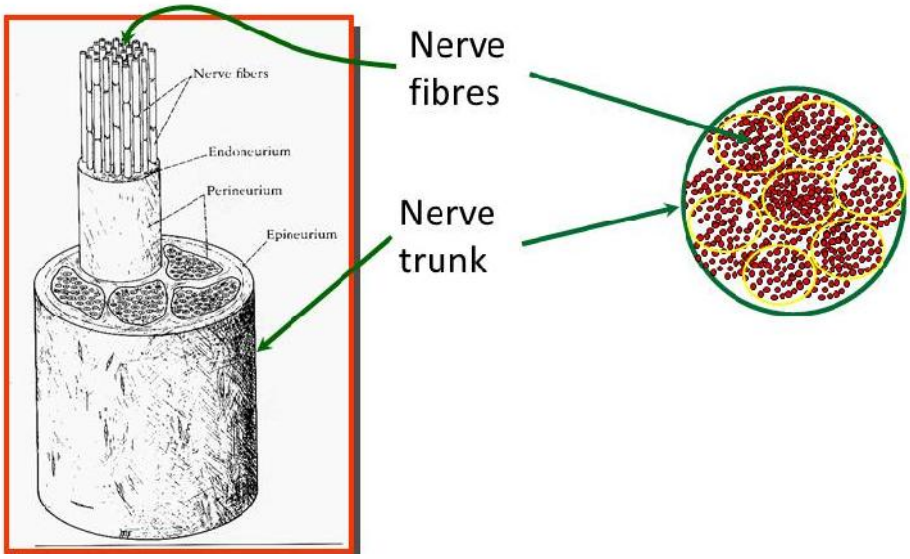

Figure 2.15.1 Internal organisation of a nerve trunk

2.13 TYPES AND GROUPS OF NERVE FIBERS

In an organism there are different types of nerve fibers. The difference can be in function, diameter, conduction velocity etc. It was Erlanger and Gasser (1937),who studied mammalian nerve fibers and classified it into various types. They observed and compared the neurologic deficits produced by careful section of nerve fibers and other nerve-cutting experiment. Based on their experiments, they classified nerve fibers into A, B, and C groups. The A group is again subdivided into A *alpha*, A *beta*, A *gamma* and A *delta* fibers. C group also has got subdivisions called dorsal root fiber and sympathetic fiber.

A, B, and C are specific type of fibers in mammals. But in general we can make conclusions based on some features. The speed of conduction is directly related to the diameter of the nerve fiber. Larger the diameter, greater is the speed of conduction. Also large axons are primarily concerned with the proprioceptive sensation, somatic motor function, conscious touch and pressure, while the smaller axons are concerned with pain and temperature sensations and autonomic functions.

The A and B fibers are myelinated axons. A *alpha* fibers has a diameter of 12-20 micro meter with a conduction velocity of 70-120 m/s. The main function is proprioception and somatic motor. A *beta fibres*carry out the functions of sensation of touch, pressure and also the motor function. It has diameter in the range of 5-12 micrometers and conduction velocity in the range of 30-70m/s. A *gamma* fibres on other hand has fiber diameters in the range of 3-6 micrometer with conduction velocity in the range of 15-30 m/s. The last subdivision of Afiber is A *delta* which carry out the functions of sensation of pain, cold and touch. These fibres have diameters in the range of 2-5 micrometer and conduction velocity in the range of 12-30 m/s.The A type fibers has a spike duration of 0.4-0.5 ms and absolute refractory period of 0.4-1 ms.

The second type is B type and it has no subdivisions.They are mainly preganglionic autonomic fibers with a fiber diameter less than 3 micrometer.The conduction velocity is about 3-15 m/s.The spike duration and absolute refractory period is 1.2 ms.

The third and the last type is C fibers.They are unmyelinated axons.They are subdivided into dorsal root and sympathetic fibers.The dorsal root carry many important sensations like pain, temperature,some mechanoreception and reflex responses.It has a fiber diameter of 0.4-1.2 micro meter and conduction velocity of 0.5-2 m/s.The sympathetic fibers carry post-ganglionic sympathetics and it has a fiber diameter of 0.3-1.3 micro meter and conduction velocity of 0.7-2.3 m/s.The spike duration and absolute refractory period of all the C type fibers are 2 ms each.

2.13.1 Motor fibres

Lower motor neurons have two kind of fibers, αand γ. Their properties are briefly summarised in Table 2.2.

Table 2.2: Motor fiber types and their properties (Ref:)

Type	Erlanger-Gasser Classification	Diameter (μm)	Myelin	Conduction velocity	Associated muscle fibers
α	Aα	13-20	Yes	80–120 m/s	Extrafusal muscle fibers
γ	Aγ	5-8	Yes	4–24 m/s	Intrafusal muscle fibers

2.13.2 Sensory fibres

Different sensory receptors are innervated by different types of nerve fibers. Proprioceptors are innervated by type Ia, Ib and II sensory fibers, mechanoreceptors by type II and III sensory fibers and nociceptorsand thermoreceptors by type III and IV sensory fibers. Their properties are summarised in Table 2.3.

Table 2.3: Sensory fiber types and their properties (Ref:)

Type	Erlanger-Gasser Classification	Diameter (μm)	Myelin	Conduction velocity	Associated sensory receptors
Ia	Aα	13-20	Yes	80–120 m/s	Primary receptors of muscle spindle
Ib	Aα	13-20	Yes	80–120 m/s	Golgi tendon organ
II	Aβ	6-12	Yes	33–75 m/s	Secondary receptors of muscle spindle All cutaneous mechanoreceptors
III	Aδ	1-5	Thin	3–30 m/s	Free nerve endings of touch and pressure Nociceptors of neospinothalamic tract Cold thermoreceptors
IV	C	0.2-1.5	No	0.5-2.0 m/s	Nociceptors of paleospinothalamic tract Warmth receptors

2.13.3 Autonomic nerve fibres

The autonomic nervous system has two kinds of peripheral fibers as given in Table 2.4

Table 2.4: Autonomic nerve fiber types and their properties

Type	Erlanger-Gasser Classification	Diameter (μm)	Myelin	Conduction velocity
preganglionic fibers	B	1-5	Yes	3–15 m/s
postganglionic fibers	C	0.2-1.5	No	0.5-2.0 m/s

2.14 DISTRIBUTION OF CONDUCTION VELOCITY (DCV)

A nerve trunk consists of thousands of nerve fibers with different conduction velocities. Their conduction properties can be best described through a statistical distribution of conduction velocity (DCV) which plots the number of fibres against conduction velocity.

Gasser and Erlanger (1937), Hurs (1939) and other have shown that for the same type of nerve fibres, the conduction velocity of action potentials is proportional to the external diameter of the fibre.Therefore a DCV may be estimated indirectly by measuring the diameters of nerve fibers in a biopsied nerve trunk. Fig. 2.16 shows a typicalDCV of myelinatednerve fibres in a nerve trunk obtained from in vitro biopsy study of the sural nerve of a normal personwhich clearly shows two peaks. The horizontal

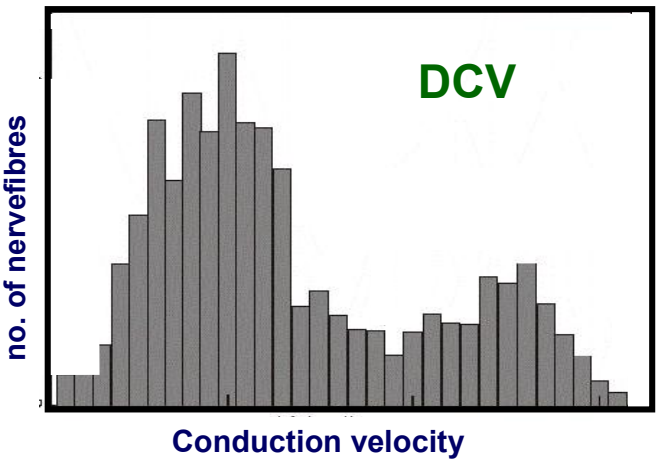

Figure 2.16: Typical DCV of A alpha and A delta fibres in a nerve trunk

axis of the original histogram was labelled in terms of diameter of nerve fibers, which have been relabelled as conduction velocity in Fig. 2.16. The first large peak on the left corresponds to A-delta and the second smaller peak to A-alphafibers. Similar distributions are expected in all peripheral nerves.

2.14 RADICULOPATHY AND MYELOPATHY

2.14.1 Radiculopathy

Radiculopathy(Fig 2.17) is defined as any disease of the spinal nerve roots and spinal nerves. It is characterized by pain which radiates outward from the spine and causes symptoms away from the site of nerve irritation.

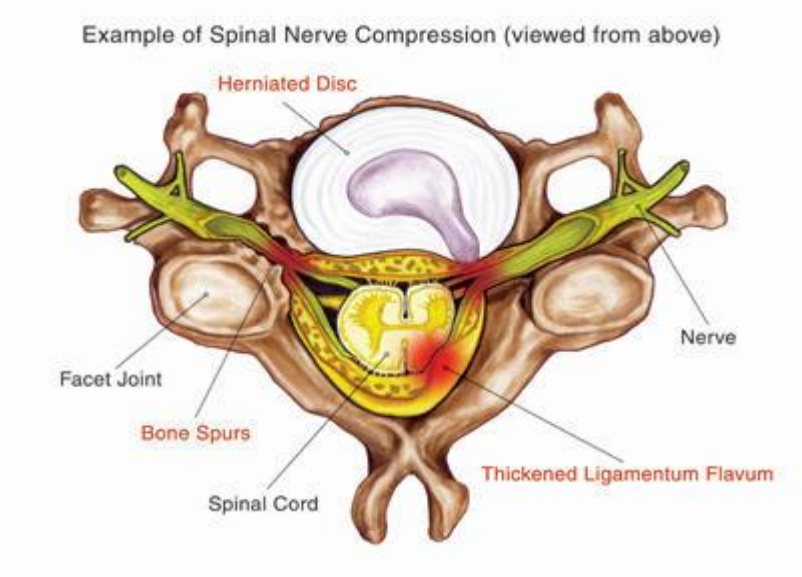

Figure 2.17A vertebral section showing Radiculopathy

As disks age they lose height and begin to bulge, also loss of water content makes the disks stiffer. As the disks lose height, the vertebrae move closer together. The body sees the collapsed disk as a possible weak area and responds by forming more bone — called spurs — around the disk to strengthen it. The bone spurs that form also contribute to the stiffening of the spine. Bone spurs may also narrow the area of the foramen and pinch the nerve root which is known as Radiculopathy.

The disk changes that occur with age are often called arthritis or spondylosis. It is important to keep in mind that all these changes are "normal" and they occur in everyone. In fact, if MRI scans were performed on all people aged 50 or older, nearly half of the scans would show worn disks and pinched nerves that do not cause painful symptoms. It is not known why some patients have symptoms and others do not (<www.Ortho info.aaos.org>).

2.14.2 Myelopathy

Myelopathy describes any neurologic deficit related to the spinal cord. Myelopathy is usually due to compression of the spinal cord by osteophyte or extruded disk material in the cervical spine. Osteophytic spurring and disk herniation may also produce myelopathy localized to the thoracic spine, though less commonly. Other common sources of myelopathy are cord compression due to extradural mass caused by carcinoma metastatic to bone, and blunt or penetrating trauma. Many primary neoplastic, infectious, inflammatory, neurodegenerative, vascular, nutritional, and idiopathic disorders result in myelopathy, though these are very much less common than discogenic disease, metastases, and trauma. A variety of cysts and benign neoplasms may also compress the cord; these tend to arise intradurally. The most common of these are meningiomas, nerve sheath tumors, epidermoid cysts, and arachnoid cysts.

Figure 2.18 Myelopathy

Disorders of the spinal cord itself generally are uncommon and difficult to treat effectively. Therefore, radiologic evaluation of myelopathy is primarily focused on extrinsic compression of the spinal cord. MR imaging is the mainstay in evaluation of myelopathy. Imaging of the spinal

cord has improved to the point that reliable diagnosis of nonexpansile spinal cord lesions is routinely possible.

CT improves depiction of bony encroachment on the spinal canal and sometimes shows cord compression by herniated disk. Bone destruction and soft tissue masses may also be seen. MR imaging has replaced CT in noninvasive evaluation of patients with painful myelopathy because of superior soft tissue resolution and multiplanar capability. Invasive evaluation by means of myelography and CT myelography may be useful for surgical planning or other specific problem solving, though less frequently (REF: David J. Seidenwurm, MD, Department of Quality & Safety, American College of Radiology, 1891 Preston White Dr, Reston, VA 20191-4397American Journal of Neuroradiology)

2.15 NERVE CONDUCTION MEASUREMENT THROUGH EVOKED RESPONSE

To measure the conduction in a nerve it is artificially stimulated at a particular point and the resulting evoked response is recorded from another point, either on the nerve for sensory conduction velocity, or from a supplied muscle, in the case of motor conduction velocity. For artificial stimulation an electrical pulse is driven through two electrodes typically placed over the skin with the target nerve underneath at a subcutaneous site. The nerve is stimulated at one, two or more points along its course, with a cathode to anode distance of 2 or 3 cm. Depolarization under the cathode results in the generation of an action potential in the nerve whereas hyperpolarization under the anode tends to block the propagation of the nerve impulse. With the cathode at the best stimulating site one stimulates the nerve with an intensity that stimulates all the nerve fibres that can be stimulated in the nerve trunk. Usually, with skin surface electrodes it is only the A-alpha group of fibres that are stimulated. Techniques for the determination of sensory and motor nerve conduction velocity are described separately below.

2.15.1 Sensory Nerve Conduction Study

For sensory conduction studies in the upper extremities, stimulation of the digital nerves elicits an orthodromic sensory nerve potential at a more proximal site. Alternatively, stimulation of the nerve trunk proximally evokes the antidromic digital (finger) potential. For example, stimulation

applied to the median or ulnar nerve at the wrist give rise to an action potential along the nerve trunk at the elbow or one in the other direction (antidromic) in the fingers. Generally sensory fibers with large diameters have lower thresholds and conduct faster than motor fibers by about 5 to 10 percent. Thus mixed nerve potentials allow determination of the fastest sensory nerve conduction velocity. The nerve action potential that is evoked in such an experiment is called compound nerve action potential (CNAP).

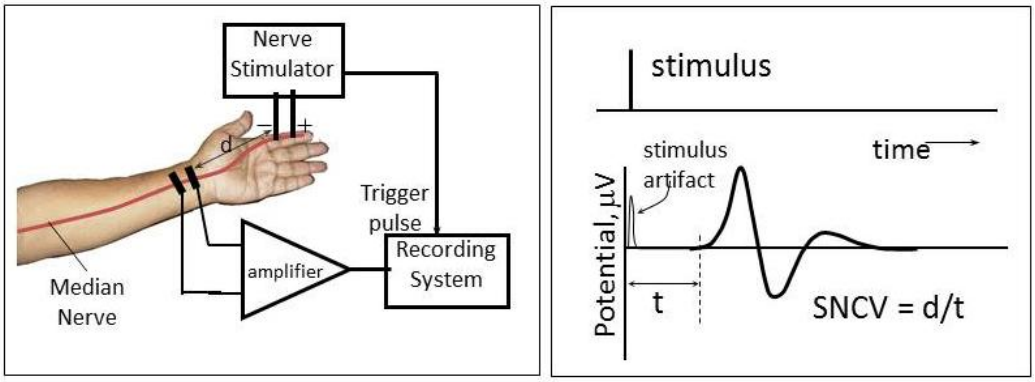

Figure 2.18a: Technique of sensory NCV measurement

For routine clinical recordings surface electrode provides adequate and reproducible information noninvasively. Some electromyographers prefer needle recording to improve the signal to noise ratio, especially in assessing temporal dispersion. Here signal averaging provides a better signal to noise ratio. Sensory NCV gives sensitive measure of early nerve damage by defining small late components that originate from demyelinated, remyelinated and regenerated fibers. Following stimulation of the nerve fiber, nerve impulses will be conducted in both directions along the nerve fibers; conduction up the sensory nerves in the normal direction is termed orthodromic conduction and conduction in the opposite direction is called antidromicconduction.

With the use of surface electrodes the antidromic potentials from digits generally have greater amplitude than the orthodromic response from the nerve trunk because the digital nerve lies nearer to the surface. For recording antidromic sensory signal conduction from digital nerves, ring electrodes are generally used. They are normally placed over the proximal and distal interphalangeal joints of a finger. For example, for recording median nerve through antidromic conduction, the recording ring electrode pair is placed over the digital nerve branches of the

index or middle finger and the nerve is stimulated either at wrist or at the elbow or both. Fig. 2.18a shows the technique of measurement as well as a typical graphical output.

Unlike motor latency which includes neuromuscular transmission, sensory latency consists only of the nerve conduction time from the stimulus point to the recording electrode. Therefore stimulation of the nerve at a single site suffices for calculation of conduction velocity. The nerve conduction velocity is estimated by dividing the distance (nerve length) between the stimulating and recording electrodes by the measured latency.

2.15.2 Motor Nerve Conduction Study

In Motor Nerve Conduction study, the stimulation is applied to a motor nerve while the resulting evoked electrical responses are recorded from the innervated muscles supplied by the particular group of nerve fibers. The obtained response is called Compound Muscle Action Potential (CMAP) or M-response. Fig. 2.18b shows the technique of measurement for conduction velocity of motor nerves through the recording of an evoked muscle response from an appropriate muscle group.

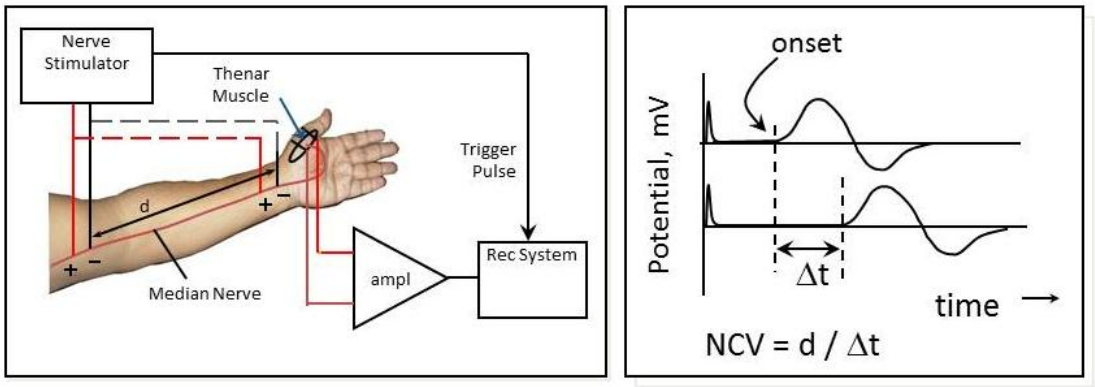

Figure 2.18b: Technique of motor NCV measurement

With this arrangement, the nerve action potential originated under the stimulating cathode will travel down the nerve, along the nerve fibers, across the neuromuscular junction and then cause anmuscle action potential (MAP) to spread along the muscle fibers. This MAP when reaches underneath the recording active lead located near the motor point will record a potential shape.

The incoming MAP will have a simple biphasic shape with initial negativity. By using an inverting amplifier this negative peak can be seen as positive deflection on the monitor. The latency of the onset of the response is measured from the stimulus artefact (shown in Fig. 2.18b). This latency consists of two components:

1. Nerve conduction time from the stimulus point to the neuromuscular junction.
2. Neuromuscular transmission time, from the axonal terminal to the motor end plate Including the time required for generation of MAP through chemical neurotransmitter.

Onset latency is a measure of the velocity of group of fastest conducting motor fibers.To measure the MNCV, it is better to consider the latency difference between the two responses elicited by stimulation at the two separate points. In this way the time for neuromuscular transmission and generation of MAP can be excluded as common factor for both cases. The latency difference represents the time required by the nerve impulse to travel between the two stimulus points. The conduction velocity is defined as the ratio between the distance from one point of stimulation to the next and the corresponding latency difference (shown in the figure).

2.15.3 Factors affecting the measured conduction velocity

A number of factors that can modify the results of motor and sensory conduction studies are described below.

2.15.3.1 .Effect of temperature

Nerve impulses conduct faster at a higher body temperature, as is seen, for example, after physical activity. The conduction velocity increases almost linearly, by 2.4 m/s, or approximately 5 percent per degree, as the temperature measured near the nerve increases from 29^0 to 38^0 C. Similarly, distal latencies increase by 0.3 ms per degree for both median and ulnar nerves upon cooling the hand.

Lower temperatures augment the amplitude of nerve and muscle potential. Cold induced slowing of Na+ channel inactivation probably accounts for the increase in amplitude, because a parallel temperature-dependent change occurs in the refractory period. Studies conducted in a warm room with ambient temperature maintained between 21^0 C and 23^0 C reduce this type of variability.

2.15.3.2. Variation among different nerves and segments:

Both motor and sensory fibers conduct substantially more slowly in the legs than in the arms. Longer nerves generally conduct more slowly than shorter nerves, as suggested by an inverse relationship between height and nerve conduction velocity. Available data further indicate a good correlation between conduction velocity and estimated axonal length in peroneal and sural nerves, but not in motor or sensory fibers of the median nerve.

The other factors possibly responsible for the velocity gradient include progressive reduction in axonal diameter, the shorter internal distances and lower distal temperatures. The nerve impulse propagates faster in the proximal than in the distal nerve segments. For example the most proximal motor nerve conduction velocity determined by the F-wave latency clearly exceeds the conventionally derived most distal conduction velocity. Calculation of the F-ratio allows comparison between motor nerve conduction time from the spinal cord to the stimulation site and that from the remaining nerve segment to the muscle. In healthy subjects the ratio is closed to unity with stimulation at the elbow or at the knee, indicating equal conduction time along the proximal and distal segments from the site of stimulation. Hence faster proximal conduction must compensate for the difference in length between the cord to elbow and elbow to muscle segments or between the cord to knee and knee to muscle segments.

2.15.3.3. Effects of age:

Nerve conduction velocities increase rapidly as the process of myelination advances from roughly half the adult value in full-term infants to the adult range at age 3 to 5 years. Conduction velocity of slower fibers also show a similar time course of maturation.Table 2.2 summarizes the results of one series showing a steep increase in conduction of the peroneal nerve through infancy and a slower maturation of the median nerve during early childhood.Premature infants have even slower conduction velocities, ranging from 17 to 25 m/s. in the ulnar nerve and from 14 to 28 m/s in the peroneal nerve.

Table 2.5: Normal motor NCV in different age groups.

Age yrs	**Ulnar m/s**	**Median m/s**	**C. Peroneal m/s**
0 to 1 week	32(21-39)	29 (21-38)	29 (19-31)
1 week to 4 months	42 (27-53)	34 (22-42)	36 (23-53)
4 months to one year	49 (40-63)	40(26-58)	48 (31-61)
1-3 years	59 (47-73)	50 (41-62)	54 (44-74)
3-8 years	66 (51-76)	58 (47-72)	57 (46-70)
8-16 years	68 (58-78)	64 (54-72)	57 (45-74)
Adults	63 (52-75)	63 (51-75)	56 (47-63)

2.15.3.4 Errors in conduction velocity measurement

The validity of the calculated nerve conduction velocity depends on the accuracy in determining the latencies and the conduction distance. Sources of error in measuring latencies include unstable or incorrect triggering of the sweep, poorly defined takeoff of the evoked response, inappropriate stimulus strength, and inaccurate calibration. Errors in estimating the conduction distance by surface measurement result from uncertainty as to the exact site of stimulation and the nonlinear course of the nerve segments. Surface determination of the nerve length yields particularly imprecise results when the nerve takes an angulated path, as in the brachial plexus or across the elbow or knee.

Because of these uncontrollable variables, the calculated velocities only approximate the absolute values of nerve conduction. On repeated testing, the results might vary occasionally as much as 10 m/s, because of the limitations inherent in the technique. Strict adherence to the

standard procedures minimizes the error and improves the reproducibility. A small range of normal values, then justifies the use of conduction studies as a clinical diagnostic test.

2.15.4 Clinical applications

Nerve conduction studies often help establish the diagnosis of the most common disorder in this category such as Guillain-Barre syndrome, Diphtheria and leprosy. By measuring the sensory conduction velocity and conduction time, it is easy to distinguish and the diabetic neuropathy and mixed sensory neuropathy.

In general axon damage or dysfunction results in loss of amplitude, whereas demyelination leads to prolongation of conduction time. Assessment of a nerve as a whole, as opposed to individual nerve fibers, usually reveals more complicated features because different types of abnormalities tend to coexist. There are three basic abnormalities that characterize motor nerve conduction study when stimulating the nerve proximally to the presumed lesion

1) Reduced amplitude with normal or slightly increased latency
2) Increased latency with relatively normal amplitude and
3) Absent response.

From the first variety, a stimulus below the lesion may elicit a normal compound muscle action potential, even though stimulation above the lesion evokes reduced amplitude. This finding indicates nerve injury in the first few days.

In the second variety slowed conduction accompanies relatively normal amplitude in the stimulation above the lesion. These changes generally imply segmental demyelination affecting a majority of the nerve fibers. Another cause diagnosed with a prolonged latency or slowing of the conduction velocity may also result from axonal neuropathy with the loss of the fast conducting fibers or entrapment neuropathy between the stimulating point to recording point.

The third variety of motor nerve conduction study is "absence of motor nerve responses" indicate that a majority of the nerve fibers fail to conduct across the site of the presumed lesion. One must then differentiate a neuropraxia lesion from nerve transaction.

2.16 F-RESPONSE

A supramaximal electric shock delivered to a peripheral nerve often elicits a delayed and reduced F-response in the innervated muscle, long after the direct M-response as shown in Fig. 2.19. The F-response or the F-wave is known to occur due to random backfiring of a few percent of the motor nerve fibers at the spinal cord after antidromic conduction. F-latencies obtained from multiple stimulations vary in latency, size and shape because of these randomness. Since the original description by Magladery and McDougal (1950), who designated it as the F wave, (presumably because they initially recorded it from intrinsic foot muscles), different authors have debated its neural source.

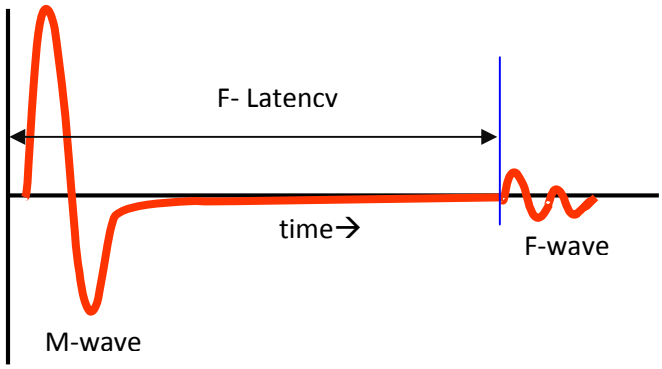

Figure 2.19: M-wave and F-wave in evoked EMG response

Conventional nerve conduction studies seldom contribute to the investigation of more proximal lesions. To study the entire length of the sensory nerve, one may record somatosensory cerebral evoked potentials. In contrast, measurement of the F-wave helps in assessing motor conduction along the most proximal segment, because it results from the backfiring of antidromically activated anterior horn cells. This technique usefully supplements the conventional nerve conduction studies, especially in characterizing demyelinating polyneuropathies, in which delay of the F wave often clearly exceeds the normal range. In addition to determination of F wave latencies, calculation of conduction velocities and the F ratio permits comparison of conduction in the proximal versus the distal nerve segments. The F wave also provides a measure of motor neuron excitability, which presumably dictates the probability of a recurrent response in individual axons. The F-wave obtained by a distal stimulation at the wrist can be used in determining the motor conduction time along the entire length of the nerve with defused or multisegmental lesions. The delay in nerve increases in proportion to the length of the tested pathways. Thus, relatively mild slowing not identifiable by conventional motor nerve conduction studies may lead to easily identifiable delayed F-waves.

2.16.1 Origin Of F-Response

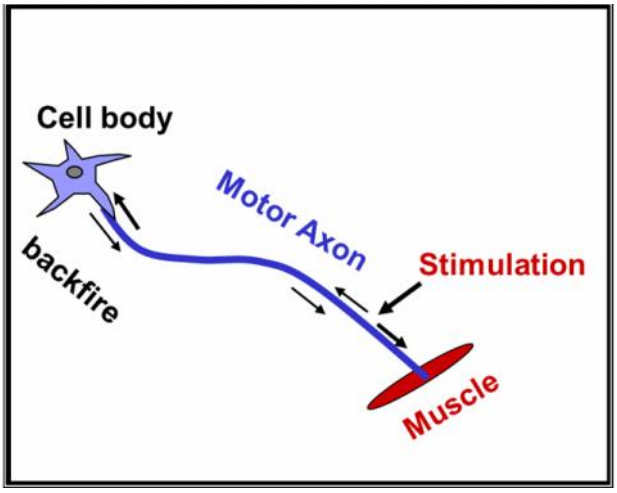

Figure 2.20: Pathway for F-response

Each peripheral nerve consists of thousands of nerve fibers with varying conduction velocities that can be well described by a frequency distribution of conduction velocities (DCV). If a supramaximal electrical stimulation is applied to a motor nerve, action potentials are produced within individual nerve fibers at the stimulation site, which travels in both directions from the point of origin. When the action potential travels in forward direction towards the muscle, then it is called orthodromic conduction and when it travels in backward direction, it is called antidromic conduction. Reaching the muscleorthodromically, the nerve action potentials elicit a compound muscle action potential, an M- response that can be recorded using surface electrodes. The action potential which travels antidromicallyreach the cell bodies in the spinal cord and are supposed to die out there. However, a few cell bodies backfire and send fresh action potentials down the nerve fibers to the muscle. As a result, a delayed compound muscle action potential, F- response is produced (fig:2.20).This F-response is much reduced in amplitude with respect to M-response, because a small number of fibers back-fire. For repeated stimulations given sufficient intervals, the M-wave occurs at the same point with the same size and shape for normal nerves and muscles. Unlike the M-response, the amplitude and latency of the F-response varies on such repeated stimulations. This occurs due to the randomness of backfiring process i.e. which nerve cells will backfire is not previously known. Sometimes no cells will backfire and there will be no F-response.

2.16.2 Physiological Characteristics Of The F-Wave

Since the F wave occurs due to the random backfiring of the antidromically activated motor neurons, it occurs after the direct motor potential or the M-response with much smaller amplitude (1-5 % of the M wave). With more proximal stimulation, the latency of the M-response increases, whereas that of the F-wave decreases. This indicates that, the impulse destined to elicit the F-wave first travels away from the recording electrodes toward the spinal cord before it returns to activate distal muscles. F-responses were found to be present even after cutting of sensory nerve. This finding is inconsistent with a reflex hypothesis where a signal travels up the spinal roots through the sensory nerves, which in turn stimulates the motor nerves, as in H-reflex. The presence of the F wave in deafferentated limbs and after transverse myelotomy strongly suggests that it depends in part on backfiring of motor neurons. Studies using single fiber electromyography have also shown that the occurence of the F-wave requires prior activation of the motor axon. The evidence of its recurrent nature, however, does not necessarily preclude the presence of reflex components that may still contribute.

2.16.3Latency And Amplitude Of The F- Wave

The incidence of the F-wave may favour the larger motor neurons with faster conducting axons. This in turn provides a rationale for using the minimal latency of the F-wave as a measure of the fastest conducting fibers. Because of a particular set of physiologic conditions required for generation and propagation of a recurrent discharge, the latency of successive F waves from a single motor axon varies only narrowly between 10 and 30 μs which is negligible compared to the total value of typical F-latency, of the order of 20 to 35ms in case of the upper limb.

When the fast conducting axons are progressively blocked by use of a collision technique, the F-wave continues to appear in proportion to the slow conducting motor axons that have escaped the collision. Hence, recurrent discharges must occur not only in the larger motor neurons with fast conducting axons, but also in the smaller motor neurons with slower conducting fibers.

The F-wave is elicited in approximately 1 to 5 percent of antidromically activated motor neurons regardless of their peripheral excitability or conduction characteristics. In normal subjects, the frequency of occurrence of F-waves varies, with a mean of 79 percent, tested during a train of 200 stimuli (Peioglou-Harmoussi, 1987).

A few-millisecond interval between the earliest and latest F-wave is in part due to the difference between the fastest and slowest motor conduction. The conduction time, however, is a function not only of the speed of the propagated impulse but also of the length of the whole nerve fibre, the major portion of which it traverses twice.

The amplitude and frequency of the F-wave provide a measure of motor neuron excitability, but the relationship is physiologically complex. No recurrent discharge is expected with an antidromic impulse producing subliminal depolarization in hypoexcitable cells. The F wave may also fail in hyperexcitable cells, which may discharge too rapidly during the refractory period of the initial axon segments. For example, despite spasticity, F-wave frequency is lower.

2.16.4Recording Procedure Of F-Wave Latency

A supramaximal electric stimulus applied at practically any point along the course of a nerve elicits the F-wave. Placing the anode distal to the cathode or off the nerve trunk avoids anodal blocking of the antidromic impulse. A surface electrode placed over the motor point of the tested muscle serves as the active lead against the reference electrode over the tendon. An optimal display of F-waves requires an amplifier gain of 200 or 500 μV/cm and an oscilloscope sweep of 5 or 10 ms/ cm, depending on the nerve length and stimulus point.

These recording parameters truncate and compress the simultaneously recorded M response into the initial portion of the tracing. Thus, one must study the M response and F wave separately, using different gains and time bases.

F-wave latencies measured from the stimulus artifact to the beginning of the evoked potential vary by a few milliseconds from one stimulus to the next. Hence for an adequate study, more than 10 F-waves must be clearly identified among 16 to 20 trials. In addition, determination of the minimal and maximal latencies reveals the degree of scatter among consecutive responses, providing a measure of temporal dispersion. Electronic averaging of a large number of responses permits easy analysis of mean latency.

2.16.5ExistingClinical Value Of F-Wave Latency And Its Limitations

Clinical uses of the F-wave suffer from inherent latency variability from one trial to the next. Determination of the shortest latency after a large number of trials can minimize this uncertainty. Recording as many as 100 F-waves at each stimulus site proved useful in special studies but is not practical in routine clinical test. Determining the latency differences between two sides or between two nerves in the same limb serves as the most sensitive means of examining a patient with a unilateral disorder affecting a single nerve. Absolute latencies suffice for evaluating the entire course of the nerve in a diffuse process. Calculation of the central latency, the F-wave conduction velocity (FWCV), and the F-ratio provides additional information not otherwise available, especially in the comparison of proximal and distal segments.

Conventionally measurement of F-wave latencies are used in identifying disorders involving proximal segments of peripheral nerves. The determination of F-wave latencies is thought to be particularly valuable in evaluating neuropathies in which focal, proximal pathology may be seen, as in Guillain-Barre syndrome and neuropathy associated with rheumatoid arthritis.

The inherent variability of the latency and configuration makes the use of F-wave less precise than that of the direct compound muscle action potential or M-response determination. Nonetheless, the technique usefully supplements the conventional nerve conduction studies, especially in characterizing demyelinating polyneuropathies, in which the delay of the F-wave often clearly exceeds the normal range. In addition to determination of F-wave latencies and calculation of conduction velocities provides a measure of motor neuron excitability, which presumably dictates the probability of a recurrent response in individual axons.

The F-wave is commonly abnormal in hereditary motor sensory neuropathy, acute or chronic demyelinating neuropathy, diabetic neuropathy, uremic neuropathy, alcoholic neuropathy and a variety of other neuropathies. Other categories of disorders associated with F-wave changes include entrapment neuropathies, amyotrophic lateral sclerosis and radiculopathies. Studies of the F-wave help in characterizing polyneuropathies in general and those associated with prominent proximal disease in particular. In the early diagnosis of more localized nerve lesions such as radiculopathies, the remaining normal segment tends to dilute a conduction delay across the much shorter segment.

2.16.6Distribution Of F-Latencies (DFL) And DCV

A peripheral nerve consists of thousands of nerve fibers with varying conduction velocities. If a motor nerve is artificially stimulated at any point, action potentials are generated within the individual nerve fibers, which travelling directly to the muscle served (orthodromic conduction), elicit a compound muscle action potential, an M-response that reproduces well on repeated supra-maximal stimulation and whose onset latency is conventionally used for obtaining a measure of NCV. From the stimulation site, the action potential also travel along the nerve fibers in the opposite direction (antidromic conduction), towards the cell bodies in the spinal cord. Most of these action potentials die out, but a few percent of the cell bodies backfire after a short delay, and send fresh action potentials down the nerve fibers to the muscle. These in effect produce a delayed compound muscle action potential called the F-response, which is very much reduced in amplitude with respect to the M-response because of the small number of fibers involved.

An important aspect of the F-response is that, unlike the M-response, it varies in shape, amplitude and latency on repeated stimulation; sometimes there will be none. The cause has been ascribed to the randomness of recruitment; which nerve cell will backfire is not previously known. It is likely to be a random process. Being a random process, it was hypothesized that, recruitment of fibers for F-response would statistically depend on the distribution of conduction velocity (DCV) for motor nerve fibers specifically of those that contribute to F-responses, and therefore, a frequency distribution of F-latencies (DFL) from such multiple F-responses would

be approximate mirror image of DCV, latency being inversely proportional to the velocity (Rabbani and Alam 2007, Rabbani, 2011).

2.17 DFL AND ITS DIAGNOSTIC IMPLICATION

First, obtaining DFL from many human subjects, it was shown that, this is a reproducible parameter for a nerve trunk of a subject, and hence reveals a new physiological phenomenon (Rabbani and Alam 2007). DFL has a single peaked distribution for normal subjects, which is also expected for the DCV of a normal healthy motor nerve. To validate its hypothesized relationship to DCV further, DFLs were obtained from both median nerves of patients with unilateral carpal tunnel syndrome (CTS). The patterns of DFL from both sides remained almost the same except for a delay shift equal to that in between the two M-responses, which lends support to this hypothesis (Rabbani and Alam 2007). As DCV is suggested to be mirror image of DFL, it appears to change systematically with certain known disorders such as cervical spondylosis (CS), even at a subclinical stage (Alam and Rabbani 2010). There appears significant differences between the DFLs of normal subject and that of a CS patient. Normal subjects having no neurological complaints show a single peaked distribution, whereas, patients having cervical spondylosis show double or triple peaks in their DFLs. Some subjects demonstrated rather broad plateau with slight indication of dual peaks, although, they did not complain of any neurological problem. This clearly indicates that, DFL may become a new and improved investigative diagnostic tool in neurophysiology

To establish DFL as a physiological phenomenon a study was conducted (Rabbani and Alam 2007) on ten adult subjects, aged between 23 and 45. To each of the median nerves of these subjects about 40 supramaximal electrical stimulations were applied at the wrist in sequence. The time sequence of the collected F-latencies from each nerve was maintained and recorded. From this protocol, 20 data sets for multiple F-latencies were collected from the right and left median nerves of 10 subjects. According to the above grouping, respective DFLs were obtained for all the 20 data sets. To test the reproducibility of the DFLs, the raw F-latency data from each nerve were separated into odd and even data points in terms of time sequence of collection, and fresh DFLs were plotted for these odd and even data sets following the latency grouping. The correlation coefficients between the respective odd and even DFLs were very high (Table

2.6)confirming the hypothesis that DFL is a physiological parameter and is an approximate mirror image of the DCV of nerve fibres. The mean and the standard deviations of the correlation coefficients are also shown.The high correlation coefficient of 0.81 established DFL as a physiologically significant phenomenon.

Table 2.6: Corelation coefficient (r) between odd and even data points for DFL from the 20 median nerves of 10 subjects. The number of F-responses (n) used in each case are also shown.

Subject identifier		Age		Right Median		Left Median	
		yrs		n	r	n	r
1.	MF	25		12	0.75	15	0.97
2.	JA	32		17	0.93	15	0.77
3.	MM	29		15	0.68	20	0.95
4.	OS	25		15	0.90	15	0.89
5.	SI	23		15	0.86	12	0.81
6.	SN	45		16	0.85	16	0.62
7.	AS	40		15	0.88	15	0.53
8.	UB	28		15	0.46	15	0.75
9.	MR	26		15	0.91	15	0.80
10.	RH	43		14	0.97	14	0.99
Summary Age: Mean: 31.6 yrs, St Dev: 8.11 yrs Corr. Coeff: Mean: 0.81, St Dev: 0.15							

To validate that DFL is a simple reflection of DCV, another experiment was performed. Carpal tunnel syndrome (CTS) is a well-understood disorder in which the median nerve is compressed at the wrist, causing a conduction delay through all the nerve fibres. The entrapment is expected to affect all the nerve fibres equally due to pressure transmission in a fluid, and it has also been demonstrated well through a shift in the M-response towards longer latencies (delays) without any significant change in its shape, unless other abnormalities are involved. This also results in a delay of the shortest F-latency. In many subjects CTS occurs only in one hand while the other hand has normal conduction. So the new multiple F-latency technique was used to obtain DFLs

from both hands of such patients, particularly those who demonstrated similar shapes of M-responses from the two hands except for the delay. This disorder is expected to shift the DCV towards lower velocities in the affected side without significant change in the relative distribution pattern.If DFL is related to DCV as suggested, then DFL will shift to longer latencies without significant change in shape as well, and the lateral time shift would be almost the same as the difference between the latencies of the M-responses. If DFL was unrelated to DCV, there would not be any such correlation between the DFLs from the two hands. Therefore, the above test may provide a validation technique for the proposed relationship between DFL and DCV.The outcome of this validation study was found to be in agreement that DFL positively correlated to DCV.

In this initial study double peaks of DFL were observed in 4 cases and triple peaks in one, and all of them reported having diagnosed Cervical Spondylotic Neuropathy (CSN), or having symptoms typical of this disorder. Through a retrospective analysis of this study an association was established that multiple peak of DFL is related to CSN (Alam and Rabbani 2010).The results of this study are summarized in thetables2.7 and 2.8.

In the course of routine clinical work one of the authors (Rabbani) also had observed double or broad peaks of DFL for the median nerve for many patients who had symptoms of CSN. Similarly, double or broad peaks of DFL were also observed for Tibial or Common Peroneal nerves for cases with Lumbo-sacral spondylosis.

To explain this association the following hypothesis was put forward (Rabbani 2011). CSN usually has two main causes. One is called Radiculopathy (CSN-R) in which nerve branches coming out of the spinal cord are compressed in the narrow channels or gaps created by the vertebral bones. This compression may be caused by bony growth in the vertebra (osteophyte), or herniation of inter-vertebral disc as shown in Fig.2.21. Either of these compressions leads to CSN, and this condition is known as radiculopathy.

The other cause of CSN is Myelopathy (CSN-M) in which one side of the spinal cord is directly pressed onto, mostly by a bulging intervertebral disc, as shown in Fig.2.22. This affects nerve fibres located in the pressed region of the spinal cord.

Table 2.7: Correspondence of DFL patterns with neurological condition in the cervical region

Subject No.	Subject identifier	Age, Years	Pattern of DFL*		Reported Clinical condition#	
			Right	Left	Right	Left
1	MF	25	B	S	Nor	Nor
2	MJA	32	B	D	Nor	CS
3	MM	29	S	D	Nor	CS
4	OS	25	S	S	Nor	Nor
5	SI	23	B	S	Nor	Nor
6	SN	45	D	B	Pain	Pain
7	AS	40	D	B	CS	Nor
8	UK	28	D	B	CS	Nor
9	MR	26	S	B	Nor	Nor
10	RH	43	S	S	Nor	Nor

* S: Single peak; D: Clear double peak; B: Broad peak (with indication of double humps), # Nor: Normal; CS: Clinically diagnosed Cervical Spondylosis; Pain: Pain in shoulder, not consulted a medical practitioner yet

Table 2.8: Collated summary of the correspondence of DFL patterns with neurological condition in the Cervical region

DFL pattern	No. of nerves	Clinical condition	Comments
Single Peak	8	All claimed normal	Single peak likely to represent normalcy
Double Peak	4	Diagnosed CS	Double peak likely to represent CS. Single case with pain possibly has CS
	1	Pain in shoulder, not yet gone for medical investigation	
Broad Peak (Plateau)	2	With single peak of DFL on opposite side	Cases with CS on one side are more likely to develop CS on the opposite side as well. Broad peak (plateau) may be an early indicator of CS.
	5	With double peak of DFL on opposite side, 4 with diagnosed CS, one with Pain in shoulder	

2.18 EXPLAINING DOUBLE AND TRIPLE PEAKS OF DFL DUE TO RADICULOPATHY AND MYELOPATHY

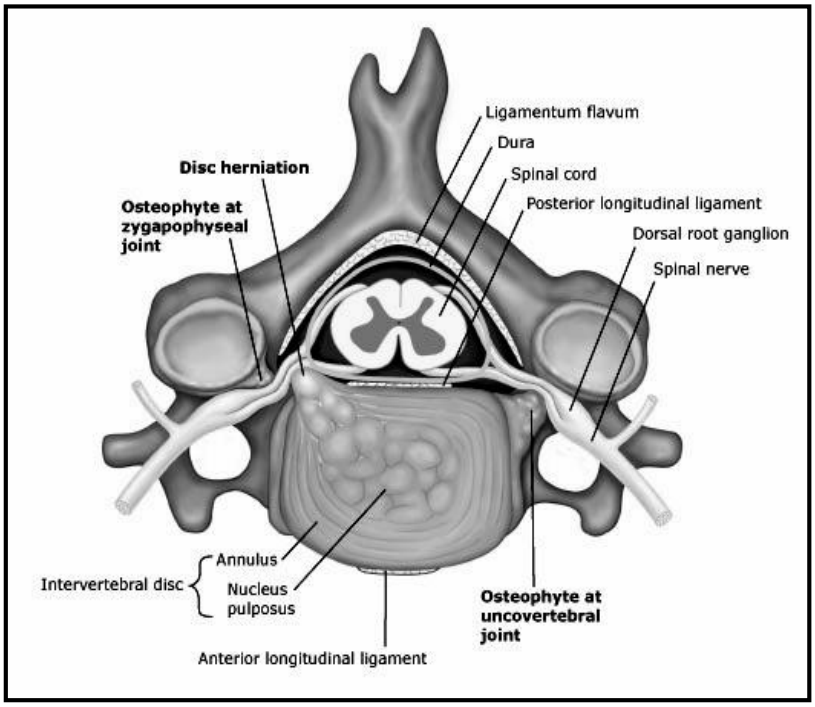

Figure 2.21Vertebral section showing radiculopathy (compression of nerve root)

For the median nerve DFL is usually obtained from the Thenar muscle (Abductor PolicisBrevis, APB) at the base of the thumb, by stimulating the nerve at the wrist. It is also known that nerve branches Cervical 8 (C8) and Thoracic 1 (T1) combine proximal to the Brachial Plexus and contribute to the median nerve to serve the Thenar muscle. Some authors claimed that a nerve branch from C7 may also contribute (Urschel et al 2000). That means three nerve branches, C7, C8 and T1 may contribute to the responses obtained from the APB muscle in the palm of the hand. This information allowed us to present a hypothesis for double or triple peaks of DFL due to radiculopathy as follows.

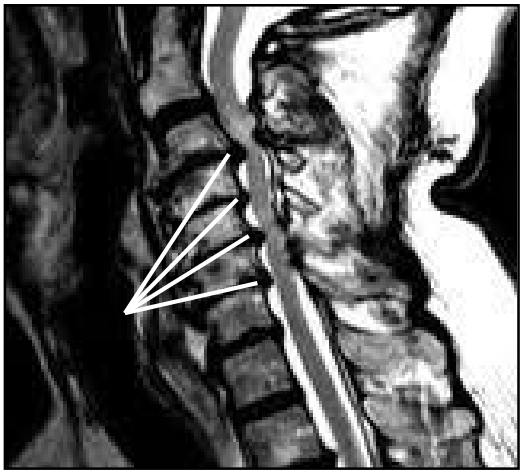

Fig. 2.22: Compression of spinal cord due to disc bulging (myelopathy)

Rabbani 2011 presented a hypothesis to relate the double or triple peak to radiculopathy which is presented below. As mentioned before, for a normal

healthy nerve trunk having many fibres, the DCV has a single peak, which gives rise to a DFL with a single peak as well. The same may be expected for the separate DCV of the fibres within each of the nerve branches C7, C8 and T1 that combine in the median nerve to serve the Thenar muscle. That is, we may expect the relative DCV from each of the nerve branches to be the same, having approximately the same conduction velocity values. This means the DFLs due to the nerve fibres in the three branches will also have similar distributions with approximately the same latency values. The combined DFL due to all the nerve fibres together would be simply a sum of all the three branch distributions, which will also have a similar pattern with a single peak at the same latency value, as shown schematically in Fig.2.23 (left). This explains why the DFL for a normal healthy nerve has a single peak.

Now suppose one of the nerve branches, say, C7 is compressed due to radiculopathy at the vertebral region while the other two, C8 and T1 are uncompressed. Therefore, all the nerve fibreswithin the C7 branch will be similarly compressed at the point of compression following

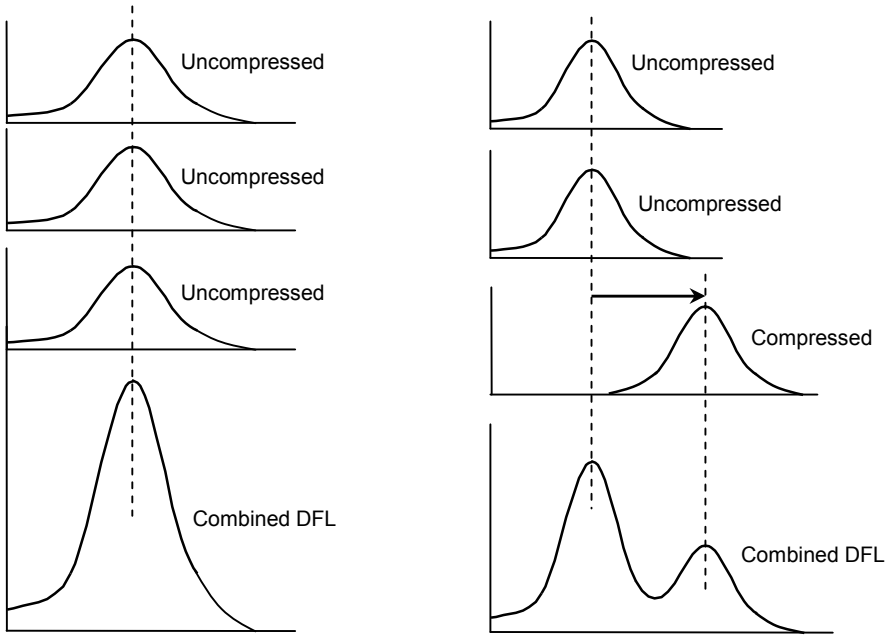

Fig.2.23: DFL due to uncompressed nerve roots (left) and due to compression in one of the three roots (right), the latter causing a double peak.

the same argument as given before for CTS. Therefore, the contribution of nerve fibres from this branch to the measured DFL will have a delay shifted pattern, same as that occurring in CTS. On

the other hand, there will be no delay in the DFL for the other two uncompressed nerve branches C8 and T1. Therefore the combined DFL due to nerve fibres from all the three branches will essentially be a sum of the three distributions, and will have a double peak. This is shown schematically in Fig.2.23 (right). This also will mean that the first uncompressed peak, being from two branches, will be larger than that from the second delayed peak, being from a single branch. This hypothesis was the first to explain the double peak of DFL in CSN. It is interesting to note that most of the experimentally observed DFLs with double peaks had the first peak larger than the second one, matching the above explanation. So this hypothesis suggests that compression of any one of the three nerve branches, C7, C8 and T1, will contribute to a DFL with double peaks.

Now if the degree of the above compression is less, as happens in the early stage of radiculopathy, the delay shift of DFL will also be less, and the two peaks of the two distributions may not get resolved in the combined DFL. So they will result in a broad peak. With an increasing degree of compression, the delay will also increase, and two humps may just be noticeable. With further compression, there will be more delay; the two peaks will be resolved and clear double peaks will be noticeable. Therefore, it was hypothesized that a broad peak of DFL indicates an early stage of radiculopathy. The subject usually does not feel anything at this stage, i.e., it is a sub-clinical phase, and this offers the possibility of early indication of neuropathy. Now, if two of the nerve branches of the three (C7, C8 and T1) are compressed to different degrees, we may obtain triple peaks, following the same arguments as above. Therefore the same hypothesis also explains the occurrence of triple peaks in DFL .

The same arguments would hold for Common Peroneal nerve and Tibial nerve in the legs due to similar differential compression of the nerve branches in the Lumbo-sacral region of the vertebra.

Conventional neurophysiological techniques have so far not produced any method to give a positive diagnosis of CSN except for excluding other peripheral nerve disorders. Using a train of 200 stimuli (Peioglou-Harmoussi et al. 1987)studied the frequency of occurrence of F-responses from ulnar nerves, frequency of identical responses and F-wave shapes to relate these to CSN. None of these led to any clear-cut method to identify CSN, as the distinctions were not well marked; however, there appears to be a correspondence with one of their observations with the

observation of DFL. They found that the F-wave appeared complex visually compared to those from controls. In the above findings, DFL is a simple distribution with a single peak for normalsubjects; therefore the backfiring nerve cells have less dispersion in latency among them,contributing to simple F-waves on combination of the individual motor unit responses.On the other hand, in case of CSN, DFL has more dispersion with double peaks, meaningthat latencies from back firing nerves may have wider separation among them, leading to more complex patterns on combination.

2.18.1Extension of hypothesis to cover other lesions

In the nerve conduction clinic of Dhaka University, sometimes double peaks of DFLwere observed in patients receiving stab injuries in the neighborhood of a nerve trunk in the arms. Although no rigorous scientific study has yet been taken up on such externally induced neuropathy, it was felt that the above hypothesis may be applied to such cases as well. In such cases, the degeneration of nerve fibres may be anticipated in a part of the nerve trunk, while the rest remaining intact. Thus the affected or degenerated part of the nerve trunk will contribute to a delay shifted DFL compared to the unaffected part, and when combined, will give rise to a double peak (Rabbani 2011). Similarly, if a tumour in the spinal canal presses onto the spinal cord, a similar degeneration of peripheral nerve fibres will result contributing to a DFL with double peaks.

2.18.2 Generalization of Hypothesis

All the above point to the fact that if a part of the whole nerve trunk is affected, whatever be the cause, resulting in a reduction of their conduction velocity, double peaks of DFL are likely to be observed. This is schematically represented in Fig.2.24. Thus DFL can be an effective screening tool for neuropathy. Of course, absence of double peaks does not exclude all neuropathy, such as CTS, but presence of double peak definitely is an indicator of neuropathy.

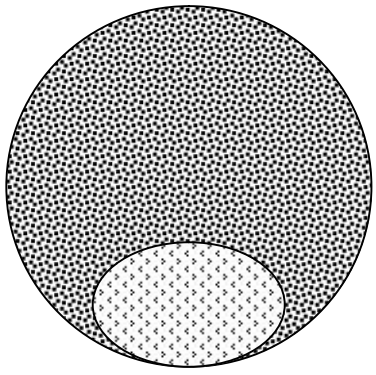

Figure 2.24: Schematic of segmental degeneration of fibres in a nerve trunk, hypothesised to cause double peak of DFL

Two studies based on the first approach stated above were carried out at Dhaka University and at Singapore General Hospital(Hossain et al, 2011, Rabbani et al 2013). The results of these studies are given below.

2.19 PAST STUDIES ON DFL AND CERVICAL SPONDYLOTIC NEUROPATHY

After the indication of the relationship between CSN and multiple peaks of DFL by Alam and Rabbani, further studies were taken up to establish this observation on firmer grounds.

In one study DFL was obtained from the median nerves of 20 subjects with age varying between 25 and 65 (Hossain et al, 2011). Firstly the DFL results were correlated to clinical findings reported by the volunteers themselves, whether they had diagnosed CSN or neck pain (which was also taken as a case of CSN). The results of this study are given in Table 2.9. As expected, the 6 normal subjects demonstrated single peak of DFL on both sides, and they did not have any neurological complain either (serial 1 to 6 in Table 2.9). One of them was investigated

Table 2.9: DFL of 12 subjects to relate their clinical condition

Subject No.	Subject ID	Age, Yrs	No. of DFL peak(s)		Clinical condition
			Right median	Left median	
1	BPL	25	S	S	NC
2	SHA	25	S	S	NC
3	ARA	25	S	S	NC
4	SID	26	S	S	NC
5	TAZ	26	S	S	NC
6	IFT	26	S	S	NC
7	HFT	26	D	S	CS
8	CHA	26	D	D	CS
9	EHS	36	S	D	CS
10	AKT	46	T	T	CS
11	SAL	49	S	D	CS
12	HUQ	64	D	D	CS

Abbreviations
S: Single peak; D: Double peak; T: Triple peak;
CS: Diagnosed Cervical Spondylosis with clinical complain;
NC: No Clinical Complain;

using X-ray, and the report came out normal, with no bony growth. The remaining 6 subjects (serial 7 to 12 in Table 1) having diagnosed CSN or neck pain demonstrated double or triple peaks of DFL.

The six subjects showing double or broad peakwere subject to X-ray or MRI investigation at regular clinics, where the radiologist gave reports without knowing the purpose of this study, or without any knowledge of the DFL findings. 3 more subjects with diagnosed CSNalsounderwent similar studies. The combined results of these 9 subjects are presented in Table 2.10. It was found that almost all of these subjects had some sort of problem in the cervical region, whether radiculopathy or myelopathy.

Table 2.10 : X-ray and MRI findings of subjects having double peak of DFL

Subject ID	Age, yrs	X-ray findings (for whom done)	MRI findings (for whom done)
HFT	26	Mild ost: C5, DSR	----
CHA	26	Marginal ost: C4, DSR	---
EHS	36	Marginal ost C7, DSR	DB: C4-C5, C5-C6, SCC
AKT	46	Mild ost: C5-C6, DSR at C4-5 and C5-6	---
SAL	49	Ost: C5, C6, C7. DSR at C5-6	DB: C5-C6, SCC
HUQ	64	Mild ost: C4, C5, DSR at C3-4, C5-6, C6-7.	---
KSR	60		DB: C5-C6, SCC
ARA	25	Cervical Rib	
AAM	26	Normal	DB: C4-5, C5-6, SCC
Abbreviations:		Ost: Osteophyte DSR: Disc space reduction	DB: Disc bulging SCC: Spinal cord compression

It is interesting to note that one of the subjects (KSR) had a broad peak with indication of two humps two years back, before the present work was taken up. His MRI at that time indicated mild disc compression on the spinal cord (myelopathy) at C5-6 intervertebral space. At present his DFL shows clear double peaks, and he feels a burning sensation around the neck and shoulders when the arms are kept high on the table, indicating mild cervical spondylotic neuropathy. This also shows that the broad peak of DFL two years back indicated the early stage when there were no symptoms.

Tables 2.9 and 2.10 indicate very conclusively that all subjects having diagnosed CS had double or triple peaks of DFL, in at least one side, while all in the normal group had single peaks. Again from Table 2.10, it can be seen that X-ray and MRI investigation carried out during this work also indicates some sort of spinal abnormality affecting the nerves in all the 9 subjects who demonstrated double or triple peaks of DFL.

If radiculopathy has to affect the thenar muscle, there should be compression of C7, C8 or T1 nerve roots. In Table 2.10 two subjects (EHS and SAL) had bony growth (osteophyte) at C7, as revealed by X-ray investigation, which may compress the nerve branch C7, and cause radiculopathy. There is also a case of cervical rib. However, in all others, disk space reduction coupled with disc bulging and compression on spinal cord are common at slightly higher levels of the vertebra. Therefore, it can be said that these cases had myelopathy, i.e., pressure on the spinal cord. This small study also indicates that myelopathy has affected more of the subjects than radiculopathy

Another study was carried out on 24 median nerves of 12 patients with suspected cervical radiculopathy over a 9 month period at the Singapore General Hospitaland analysed at Dhaka (Rabbani et al 2013). Initially only double peaks of DFL, prepared using 2ms bin intervals, were assumed to indicate radiculo-myelopathy. However, when compared with the MRI findings there was a significant percentage of false negatives; diagnosed as free of lesion through DFL, while MRI suggested otherwise. It was observed though that many of the false negatives had two adjacent frequency values (at a separation of 2ms) significantly high and with low values further out, which were considered as single peaks in this analysis. At this point the broad peaks of DFLwere redefined to include such patterns of DFL, which were considered as marginal broad peaks. Through a comparison with the MRI findings a rule of thumb was made to define such a broad peak; it will be termed a broad peak if an adjacent (at a separation of 2 ms) frequency to a peak is more than one third the peak. This was considered in addition to the original definition of a broad peak. Thus the definition of broad peak was revised to include broad peaks as that where the adjacent frequency of occurrence was greater than one third of the peak frequency, or where non-zero frequency exists at 4 ms difference from the position of the peak .

The findings are summarized in tables 2.11 and analysed in Tables 2.11A, 2.12 and 2.13. The first analysis (Table 2.11A) is based on the initial definition of broad peak of DFL which was considered to have CSN. The clear multiple peaks were obviously considered as abnormal. Table 2.12was based on the revised definition of broad peak as defined above, which were also

considered to have CSN.Table 2.13 considers a subject with sensori-motor neuropathy as abnormal although MRI did not show radiculo-myelopathy. In the previous two analyses this case was considered normal.

Table-2.11: Analysis-1: Comparison of diagnosis using DFL and MRI considering only double, triple or clearly defined broad peaks of DFL as abnormal (single peak and marginal broad peak considered normal)

	Right		Left	
Patient	DFL	MRI	DFL	MRI
TCS	Y	Y[1]	Y	Y[1]
SJJ	N	N	N	N
GIGC	Y	N[2]	Y	N[2]
CTS	Y	Y[3]	Y	Y[3]
TCW	N	Y[3]	N	Y[3]
SBC	N	Y[4]	Y	Y[4]
NWK	N	Y[5]	N	Y[5]
LWK	N	Y[3*]	N	Y[3]
LKT	N	Y[6]	N	N
LCK	N	Y[7]	Y	Y[7]
GBK	Y	Y[8]	N	Y[8]
CSW	Y	Y[9]	Y	Y[9]

[1]Severe spondylosis with spinal cord impingement and foramina stenosis
[2]Sensorimotor neuropathy but no exit or foramina stenosis
[3] Canal and foramina stenosis
[4]C2/3, C5/6 foramina stenosis
[5] C7 Infective but foramina stenosis
[6] C3/4/5 mild canal and foramina stenosis
[7] Mild foraminaexitstenosis
[8] C6-8 Foramina stenosis
[9]Spinal cord compression and foramina stenosis

Table-2.11A:Prediction capability of Analysis-1 with MRI as reference (considering only double, triple or clearly defined broad peaks of DFL as abnormal)

Correct positive: 9/24 (37.5%)	False positive: 2/24 (8.3%)
Correct negative: 3/24 (12.5%)	False negative: 10/24 (41.7%)
Correctly predicted 12/24 (50%)	Wrongly predicted 12/24 (50%)
Sensitivity: 47.4%	Specificity: 60%

Table-2.12:Prediction capability of Analysis-2 with MRI as reference (considering marginal broad peaks in addition to that for Analysis-1 as abnormal)

Correct positive: 17/24 (70.8%)	False positive: 3/24 (12.5%)
Correct negative: 2 (8.3%)	False negative: 2/24 (8.3%)
Correctly predicted 19/24 (79.2%)	Wrongly predicted 5/24 (20.8%)
Sensitivity: 89.5%	Specificity: 40%

Table-2.13: Prediction capability of Analysis-3 (considering a case of clinically diagnosed sensori-motor neuropathy as abnormal in addition to that for Analysis-2)

Correct positive: 19/24 (79.1%)	False positive: 1/24 (4.2%)
Correct negative: 2/24 (8.3%)	False negative: 2/24 (8.3%)
Correctly predicted 21/24 (87.5%)	Wrongly predicted 3/24 (12.5%)
Sensitivity: 90.5%	Specificity: 66.7%

2.19.1 Improved definition of a broad peak (from Singapore work)

One of the important outcomes of the Singapore work was the definition of a broad peak of DFL. Earlier a clear broad peak was defined where non-zero frequency exists at 4 ms difference from the position of the peak of DFL (considering a bin size of 2 ms). However, this work helped in redefining the broad peak to include shapes that were only marginally broad. Through a comparison with the MRI findings a rule of thumb was made to define such a broad peak; it will be termed a broad peak if an adjacent (at a separation of 2 ms) frequency to a peak is more than one third the peak. Thus the new definition of broad peak will improve the outcome of the diagnosis of CSN using DFL.

2.10 NEED FOR A DOUBLE BLIND TRIAL

The previous work described above paves the path towards the detection of CSN using DFL. However, in order to use it clinically, particularly if we want to put forward DFL as an alternative to MRI investigations in the detection of CSN, a double blind trial is needed giving a clinical worthiness of the new technique. This has to be done using ROC analysis involving the occurrences of true positive, true negative, false positive and false negative findings. The present work was taken up with this objective which is presented in the chapters that follow.

CHAPTER 3

Methods

The aim of the present work was to study the effectiveness of DFL for diagnosis or screening of cervical spondylotic neuropathy (CSN). In the diagnosis of CSN, MRI is the standard investigation carried out. So we decided to do carry out a double blind trial involving both MRI and DFL.

These investigations were carried out on both symptomatic and asymptomatic subjects. The Radiologist conducting MRI was not informed of the DFL findings. Also the investigator assessing the DFLs was unaware of the MRI results. This was done to keep the trial double blind and minimize bias.

Subject selection

A pool of 31 volunteers was chosen to take part in the investigation. The selection process was random. The pool was divided into two age groups. One group consisted of subjects aged from 25 to 50 and the other group consisted of subjects over 50. This grouping was done on the basis of the conventional understanding that cervical spondylosis was more prevalent in older age.

Informed consent was taken from the subjects prior to testing, and it was noted whether the patient had any history of cervical pain or prior diagnosis of cervical spondylotic neuropathy. Then they were subjected to MRI test at the Square hospital and later tested for DFL at the Trauma Center, both located in Dhaka, using a nerve conduction equipment developed locally by our extended group earlier in 1988 with the support of scientists from UK. Clinical neurologic evaluation of the subjects was not done.

The F – responses of individual subjects were taken from each hand by stimulating the Median nerve at the wrist and the F- response was recorded at the thenar muscle of the palm, at the base of the thumb (APB muscle).

The Median nerve was stimulated in four blocks of ten stimulations each for a total of 40 stimulations. The F- responses were recorded and then sorted into latency bins of 2ms duration. Then the distribution of F- latency was plotted as a frequency distribution.

The DFL results were evaluated according to predetermined criteria as follows

i. The bin with the highest frequency was noted and if the frequency of the adjacent bin was more than one third as high as the highest frequency then the distribution was considered to be indicative of cervical spondylosis
ii. The DFL was also considered to be indicative of cervical spondylosis if there were non zero frequencies recorded with a separation of more than 4ms from the highest frequency

MRI investigation of the cervical spine was done of each subject using a GE Signa 1.5 Tesla machine supplied by General Electric Corp at the Square Hospital, Dhaka.

Two sequences were taken (Sagittal and Axial) and the protocols were as follows

T2 (Sagittal) T(R) – 3060 ms, T(E)- 116.5 ms

T2 (Axial) T(R)- 500ms, T(E)- 15.2 ms

The results were evaluated for spinal cord compression because of disc herniation, and nerve root compression because of osteophytes or disc herniation, at the level of the cervical spine.

Since the APB muscle is supplied by nerve roots C7, C8 and T1, root compression at these levels were only considered as positive for radiculopathic CSN that could be detected using DFL. Again, spinal cord compression due to disc herniation at slightly higher levels, C4/5, C5/6, C6/7 and C7/T1 were considered to contribute to double or broad peaks indirectly. It was hypothesized that nerve cell degeneration at one position in the conduction pathway in a descending nerve would lead to atrophy or degeneration of the lower nerve fibers with which it synapses. So if the anterior horn cells of a motor nerve was degenerated in this way it would also show up as broadened peak in DFL (Rabbani 2011).

The DFL and MRI findings were evaluated separately and only brought together for comparison at the end of the investigation to ensure the double blind nature of the study. Here the MRI result was assumed standard against which the DFL outcomes were compared. The DFL results were grouped as i) True positive ii) False positive iii) True negative and iv) False negative.

There were a few instances where the MRI findings were very subtle and judged to be within normal limits by the radiologist in spite of mild cord and root compression. At each level the severity of the defect was indicated by the number of stars (*): single star (*) indicates mild abnormality, double star (**) indicates moderate abnormality and triple star (***) indicates severe abnormality. The absence of star indicates normal condition.

The data were also analysed based on two age groups as mentioned above.

Thus the results were tabulated and analyzed in the following four ways

1. The whole data set with single star (*) considered as negative.
2. The whole data set with single star (*) considered as positive.
3. The group consisting of subjects aged between 20 and 50 yrs with single star (*) considered as positive.
4. The group consisting of subjects aged above 50 yrs with single star (*) considered as positive.

From the above analysis the prediction capability of DFL were analysed in terms of Correctly Predicted percentage, Wrongly predicted percentage, Sensitivity and Specificity.

All the results and analyses are given in Chapter 4

CHAPTER 4

RESULTS

Presence of Cervical Spondylotic Neuropathy (CSN) in all the subjects as indicated by DFL based on our defined conditions in the previous chapter isgiven in Table 4.1. The abbreviations used are defined in the table caption. Each subject has two nerves on two sides under study. Thus for 31 subjects studied, the number of samples is twice this, i.e., 62. Some subjects had symptoms of CSN as radiating pain from the neck. This is indicated in one column, although no analyses were performed based on this information. The diagnosis is given in terms of Yes (Y) or No (N) on both right and left sides.

Corresponding MRI findings of the same subjects are given in Table 4.2. Again, the abbreviations used are defined in the table caption. This table also has a column showing our interest, either in Myelopathy (M) or in Radiculopathy (R), or in both, at particular vertebral levels. As mentioned in the previous chapter, at each level the severity of the defect was indicated by the number of stars (*): single star (*) indicates mild abnormality, double star (**)indicates moderate abnormality and triple star (***) indicates severe abnormality. The absence of star indicates normal condition.As mentioned in the previous chapter this is specifically addressed to the measurement on the APB muscle which is supplied by nerve roots from C7, C8 and T1 (corresponding vertebral spaces: C6-7, C7-T1, T1-T2). Therefore, radiculopathy in these three roots were of interest. Again, Myelopathy at immediate one or two levels above were of interest (corresponding vertebral spaces: C4-5, C5-6, C6-7, C7-T1). Abnormal DFL is expected to occur for both these types of neuropathy as mentioned before.

The two tables 4.1 and 4.2 were combined into a single table (Table 4.3).

The comparisons of DFL and MRI results performed according to the four analyses mentioned in the previous chapter are shown in Tables 4.4, 4.5, 4.6 and 4.7 respectively. These tables also give the counts for True Positive (TP), True Negative (TN), False Positive (FP) and False Negative (FN) events which are subsequently used to obtain figures for correct prediction, wrong prediction, Sensitivity and Specificity. The corresponding results of these analyses are given in Tables, 4.4A, 4.5A 4.6A and 4.7A respectively. These results will indicate the utility of the new test method, DFL, in diagnosis or screening of CSN which are discussed in the next chapter.

Table 4.1: Presence of CSN in all the subjects as indicated by DFL pattern (Y: positive, N: negative).
[Abbreviations are; S: Symptomatic, BP: Broad peak, DP: Double peak,SP: Single peak]

Sl No	Subject Code	Age	sex	Whether Symp-tomatic	Findings		diagnosis	
					Right	left	Right	left
1	EH	58	M	S	DP	DP	Y	Y
2	SP	27	F	S	BP	BP	Y	Y
3	KB	39	F	S	DP	SP	Y	N
4	AIK	24	M		BP	SP	Y	N
5	OR	39	M	S	SP	BP	N	Y
6	MATS	62	M	S	BP	BP	Y	Y
7	MSH	24	M		BP	BP	Y	Y
8	AKMDBZ	25	M		BP	BP	Y	Y
9	PA	24	M		SP	SP	N	N
10	MZT	25	M		BP	BP	Y	Y
11	MKH	26	M		SP	BP	N	Y
12	MAY	30	M		DP	DP	Y	Y
13	AM	26	M		BP	SP	Y	N
14	RS	24	F	S	BP	SP	Y	N
15	AR	37	M	S	SP	BP	N	Y
16	MMM	32	M	S	BP	SP	Y	N
17	AAM	29	M	S	BP	BP	Y	Y
18	NNL	22	F		DP	SP	Y	N
19	MMM(1)	30	M	S	DP	DP	Y	Y
20	NCD	63	M	S	BP	BP	Y	Y
21	SR	53	M		BP	BP	Y	Y
22	FA	55	F	S	BD	BP	Y	Y
23	MDB	55	M		BP	SP	Y	N
24	MUA	55	M		BP	DP	Y	Y
25	KU	64	M	S	BP	DP	Y	Y
26	PD	26	M	S	BP	BP	Y	Y
27	NI	43	M		BP	DP	Y	Y
28	R	50	F	S	BP	SP	Y	N
29	AJ	60	M		BP	SP	Y	N
30	BKD	27	M		BP	SP	Y	N
31	RA	25	M	S	DP	DP	Y	Y

Table 4.2: MRI findings for CSN.

[Abbreviations are: PDH – posterior disc herniation, TSH – Thecal sac indentation, O- osteophyte, FN- foraminal narrowing, DHR-disc height reduction, FDH – foraminal disc herniation, l- left, r- right, bl – bilateral, M- Myelopathy, R- Radiculopathy. A single '*' in columns 8 to 11 indicates presence of the particular feature, double '**'and triple '***" represents increased severity]

Sl No	Code	age	sex	Spinal level	Our interest	Finding	Cord compression		Root compression	
							Rt	Lt	Rt	Lt
1	EHC	56		C4-5	M	DHR,	*	*	*	***
				C 5-6	M	DH	**	**	**	*
				C6-7	R	FDH (L-R)			**	*
2	SP	27	F							
				C4-5	M	TSI,O	*	*		**
				C6-7	R	O, FN				**
3	KB	39	F	C4-5	M	TSI	**	**		
				C6-7	M,R	TSI	*	*		
4	AIK	23	M	C5-6	M	DH (Rt)	***	**	**	**
5	OR	38	M	C4-5	M	TSI(mild)	*	*		
				C5-6 C6-7	M M,R	O, FN, TSI(mild)		*		*
				C7-T1	M,R	O				*
6	MATS	62	M							
				C4-5	M	TSI(mild)	*		*	*
				C5-6	M	TSI, FN	*	*	*	*
				C6-7	M,R	FN	*	*	*	*
7	MSH	24	M							
				C5-6	M	DH, O(mild)			*	**
8	MBZ	25	M	C4-5	M	O (MILD)				*
9	PA	24	M	C4-5	M	O (MILD)				
10	MZT	25	M	C5-6	M	DH(MILD)			*	
				C6-7	M,R	DH(MILD)			*	*
11	MKH	26	M	C4-5	M	FN(MILD)	*	*	*	*
				C5-6	M	TSI(mild)	*	*	*	*
				C6-7	M,R	FN(MILD)	*	*	*	*
12	MAY	30	M	C4-5 C5-6	M M	DH-(MILD)	*	*		
13	AM	26	M							
				C4-5	M	DH, TSI(mild)	*	*		
				C5-6	M	DH,FN	*	*	*	*
				C6-7	M,R	DH,FN(mild)	*	*	*	*
				C7-T1	M,R	FN				*
14	RS	24	F	C5-6 C6-7	M R	TSI,FN	*	*	*	*
15	AR	37	M							
				C4-5 C5-6 C6-7	M M R	DH, TSI,FN	*	*	*	*
16	MMM(1)	32	M							
				C5-6	M	DH,FN	*	*	*	*
				C6-7	M	DH.TSI,FN	*	*	*	*
17	AAM	29	M	C4-5	M	DH,FN(mild)	*	*		*
				C5-6	M	DH,FN(mild)	*	*	*	*
18	NNL	22	F	C5-6 C6-7	M M,R	O (minimal)	*	*		

Table continued to next page

Sl No	Code	age	sex	Spinal level	Our interest	Finding	Cord compression		Root compression	
							Rt	Lt	Rt	Lt
19	MMM(2)	30	M							
				C4-5	M	DH(mild)TSI, FN	*	*	*	**
				C5-6	M	FN,DH	*	*	*	**
20	NCD	63	M							
				C4-5	M	DH,FN	*	*	**	*
				C6-7	M,R	DH,FN	*	*	*	*
21	SR	53	M							
				C4-5	M	, DH,FN,TSI	**	**	**	**
				C5-6	M	DH,FN,TSI	*	**	***	**
				C6-7	M	DH,FN,TSI	*	**	**	*
				C7-T1	M,R	DH,(mild)FN,TSI	*	*	*	*
22	FA	55	F							
				C5-6	M	DH,FN	*	*	*	*
				C6-7	M,R	DH	*	*	*	**
23	MDB	55	M							
				C4-5	M	DH,O,FN,	*	*	*	*
				C5-6	M	DH,O	*	*	*	**
				C6-7	M,R	DH,O,FN	*	**	*	*
24	MUA	55	M	C5-6	M	DH	**			
				C6-7	M,R	DH		**		
25	KU	64	M							
				C4-5	M	DH.O,FN	**	**	**	**
				C5-6	M	DH,FN	**	**	**	**
				C6-7	M,R	DH,O,FN	**	**	**	**
26	PD	26	M							
				C4-5	M	DH,O(mild)	*	**	*	**
				C5-6 C6-7	M M,R	DH,O,FN	*	*	*	*
27	NI	43	M							
				C4-5	M	DH,O,FN	*	*	*	*
				C5-6 C6-7	M M,R	DH,O,FN	*	*	*	*
				C7-T1	M,R	O,FN	*	*	*	*
28	R	50	F							
				C4-5	M	DH	*	*		
				C5-6	M	DH,FN	*	**		*
29	AJ	60	M							
				C5-6	M	DH,O,FN	**	**	***	***
				C6-7	M,R	DH,O,FN	**	**	*	*
30	BKD	27	M	C5-6		DH,FN(mild)	*	*	*	*
				C6-7		DH,FN(mild)	*	*	*	*
31	RA	25	M							
				C5-6,6-7	M	DH,	**	*	**	*

Table 4.3: MRI findings for CSN.

[Abbreviations: PDH – posterior disc herniation, TSI – Thecal sac indentation, O- osteophyte, FN- foraminal narrowing, DHR-disc height reduction, FDH – foraminal disc herniation, L-left, R- right, bl – bilateral, M- Myelopathy, R- Radiculopathy. A single '*' in columns 8 to 11 indicates mild presence of the particular feature, double '**' and triple'***" represents increased severity]

	MRI findings											DFL findings				
Sl No	Subj. Code	Age	Sex	Spinal level	Our interest	Finding	Cord compression		Root compression		Radiologist's Impression	Symp -tom	Findings		Diagnosis	
							Rt	Lt	Rt	Lt			Right	Left	Right	Left
1	EHC	56	M	C4-5	M	DHR	*	*	*	***	Spinal stenosis, M (bl), R(bl, rt dominant)	Y	DP	DP	Y	Y
				C 5-6	M	DH,	**	**	**	*						
				C6-7	R	FDH(L-R)	*	*	**	*						
2	SP	27	F	C4-5	M	TSI,O				**	M, R(lt)	Y	BP	BP	Y	Y
				C6-7	M,R	O, FN				**						
3	KB	39	F	C4-5	M	TSI	**	**			M (bl)	Y	DP	SP	Y	N
				C6-7	M,R		*	*								
4	AIK	23	M	C5-6	M	DH(Rt)	***	**	**	**	Spinal canal stenosis, M(rt dominant)	N	BP	SP	Y	N
5	OR	38	M	C4-5	M	TSI(mild)	*	*			R(lt)	Y	SP	BP	N	Y
				C5-6	M	O, FN,		*		*						
				C6-7	M,R	TSI(mild)		*		*						
				C7-T1	M,R	O				*						
6	MATS	62	M	C4-5	M	TSI(mild), FN	*		*	*	M(bl), R(bl)	Y	BP	BP	Y	Y
				C5-6	M	TSI, FN	*	*	*	*						
				C6-7	M,R	FN,DH	*	*	*	*						
7	MSH	24	M	C5-6	R	DH, O(mild)			*	**	Normal. (mild Cord compr.)	N	BP	BP	Y	Y
				C6-7	M,R				*	*						
8	MBZ	25	M	C4-5	M	O (mild)				*	Normal	N	BP	BP	Y	Y
9	PA	24	M	C4-5	M	O (mild), TSI(mild)					Normal	N	SP	SP	N	N
10	MZT	25		C4-5	M	FN			*							
			M	C5-6	M	DH(mild)			*		Normal	N	BP	BP	Y	Y
				C6-7	M,R				*	*						
11	MKH	26	M	C4-5	M	FN (mild), TSI(m)	*	*	*	*	Normal (mild root compr.)	N	SP	BP	N	Y
				C5-6	M	TSI(mild), FN	*	*	*	*						
				C6-7	M,R	FN(MILD), TSI	*	*	*	*						
12	MAY	30	M	C4-5	M	DH (mild)	*	*			Normal	N	DP	DP	Y	Y
				C5-6	M		*	*								

Sl No	Code	age	sex	Spinal level	Our interest	Finding	Cord compression		Root compression		Radiologist's Impression	Symptom				
							Rt	Lt	Rt	Lt						
13	AM	26	M	C4-5	M	DH, TSI(mild)	*	*			M(bl), R(lt)	N	BP	SP	Y	N
				C5-6	M	DH,FN	*	*	*	*						
				C6-7	M,R	DH,FN(mild)	*	*	*	*						
				C7-T1	M,R	FN				*						
14	RS	24	F	C5-6 C6-7	M R	TSI,FN	*	*	*	*	M (mild, bl)	Y	BP	SP	Y	N
15	AR	37	M	C4-5 C5-6 C6-7	M M R	DH, TSI,FN	*	*	*	*	M (bl).	Y	SP	BP	N	Y
16	MMM (1)	32	M	C5-6	M	DH,FN	*	*	*	*	M (bl).	Y	BP	SP	Y	N
				C6-7	M	DH.TSI,FN	*	*	*	*						
17	AAM	29	M	C4-5	M	DH,FN(mild)	*	*		*	M (mild, bl)	Y	BP	BP	Y	Y
				C5-6	M	DH,FN(mild)	*	*	*	*						
18	NNL	22	F	C5-6 C6-7	M M,R	O (minimal)	*	*			Normal	N	DP	SP	Y	N
19	MMM (2)	30	M	C4-5	M	DH(mild)TSI, FN	*	*	*	**	R (bl)	Y	DP	DP	Y	Y
				C5-6	M	FN,DH	*	*	*	**						
20	NCD	63	M	C4-5C5-6	M	DH,FN	*	*	**	*	R(rt)	Y	BP	BP	Y	Y
				C6-7	M,R	DH,FN	*	*	*	*						
21	SR	53	M	C4-5	M	DH,FN,TSI	**	**	**	**	M(bl), R (bl)	N	BP	BP	Y	Y
				C5-6	M	DH,FN,TSI	*	**	***	**						
				C6-7	M	DH,FN,TSI	*	**	**	*						
				C7-T1	M,R	DH,(mild), FN,TSI	*	*	*	*						
22	FA	55	F	C5-6	M	DH,FN	*	*	*	*	Cord compr.(?)	Y	BP	BP	Y	Y
				C6-7	M,R	DH,TSI	*	*	*	**						
23	MDB	55	M	C4-5	M	DH,O,FN,	*	*	*	*	M(lt) R.(bl) (?)	N	BP	SP	Y	N
				C5-6	M	DH,O, FN	*	*	*	**						
				C6-7	M,R	DH,O,FN	*	**	*	*						
24	MUA	55	M	C5-6	M	DH	**				M(bl)	N	BP	DP	Y	Y
				C6-7	M,R	DH		**								
25	KU	64	M	C4-5	M	DH.O,FN	**	**	**	**	Cord compr.	Y	BP	DP	Y	Y
				C5-6	M	DH,FN	**	**	**	**						
				C6-7	M,R	DH,O,FN	**	**	**	**	Cord & Root Compr.					

Sl No	Code	age	sex	Spinal level	Our interest	Finding	Cord compression		Root compression		Radiologist's Impression	Symptom				
							Rt	Lt	Rt	Lt						
26	PD	26	M	C4-5	M	DH,O∗	*	**	*	**	Cord & root compr.	Y	BP	BP	Y	Y
				C5-6 C6-7	M M,R	DH,O,FN	*	*	*	*						
27	NI	43	M	C4-5	M	DH,O,FN	*	*	*	*	Cord & Root compr.	N	BP	DP	Y	Y
				C5-6 C6-7	M M,R	DH,O,FN	*	*	*	*						
				C7-T1	M,R	O,∗FN∗	*	*	*	*						
28	R	50	F	C4-5	M	DH	*	*			Cord & Root compr.(minimal)	Y	BP	SP	Y	N
				C5-6	M	DH,FN∗	*	**		*						
29	AJ	60	M	C5-6	M	DH,O∗,FN∗	**	**	***	***	Cord compr.	N	BP	SP	Y	N
				C6-7	M,R∗	DH,O,FN	**	**	*	*						
30	BKD	27	M	C5-6	M ∗	DH,FN∗	*	*	*	*	Cord compr	N	BP	SP	Y	N
				C6-7	M ∗	DH∗,FN∗	*	*	*	*						
31	RA	25	M	C5-6 C6-7	M	DH,	**	*	**	*	Cord compr	Y	DP	DP	Y	Y

Table 4.4: Comparison of MRI and DFL findings, assuming single* to represent absence of CSN.
[Y: Yes (positive for CSN), N: No (negative for CSN).TP: True positive, TN: True negative, FP: False positive, FN: False negative]

Sl No	Code	age	sex	Spinal level	MRI Finding		DFL Findings		TP	TN	FP	FN
					Rt	Lt	Rt	Lt				
1	EHC	56	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C6-7	Y	Y						
2	SP	27	F	C4-5	Y	Y	Y	Y	1	0	1	0
				C6-7	N	Y						
3	KB	39	F	C2-3			Y	N	1	0	0	1
				C4-5	Y	Y						
				C6-7	Y	Y						
4	AIK	23	M	C5-6	Y	N*	Y	N	1	0	0	1
5	OR	38	M	C4-5	Y*	Y*	N	Y	0	1	1	0
				C5-6	N	Y						
				C6-7	N	Y						
				C7-T1	N	Y						
6	MATS	62	M	C4-5	Y*	Y*	Y	Y	0	0	2	0
				C5-6	Y	Y						
				C6-7	Y	Y						
7	MSH	24	M	C5-6	Y*	Y*	Y	Y	1	0	1	0
8	MBZ	25	M	C4-5	N	N*	Y	Y	0	0	2	0
9	PA	24	M	C4-5	N	N*	N	N	0	2	0	0
10	MZT	25	M	C5-6	N*	N*	Y	Y	0	0	2	0
				C6-7	N*	N*						
11	MKH	26	M	C4-5	N*	N*	N	Y	0	1	1	0
				C5-6	N*	N*						
				C6-7	N*	N*						
12	MAY	30	M	C4-5	N*	N*	Y	Y	0	0	2	0
				C5-6	N*	N*						
13	AM	26	M	C4-5	Y*	Y*	Y	N	0	1	1	0
				C5-6	Y	Y						
				C6-7	Y*	Y*						
				C7-T1	N	Y						
14	RS	24	F	C5-6	Y	Y	Y	N	0	1	1	0
				C6-7	Y	Y						
15	AR	37	M	C4-5	Y	Y	N	Y	0	1	1	0
				C5-6	Y	Y						
				C6-7	Y	Y						
16	MMM	32	M	C5-6	Y	Y	Y	Y	0	1	1	0
				C6-7	Y	Y						
17	AAM	29	M	C4-5	Y	Y	Y	Y	0	0	2	0
				C5-6	Y	Y						
18	NNL	22	F	C5-6	N*	N*	Y	N	0	1	1	0
				C6-7	N*	N*						
Sub Total-A									6	9	19	2

Table continued to next page

Table 4.4continued …

Sl No	Code	age	sex	Spinal level	MRI Findings		DFL Findings		TP	TN	FP	FN
					Rt	Lt	Rt	Lt				
19	MMM (1)	30	M	C4-5	Y	Y	Y	Y	1	0	1	0
				C5-6	Y	Y (R)						
20	NCD	63	M	C4-5	Y (R)	Y	Y	Y	1	0	1	0
				C6-7	Y	Y						
21	SR	53	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
				C7-T1	Y	Y						
22	FA	55	F	C5-6	Y	Y			1	0	1	0
				C6-7	Y	Y	Y	Y				
23	MDB	55	M	C4-5	Y	Y			0	0	1	1
				C5-6	Y	Y (M)	Y	N				
				C6-7	Y	Y (M)						
24	MUA	55	M	C5-6	Y (M)	N*	Y	Y	2	0	0	0
				C6-7	N*	Y (M)						
25	KU	64	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
26	PD	26	M	C4-5	Y	Y	Y	Y	1	0	1	0
				C5-6	Y	Y						
				C6-7	Y	Y						
27	NI	43	M	C4-5	Y	Y	Y	Y	0	0	2	0
				C5-6	Y	Y						
				C6-7	Y	Y						
				C7-T1	Y	Y						
28	R	50	F	C4-5	Y	Y	Y	Y	0	1	1	0
				C5-6	Y (M)	Y						
29	AJ	60	M	C5-6	Y	Y	Y	N	1	0	0	1
				C6-7	Y	Y						
30	BKD	27	M	C5-6	Y	Y	Y	N	0	1	1	0
				C6-7	Y	Y						
31	RA	25	M	C5-6	Y (M	Y	Y	Y	1	0	1	0
				C6-7	Y (M	Y						
Sub Total-B									12	2	10	2
TOTAL (A+B)									**18**	**11**	**29**	**4**

Table 4.4-A: Analysis -1 for DFL as an indicator of CSN, appropriate for Table 4.3.

TP	TN	FP	FN	Correctly Predicted %	Wrongly Predicted %	Sensitivity %	Specificity %
18	**11**	**29**	**4**	**47**	**53**	**82**	**28**

Table 4.5: Comparison of MRI and DFL findings, assuming single* to represent presence of CSN.
[Y: Yes (positive for CSN), N: No (negative for CSN).TP: True positive, TN: True negative, FP: False positive, FN: False negative]

Sl No	Code	age	sex	Spinal level	MRI Finding		DFL Findings		TP	TN	FP	FN
					Rt	Lt	Rt	Lt				
1	EHC	56	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C6-7	Y	Y						
2	SP	27	F	C4-5	Y	Y	Y	Y	1	0	1	0
				C6-7	N	Y						
3	KB	39	F	C2-3			Y	N	1	0	0	1
				C4-5	Y	Y						
				C6-7	Y	Y						
4	AIK	23	M	C5-6	Y	N* (Y)	Y	N	1	0	0	1
5	OR	38	M	C4-5	Y*	Y*	N	Y	1	0	0	1
				C5-6	N	Y						
				C6-7	N	Y						
				C7-T1	N	Y						
6	MATS	62	M	C4-5	Y*	Y*	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
7	MSH	24	M	C5-6	Y*	Y*	Y	Y	2	0	0	0
8	MBZ	25	M	C4-5	N	N*(Y)	Y	Y	1	0	1	0
9	PA	24	M	C4-5	N	N*(Y)	N	N	0	2	0	0
10	MZT	25	M	C5-6	N*(Y)	N*(Y)	Y	Y	2	0	0	0
				C6-7	N*(Y)	N*(Y)						
11	MKH	26	M	C4-5	N*(Y)	N*(Y)	N	Y	1	0	0	1
				C5-6	N*(Y)	N*(Y)						
				C6-7	N*(Y)	N*(Y)						
12	MAY	30	M	C4-5	N*(Y)	N*(Y)	Y	Y	2	0	0	0
				C5-6	N*(Y)	N*(Y)						
13	AM	26	M	C4-5	Y*	Y*	Y	N	1	0	0	1
				C5-6	Y	Y						
				C6-7	Y*	Y*						
				C7-T1	N	Y						
14	RS	24	F	C5-6	Y	Y	Y	N	1	0	0	1
				C6-7	Y	Y						
15	AR	37	M	C4-5	Y	Y	N	Y	1	0	0	1
				C5-6	Y	Y						
				C6-7	Y	Y						
16	MMM	32	M	C5-6	Y	Y	Y	Y	1	0	0	1
				C6-7	Y	Y						
17	AAM	29	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
18	NNL	22	F	C5-6	N*(Y)	N*(Y)	Y	N	1	0	0	1
				C6-7	N*(Y)	N*(Y)						
Sub Total-C									22	2	2	10

Table continued to next page

Table 4.5continued …

Sl No	Code	age	sex	Spinal level	MRI Findings		DFL Findings		TP	TN	FP	FN
					Rt	Lt	Rt	Lt				
19	MMM (1)	30	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y (R)						
20	NCD	63	M	C4-5	Y (R)	Y	Y	Y	2	0	0	0
				C6-7	Y	Y						
21	SR	53	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
				C7-T1	Y	Y						
22	FA	55	F	C5-6	Y	Y	Y	Y	2	0	0	0
				C6-7	Y	Y						
23	MDB	55	M	C4-5	Y	Y	Y	N	1	0	0	1
				C5-6	Y	Y (M)						
				C6-7	Y	Y (M)						
24	MUA	55	M	C5-6	Y (M)	N*(Y)	Y	Y	2	0	0	0
				C6-7	N*(Y)	Y (M)						
25	KU	64	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
26	PD	26	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
27	NI	43	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
				C7-T1	Y	Y						
28	R	50	F	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y (M)	Y						
29	AJ	60	M	C5-6	Y	Y	Y	N	1	0	0	1
				C6-7	Y	Y						
30	BKD	27	M	C5-6	Y	Y	Y	N	1	0	0	1
				C6-7	Y	Y						
31	RA	25	M	C5-6	Y (M	Y	Y	Y	2	0	0	0
				C6-7	Y (M	Y						
Sub Total-D									23	0	0	3
Sub Total-C									22	2	2	10
TOTAL (C+D)									**45**	**2**	**2**	**13**

Table 4.5-A: Analysis -2 for DFL as an indicator of CSN, appropriate for Table 4.4.

TP	TN	FP	FN	Correctly Predicted %	Wrongly Predicted %	Sensitivity %	Specificity %
45	**2**	**2**	**13**	**76**	**24**	**78**	**50**

Table 4.6: For age group 20 to 50 (inclusive): Comparison of MRI and DFL findings, assuming single* to represent presence of CSN.
[Y: Yes (positive for CSN), N: No (negative for CSN).TP: True positive, TN: True negative, FP: False positive, FN: False negative]

Sl No	Code	age	sex	Spinal level	MRI Finding		DFL Findings		TP	TN	FP	FN
					Rt	Lt	Rt	Lt				
1	SP	27	F	C4-5	N	Y	Y	Y	1	0	1	0
				C6-7	N	Y						
2	KB	39	F	C2-3			Y	N	1	0	0	1
				C4-5	Y	Y						
				C6-7	Y	Y						
3	AIK	23	M	C5-6	Y	N* (Y)	Y	N	1	0	0	1
4	OR	38	M	C4-5	Y*	Y*	N	Y	1	0	0	1
				C5-6	N	Y						
				C6-7	N	Y						
				C7-T1	N	Y						
5	MSH	24	M	C5-6	Y*	Y*	Y	Y	2	0	0	0
6	MBZ	25	M	C4-5	N	N*(Y)	Y	Y	1	0	1	0
7	PA	24	M	C4-5	N	N*(Y)	N	N	0	2	0	0
8	MZT	25	M	C5-6	N*(Y)	N*(Y)	Y	Y	2	0	0	0
				C6-7	N*(Y)	N*(Y)						
9	MKH	26	M	C4-5	N*(Y)	N*(Y)	N	Y	1	0	0	1
				C5-6	N*(Y)	N*(Y)						
				C6-7	N*(Y)	N*(Y)						
10	MAY	30	M	C4-5	N*(Y)	N*(Y)	Y	Y	2	0	0	0
				C5-6	N*(Y)	N*(Y)						
11	AM	26	M	C4-5	Y*	Y*	Y	N	1	0	0	1
				C5-6	Y	Y						
				C6-7	Y*	Y*						
				C7-T1	N	Y						
12	RS	24	F	C5-6	Y	Y	Y	N	1	0	0	1
				C6-7	Y	Y						
13	AR	37	M	C4-5	Y	Y	N	Y	1	0	0	1
				C5-6	Y	Y						
				C6-7	Y	Y						
14	MMM	32	M	C5-6	Y	Y	Y	Y	1	0	0	1
				C6-7	Y	Y						
15	AAM	29	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
16	NNL	22	F	C5-6	N*(Y)	N*(Y)	Y	N	1	0	0	1
				C6-7	N*(Y)	N*(Y)						
17	MMM (1)	30	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y (R)						
18	PD	26	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
19	NI	43	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
				C7-T1	Y	Y						
20	R	50	F	C4-5	Y	Y	Y	Y	1	0		1
				C5-6	Y (M)	Y					0	
21	BKD	27	M	C5-6	Y	Y	Y	N	1	0		1
				C6-7	Y	Y					0	
22	RA	25	M	C5-6	Y (M	Y	Y	Y	2	0	0	0
				C6-7	Y (M	Y						
Total-E									**29**	**2**	**2**	**11**

Table 4.6-A: Analysis -3 for DFL as an indicator of CSN, appropriate for Table 4.5, (20 to 50yrs)

TP	TN	FP	FN	Correctly Predicted %	Wrongly Predicted %	Sensitivity %	Specificity %
29	**2**	**2**	**11**	**70**	**30**	**73**	**50**
40 (= 29 + 11) nerves out of 44 (91%) has CSN (based on MRI result)							

Table 4.7: For age group above 50 yrs: Comparison of MRI and DFL findings, assuming single* to represent presence of CSN.
[Y: Yes (positive for CSN), N: No (negative for CSN).TP: True positive, TN: True negative, FP: False positive, FN: False negative]

Sl No	Code	age	sex	Spinal level	MRI Findings		DFL Findings		TP	TN	FP	FN
					Rt	Lt	Rt	Lt				
1	EHC	56	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C6-7	Y	Y						
2	MATS	62	M	C4-5	Y*	Y*	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
3	NCD	63	M	C4-5	Y (R)	Y	Y	Y	2	0	0	0
				C6-7	Y	Y						
4	SR	53	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
				C7-T1	Y	Y						
5	FA	55	F	C5-6	Y	Y	Y	Y	2	0	0	0
				C6-7	Y	Y						
6	MDB	55	M	C4-5	Y	Y	Y	N	1	0	0	1
				C5-6	Y	Y (M)						
				C6-7	Y	Y (M)						
7	MUA	55	M	C5-6	Y (M)	N*(Y)	Y	Y	2	0	0	0
				C6-7	N*(Y)	Y (M)						
8	KU	64	M	C4-5	Y	Y	Y	Y	2	0	0	0
				C5-6	Y	Y						
				C6-7	Y	Y						
9	AJ	60	M	C5-6	Y	Y	Y	N	1	0	0	1
				C6-7	Y	Y						
Total-F									**16**	**0**	**0**	**2**

Table 4.7-A: Analysis -4 for DFL as an indicator of CSN, appropriate for Table 4.6, (> 50yrs)

TP	TN	FP	FN	Correctly Predicted %	Wrongly Predicted %	Sensitivity %	Specificity %
16	**0**	**0**	**2**	**89**	**11**	**89**	***
18 (= 16 +2) out of 18 (100%) has CSN (based on MRI result)							

*** Since both TN and FP have zero value, specificity could not be calculated.

CHAPTER 5

Discussion

The work on DFL (which is a statistical frequency distribution of F-latencies from multiple F-responses) and the exploration of its benefit in the diagnosis of cervical spondylosis has progressed through several steps. First came the conceptual realization that it was an approximate mirror image of DCV of nerve fibers which can be electrically stimulated. Secondly, a study was conducted to establish that DFL was a repeatable thus physiological parameter which returns consistently similar results upon repeated testing of the same individual nerve which in turn verified the above concept. The third step was the establishment that it was sensitive to nerve compression due to any cause, resulting in a delay shift of the DFL. During this study there was a fortuitous observation that among the subjects tested, the ones returning a broad, double or triple peak of DFL were diagnosed cases of cervical spondylosis, or alternately suffering from neck pain while normal subjects demonstrated a single peak. This observation brought about a question as to whether DFL was correlated to cervical spondylosis. A set of hypotheses invoking the segmental compression or degeneration of nerves were formulated based on physiological and statistical arguments to explain the observations. The fourth study attempted to verify the hypotheses through a correlation between the DFL and X-ray findings (with a few MRI) of known cases of cervical spondylosis. This finding was further confirmed through comparison of DFL and MRI in a study conducted at Singapore General Hospital on patients with radiculopathy.

One of the important outcomes of the Singapore work was the definition of a broad peak of DFL. Earlier a clear broad peak was defined where non-zero frequency exists at 4 ms difference from the position of the peak of DFL (considering a bin size of 2 ms for the frequency distribution). However, this work helped in redefining the broad peak to include shapes that were only marginally broad. Through a comparison with the MRI findings a rule of thumb was made to define such a broad peak; it will be termed a broad peak if an adjacent (at a separation of 2 ms) frequency to a peak is more than one third that at the peak. Thus the new definition of broad peak (though still arbitrary) has improved the correlation with MRI findings. The Singapore study was

a valuable learning experience and the redefined criteria for broad peak thus obtained, was used in the analysis of the current study.

The current trial tries to establish the cost effectiveness of using DFL as an alternative to MRI in the detection of CSN through a double blind study. MRI is so far considered the gold standard in the diagnosis of CSN, but it is expensive, time consuming, and the evaluation is qualitative rather than quantitative. Besides, it is also dependent on the expertise and experience of the investigator. DFL on the other hand is a functional and objective test, and uses equipment that can be made at a low cost, with almost zero consumable expense. Therefore if the efficacy of DFL in the detection of CSN is borne out through the present work, this could provide an important milestone in neuromedicine.

In the present work patient selection was done keeping the prevailing idea about the epidemiology of radiculopathy and myelopathy in consideration. It is conventionally accepted that radiculopathy and myelopathy is mainly to be found in subjects over the age of 50. So the selected subjects were divided into two age groups, the first group was composed of individuals within the age range of 20 to 50 (inclusive), while the second group was composed of those who were above 50 years. Whether the subjects had symptoms was also duly noted although this information was not used for any analysis.

The stimulation interval used to obtain the F responses was set at one second to ensure that refractory period of action potentials did not affect the output since DFL requires each event related to a stimulation to be random. Stimulation induced physiological processes are expected to end much before the next stimulus in this case, thus making each event independent of history.

The centre that performed MRI in the present work does not image the T1 vertebral section routinely. Because of this oversight, information of the contribution of radiculopathy at this level is missing from the present MRI findings. This definitely could affect the results. However, since involvement of C4 to C8 is present, statistically the role of T1 will not be too much. Besides, it is reported that the prevalence of cervical myelopathy is much higher than that of cervical radiculopathy (Young, 2000), so the results will be affected only slightly through this omission. In fact if there were T1 lesions in the present case the efficacy of DFL would improve further since it would decrease the number of false positives.

The instances where the MRI reports indicated the deformity to be mild (indicated by single *) and was taken to indicate absence of neuropathy yielded results with a correct prediction score of only 47%. This was low as there was a high false positive score of 29 against true positive of 18 and true negative of 11. On the other hand the correct prediction score was significantly improved when the same MRI findings with mild compression were taken to indicate abnormality, raising the correct prediction score to 76%. This indicates that DFL is a very sensitive tool for identification of CSN. In fact in many of the cases, the person did not have any complain, but DFL indicated abnormality. That means DFL can detect CSN even in the subclinical phase increasing its utility in clinical management.

In terms of the details, the sensitivity and specificity values for the combined population were 82% and 28% respectively with mild compressions considered as normal and 78% and 50% respectively with mild compressions considered as abnormal. This shows that the overall performance increases if the mild compressions are considered abnormal. Therefore the subsequent analyses for the two age groups were performed only on this basis. Of course the specificity seems to be rather low which is because there were not too many cases without CSN, an important point revealed by this work about which we will discuss more later.

For the study of the two age groups, the lower age group (20-50yrs) gives the scores of correct prediction and sensitivity as 70% and 73% respectively while that for the older age group (50-70 yrs) were both 89%. The slightly low value for the lower age group was due to a rather large false negative score (11 out of 44) which reveals some limitations of the DFL technique. A close observation indicates that for most of these false negative cases the subject had compressions at multiple vertebral levels. If these compressions lead to a similar degree of delay shift of DFL through each of the nerve branches, the combined DFL would not show broad peak or double peak, thus leading to an erroneous conclusion. Therefore, this aspect of DFL needs to be looked into for future improvement. Even then the sensitivity score of 73% is good for a new, simple and low cost diagnostic method. For the elderly, the prediction rate and sensitivity are both high, both being 89%. Therefore, the efficacy of this technique for a screening test of elderly looks promising. The specificity for the younger age group was 50%, while it could not be obtained at all for the higher age group. This is because of the low incidence of actually negative cases. In

the lower age group the true negative and false positives were both 2 while these were both zero for the higher age group.

The present study shows that DFL is well correlated with MRI with reasonably high sensitivity and moderate specificity. So it is very promising as a screening tool. The final aim is to find out if DFL is a dependable alternative to MRI in the investigation and diagnosis of radiculopathy and myelopathy. This can be found out taking a larger sample of test subjects, including both symptom free and symptomatic individuals and reducing observer bias by being double blind.

However, taking MRI as a gold standard is also questionable since the resolution of the images may put a limitation on the assessment of compression. In many cases Thecal sac indentation was rather blunt and it was not clear whether it affected one side more than the other. On the other hand, DFL gives clear and distinct side discrimination. This could have affected the results of the present study as well. Therefore, the low values of specificity obtained in this work could have been due to this limitation of MRI. Perhaps studies with an MRI with greater magnetic field strength may give a better answer. In fact DFL is a very sensitive technique as it can detect subclinical CSN.

The capability of DFL in detecting subclinical stages of CSN holds a promise as an awareness development tool alongside screening for prevalence of neuropathy. Those individuals who are diagnosed as positive for CSN and are still asymptomatic could be persuaded to make changes of lifestyle to lessen the chance of progression of their health condition.

Further study could be carried out in investigating Lumbosacral Spondylotic neuropathy by examining the tibial and common peroneal nerves. Presently DFL is limited in that it cannot determine the location and type of lesion (whether radiculopathy, myelopathy, trauma or other lesions) involved. Further work has already been taken up to differentiate radiculopathy from myelopathy using DFL in conjunction with the M-response, which is acquired as a standard procedure in nerve conduction measurements. Besides, to identify the levels of the lesion, it is being planned to use DFL together with other nerve conduction parameters and standard clinical examinations.

Other neurologic conditions such as Gullian Barre syndrome, diabetic and uremic neuropathy etc, could also be explored with this technique. The present study can be extended further to

include the examination of Lumbosacral spondylotic neuropathy by evaluating the Tibial and Common Peroneal nerves which have already shown similar features.

The current study along with past clinical experience in our laboratory indicates that there is a high prevalence of undiagnosed or early stage cervical spondylotic neuropathy even in the younger age group. From tables 4.5A and 4.6A it can be seen that about 91% of 44 median nerves of 22 subjects aged between 20 to 50yrs had positive CSN of varying degrees, while 100% of 18 median nerves of 9 subjects aged above 50yrs had positive CSN, both based on the MRI results. This finding for the lower age group came rather as a surprise, since conventional wisdom suggests CSN to be a feature of mainly the old age. Therefore, the present study brings to light a new area of research; that of taking up a prevalence study of CSN in population samples taken from different backgrounds, economic and social conditions, occupation, etc.

No extensive prevalence data for CSN are available in the literature; the limited availability and the high cost of MRI equipment may be the cause behind. Most reports deal with cases that come to a hospital for treatment only, which is of no use for a general prevalence study. A large population will not come to a hospital although they may have CSN but to a tolerable level. Most studies suggest that the incidence of cervical myelopathy is much higher than that of radiculopathy and that cervical myelopathy is the most common spinal cord disorder in individuals aged 55 and older in the US (Young, 2000). Baron et al (2005) reported that the prevalence of cervical spondylotic myelopathy is 50% in men and 33% in women by 60 years of age.

Therefore, large screening studies should be conducted using DFL to further explore the finding of the high incidence of CSN in the younger population as well as in the aged. In conclusion, DFL could become a screening tool for early detection of cervical spondylosis, and used as an awareness building tool of choice.

The present study establishes DFL on a stronger footing for assessment of cervical spondylotic neuropathy, whether due to spinal cord or nerve root compression. With further development, the performance is expected to improve making it more effective. A dedicated portable equipment giving M-response and DFL on a computer monitor can be made at reasonably low cost, and our extended group at Dhaka is already working on this. Being a non-invasive technique requiring

virtually zero expenditure in consumables, it promises greater access to patients, and could be used for extensive prevalence study.

Thus the present work has been successful in establishing the new technique of DFL in the detection of cervical spondylotic neuropathy with greater confidence. This study could be a stepping stone for its global acceptance.

References

1. Alam MJ and Rabbani KS, 2010. *Possible detection of cervical spondylotic neuropathy using Distribution of F- latency (DFL), a new neurophysiological parameter.* BMC Research Notes; 3:112-116.
2. Baron EM and Young WF, 2005, *Cervical Spondylosis: Diagnosis and Management*, eMedicine.
3. Cameron J.R. & Skofronick J.G 1978.**:** "Medical Physics" John Willy & Sons, Inc.
4. Charles R. Noback, Norman L. Strominger, Robert J. Demarest, David A. Ruggiero**:** The Human Nervous System: Structures and Functions, 6th Ed. Humana press, New Jersey.
5. Chummy S. Sinnatamby**:** Lasts Anatomy: Regional and Applied, 10th Ed.
6. Gray's anatomy, 1995. 38th English ed. New York: Churchill Livingstone, p.859.
7. Harayama H, Shinozawa K, Kondo H, et al, 1991. *A new method to measure the distribution of motor conduction velocity in man.*Electroenceph Clin Neurophysiol; 81:323-331.
8. Hossain MI, Chowdhury EA, Mamun AA, Salam A, Baig TN and Rabbani KS, 2011. *Use of distribution of F-latency (DFL) in the detection of cervical spondylotic neuropathy,* Bangladesh J of Med Phys; 4:37-42.
9. Ingram DA, Davis GR and Swash M,1987. *The collision technique: a new method for measurement of the motor nerve refractory period distribution in man.* Electroenceph Clin Neurophysiol; 66:225-234.
10. Kimura J, 1989. *Electrodiagnosis in diseases of nerve and muscle: Principles and practice,* 2nd ed. Philadelphia: FA Davis company,.
11. Peioglou-Harmoussi S, Fawcett PR, Howel D and Barwick DD, 1987: *F-response frequency in motor neuron disease and cervical spondylosis*. Journal of Neurology, Neurosurgery, and Psychiatry, 50, 593-599.
12. Rabbani KS, 2011. *Hypotheses to explain the occurrence of multiple peaks of DFL in nerve conduction measurement.* Bangladesh J of Med Phys; 4:27-36.
13. Rabbani KS, Alam MJ and Salam MA,2007. *Frequency Distribution of F-Latencies (DFL) has physiological significance and gives Distribution of Conduction Velocity (DCV) of motor nerve fibres with implications for diagnosis*. J of BiolPhys;33:291-303.
14. Rabbani KS, NorazeidaYassin, Y L Lo, 2013, *Identification of Cervical Spondylotic Radiculo-Myelopathy using distribution of F-Latency (DFL), a new nerve conduction parameter*. Submitted , Journal of clinical neurophysiology.
15. Seidenwurm DJ, 2008, American Journal of Neuroradiology, 29:1032-1034
16. Urschel Jr HC and Razzuk MMA, 2000. Ann Thorac Surg correspondence; 69: 665.
17. Young WF, 2000, *Cervical Spondylotic Myelopathy: A Common Cause of Spinal Cord Dysfunction in Older Persons,* Am Family Physician; 62(5):1064-1070.

APPENDIX

DFL graphs

MRI reports