Chapter one

:Introduction 1-1

MS is a chronic, progressive, degenerative disorder of the central nervous system (CNS) characterized by disseminated demyelization of nerve fibers of the brain and spinal cord, MS usually affects young to middle- aged adults, with onset between 15 and 50 years of age the women affected more than men it's unknown etiological cause it's may be related to infectious, immunologic, and genetic factors possible precipitating factors include (physical injury, emotional stress, pregnancy, poor state of health. Pathophysiology of mylelin sheath affected by segmented lamination that wraps axons of many nerve cells increases velocity of nerve impulse conduction in the axons, composed of myelin, a substance with high lipid content (Kalb & P. D.R.C 2008). Characterized by chronic inflammation, demyelination, and gliosis (scarring) in the CNS, initially triggered by a virus in genetically susceptible individuals subsequent antigen-antibody reaction leads to demyelination of axons .Disease process consists of loss of myelin, disappearance of oligodendrocytes, and proliferation of astrocytes changes result in plaque formation with plaques scattered throughout the CNS, initially the myelin sheaths of the neurons in the brain and spinal cord are attacked, but the nerve fiber is not affected, patient may complain of noticeable impairment of function, myelin can regenerate, and symptoms disappear, resulting in a .(remission (Kalb & P. D.R.C 2008

The characteristic abnormalities of MS in the brain consist of multiple white matter lesions with a high signal intensity (SI) on fluid attenuation inversion recovery (FLAIR), proton density (PD)-weighted image(WI), and T2-WI and low signal intensity (SI) on T1-WI. Lesions are found predominantly in a periventricular distribution, Centrum semiovale, and the callososeptal interface. Additional sites of involvement include other parts of the cerebral white matter such as the sub cortical a penetrating

medullary vein. Atypical lesions and mass-like lesions occur with sufficient frequency to cause diagnostic errors. MS lesions may enhance after contrast administration on T1-WI, depending on the age and activity of the lesion. New and active lesions commonly show contrast enhancement, due to BBB breakdown. New lesions tend to show solid enhancement, whereas .(reactivated lesions enhance in a ring-like fashion (Fazekas F et al 1999

After 2 months, the integrity of the BBB is restored, and the majority of lesions no longer show contrast enhancement. As with unenhanced lesions, the contrast-enhancing lesions are smaller than the corresponding lesions on the T2-W scan. The discrepancy between the size of the lesion on T1-WI and T2-WI reflects the different components of the local process: edema, inflammation, and demyelization. The poor correlation between the MRI findings and the clinical events is demonstrated by the frequent finding of enhancing lesions in clinically stable patients.White matter, optic nerves, corpus callosum, internal capsule, cerebellar peduncles, brainstem, and spinal cord. Demyelinating lesions appear smaller on T1-WI than on T2-WI. Occasionally, they show a hyper intense border on T1-WI .((Fazekas F et al 1999

Lesions in MS can be small, large, or confluent the typical configuration is that of an ovoid lesion extending perpendicularly from the ventricular surface (Dawson’s finger).This probably reflects the perivascular inflammation along found in the corpus callosum. Typically, these lesions occur along the inner callosal-ventricular margin, creating an irregular ventricular surface of the corpus callosum. This aspect can be differentiated from callosal atrophy due to the lobar white-matter lesions. The existence of callosal lesions improves both the sensitivity and the specificity of MRI for the diagnosis of MS. The absence of callosal lesions renders the diagnosis of MS less likely, but does not exclude it. A frequent initial presentation of MS is optic neuritis, although there is controversy regarding the likelihood of definitive MS developing in patients who have .(had an optic neuritis (Gray O, McDonnell GV and Forbes RB 2004

Brainstem lesions are common, and a lesion in the medial longitudinal bundle affects approximately one-third of MS patients. In patients with clinically possible MS and a normal MRI study of the brain, a spinal MRI study should be performed. MS is an inflammatory demyelinating disease of the CNS. It is the most common demyelinating disease after vascular- and age-related demyelination. MS is characterized by multiple “plaques” of demyelination in the white matter of the brain and spinal cord. The primary lesions are found in the perivascular spaces along penetrating veins. Though the etiology of MS is not fully understood, the destruction of myelin is most likely caused by an autoimmune process. Initial symptoms can sometimes be triggered by trauma or a viral infection, but a convincing link to the disease has not been made. (Gray O , 2004 McDonnell GV and Forbes RB).

The clinical course of MS is highly variable. The age of symptom onset in MS is usually between 18 and 40 years; onset is uncommon in childhood and after the age of 50 years. Initial symptoms may include numbness, dysesthesia, double vision, or problems with balance and coordination. Loss of motor function is also a frequent initial presentation. Less commonly, spinal-cord-related symptoms constitute the initial presentation of MS. There is a female: male ratio of 3:2. The most common clinical presentation is “relapsing- remitting” MS (70% of cases) (Rae-Grant et al 1999).

Patients experience symptomatic episodes (known as “attack”), which can last from 24 h to several weeks, followed by complete or partial disappearance of symptoms (remission). The interval between relapses may be weeks to years (and even decades). As white-matter lesions increase over time, and neurologic disabilities increase, the disease frequently becomes “secondary progressive.” Accumulating neurological deficits eventually lead to permanent disability. The evolution from relapsing-remitting to secondary-progressive MS occurs in approximately half of patients within 10 years after onset. Alternatively, in

10–20% of cases, MS can follow a “primary progressive” course; in this type of disease, there is a continuous, gradual evolution from the beginning, rather than relapses (Rae-Grant et al 1999).

1.2 Research problems:

Prevalence of MS patients whom were referred to the MRI department to examine brain, among The Sudanese population, in routine MRI brain protocols a hidden small MS does not seen due to a thicker slice (5 mm) and slice gab (1mm), in some cases enhanced T1w with using contrast is the necessary to view inactive MS and to aid the deferential diagnosis between the MS and small vascular disease.

1.3 Research objectives:

1.3.1 General objectives:

To standardized MRI protocol to meets the challenge of MS diagnosis.

1.3.2 Specific objectives

To reassessment the MS patients for initiation or modification of treatment unexpected clinical worsening.

To evaluate agreed role of gadolinium to provides useful additional information about new activity.

To put optimum protocol to diagnose MS.

Correlation between patient age and symptoms and MRI finding.

1.4 Thesis outline

Chapter one: consist of introduction, statement of the problem, objectives of the study, and thesis outline).

Chapter two: the literature review (Anatomy, Physiology, Pathology

.(of the brain, previous studies

.Chapter three: methodomatriel and method

.Chapter four: result

,Chapter five: dissection ,Conclusions, Recommendation

References . -

Appendix . -

Chapter tow

Theoretical Background 2.1

Anatomy of the Brain 2.1.1

There are different ways of dividing the brain anatomically into regions. Let’s use a common method and divide the brain into three main regions based on embryonic development is the forebrain, midbrain and hindbrain. The forebrain (or prosencephalon) is made up of our incredible cerebrum, thalamus, hypothalamus and pineal gland among other features. Neuroanatomists call the cerebral area the telencephalon and use the term diencephalon (or interbrain) to refer to the area where our thalamus, hypothalamus and pineal gland reside The midbrain (or mesencephalon), located near the very center of the brain between the interbrain and the hindbrain, is composed of a portion of the brainstem. The hindbrain (or rhombencephalon) consists of the remaining brainstem as well as our cerebellum and pons. Neuroanatomists have a word to describe the brainstem sub-region of our hindbrain, calling it the myelencephalon, while they use the word metencephalon in reference to .(our cerebellum and pons collectively. (Siesjo BK 1989

The tissue of the brain can be broken down into two major classes gray matter and white matter. Gray matter is made of mostly unmyelinated neurons, most of which are interneurons, the gray matter regions are the areas of nerve connections and processing. White matter is made of mostly myelinated neurons that connect the regions of gray matter to each other and to the rest of the body. Myelinated neurons transmit nerve signals much faster than unmyelinated axons do. The white matter acts as the information highway of the brain to speed the connections between .(distant parts of the brain and body (Afshar et al 1978

(Hindbrain (Rhomb encephalon 2.1.1.1

Brainstem 2.1.1.1.1

Connecting the brain to the spinal cord, the brainstem is the most inferior portion of our brain. Many of the most basic survival functions of the brain are controlled by the brainstem. The brainstem is made of three

regions: the medulla oblongata, the pons, and the midbrain. A net-like structure of mixed gray and white matter known as the reticular formation is found in all three regions of the brainstem. The reticular formation controls muscle tone in the body and acts as the switch between consciousness and sleep in the brain. The medulla oblongata is a roughly cylindrical mass of nervous tissue that connects to the spinal cord on its inferior border and to the pons on its superior border. The medulla contains mostly white matter that carries nerve signals ascending into the brain and descending into the spinal cord. Within the medulla are several regions of gray matter that process involuntary body functions related to .(homeostasis (Afshar et al 1978

The cardiovascular center of the medulla monitors blood pressure and oxygen levels and regulates heart rate to provide sufficient oxygen supplies to the body's tissues. The medullary rhythmicity center controls the rate of breathing to provide oxygen to the body. Vomiting, sneezing, coughing, and swallowing reflexes are coordinated in this region of the brain as well. The pons is the region of the brainstem found superior to the medulla oblongata, inferior to the midbrain, and anterior to the cerebellum. Together with the cerebellum, it forms what is called the metencephalon. About an inch long and somewhat larger and wider than the medulla, the pons acts as the bridge for nerve signals traveling to and from the cerebellum and carries signals between the superior regions of .(the brain and the medulla and spinal cord (Naidich et al 2009

2.1.1.1.2Cerebellum

The cerebellum is a wrinkled, hemispherical region of the brain located posterior to the brainstem and inferior to the cerebrum. The outer layer of the cerebellum, known as the cerebellar cortex, is made of tightly folded gray matter that provides the processing power of the cerebellum. Deep to the cerebellar cortex is a tree-shaped layer of white matter called the arbor vitae, which means 'tree of life'. The arbor vitae connects the processing regions of cerebellar cortex to the rest of the brain and body .((Duvernoy & H.M 1999

The cerebellum helps to control motor functions such as balance, posture, and coordination of complex muscle activities. The cerebellum receives sensory inputs from the muscles and joints of the body and uses this information to keep the body balanced and to maintain posture. The cerebellum also controls the timing and finesse of complex motor actions .(such as walking, writing, and speech (Duvernoy & H.M 1999

(2.1.1.2Midbrain(MESENCEPHALON

The midbrain, also known as the mesencephalon, is the most superior region of the brainstem. Found between the pons and the diencephalon, the midbrain can be further subdivided into 2 main regions: the tectum and the cerebral peduncles. The tectum is the posterior region of the midbrain, containing relays for reflexes that involve auditory and visual information. The pupillary reflex (adjustment for light intensity), accommodation reflex (focus on near or far away objects), and startle reflexes are among the many reflexes relayed through this region, forming the anterior region of the midbrain, the cerebral peduncles contain many nerve tracts and the substantia nigra. Nerve tracts passing through the cerebral peduncles connect regions of the cerebrum and thalamus to the spinal cord and lower regions of the brainstem. The substantia nigra is a region of dark melanin-containing neurons that is involved in the inhibition of movement. Degeneration of the substantia nigra leads to a loss of .(motor control known as Parkinson’s disease (Duvernoy & H.M 1999

(Forebrain (Proencephalon 2.1.1.3

2.1.1.3.1.1Diencephalon

Superior and anterior to the midbrain is the region known as the interbrain, or diencephalon. The thalamus, hypothalamus, and pineal glands make up the major regions of the diencephalon. The thalamus consists of a pair of oval masses of gray matter inferior to the lateral ventricles and surrounding the third ventricle. Sensory neurons entering the brain from the peripheral nervous system form relays with neurons in the thalamus that continue on to the cerebral cortex. In this way the

thalamus acts like the switchboard operator of the brain by routing sensory inputs to the correct regions of the cerebral cortex. The thalamus has an important role in learning by routing sensory information into processing .(and memory centers of the cerebrum (Woolsey et al 2003

The hypothalamus is a region of the brain located inferior to the thalamus and superior to the pituitary gland. The hypothalamus acts as the brain's control center for body temperature, hunger, thirst, blood pressure, heart rate, and the production of hormones. In response to changes in the condition of the body detected by sensory receptors, the hypothalamus sends signals to glands, smooth muscles, and the heart to counteract these changes. For example, in response to increases in body temperature, the hypothalamus stimulates the secretion of sweat by sweat glands in the skin. The hypothalamus also sends signals to the cerebral cortex to produce the feelings of hunger and thirst when the body is lacking food or water. These signals stimulate the conscious mind to seek out food or water to correct this situation. The hypothalamus also directly controls the pituitary gland by producing hormones. Some of these hormones, such as oxytocin and antidiuretic hormone, are produced in the hypothalamus and stored in the posterior pituitary gland. Other hormones, such as releasing and inhibiting hormones, are secreted into the blood to stimulate or inhibit hormone production in the anterior pituitary gland (Van .(Buren et al 1972

The pineal gland is a small gland located posterior to the thalamus in a sub-region called the epithalamus. The pineal gland produces the hormone melatonin. Light striking the retina of the eyes sends signals to inhibit the function of the pineal gland. In the dark, the pineal gland secretes melatonin, which has a sedative effect on the brain and helps to induce sleep. This function of the pineal gland helps to explain why darkness is sleep-inducing and light tends to disturb sleep. Babies produce large amounts of melatonin, allowing them to sleep as long as 16 hours per day. The pineal gland produces less melatonin as people age, resulting in .(difficulty sleeping during adulthood. (Van Buren et al 1972

:2.1.1.3.2Cerebrum

The largest region of the human brain, our cerebrum controls higher brain functions such as language, logic, reasoning, and creativity. The cerebrum surrounds the diencephalon and is located superior to the cerebellum and brainstem. A deep furrow known as the longitudinal fissure runs midsagittally down the center of the cerebrum, dividing the cerebrum into the left and right hemispheres. Each hemisphere can be further divided into 4 lobes: frontal, parietal, temporal, and occipital. The lobes are named for the skull bones that cover them. The surface of the cerebrum is a convoluted layer of gray matter known as the cerebral cortex. Most of the processing of the cerebrum takes place within the cerebral cortex. The bulges of cortex are called gyri (singular: gyrus) while the indentations are .(called sulci (singular: sulcus) (Schitzlein, H.N, Murtagh and F.R 1990

Deep to the cerebral cortex is a layer of cerebral white matter. White matter contains the connections between the regions of the cerebrum as well as between the cerebrum and the rest of the body. A band of white matter called the corpus callosum connects the left and right hemispheres of the cerebrum and allows the hemispheres to communicate with each other. Deep within the cerebral white matter are several regions of gray matter that make up the basal nuclei and the limbic system. The basal nuclei, including the globus pallidus, striatum, and sub thalamic nucleus, work together with the substantia nigra of the midbrain to regulate and control muscle movements. Specifically, these regions help to control muscle tone, posture, and subconscious skeletal muscle (Schitzlein, H.N, .(Murtagh and F.R 1990

The limbic system is another group of deep gray matter regions, including the hippocampus and amygdala, which are involved in memory, survival, and emotions. The limbic system helps the body to react to emergency and highly emotional situations with fast, almost involuntary actions, with so many vital functions under the control of a single incredible organ - and so many important functions carried out in its outer layers - how does our body protect the brain from damage? Our skull

clearly offers quite a bit of protection, but what protects the brain from the skull itself? (Schitzlein, H.N, Murtagh and F.R 1990).

2.1.1.3.3Meninges

three layers of tissue, collectively known as the meninges, surround and protect the brain and spinal cord. The dura mater forms the leathery, outermost layer of the meninges. Dense irregular connective tissue made of tough collagen fibers gives the dura mater its strength. The dura mater forms a pocket around the brain and spinal cord to hold the cerebrospinal fluid and prevent mechanical damage to the soft nervous tissue. The name dura mater comes from the Latin for “tough mother,” due to its protective nature.The arachnoid mater is found lining the inside of the dura mater. Much thinner and more delicate than the dura mater, it contains many thin fibers that connect the dura mater and piamater. The name arachnoid mater comes from the Latin for “spider-like mother”, as its fibers resemble a spider web. Beneath the arachnoid mater is a fluid-filled region known as the subarachnoid space (Morel et al 1997).

2.1.1.4.CerebroSpinal Fluid:

Cerebrospinal fluid (CSF) a clear fluid that surrounds the brain and spinal cord provides many important functions to the central nervous system. Rather than being firmly anchored to their surrounding bones, the brain and spinal cord float within the CSF. CSF fills the subarachnoid space and exerts pressure on the outside of the brain and spinal cord. The pressure of the CSF acts as a stabilizer and shock absorber for the brain and spinal cord as they float within the hollow spaces of the skull and vertebrae. Inside of the brain, small CSF-filled cavities called ventricles expand under the pressure of CSF to lift and inflate the soft brain tissue. Cerebrospinal fluid is produced in the brain by capillaries lined with ependymal cells known as choroid plexuses. Blood plasma passing through the capillaries is filtered by the ependymal cells and released into the subarachnoid space as CSF. The CSF contains glucose, oxygen, and ions, which it helps to distribute throughout the nervous tissue. CSF also

transports waste products away from nervous tissues (Orrison Jr., W.W .(2008

After circulating around the brain and spinal cord, CSF enters small structures known as arachnoid villi where it is reabsorbed into the bloodstream. Arachnoid villi are finger-like extensions of the arachnoid mater that pass through the dura mater and into the superior sagittal sinus. The superior sagittal sinus is a vein that runs through the longitudinal fissure of the brain and carries blood and cerebrospinal fluid .(from the brain back to the heart (Orrison Jr., W.W 2008

Neurons and glia .2.1.1.5

The basic structural and functional unit of the nervous system is the nerve cell or neuron. It is important to come to grips with the neuron and the terminology relating to its parts now, otherwise much of the material on organization of the nervous system will not make sense to you. Here is a schematic drawing of a typical nerve cell .All neurons have a cell body (or soma) which contains cellular organelles which are typical of most of the cells in the body, including a nucleus, a nucleolus, lots of rough endoplasmic reticulum, and so on. Most nerve cells have processes called (dendrites), which act like antennae for the cell, in that they receive input to the cell. Most neurons also have a single long process called an axon which is capable of transmitting a pulse of electricity (nerve impulse or action pottential) from the cell body to some distant target in the brain or .(the periphery (Woolsey et al 2003

These axons may be quite long (up to a meter or more in the case of a nerve cell whose some sits in the spinal cord and has an axon which contacts a muscle in the foot). Axons usually break up into smaller branches (terminal branches) near their target. These terminal branches end in swellings which make a specialized contact with the target cell. If the target cell is another neuron, the swelling is called a (BOUTON), and the specialized contact is called a SYNAPSE. If the target is a muscle fiber, the bouton is often called a (mootor) and the synapse is often referred to as a (neuromuscular junction). There is usually a gap between the terminal

swelling and the target cell (postsynaptic cell). The electrical impulse does not cross this gap, but rather causes a chemical (neurotransmitter) to be .(released from the axon terminals (Woolsey et al 2003

The neurotransmitter diffuses across the gap and causes electrical changes to occur in the postsynaptic cell, neurons come in all sizes and shapes, but the basic functions of all neurons are more or less similar: they receive (and integrate) inputs, and relay their output, in the form of an action potential, to some other target cell. The cell body is mainly responsible for meeting the metabolic needs of the cell and its position with respect to the axon and dendrites is somewhat variable. The drawing below shows you a type of neuron you will encounter in your study of the peripheral nervous system. It is a dorsal root ganglion cell, or primary .(sensory neuron (Woolsey et al 2003

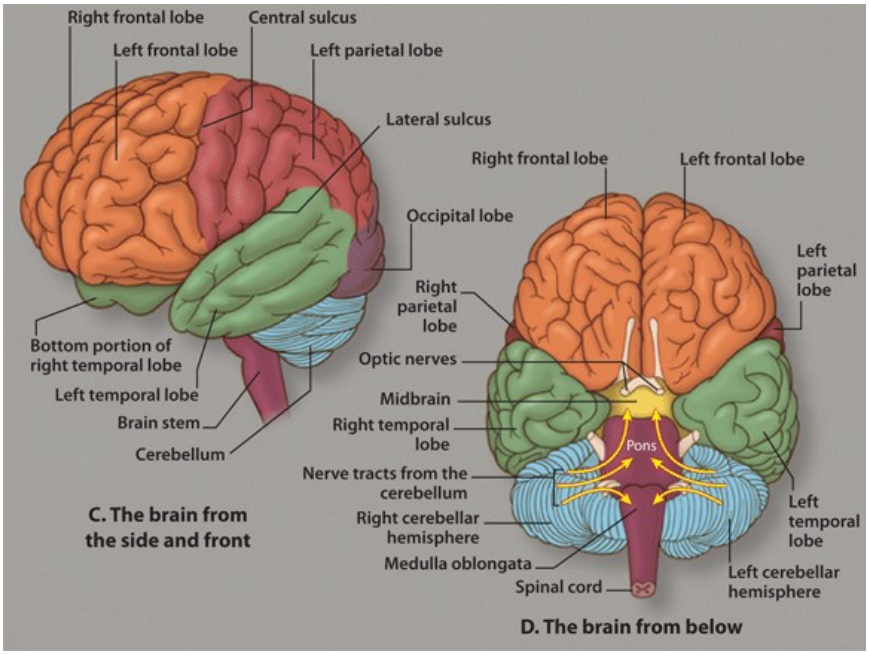


Figure (2.1) Anatomy of the brain

http://www.birthinjury.org/assets/images/CP_BI/illustrations/CP-Illustration-) (%28Brain-Anatomy-2%29.gif

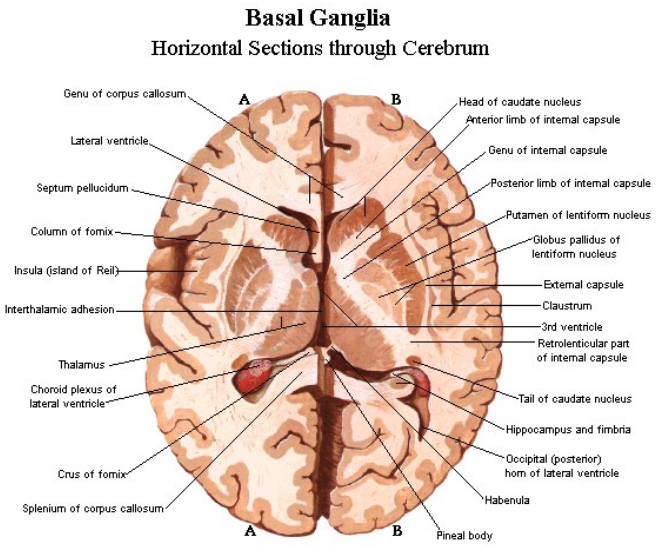


Figure (2.2) Anatomy of brain

((http://www.aboutcancer.com/brain_anatomy_net_6.gif

Physiology of the Brain .2.2.2

Metabolism .2.1.2.1

Despite weighing only about 3 pounds, the brain consumes as much as 20% of the oxygen and glucose taken in by the body. Nervous tissue in the brain has a very high metabolic rate due to the sheer number of decisions and processes taking place within the brain at any given time. Large volumes of blood must be constantly delivered to the brain in order to maintain proper brain function. Any interruption in the delivery of blood to the brain leads very quickly to dizziness, disorientation, and eventually unconsciousness. (Carola et al 1992).

:2.1.2.2Sensory

The brain receives information about the body's condition and surroundings from all of the sensory receptors in the body. All of this information is fed into sensory areas of the brain, which put this information together to create a perception of the body's internal and external conditions. Some of this sensory information is autonomic sensory information that tells the brain subconsciously about the condition of the

body. Body temperature, heart rate, and blood pressure are all autonomic senses that the body receives. Other information is somatic sensory information that the brain is consciously aware of. Touch, sight, sound, and .(hearing are all examples of somatic senses (Carola et al 1992

:MotorControl.2.1.2.3

The brain directly controls almost all movement in the body. A region of the cerebral cortex known as the motor area sends signals to the skeletal muscles to produce all voluntary movements. The basal nuclei of the cerebrum and gray matter in the brainstem help to control these movements subconsciously and prevent extraneous motions that are undesired. The cerebellum helps with the timing and coordination of these movements during complex motions. Finally, smooth muscle tissue, cardiac muscle tissue, and glands are stimulated by motor outputs of the .(autonomic regions of the brain (Carola et al 1992

:Processing.2.1.2.4

Once sensory information has entered the brain, the association areas of the brain go to work processing and analyzing this information. Sensory information is combined, evaluated, and compared to prior experiences, providing the brain with an accurate picture of its conditions. The association areas also work to develop plans of action that are sent to the brain’s motor regions in order to produce a change in the body through muscles or glands. Association areas also work to create our thoughts, .(plans, and personality (Carola et al 1992

learning and memory .2.1.2.5

The brain needs to store many different types of information that it receives from the senses and that it develops through thinking in the association areas. Information in the brain is stored in a few different ways depending on its source and how long it is needed. Our brain maintains short-term memory to keep track of the tasks in which the brain is currently engaged. Short-term memory is believed to consist of a group of neurons that stimulate each other in a loop to keep data in the brain’s

memory. New information replaces the old information in short-term memory within a few seconds or minutes, unless the information gets moved to long-term memory, long-term memory is stored in the brain by the hippocampus. The hippocampus transfers information from short-term memory to memory-storage regions of the brain, particularly in the cerebral cortex of the temporal lobes. Memory related to motor skills (known as procedural memory) is stored by the cerebellum and basal .(nuclei (Carola et al 1992

Homeostasis .2.1.2.6

The brain acts as the body's control center by maintaining the homeostasis of many diverse functions such as breathing, heart rate, body temperature, and hunger. The brainstem and the hypothalamus are the brain structures most concerned with homeostasis. In the brainstem, the medulla oblongata contains the cardiovascular center that monitors the levels of dissolved carbon dioxide and oxygen in the blood, along with blood pressure. The cardiovascular center adjusts the heart rate and blood vessel dilation to maintain healthy levels of dissolved gases in the blood and to maintain a healthy blood pressure. The medullary rhythmicity center of the medulla monitors oxygen and carbon dioxide levels in the blood and adjusts the rate of breathing to keep these levels in balance .((John Bullock et.al. 1995

The hypothalamus controls the homeostasis of body temperature, blood pressure, sleep, thirst, and hunger. Many autonomic sensory receptors for temperature, pressure, and chemicals feed into the hypothalamus. The hypothalamus processes the sensory information that it receives and sends the output to autonomic effectors in the body such as sweat glands, .(the heart, and the kidneys (John Bullock et.al. 1995

Sleep.2.1.2.7

While sleep may seem to be a time of rest for the brain, this organ is actually extremely active during sleep. The hypothalamus maintains the body's 24 hour biological clock, known as the circadian clock. When the

circadian clock indicates that the time for sleep has arrived, it sends signals to the reticular activating system of the brainstem to reduce its stimulation of the cerebral cortex. Reduction in the stimulation of the cerebral cortex leads to a sense of sleepiness and eventually leads to sleep. In a state of sleep, the brain stops maintaining consciousness, reduces some of its sensitivity to sensory input, relaxes skeletal muscles, and completes many administrative functions. These administrative functions include the consolidation and storage of memory, dreaming, and development of nervous tissue (De Loris Wenzel and David 1996).

There are two main stages of sleep: rapid eye movement (REM) and non-rapid eye movement (NREM). During REM sleep, the body becomes paralyzed while the eyes move back and forth quickly. Dreaming is common during REM sleep and it is believed that some memories are stored during this phase. NREM sleep is a period of slow eye movement or no eye movement, culminating in a deep sleep of low brain electrical activity. Dreaming during NREM sleep is rare, but memories are still processed and stored during this time (De Loris Wenzel and David 1996).

Reflexes.2.1.2.8

A reflex is a fast, involuntary reaction to a form of internal or external stimulus. Many reflexes in the body are integrated in the brain, including the pupillary light reflex, coughing, and sneezing. Many reflexes protect the body from harm. For instance, coughing and sneezing clear the airways of the lungs. Other reflexes help the body respond to stimuli, such as adjusting the pupils to bright or dim light. All reflexes happen quickly by bypassing the control centers of the cerebral cortex and integrating in the lower regions of the brain such as the midbrain or limbic system (David T. Lindsay 1996).

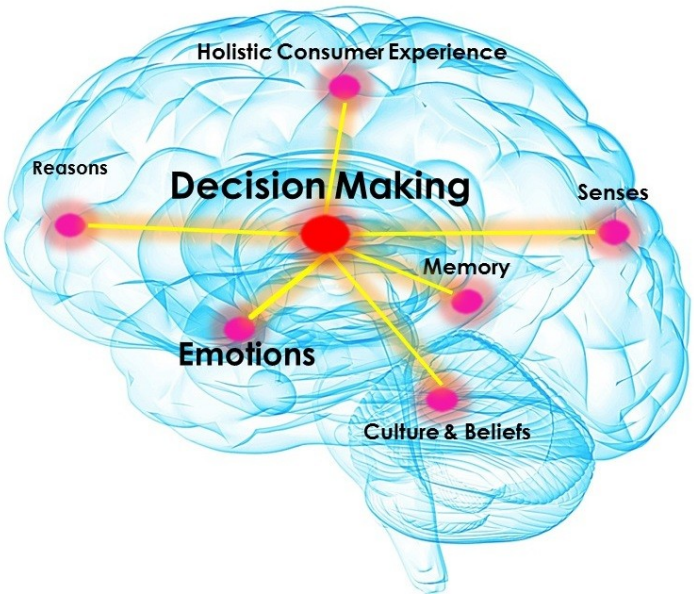


Figure (2.3).physiology of the brain (http://iammoulude.files.wordpress.com/2014/07/decisionmaking_brain.jpg)

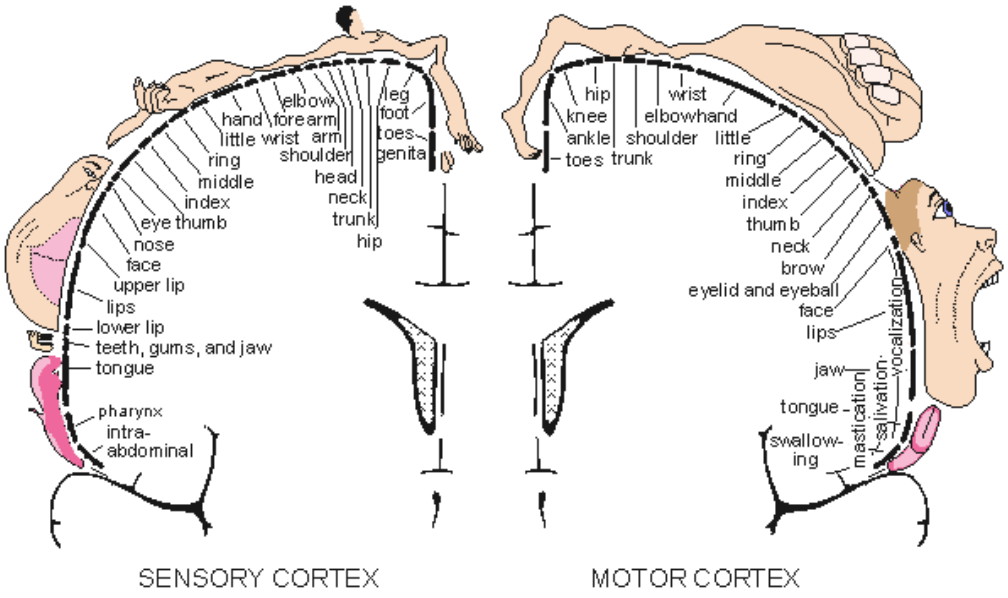


Figure (2.4).physiology of the brain (http://www.bem.fi/book/05/fi/0506.gif)

2.1.3.pathology:

2.1.3.1.Multiple Sclerosis

Multiple Sclerosis (MS) is a debilitating disease, which affects the central nervous system. The nerve fibres, which make up our central nervous system and transmit messages from our brain, throughout our body, are wrapped in a fatty sheath, made of a substance known as Myelin. In MS, the Myelin sheath is attacked causing inflammation or damage. Areas of scarring (Sclerosis) result and these scars can disrupt or even block signals within the brain and spinal cord. These scars may cause loss of nerve fibres as well as their ensheathing myelin. The disruption or blocking of nerve signals within the central nervous system causes a variety of symptoms, depending on which areas of the brain and spinal cord are affected., Loss of bladder/bowel control , Extreme fatigue , Sight impairments , Memory lapses Vertigo , Weakness, Impaired sensation Early symptoms are usually mild. MS is a progressive disease and as time goes on, symptoms may become more severe (Charil et al 2006).

Secondary Progressive MS – patient originally has relapse-remitting MS, which develops into progressive disability, often with superimposed relapses. Affects approximately 40% of patients. Primary Progressive MS a lack of distinct attacks, a slow onset and steady worsening of symptoms. Deficits and disability accumulate and may level off at some point, or continue over months and years. Affects approximately 15% of patients. Relapsing Progressive MS a gradual progression of disability from the onset of the disease, accompanied by one or more relapses. Affects approximately 5% of patients. Benign MS after one or two attacks with complete recovery (initial symptoms tend to be less severe) there is no worsening or permanent disability after 15 years. Affects approximately 5% of patients. (Charil et al 2006).

MS typically strikes young adults, with symptoms beginning between the ages of 20 and 50. MS is the most common cause of chronic

neurological impairment in young people and affects more than 1 million adults worldwide. MS is not hereditary but having a first degree relative with MS does increase a person's risk. MS strikes 50% more women than men, and is five times more common in temperate climates than in the tropics. The cause of MS is still unknown, however many believe that MS is an autoimmune disease, where the patient's immune system defensive cells mistakenly attack the myelin sheaths. Some believe the cause to be viral; others believe it to be physical or emotional stress. It has yet to be proven that any one virus triggers MS.(Uitdehaag, et al 2005).

Diagnosing MS can be difficult as patient's exhibit similar warning signs to other diseases of the central nervous system. Doctors faced with a sudden appearance of symptoms (like those listed above), signaling central nervous system damage, may suspect MS. There is no single test to diagnose MS. If your doctor suspects MS they will order a MRI (magnetic resonance imaging) scan of your brain and/or spinal cord to check for areas of scarring and inflammation in the myelin sheath. This will be done in conjunction with a clinical exam to review coordination, motor skills, vision, balance, sensory, language and emotional function. Other tests your doctor may order can include an eye examination by an ophthalmologist and a lumbar puncture (spinal tap) and electrophysiological tests to assess the passage of nerve impulses through the central nervous system.(McDonald et al 2001).

There is more than one area of damage in the central nervous system.

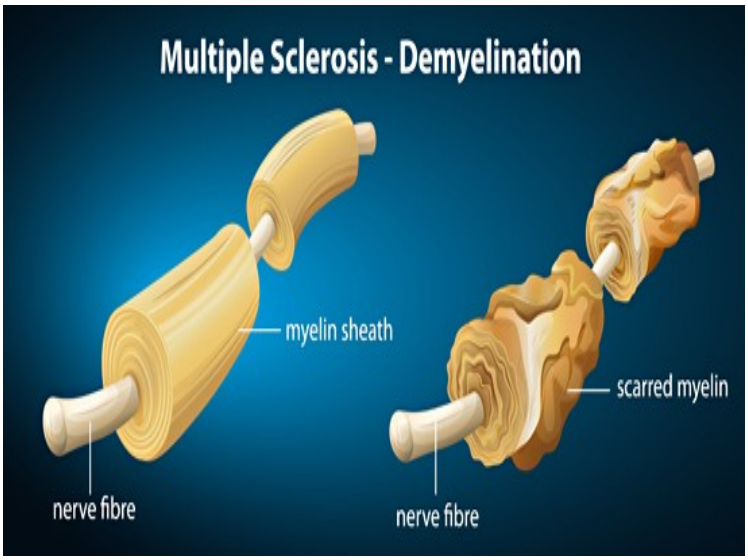


Figure (2.5).Demyelination

2.1.3.1.1.Treatment

There is no cure for MS. There are two types of treatments that may be used: treatment to modify the immune system and suppress the disease; and treatment to improve the symptoms.

Drug treatments targeting the immune system may include:
Immunotherapy drugs are taken by injection under the skin or into the muscle, the medication slows the frequency and severity of the attacks by about 30%, resulting in less damage to the myelin sheaths.

Methotrexate this drug is traditionally used to treat rheumatoid arthritis and was reported to have a modest effect on some aspects of progressive MS. It is not commonly used. (Comi et al 2001).

Mitoxantrone a drug used in oncology has been reported to have modest benefits in patients with rapidly progressive MS with frequent attacks. Because of its potential harmful side effects its use is limited to patients who show progressive disability, despite the use of the safer drugs such as beta interferons or Copaxone.
Methylprednisolone , this is a steroid given by injection to patients who have suffered an attack to shorten the duration of disability. It has no benefit when given continuously a similar drug Prednisone, may be given orally.

Patients may experience drug treatment side effects such as drowsiness, fluid retention, flu symptoms etc.

Treatments can target specific symptoms, for instance:

Muscle problems drugs and/or physical therapy can ease stiffness and tremors and improve strength. (Comi et al 2001).

Fatigue some studies have found that drugs used to treat narcolepsy can be helpful in controlling fatigue.

Neurological symptoms such as visual disturbances can be helped with drugs.

Continence – special exercises, aids and dietary changes can improve continence problems.

Neuropsychological problems depression may be treated with counseling or medication. Other cognitive difficulties such as memory loss can be better managed with help from a neuropsychologist. (Kappos et al 2006).

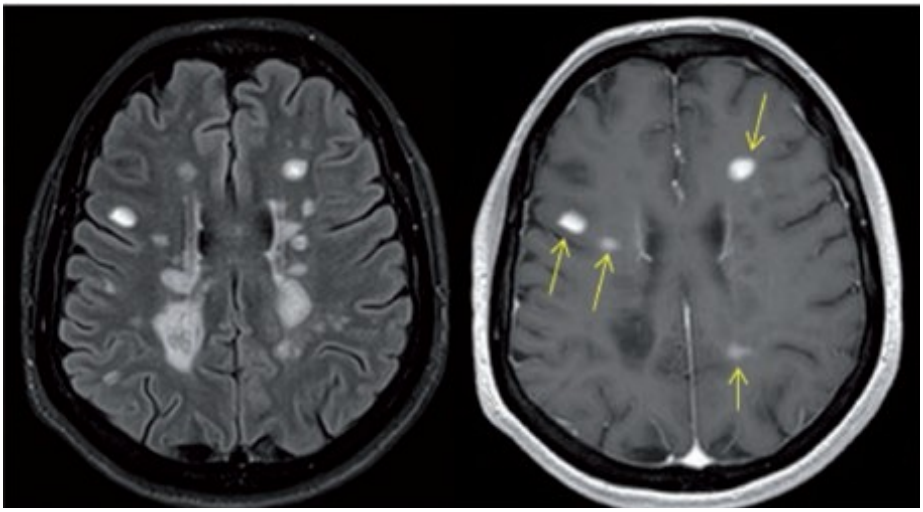


Figure (2.6).Conventional brain MR imaging in a patient with a diagnosis of MS. The flair-image (left) shows the typical multifocal dem-[yelinating lesions involving the white matter of both brain hemispheres. The contrast-enhanced T1-weighted image (right) demonstrates those lesions with abnormal blood brain barrier permeability (arrows), a marker of .(inflammatory activity.(Tintore´ M et al2003

:Diagnostic imaging 2.1.4

:MRI principle .1.4.1.-2

Magnetic resonance imaging (MRI) is a type of scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body. An MRI scanner is a large tube that contains powerful magnets. You lie inside the tube during the scan. An MRI scan can be used :to examine almost any part of the body, including the brain and spinal cord, bones and joints , breasts, heart and blood vessels , internal organs, such as the liver, womb or prostate gland The results of an MRI scan can be used to help diagnose conditions, plan treatments and .(assess how effective previous treatment has been (Slichter & C.P 1978

During an MRI scan, you lie on a flat bed that is moved into the scanner. Depending on the part of your body being scanned, you will be moved into .the scanner either head first or feet first

The MRI scanner is operated by a radiographer, who is trained in carrying out X-rays and similar procedures. They control the scanner using a computer, which is in a different room to keep it away from the magnetic field generated by the scanner. You will be able to talk to the radiographer through an intercom and they will be able to see you on a television monitor throughout the scan. At certain times during the scan, the scanner will make loud tapping noises. This is the electric current in the scanner coils being turned on and off. You will be given earplugs or headphones to wear (Slichter & C.P 1978). It is very important that you keep as still as possible during your MRI scan. The scan will last between 15 and 90 minutes, depending on the size of the area being scanned and how many .images are taken

:MRI Safety.2.1.4.1.1

MRI scan is a painless and safe procedure. You may find it uncomfortable if you have claustrophobia (fear of enclosed spaces), but most people find this manageable with support from the radiographer. Sometimes going into the scanner feet first may be easier, although this is not always possible (Slichter & C.P 1978).

MRI scans do not involve exposing the body to X-ray radiation. This means people who may be particularly vulnerable to the effects of radiation, such as pregnant women and babies, can use them if necessary. However, not everyone can have an MRI scan. For example, they are not always possible for people who have certain types of implants fitted, such as a pacemaker (a battery-operated device that helps control an irregular heartbeat). Extensive research has been carried out into whether the magnetic fields and radio waves used during MRI scans could pose a risk to the human body. No evidence has been found to suggest that there is a risk, which means that MRI is one of the safest medical procedures currently available (Kucinski et al 2003).

Figure 2.7.The MRI machine

(Barkhof F, Rocca M et al 2003)

:Coils .2.1.4.1.2

A coil consists of one or more loops of conductive wire, looped around the core of the coil. Coils are part of the hardware of MRI machines and are used to create a magnetic field or to detect a changing magnetic field by .voltage induced in the wire.A coil is usually a physically small antenna

The perfect coil produces a uniform magnetic field without significant radiation. Different types of MRI coils are used in MR systems: Gradient coils are used to produce controlled variations in the main magnetic field (B0) to provide spatial localization of the signals and to apply reversal pulses in some imaging techniques. MR imaging radio frequency coils to .receive and/or transmit the RF signal

Shim coils provide auxiliary magnetic fields in order to compensate for in homogeneities in the main magnetic field of the MRI machine (Nitz, W. R. .(1999

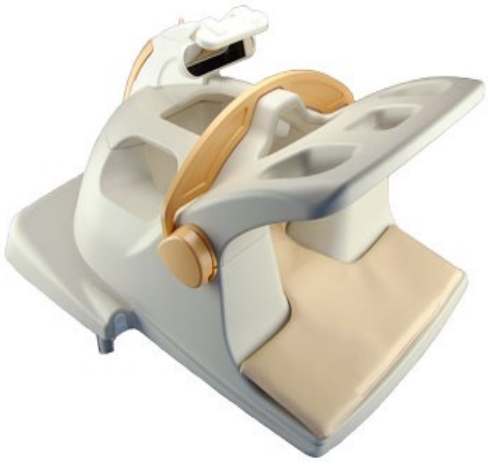
MRI head coils / MRI brain coils are typically birdcage coils. Multi channel coils allow to speed up the scan time with parallel imaging particularly at 3T (coils with 8 to 16 channel / elements are common).Transmit receive coils with their low image noise are particularly useful for spectroscopic imaging techniques.Multi channel neuro coils enable to combine cervical spine MRI, brain MRI, and neurovascular MRI. MRI spine coils consist usually of up to 15 phased array elements with a lower number of .(channels. (Nitz, W. R. 1999

Knee MRI coils are usually volume coils; multi channel coils are designed for high SNR and parallel imaging; transmit receive quadrature coils are also available. Specialized extremity coils are build for high resolution images; obtainable are for example wrist MRI coils, shoulder MRI coils, foot coils, finger coils, etc. Dedicated bilateral breast MRI coils provide easy positioning and maximum access also for MR guided interventions. An endorectal MRI coil is a RF coil used to obtain high quality images of the rectum area; particularly for

.prostate imaging

For general purpose all manufacturers offer surface coils with different designs for a high signal to noise ratio, faster image acquisition and .patient throughput or higher image resolution

The body coil, usually integrated in whole body MRI systems provides the .(possibility to image larger patients. (Nitz, W. R. 1999



(Figure (2.8) Neurovascular coil of the brain (Barkhof F, Rocca M et al 2003

: The common brain protocol.2.1.4.1.3

.Axial : T1,T2 and FLAIR

.Sagital: T1

.Coronal :T2

.Slice gap : 1mm

.Slice thickness : 5mm

2.2. Pervious study:

:Results

The following consensus recommendations were made: (1) When available, standardized brain MRI [1.0Teslaand higher, 3mm(preferred)-thick, non-gapped, sagittal fluid attenuating inversion recovery(FLAIR), axial FLAIR/T2weighted (T2)] should be performed in the initial evaluation

of suspected MS and baseline evaluation in established MS.(2) Brain and spinal cord [sagittal T1-weighted(T1), proton density (PD)/T2W with axial fast (or turbo) spin echo(FSE)T2throughsuspiciouslesions] MRI are indicated if the presenting symptoms are unresolved and at the level of the spinalcord and also when the brain MRI is equivocal. (3) In suspected MS, follow-up MRI to establish diagnosis by identifying disease disseminated in time and/or space is indicated. (4) In established MS, routine follow-up MRI scans at predefined intervals are not recommended, in the absence of clinical indications, which include unexpected clinical worsening, reassessment for initiation or modification of treatment and suspicion of secondary diagnosis. (5) Use of gadolinium (0.1 mmol/kg with minimum 5 minute delay) is recommended in suspected MS to identify disease disseminated in time butotherwise optional. (6) The indication (diagnosis, baseline or follow-up evaluation) for the study should always be provided. (7) The radiology report should include a description of findings, comparison with previous studies and interpretation. (8) MRI studies .should be permanently retained and available

A number of implementation strategies, including presentations at national and international meetings, publications, endorsement and support from MRI technologists, neurological and radiological professional societies, .(web-basedinstructions and CME were discussed. (D. K. Li1,et al 2004

Chapter three

Material and Method

3.1 Material

3.1.1 Patients (Study sample)

This study will be a practical study will be include a samples of 20 patients 11male and 9female under wemt to MRI department for brain MRI

suspected MS in different genders and age groups. whom will be referred to the radiology department in modern medical centers in Khartoum with a suspected case of multiple sclerosis, undergone MRI examination, to standardize protocol to diagnose MS, child's and patient with brain tumor excluded from the study, all patients will informed to obtain their consent before the exam and their information's will be used in this study, the data .will be collected and interpreted by radiologist reports

3.1.2. Machine used

Machine used in this study MRI scanner PHILIPS and GE (1.5 tesla),
Philips machine in alamal national hospital,and GE machine in antalea diagnostic center. Coil used neurovascular head coil, ear plug, .immobilization bad

:Method.3.2

3.2.1. Technique used

:The following MRI technique was used

.Field Strength: 1.5 T

. Slices: < 3 mm and no gap of plane resolution of < 1 mm for brain

.1st: Sagittal FLAIR Sequences:

. 2nd: Axial T2

.3rd: Axial FLAIR

.(4th: Gadolinium enhanced T1 (in follow-up

Data Interpretation 3.2.2

The data result collected from the result of MRI scan finding and supported the result by radiologist reports. determine by SI as hyper, hypo and iso compare to normal brain area by observation and by .measuring SI of affected area

:Data collection .3.2.3

Data will be collected from findings which appear in different MRI .cuts and the data will be represented in tables and graphs

The data's will include the general patients data (Age, genders and weight) and will be accompanied by the related to Symptoms and clinical information such as clinical signs (A numb or weak feeling in the face, ,trouble speaking, blurred or poor vision, loss of balance, headache

The risk factors and patients history (hypertension, D.M , heart .(disease

Data analysis .3.2.4

All data wered entered and analysed using Microsoft Excel and statistical analysis soft wered statistical package for social sciences(SPSS) version 22 statistical analysis included description statistic of frequency tables, graphs, cross tabulation and t test was applied to compare the variables, the difference was considered significant when p-value is less **.**(or equal (0.05

Chapter four

Result

Table (4.1) illustrates the frequency of multiple sclerosis patients according to .the gender

This result from 20 patient age between 22 to 60year underwent to MRI .examination and diagnosed MS according to their sign and symptoms

percentage	Frequency	Gender
% 55	**11**	**Male**
% 45	**9**	**Female**
% 100	**20**	**Total**

Figure (4.1) illustrate the frequency of multiple sclerosis .patients according to the gender

Table (4.2) illustrates the frequency of multiple sclerosis patients according to .the Age

Percentage	Frequency	Age
% 55	9	Lower than 35 yrs
% 45	11	Higher than 35 yrs
% 100	**20**	**Total**

Figure (4.2) the frequency of multiple sclerosis patients according to the Age.

Table (4.3) represents the clinical diagnosis in patients with multiple sclerosis.

Frequency	Clinical diagnosis
7	**Head ache**
6	**Headache + vertigo**
1	**Headache + lose of imbalance**
1	**Headache + defect in memory**
2	**Head ache +blurring of vision**
2	**Migraine Headache**
1	**Headache + Blurring Of vision**

Figure (4.3) represent the frequency of clinical diagnosis in .patients with multiple sclerosis

Figure (4.4) represent the percentage % of clinical diagnosis in .patients with multiple sclerosis

Table (4.4) illustrates the mean of finding MS in protocol 1 and .protocol 2

P. vlaue	Mean of finding	Number	Measurement
0.000	15.8	20	Protocol 1
	30.5	20	Protocol 2

Result given in mean

Significant difference at P. value <0.05 *

Figure (4.5) show new diagnosis and follow up patient

.with multiple sclerosis

CHAPTER FIVE

Discussion 5.1

The preliminary investigations obtained from this study revealed that the MS patient's participated in this study, patients with ages rather than 35 years was more affected than patient's with age less than 35 years , and this remarks are reported by (Herna´n MA. et al 2001), who .postulated that the risk of MS rises significantly with age After 35

In our study data among the patients , symptoms more frequently founded was headache and headache + vertigo and this result in agreement with (McDonald et al., 2001).

One of the most interesting observations obtained from this study is to cover all M.S in the brain and detected anew M.S by using modified MRI protocol, in this study represented by (protocol 2). Protocol 2: routine MRI brain and the most important sequence is FLAIR axial and sagital with 3mm slice thickness and slice gap 0.0mm to cover any M.S in the brain.

The common brain MRI protocol applied in radiological center in this study represented by (protocol 1).

Protocol 1: in radiological center used axial T1,T2, FLAIR sagitalT1 and coronalT2 with slice thickness 5mm and gap 1mm this protocol is good in survey brain but it cannot cover all M.S in the brain . (D. K. Li, et al 2004).

From this result, the analysis show the mean of finding MS in protocol 1was 15.8 and protocol 2 was 30.5. The P Value was 0.00, the difference was considered significant when p-value is less or equal 0.05.

This result show that there is a significance difference between the two protocols

The result indicate that , protocol 2 is more accuracy than protocol 1 in detection all M.S in the brain.

Conclusions 5.2

This study conclude that Advances neuroimaging have improved ability to diagnose and monitor MS and have provided insight into the pathophysiology of the disease. Conventional MRI of the central nervous system plays a prominent role in establishing the diagnosis of MS and in differentiating MS-mimics and demyelinating disease subtypes. Moreover, it allows an earlier and accurate diagnosis of the disease, as it can support or even replace some clinical criteria. accurate diagnosis is essential to allow earlier therapeutic intervention that appears to be beneficial on delaying the accumulation of irreversible neurologic damage and .consequent disability

Through the study found the best MRI protocol for detection and diagnose M.S is the .(modified protocol (protocol 2

Recommendations 5.3

- Flair axial and sagital with slice thickness 3mm and gap 0.0 should be basic protocol for MS patient.
- Farther study with large sample of patient.
- Training for technologist and radiologist for MRI sequence and MS protocol.
- All neurologist and physician should be awarded with MS protocol.

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APPENDIX

Name	
Age	
Gender	
pregnancy	
Weight	
Height	
Occupation	
Habits	( ) Smoking ( ) D. alcohol ( ) Others
Tribe	

: Examination regard

Clinical diagnosis	
Protocol of MRI brain	Slice thickness / Spacing
1st Protocol	5.0 / 1.0
2nd protcol	3.0 / 0.0

NO. OF **MS**

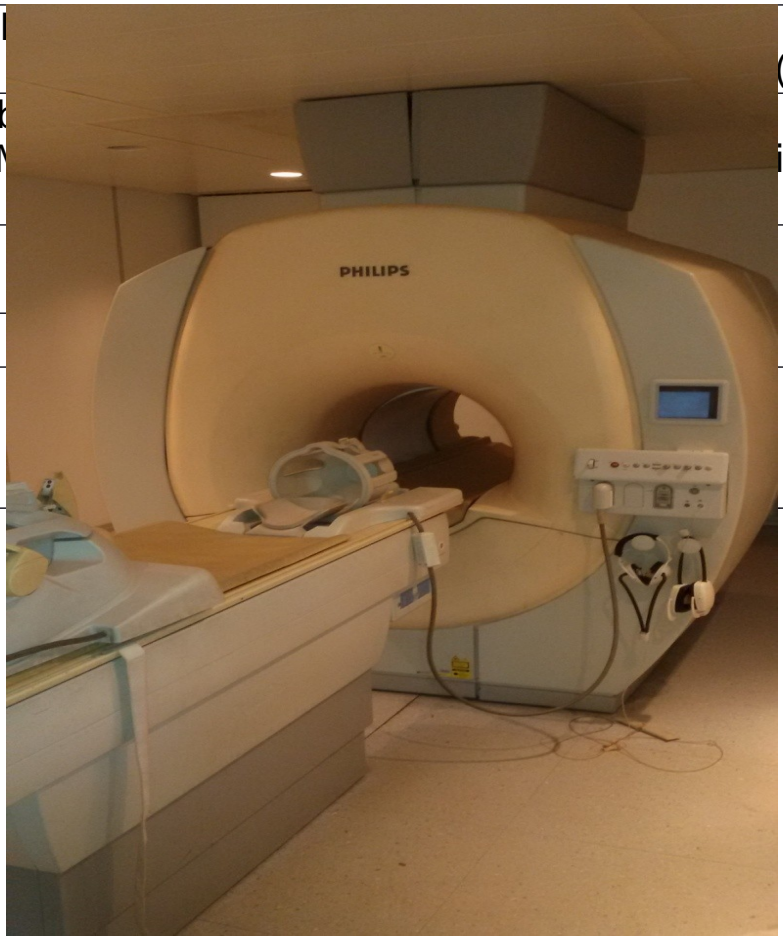
ENHANCEI		No ( )	Contrast : used
Compare b (old M		New iagnos is	Diagnosis :of MS
			Other findings
:n’s		Patient informatio	

IMAGE 1. CLOSED PHLIPS MRI MACHINE (1.5 TESLA) HOLLAND, .((ALAMAL DIAGONSTIC CENTER

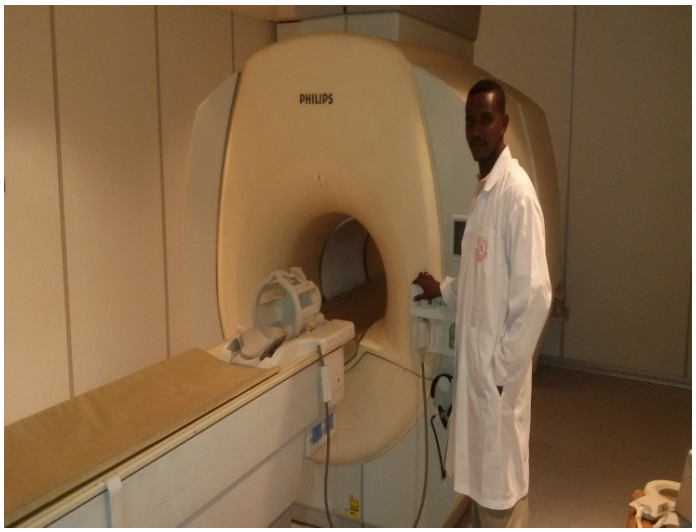


IMAGE 2. CLOSED PHLIPS MRI MACHINE (1.5 TESLA) HOLLAND, (ALAMAL .(DIAGONSTIC CENTER

IMAGE 3 . NEUROVASCULAR COIL PHLIPS MRI .(MACHINE(HOLLAND),(ALAMAL DIAGONSTIC CENTER

IMAGE 4 . HEAD COIL PHLIPS MRI MACHINE (HOLLAND), (ALAMAL DIAGONSTIC CENTER.)

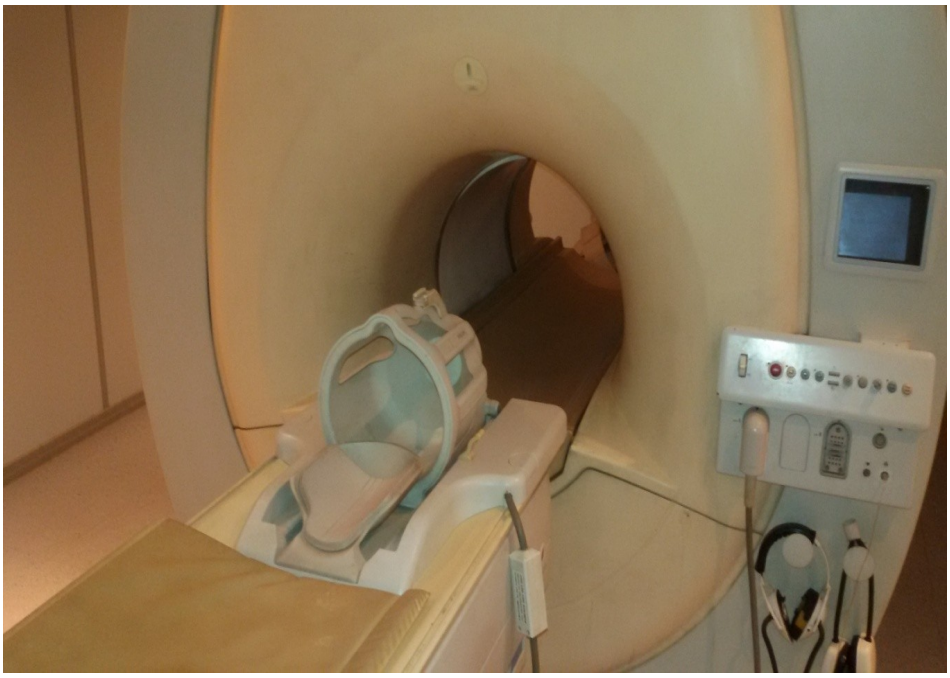


IMAGE 5 axial FLAIR sequence, image on the left side, use modified protocol(slice thickness3mm & gap 0.0mm) and image .(on the right used routine protocol (thickness 5mm & gap 1mm