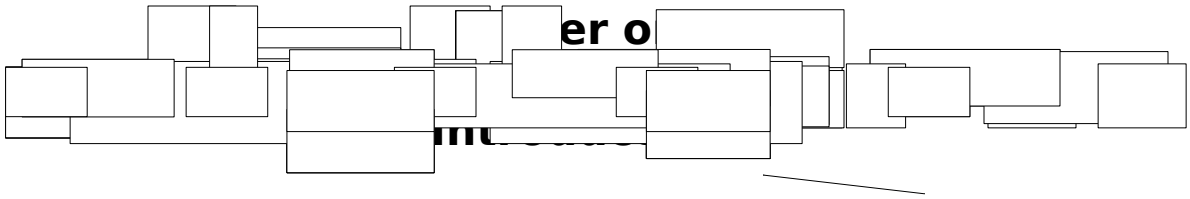

1.1 Prelude:-

The substantia nigra is a brain structure located in the mesencephalon (midbrain), that plays an important role in reward, addiction, and movement, an area of pigmented cells in the midbrain which is responsible for producing the neurotransmitter dopamine. This section of the brain plays an important role in the control of movement, and it also appears to interact in the process of addiction. It is located in the midbrain, right at the tip of the brainstem between the cru- cerebri and the tegmentium, lateral to the red nucleolus and medial to the cerebri. (Rabey et al, 1990*)*

In Latin substantia nigra means black substance. It was so named because of its black appearance on microscopic examinations, reflecting the fact that parts of the substantia nigra appears darker than neighboring areas; this is due to high level of melanin dopaminergic neurons. Substantia nigra produces and uses dopamine which is a chemical that crosses the gap between nerve to connect and stimulate them. Dopamine is a neurotransmitter which plays an important role in brain function, addiction, movement and Parkinson disease. *(*Rabey et al, 1990*)*.

Substantia nigra actually consist of two parts with very different connection and function, the pars compacta and pars reticula.the

pars compacta serves mainly as an input to the basal ganglia circit,supplying the striatum with dopamine. It contains melanin pigment. The pars reticula, on the other hand, serves mainly as an output, conveying signals from the basal ganglia to numerous other brain structures. (Danner et al, 2003).

Because the substantia nigra is so critical to movement, having a healthy substantin nigra is important, if lesions appear on this region of the brain, people can experience movement disorder. Parkinson disease is linked with lesions and decreases activity in the substantia nigra depending on how severe the damage is. Patients may simply have difficulties with coordination and other movement problems. (Whishaw et al, 2011)

Schizophrenia is a is a mental disorder often characterized by abnormal social behavior and failure to recognize what is real, Common symptoms include false beliefs, unclear or confused thinking, auditory hallucinations, that affects the way a person behaves, thinks, and sees the world. People with schizophrenia often have an altered perception of reality. They may see or hear things that don’t exist, speak in strange or confusing ways, believe that others are trying to harm them, or feel like they’re being constantly watched. This can make it difficult to negotiate the activities of daily life, and people with schizophrenia may withdraw from the outside world or act out in confusion and fear. Although Schizophrenia is a chronic disorder, there is help available. With support, medication, and therapy, many people

with schizophrenia are able to function independently and live fulfilling lives. *(*Picchioni 2007).

Epilepsy is a group of neurological diseases characterized by epileptic seizures. Epileptic seizures are episodes that can vary from brief and nearly undetectable to long periods of vigorous shaking. In epilepsy, seizures tend to recurrent, and have no immediate underlying cause. Many people with epilepsy have more than one type of seizure and may have other symptoms of neurological problems as well.

(Lowenstein *et al 2003)*

The human brain is the source of human epilepsy. Although the symptoms of a seizure may affect any part of the body, the electrical events that produce the symptoms occur in the brain. The location of that event, how it spreads and how much of the brain is affected, and how long it lasts all have profound effects. These factors determine the character of a seizure and its impact on the individual. (Sirven et al, 2014).

A person is diagnosed with epilepsy if they have had at least two seizures that were not caused by some known and reversible medical condition like alcohol withdrawal or extremely low blood sugar. The cause of most cases of epilepsy is unknown, although some people develop epilepsy as the result of brain injury, stroke, and tumors. The seizures in epilepsy may be related to a brain injury or a family tendency. The word "epilepsy" does not indicate anything about

the cause of the person's seizures or their severity. (Longo, et al 2012).

The midbrain extends from the Pons to the diencephalon, and is about 2.5 cm long. The aqueduct of the midbrain (cerebral aqueduct) passes through the midbrain, connecting the third ventricle above with the forth ventricle below. Like the medulla and the pons, the midbrain contains both nuclei and tracts.

The midbrain contains several other nuclei, including the left and right substantia nigrae, which are large and darkly pigmented. Neurons that release dopamine help control subconscious muscles activities.loss of these neurons are associated with Parkinson disease (Bergen, 2003).

MRI allows cross sectional viewing of the body with unprecedented tissue contrast. It does not use any ionizing radiation and has rabidly evolved into an accepted modality for medical imaging of disease processes in the musculoskeletal system. MR imaging is increasingly being recognized as the modality for assessment of pathological condition. (Freimarck, 1995).

MRI stands for magnetic resonance imaging once called nuclear magnetic resonance imaging. The (nuclear) was dropped off because of fear that people would think was something radioactive involve, which there is not. MRI is a way of getting picture of various parts of human body without the use of X-ray.

Unlike regular x-rays pictures and CT scan.MRI scanner consists of a large and very strong magnet in which the patient lies. A rdiowave antenna is used to send signal to the body and then receive signals back. These returning signals are converted into pictures by computer attached to the scanner. Pictures of almost any part of the body can be obtained at any particular angle. These radio wave signals are actually a varying or changing magnetic field that is much weaker than the steady strong magnetic field of the main magnet.MRI is quite safe in the majority of patients. Certain patients may not be able to have an MRI, these include people who get nervous in small places (claustrophobic) and those with implants medical devices such as aneurism clips in the brain, heart pacemakers and cochlear (inner ear. *(*Freimarck, 1995).

1.2 Problems of the study:-

Nigra control most of the sense in the body and muscular function, age and disease affect the nigra characteristics in various methods. They were subjectively done, therefore characterization of this part of the brain by objective method will facilitate bases of a good explanation for the associated pathology.

1.3 Objectives:-

1.3.1 **General objectives**:-

To characterize substantia nigra using MRI in order to use quantitative measurement as indication for the pathological condition.

1.3.2 Specific objective:-

-To measure the nigra width and length in different types of brain disease (Parkinson, schizophrenia and epilepsy).

-To measure the nigra width and length in normal control group.

-To compare the measurement of substantia nigra between disease groups and normal groups.

-To correlate the measurement with age and gender.

-To measure the ventricles and temporal lobe and putamen.

-To compare the nigra measurement between the disease group Parkinson, schizophrenia.

1.4 Over view of the study:-

This study falls into five chapters, Chapter one, which is an introduction, deals with theoretical frame work of the study. It presents the statement of the of the study problems, objectives of the study, chapter two, is divided into two sections, section one deals with the anatomy and pathology. Section two deals with literature review (previous studies). Chapter three deals with material and method, Chapter fours deals with (results) data presentation. Chapter five discusses the data (discussion), analysis recommendations, conclusion and references.

Chapter two

Literature Review

2.1 Anatomy and Physiology

2.1.1The midbrain:-

The midbrain comprises two lateral halfs, called the cerebral peduncles, each of these is divided into an anterior part, the crus cerebri,and a posterior part, the tegmentum,by a pigmented band of gray matter, the substantia nigra(Snell, 1999).

The narrow cavity of the midbrain is the cerebral aqueduct, which connects the third and fourth ventricles. The tectum is the part of the midbrain posterior to the cerebral aqueduct; it has four small surface swellings, namely, the two superior and two inferior colliculi. The colliculi are deeply placed between the cerebellum and the cerebral hemispheres.

The pineal body is a small glandular structure that lies between the superior colliculi.It is attached by a stalk to the region of the posterior wall of the third ventricle. The pineal commonly calcifies

in middle age, and thus it can be visualized on radiographs. (Snell, 2010).

2.1.2 Subnstantia nigra:-

Is a large motor nucleus situated between the tegmentum and the crus cerebri, it is curve plate of grey matter. and is found throughout the mid brain .it contains many large nerve cells with a considerable amount of melanin in their cytoplasm.these cells have connections with the tegementium of the midbrain and with the corpus stratium.it play an important part in the control of muscle,activity,and produce dopamine which is passed along their axon to the corpus stratium. (Richard S.Snell, 2010).

The substantia nigra extend from the superior border of the pons into the infrolateral part of the hypothalamus, superior to the midbrain (G.J Roman's, 1998).

Substantia nigra is an area of pigmented cells in the midbrain responsible of producing neurotransmitter dopamine. It play an important role in the control of movement, it also appear to intact in the process of addiction. It is a part of the basal ganglia, a complex network which control movement, learning, emotion.

*(*Rabey et al, 1990*)) .*

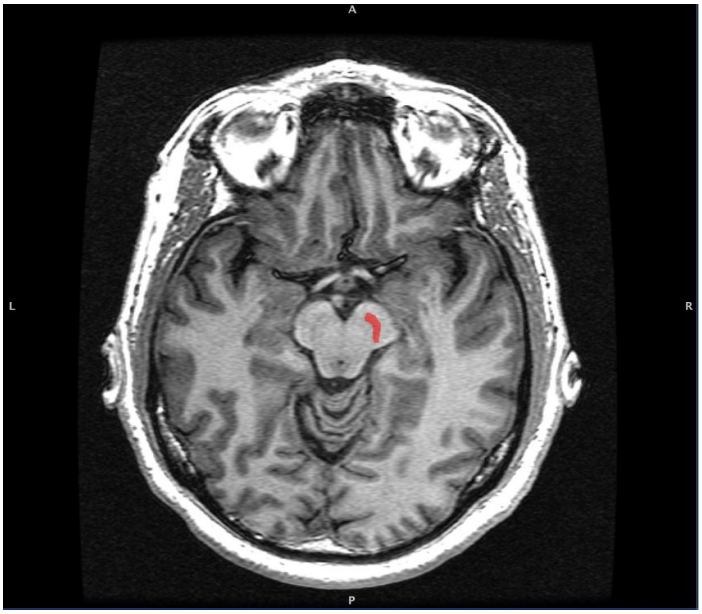

Figure (2.1) Axial MRI (T1W) slice with highlighting indicating location of the substantia nigra .

(https://upload.wikimedia.org/wikipedia/commons/2/2f/Substantia -Nigra.jpg)

2 /2/ 2013, 22:21.

Dopamine plays an important role in the motivation and reward cycle for the brain, which mean that it can play directly into addiction, when the brain learns that a behavior will be rewarded, it will encourage to engage in that behavior as often as possible. With dopamine, receptors becoming more active whenever you engage in that behavior, dopamine is also involve in mood and sleep regulation.The substantia nigra contains two parts: the substantia nigra pars compacta and the substantia nigra pars reticulate.The pars compacta obtains input from the putamen and caudate, and sends information back. The pars reticulate also

obtains input from the putamen and caudate. However, it sends the input outside the basal ganglia to control head and eye movement. The pars compacta produces dopamine, which is crucial for movements. The pars compacta is the part which degenerates during Parkinson disease. (http://en.wikipedia.org/wiki/Substantia nigra).

2.1.3 Putamen:-

The putamen is structure in the brain which forms part of the basal ganglia,the basal ganglia is a series of related structures located at the base of theforebrain and they are involved in a number of different processess(regulation of movement and learning).

Disorder in basal ganglia can cause a variety of disorders,depending of the areas affected and the nature of the disorder.in the case of the putamen ,the structure is a part of larger structure known as stratium,together with the caudate nucleus,the putamen sends message to other areas of the basal ganglia for the purpose of regulating various activities,and receives messages from the cerebral cortex.

Along with the other parts of the basal ganglia,putamen is involved in body movement,with the assisstance of dopamine ,an important neurotransmitter produces in the substantia nigra. Putamen contains a number of colinergic neurons which are senstized to acetylcoline.

parkinson disease is a common neurological condition which can involve the putamen,people with this condition do not produce enough dopamine and are not as sensitive to it as other people,they devolop movement disorders in adition to difficulty speaking and learning.

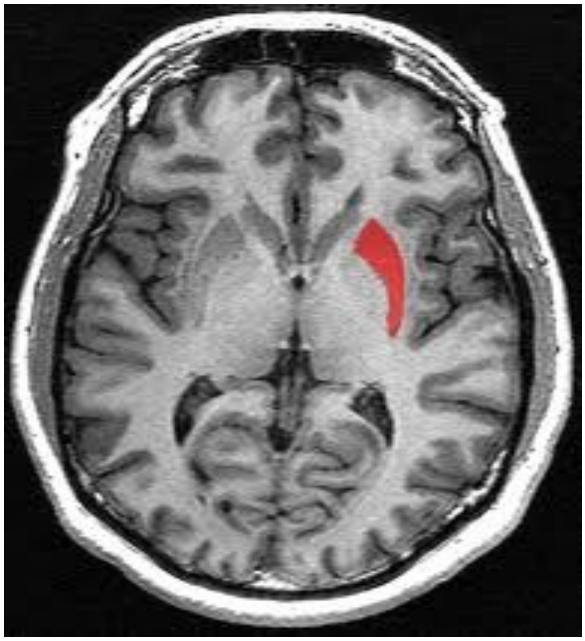

Figure (2.2) Axial MRI T1W image of brain shows the put amen (https://en.wikipedia.org/wiki/Putamen 2/2/2013).

2.1.4 Pons:-

The Pons is anterior to the cerebellum, and connects the medulla oblongata to the mid brain. The anterior surface of the Pons is convex from side to side and shows many transverse fibers that converge on each side to form the middle cerebellar peduncle. The posterior surface of the Pons is hidden from view by the cerebellum. It forms the upper half of the floor of the forth ventricles and is triangular in shape. The Pons is a formation

consisting of nerve fibers that is located on the brainstem, it is situated directly above the medulla and bellow midbrain, the main function is to pass information between the cerebellum and cerebrum. In addition, it helps to send other messages to the brain. It is responsible for rapid eye movement (rem) sleep. It is composed mainly of nerve fibers, which connect the two halves of the cerebellum. It also contains ascending and descending fibers connecting the forebrain, the midbrain, and the spinal cord. Some of the nerve cells within the Pons serve as relay stations, whereas others form cranial nerve nuclei. The pons Looks like an elongated door knob; it is formed from nerves that run horizontally from the left to the right. The back of it forms the forth ventricle. (Snell, 2010).

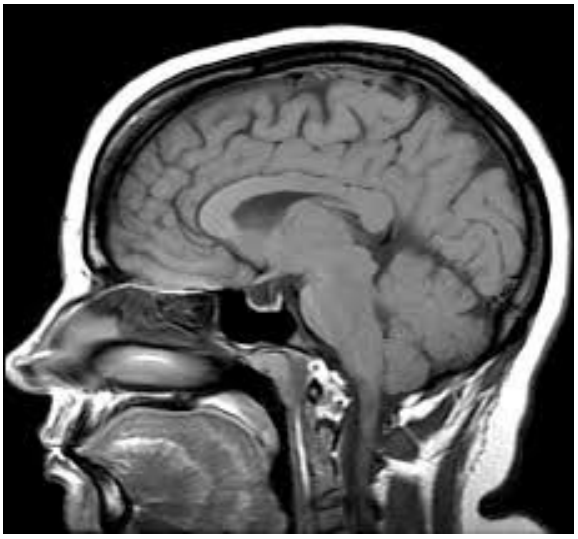

Figure (2.3)MRI of the brain, T2-weighted sagittal view of the pons

http://www-radiology.com/pons.php5/3/2013

2.1.5 Temporal lobe:-

Temporal lobe is an area of cerebral cortex, a sheet of layered neural tissue on the brain, lies inferior to the lateral sulcus and anterior to the occipital lobe.These lobes are responsible for auditory perception, and they play a rule in speech, vision and long term memory. The temporal lobes process the majority of sensory input. It is responsible for a person's fight –or-flight response. It is associated with known function includes the auditory cortex and the temporal association cortex. The auditory cortex is found on the superior temporal gyrus, the auditory cortex's function is the reception of auditory stimuli, and the temporal association cortex Situated around the auditory cortex, this area is involved with the recognition and integration of auditory stimuli. Language is somewhat influence by the temporal lobe.leisons appearing on the left temporal lobe can make the recognition of words difficult. If lesions affect the right temporal lobe, these can be a major loss inhibition when talking. Some forms of epilepsy are known to originate in the temporal lobes,epilepcy affecting these areas of the brain can have a major impact on the personality of the person suffering from the condition.odd sensoryperceptio perception and paranoia also are common in temporal lobe epilepsy.(www.wisegeek what is temporal lobe.htm)

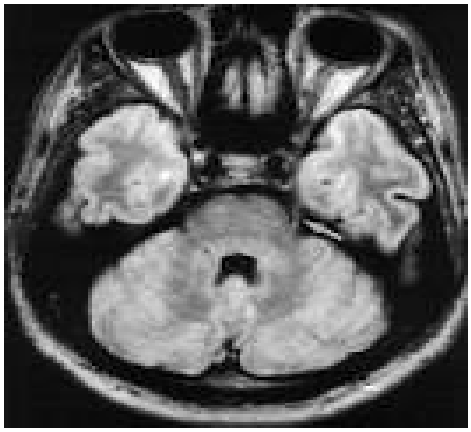

Figure (2.4) Axial MRI T2 shows temporal lobe

(https://www.google.com/search-temporallobeMRIIMAGES&biw-911-433. 13/8/2013)

2.1.6 Ventricles of the brain:-

The ventricles of the brain consist of the two lateral ventricles, the third ventricle, and the fourth ventricle. The two lateral ventricles communicate with the third ventricle through the interventricular foramina. The third ventricle communicates with the fourth ventricle by the cerebral aqueduct. The fourth ventricle, in turn, is continuous with the narrow central canal of the spinal cord and, through the three foramina in its roof, with the subarachnoid space. The ventricles are filled with cerebrospinal fluid, which is produced by the choroid plexuses of the two lateral ventricles, the third ventricle, and the fourth ventricle. The size and shape of the cerebral ventricles may be visualized clinically using computed tomography (CT) scan and magnetic resonance imaging (Snell, 2010).

The lateral ventricle is located in each hemisphere of the cerebrum.anteriorly; the lateral ventricles are separated by a thin membrane, the septum pellucidum.

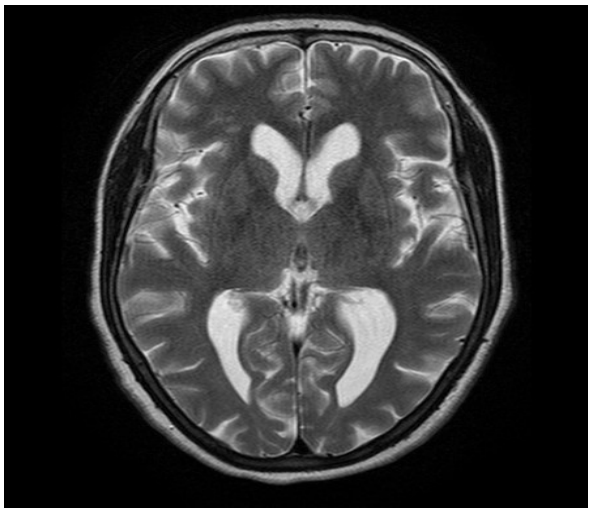

Figure (2.5)Axial MRI T2of Lateral ventricle

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The third ventricle is a narrow cavity along the midline superior to the hypothalamus and between the right and left halves of the thalamus.

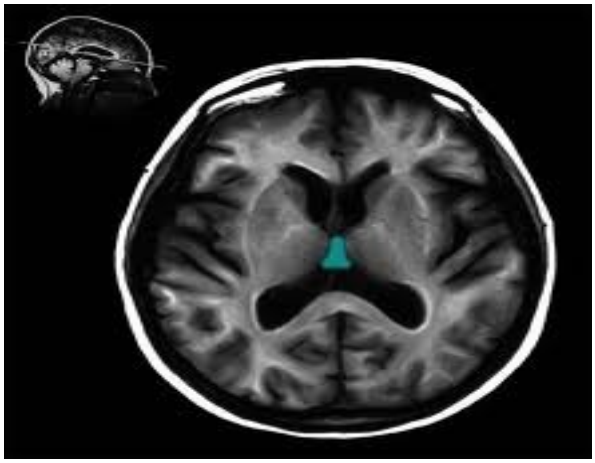


Figure (2.6) Axial MRI T1 of third ventricle

http//www/search/google-mri image of lateral ventricle,biw-911-433 –tbm.7/9/2013

The forth ventricle lies between the brain stem and the cerebellum (Bergen, 2003).

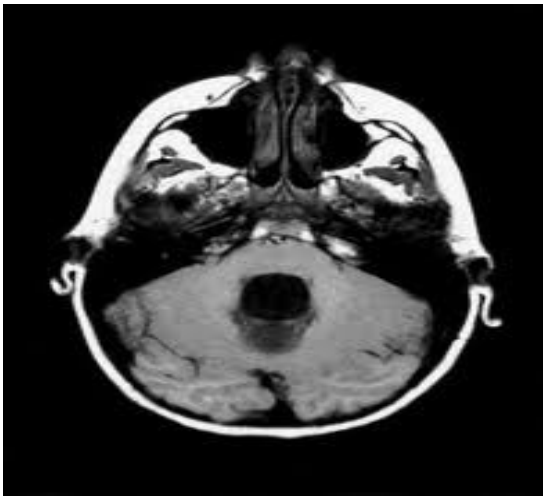


Figure (2.7) Axial MRI T1of forth ventricle

http//www/search/google-mri image of lateral ventricle,biw-911-433 –tbm.7/9/2013

2.2 Blood Supply of the Brain

2.2.1 Arteries of the Brain

The brain is supplied by the two internal carotid and the two vertebral arteries. The four arteries anastomose on the inferior surface of the brain and form the circle of Willis (circulus arteriosus).

2.2.2 Veins of the Brain

The veins of the brain have no muscular tissue in their thin walls, and they possess no valves. They emerge from the brain and drain into the cranial venous sinuses Cerebral and cerebellar veins and veins of the brainstem are present. The great cerebral vein is formed by the union of the two internal cerebral veins and drains into the straight sinus. (Snell, 1999).

2.3. Parkinson's disease:-

Parkinson's disease is a progressive disease of unknown cause,it is associated with

degeneration in the substantia nigra and,to a lesser ,in the putamen,the degeneration of the neurons of the substantia nigra that send their axons to the corpus stratium result in a reduction in the release of the neurotransmitter dopamine within the corpus stratium.(Snell,2010).

2.3.1 Signs and symptoms:-

2.3.1.1 Tremor: - is the most apparent and well-known symptom. It is the most common; around 30% of individuals with

PD do not have tremor at disease onset, and most develop it as the disease progresses. It is usually a rest tremor. Maximal when the limb is at rest and disappearing with voluntary movement and sleep. It affects to a greater extent the most distal part of the limb and at onset typically appears in only a single arm or leg, becoming bilateral later, this is the result of the alternating contraction of agonists and antagonists. *(*Jankovic, 2008).

Tremors are involuntary regular contraction of muscles. Which occur at rest (thus the name static tremors), but they may continue during voluntary movement, these tremors consist of flexion and extension. (Sukkar, 2000).

2.3.1.2 Rigidity: - Is stiffness and resistance to limb movement caused by increased muscle tone, an excessive and continuous contraction of muscles. In Parkinson the rigidity can be uniform (lead-pipe rigidity) or ratchety (cogwheel rigidity). The combination of tremor and increased tone is considered to be at the origin of cogwheel rigidity. Rigidity may be associated with joint pain; such pain being a frequent initial manifestation of the disease. In early stages of Parkinson's disease, rigidity is often asymmetrical and it tends to affect the neck and shoulder muscles prior to the muscles of the face and extremities with the progression of the disease, rigidity typically affects the whole body and reduces the ability to move. Muscle stiffness may occur in any part of the body. The stiff muscles can limit the range of motion and cause a pain. *(*Thompson et al, 2007).

2.31.3 Bradykinesia:-There is a difficulty in initiating (akinesia) and performing a new movement, the movement is slow. The face is expression, and the voice is slurred and unmodulated. Over time, Parkinson's disease may reduce the ability to move and slow movement, making simple tasks difficult and time-consuming. The steps may become shorter. (Snell, 2010). Akinesia is the most incapacitating of the motor abnormalities that patient experience.the patient find the greatest difficulty in initiating voluntary movement, which occur out slow and rigid as a result, movement become scare(poverity of movement)and a patient looks like a statue (Sukkar, 2000).

2.3.1.4 Postural disturbance (gait):-

The patient stand with stoop and his or her arms are flexed. The patient walks by taking short steps and often is unable to stop. In fact he or she may break into shuffling run to maintain balance. Other symptoms include depression.(Snell, 2010).

Parkinson's disease can cause neuropsychiatric disturbances which can range from mild to severe. This includes disorders of speech, cognition, mood, behavior, and thought. Cognitive disturbances can occur in the initial stages of the disease and sometimes prior to diagnosis, and increase in prevalence with duration of the disease. The most common cognitive deficit in affected individuals is executive dysfunction. Parkinsonian symptoms do not appear until up to 50-80% of substantia nigra dopaminergic neurons have died. Most of this plasticity occurs at the neurochemical level; dopamine transport systems are slowed,

allowing dopamine to linger for longer periods of time in the chemical synapses in the striatum. Parkinson disease (PD) is a degenerative disorder of the central nervous system, more commonly seen in the elderly .The main pathological change of PD is the death of dopamine-generating cells in the substantia nigra, a region of the midbrain; then it causes obvious dopamine DA to reduce in the corpus striatum. *(*Caballol et al, 2007).

2.4 Neurodegeneration in Parkinson disease:-

Parkinson's disease is caused by a degeneration of dopaminergic neurons in the substantia nigra of the midbrain. It is considered a disorder of the basal ganglia because the major projection from the substantia nigra is to nuclei of the basal ganglia. The schematic provides a simplified illustration of the connectivity of the basal ganglia. The basal ganglia receive inputs from multiple cortical areas, and then project to the motor cortex via the thalamus. The substantia nigra is interconnected with nuclei in the basal ganglia. The basal ganglia integrate these multiple inputs to modulate the output of the motor cortex. Some of the connections are excitatory and some are inhibitory. The loss of dopaminergic input from the substantia nigra alters the balance of the output from the basal ganglia to the motor cortex, and this underlies the symptoms that are seen. Parkinson disease

Is a progressive neurodegenerative disorder, and over the course of the disease, symptoms will worsen. There are pharmacologic and surgical therapies that do work to decrease the symptoms (Nutt et al 2005).

2.5 Treatment:-

Parkinson disease may be treated by elevating the brain dopamine level. Unfortunately, dopamine cannot cross the blood-brain barrier, but its immediate precursor L-Dopa can, and is used in its place. L Dopa is taken up by the dopaminergic neurons in the basal nuclei and converted to dopamine. Snell, 2010).

The basal ganglia are stimulated by acetyl-choline and inhibited by dopamine,and balance between them is necessary for normal muscle tone.

Treatment of Parkinson consist of promoting dopamine activity by levo-dopa(L-dopa) and reducing acetylcoline activity. (Sukkar, (2000).

The substantia nigra is the target of chemical therapeutics for the treatment of Parkinson's disease. Levodopa (L-DOPA), the dopamine precursor, is the most commonly prescribed medication for Parkinson's disease. Despite controversy concerning the neurotoxicity of dopamine, it remains the most common treatment for Parkinson's disease. The drug is especially effective in treating patients in the early stages of Parkinson's, although the drug does lose its efficacy over time. Levodopa can cross the blood brain barrier, and increases dopamine levels in the substantia nigra, thus alleviating the symptoms of Parkinson's disease. (Neng et al 1996).

2.6. Schizophrenia:-

Schizophrenia is a mental disorder often characterized by abnormal social behavior and failure to recognize what is real.

Common symptoms include false beliefs, auditory hallucinations, confused or unclear thinking, inactivity, and reduced social engagement and emotional expression. Diagnosis is based on observed behavior and the person's reported experiences. (http://en.wikipedia.org/wiki/Schizophrenia)

2.6.1.Causes of schizophrenia:-

A combination of genetic and environmental factors plays a role in the development of schizophrenia. People with a family history of schizophrenia who have a transient psychosis have a 20–40% chance of being diagnosed one year later. (http://en.wikipedia.org/wiki/Schizophrenia)24/5

Increased levels of dopamine have long been implicated in the development of shisophrenia. However, much debate continues to this day surrounding this dopamine hypothesis of schizophrenia. Despite the controversy, dopamine antagonists remain a standard and successful treatment for schizophrenia. These antagonists include first generation (typical) antipsychotics such as butyrophenones, phenothiazines, and thioxanthenes. These drugs have largely been replaced by second-generation (atypical) antipsychotics such as clozapine and paliperidone. It should be noted that, in general, these drugs do not act on dopamine-producing neurons themselves but on the receptors on the post-synaptic neuron. (Cunha, et al, 2006).

2.6.2 Symptoms:-

Individuals with schizophrenia may experience hallucinations (most reported are hearing voices), delusions (often bizarre or persecutory in nature), and disorganized thinking and speech. The last may range from loss of train of thought, to sentences only loosely connected in meaning, to speech that is not understandable known as word salad. In men, schizophrenia symptoms typically start in the early to mid-20s. In women, symptoms typically begin in the late 20s. It's uncommon for children to be diagnosed with schizophrenia and rare for those

Older than 45years **(**Carson et al 2000).

2.6.2.1. Delusions: - These are false beliefs that are not based in reality. For example, you're being harmed or harassed, certain gestures or comments are directed at you, you have exceptional ability or fame, another person is in love with you, a major catastrophe is about to occur, or your body is not functioning properly. Delusions occur in as many as 4 out of 5 people with schizophrenia. The individual thinks that, harm is occurring, or is going to occur. The persecutor(s) has (have) the intention to cause harm, they are constantly being prejudged. (Freeman, et al (2004).

2.6.2.2 Hallucinations: - is a perception in the absence of external stimulus that has qualities of real perception. They are distinguishable from these related phenomena, dreaming, which does not involve wakefulness, illusion, which involves distorted or misinterpreted real perception, imagery, which does not mimic real perception and is under voluntary control. These usually

involve seeing or hearing things that don't exist. Yet for the person with schizophrenia, they have the full force and impact of a normal experience. Hallucinations can be in any of the senses, but hearing voices is the most common hallucinatio *(*Chiu et al, 1989).

2.6.2.3 Disorganized thinking (speech):- Disorganized thinking is inferred from disorganized speech. Effective communication can be impaired, and answers to questions may be partially or completely unrelated. Rarely, speech may include putting together meaningless words that can't be understood, sometimes known as word salad. (http://www.mayoclinic.org/disease)

2.6.2.4 Negative symptoms: - are deficits of normal emotional responses or of other thought processes, and are less responsive to medication. This refers to reduced ability or lack of ability to function normally. For example, the person appears to lack emotion, such as not making eye contact, not changing facial expressions, speaking without inflection or monotone, or not adding hand or head movements that normally provide the emotional emphasis in speech. Also, the person may have a reduced ability to plan or carry out activities, such as decreased talking and neglect of personal hygiene, or have a loss of interest in everyday activities, social withdrawal. (Carson.et al, 2000).

2.7 physiology:-

The substantia nigra is responsible for producing the neurotransmitter dopamine.

2.7.1 Dopamine:-

Is a hormone and neurotransmitter of the catecholamine and phenethylamine families that plays a number of important roles in the human brain and body. Its name derives from its chemical structure: it is an amine that is formed by removing a carboxyl from a molecule of L-DOPA. In the brain, dopamine functions as a neurotransmitter, a chemical released by nerve cells to send signals to other Cells. The brain includes several distinct dopamine systems, one of which plays a major role in reward-motivated behavior. Most types of reward increase the level of dopamine in the brain, and a variety of addictive drugs increase dopamine neuronal activity. Other brain dopamine systems are involved in motor control and in controlling the release of several other important hormones. Several important diseases of the nervous system are associated with dysfunctions of the dopamine system. Parkinson disease a degenerative condition causing tremor and motor impairment, is caused by loss of dopamine-secreting neurons in the midbrain area called the substantia nigra. There is evidence that schizophrenia involves altered levels of dopamine activity, and the antipsychotic drugs that are frequently used to treat it have a primary effect of attenuating dopamine activity. *(Moncrieff* et al, 2008).

Outside the nervous system, dopamine functions in several parts of the body as a local chemical messenger. In the blood vessels, it inhibits norepinephrine release and acts as a vasodilator, in the kidneys, it increases sodium excretion and urine output, in the

pancreas, it reduces insulin production, in the digestive system, it reduces gastrointestinal motility and protects intestinal mucosa, and in the immune system, it reduces the activity of lymphocytes. With the exception of the blood vessels, dopamine in each of these peripheral systems is synthesized locally and exerts its effects on cells that are located near the cells that release it. A variety of Important drugs work by altering the way the body makes or uses dopamine. Dopamine itself is available for intravenous injection: although it cannot reach the brain from the bloodstream, its peripheral effects make it useful in the treatment of heart failure or shock, especially in newborn babies. L-dopa, the metabolic precursor of dopamine, does reach the brain and is the most widely used treatment for Parkinson's disease. Dopaminergic stimulants can be addictive in high doses, (http://en.wikipedia.org/wiki/Dopamine) 11/6/2014.

2.8 Epilepsy:-

Epilepsy is a group of neurological diseases characterized by epileptic seizures. a central nervous system disorder (neurological disorder) in which nerve cell activity in the brain becomes disrupted, causing seizures or periods of unusual behavior, sensations and sometimes loss of consciousness.*(* Chang et al, 2003).

The signs and symptoms of seizures vary depending on the type. The most common type of seizures is convulsive (60%). Two-thirds of these begin as focal seizures and become generalized while one third begins as generalized seizures. The remaining 40% of seizures are non-convulsive. Some people with epilepsy simply

stare blankly for a few seconds during a seizure, while others repeatedly twitch their arms or legs. *(Peter et al, 2006).* Seizure signs and symptoms may include, Temporary confusion, a staring spell, uncontrollable jerking movements of the arms and legs and Loss of consciousness or awareness.

2.8.1 Symptoms:-

Symptoms vary depending on the type of seizure. In most cases, a person with epilepsy will tend to have the same type of seizure each time, so the symptoms will be similar from episode to episode.

2.8.1.1 Focal seizures:

When seizures appear to result from abnormal activity in just one area of the brain, they're called focal (partial) seizures. These seizures fall into two categories.

- Focal seizures without loss of consciousness (simple partial seizures). These seizures don't cause a loss of consciousness. They may alter emotions or change the way things look, smell, feel, taste or sound. They may also result in involuntary jerking of a body part, such as an arm or leg, and spontaneous sensory symptoms such as tingling, dizziness and flashing lights.
- Focal dyscognitive seizures (complex partial seizures). These seizures involve a change or loss of consciousness or awareness. During a complex partial seizure, you may stare into space and not respond normally to your environment or perform repetitive movements, such as hand rubbing, chewing, swallowing or walking in circles.

Symptoms of focal seizures may be confused with other neurological disorders, such as migraine, narcolepsy or mental illness. A thorough examination and testing are needed to distinguish epilepsy from other disorders.

2.8.1.2 Generalized seizures:-

Seizures that appear to involve all areas of the brain are called generalized seizures. Six types of generalized seizures exist.

Absence seizures: - Absence seizures, previously known as petit mal seizures, often occur in children and are characterized by staring into space or subtle body movements such as eye blinking or lip smacking. These seizures may occur in clusters and cause a brief loss of awareness.

Tonic seizures: - Tonic seizures cause stiffening of your muscles. These seizures usually affect muscles in your back, arms and legs and may cause you to fall to the ground.

Atonic seizures:- Atonic seizures, also known as drop seizures, cause a loss of muscle control, which may cause you to suddenly collapse or fall down.Clonic seizures:- Clonic seizures are associated with repeated or rhythmic, jerking muscle movements. These seizures usually affect the neck, face and arms.

Myoclonic seizures: - Myoclonic seizures usually appear as sudden brief jerks or twitches of your arms and legs.

Tonic-clonic seizures: - previously known as grand mal seizures, are the most dramatic type of epileptic seizure and can cause an abrupt loss of consciousness, body stiffening and shaking, and sometimes loss of bladder control or biting your tongue.

(http://www.mayoclinic.org/diseases-conditions/epilepsy/symptoms-causes/dxc-20117207)

2.9 MRI Historical background

The story of MRI starts in about 1946 when Felix Bloch proposed in a Nobel Prize winning paper. He stated that the nucleus behaves like a magnet. He realized that a charged particle, such as a proton, spinning around its own axis has a magnetic field, known as a magnetic momentum. He wrote down his finding in what we know as the Bloch Equations. It would take until the early 1950s before his theories could be verified experimentally. In 1960 Nuclear Magnetic Resonance spectrometers were introduced for analytical purposes. During the 1960s and 1970s NMR spectrometers were widely used in academic and industrial research. Spectrometry is used to analyze the molecular configuration of material based on its NMR spectrum.

In the late 1960s Raymond Damadian discovered that malignant tissue had different NMR parameters than normal tissue. He mused that, based on these differences, it should be possible to do tissue characterization. Based on this discovery he produced the first ever NMR image of rat tumor in 1974. In 1977 Damadian and his team constructed the first super conducting NMR scanner (known as The Indomitable) and produced the first image of the human body, which took almost 5 hours to scan.

At the same time Paul Lauterbur was pioneering in the same field. One could discuss who was responsible for bringing MRI to

us, although, in all fairness, one could accept that both gentlemen had their contribution.

The name Nuclear Magnetic Resonance (NMR) was changed into Magnetic Resonance Imaging (MRI) because it was believed that the word nuclear would not find wide acceptance amongst the public.

In the early 1980s just about every major medical imaging equipment manufacturer researched and produced MRI scanners. Then a lot happened in term

of development. The hardware and software became faster, more intelligent and easier to use. Because of the development of advanced MRI pulse sequences more applications for MRI opened up, such as MR Angiography, Functional Imaging and Perfusion / Diffusion scanning.

And yet, the end is not in sight. The development of MR is still in full swing and only time will tell what the future has in store for us. (Brown, *2003).*

2. 10 MRI component:-

2.10.1 The Magnet:-

The magnet is the basic component of the MR scanner. Magnet is available in a variety of field strength, shapes and materials. All magnet fields are measured in unit of Tesla or gauss (1 tesla=10000 gauss) magnet are usually categorized as low(less than 0.5 T,medium(between 0.5-1T or high field strength (more than1T). Magnet are also characterize by the material used in their composition.perminant magnet are manufactured from

metal that remains magnetic for a long time (years),other types are electromagnets in which the flow of electrical current through wire coil produces the magnetic field. The most common type of magnet is superconductive using niobilum-titanium wire immersed in liquid helium. Some low field magnets are permanent or resistive but for all scanners above 1.0 Tesla the magnet are superconductive, that has zero electrical resistance below a critical temperature. To maintain this temperature the magnet is enclosed and cooled by a cryogen containing liquid helium (sometimes also nitrogen) which has to be topped-up on a monthly basis. Imperfections in the superconductive windings (soldered joins) mean that the scanner will lose 5-10 G per year. Far more serious is a quench when the magnet suddenly loses its superconductivity and begins to heat up causing the cryogens to boil and escape (Brown , *2003).*

2.10.2 RF system and coils:-

The radio frequency transmitted system is responsible for generating and broadcasting the RF pulses used to excite the proton. RF transmitter system contains four main components: a frequency synthesizes the digital envelope of RF frequencies, a high-power amplifier and a coil or antenna. The frequency synthesizer produces the center frequency for the RF pulse.

RF coils are used for transmitting energy and receiving signals. There are three types, transmit receive coils, receive only coil, transmit only coil. RF coils are needed to transmit and/or receive the MR signal. In order to optimize signal-to-noise ratio (SNR), the

RF coil should cover only the volume of interest. This is because the coil is sensitive to noise from the whole volume while the signal comes from the slice of interest. To this end there are many types of RF coil with trade-offs in terms of coverage and sensitivity. The most homogenous coils are of a 'birdcage' design. Examples of these include the head and body coils. Both these coils act as transreceivers i.e. they transmit and receive. The body coil is integrated into the scanner bore and cannot be coils, as the name suggests, are used for imaging anatomy near to the coil. They are simple loop designs and have excellent SNR close to the coil but the sensitivity drops off rapidly with distance from the coil. These are only used as receivers, the body coil acting as the transmitter. Multiple loops can be connected into a phased array design, combining the excellent SNR with greater volume coverage. Quadrature or circularly-polarized coils comprise two coils 90° apart to improve SNR. (Brown, *2003).*

Figure (2.8) Phased array head coil

2.10.3 Gradient coils:-

The principle role of the gradient coils are to produce linear changes in magnetic field in each of the x, y and z directions. By combining gradients in pairs of directions, oblique imaging can be performed. Gradient specifications are stated in terms of a slew rate which is equal to the maximum achievable amplitude divided by the rise time. Typical modern slew rates are 150 T/m-s. The gradient coils are shielded in a similar manner to the main windings. This is to reduce eddy currents induced in the cryogen which would degrade image quality.

2.10.4. Pulse sequence:-

Spin echo sequence (SE) also known as conventional spin echo (CSE).usually uses a 90 excitation pulse followed by 180 rephrasing pulse to produce spin echo.SE sequence can be used to generate one or several spin echoes. One echo usually used for T1W, while two echoes used for proton density and T2W.

For T1W used short TE min-20ms, short TR 250-600ms.for T2 W used long TE 70ms and longer 2000ms.(Westbrook,1999).

Fast spin echo (FSE) uses 90 flip angle followed by several 180 rephrasing pulses to produce several spin echoes in a given TR. Some contrast characteristic of FSE sequence differs from SE sequence, fat remains bright. On T2W and fat suppression technique may be needed to compensate for this.

For T2W used longer 90ms, long TR 4000ms, long ETL 16 .for PD used short TE 20ms and longer 4000ms, ETL 8-12.

Inversion recovery pulse sequence (IR):-begins with a 180 pulse that inverts the net magnetization vector into full saturation. A 90 excitation pulse is applied which transfers proportion of magnetization into the transverse plane. This transverse magnetization is then rephrased by a 180 rephrasing pulse to produce an echo. In IR several 180 rephrasing pulses are applied, so reducing scan time.

For STIR used TE 60ms, TR 6000ms, long ETL 16 .for Flair used TE 60ms and longer 6000-10000ms, ETL 16. (Westbrook, 1999).

2.10.5 MRI parameter:-

Repetition time (TR) measured in ms, is the time between successive RF excitation pulses applied to a given volume of tissue.TR determine the amount of T1W.

Echo time (TE) measured in ms, is the time between the excitation pulse and the echo (signal) maximum. It determines the amount of T2W.

Inversion time (TI) measured in ms, is the time between the 180 inversion pulse and the imaging excitation pulse.

Echo train length (ETL) also known as turbo factor, is the number of echoes (number of phase-encoding steps) measured following

an excitation pulse that are used to create an image. (Brown, 2003).

Signal to noise ratio (SNR) is defined as the ratio of the amplitude of signal received by the coil to the amplitude of the noise. The signal is the voltage induced the receiver coil and the noise is a constant value depending on the area under examination and the background electrical noise of the system.

Contrast to noise ratio (CNR), is the difference in the SNR between two adjacent areas. All examinations should include images that demonstrate a good CNR between pathology and the surrounding normal anatomy.

Spatial resolution is the ability to distinguish between two points as separate and distinct. It is controlled by voxel size. Spatial resolution may be increased by selecting thin slices, fine matrix and small FOV.

Scan time, is the time to complete the acquisition of data. The scan time may be decreased by using a short TR, a coarse matrix and a lowest NEX. (Westbrook, 1999).

2.11 MRI physics:-

Over the past 10 years magnetic resonance imaging has become accepted as a powerful tool. It uses the magnetic proprieties of hydrogen atom to produce the Images. The nucleus of the hydrogen atom is a single proton, being spinning, charge particles. It has magnetic properities, so it acts as a small magnet

bar, with north and south poles. The first step in MR is the application of strong external magnet for this purpose. The patient is placed within a large magnet, either permanent or superconductive. Hydrogen atoms within the patient align in a direction either parallel or antiparallel to the strong external field. A greater proportion aligning in the parallel direction, so that the net vector of their alignment, the net vector will be in the direction of the external field.

Each nucleus of the hydrogen atom spins around the line of the field (precession), the frequency of precession known as larmor frequency (10 MHz).

A second magnetic field applied at right angles to the external field at the same frequency as the larmer frequency (RF pulses).a second magnetic coil, the RF coil, applies the RF pulses, the magnetization vector of the hydrogen atoms turn towards the transverse plane. As such the RF adds energy to the system; the extra energy is dissipated to the surrounding chemical lattice in a process known as T1 relaxation

Time. The RF pulse brings the precessing protons into phase, the process of dephasing,which occurs due to tiny inhomogenities in the nuclear magnetic environments is known as T2 relaxation.

The component of the net magnetization vector in the transverse plane induces a current in the magnetic coils (RF receiver coils),

this current is known as the MR signal, and is the basis for formation of an image (Lisle, 2001).

2.12 Image optimization

The SNR and contrast characteristics of the brain are usually good. The quadrature head coil and phased array coils yield high and uniform signal.FSE can be utilized to produce images with good grey matter/white matter contrast in a short time. As the TR increase above 2000 ms the signal intensity of CSF increase due to its high proton density, this may reduce contrast between some preventricular lesions. In order to optimize contrast, two separate acquisition may be necessary, one for proton density, the other for T2.In such an acquisitions, a TR of 2000-2400 ms may be selected along with an ETL of no higher than 4 (Westbrook , 1999).

2.13 Image Contrast

An image has a contrast if there are areas of high signal (white on the image), as

Well As areas of low signal (dark on the image). Some areas have an intermediate signal (shades of grey in-between white and black). The NMV can be separated into the individual vectors of the tissues present in the patient such as fat, cerebro-spinal fluid (CSF) and muscle.

A tissue has a high signal (white) if it has a large transverse component of

magnetization.Image contrast is controlled by extrinsic contrast parameters (those that are controlled by the system operator). These include the following:-

Repetition time (TR), Echo time (TE), Flip angle, Turbo-factor or echo train length (ETL/TF) and Time from inversion (TI).

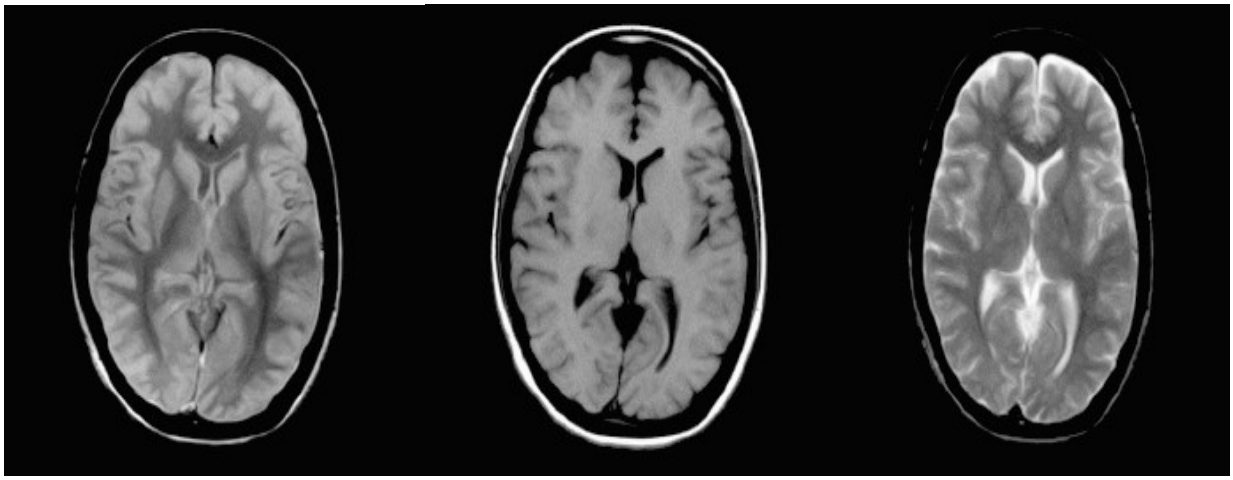
Image contrast is also controlled by intrinsic contrast mechanisms, those do not

Come under the operator's control). These includeT1 recovery,T2 decay and proton density (Westbrook(2002).

One of the great advantages of MRI is its excellent soft-tissue contrast which can be widely manipulated. In a typical image acquisition the basic unit of each sequence (i.e. the 90°-180°-signal detection) is repeated hundreds of times over. By altering the echo time (TE) or repetition time (TR), i.e. the time between successive 90° pulses, the signal contrast can be altered or weighted. For example if a long TE is used, inherent differences in T_2 times of tissues will become apparent. Tissues with a long T_2 (e.g. water) will take longer to decay and their signal will be greater (or appear brighter in the image) than the signal from tissue with a short T_2 (fat). In a similar manner TR governs T_1 contrast. Tissue with a long TR (water) will take a long time to recover back to the equilibrium magnetization value, so therefore a short TR interval will make this tissue appear dark compared to tissue with a short T_1 (fat). When TE and TR are chosen to minimize both these weightings, the signal contrast is only

derived from the number or density of spins in a given tissue. This image is said to be 'proton-density weighted image.

T_2-weighting requires long TE, long TR, T_1-weighting requires short TE, short TR and PD-weighting requires short TE, long TR (Blink2004)

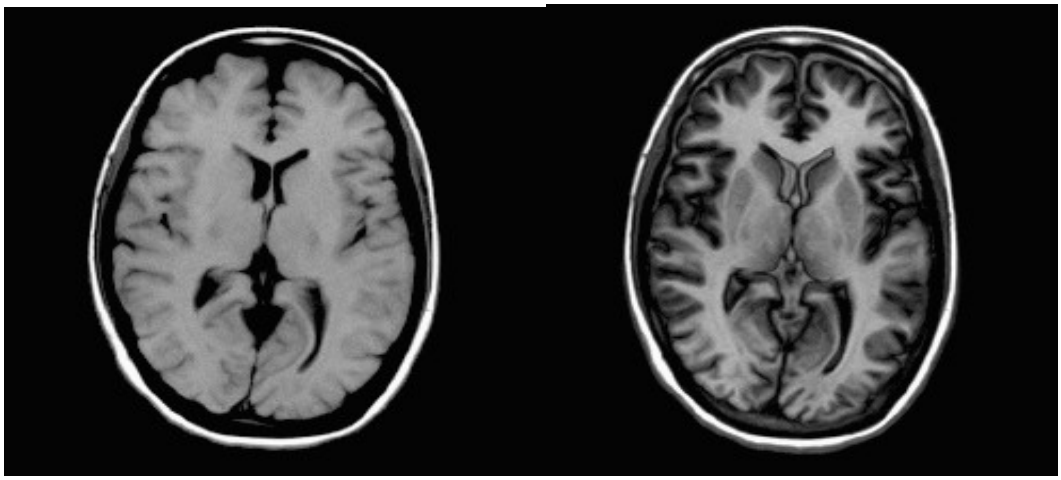


PD T1

T2

Figure (2.9) shows examples of various image contrast https://www.google.com/search-examples of various mri images PD,T1,T2-biw,911-433-tbm.4/1/2014 .

For clear delineation of anatomical structures a T1W or even, an IR sequence is the best choice.

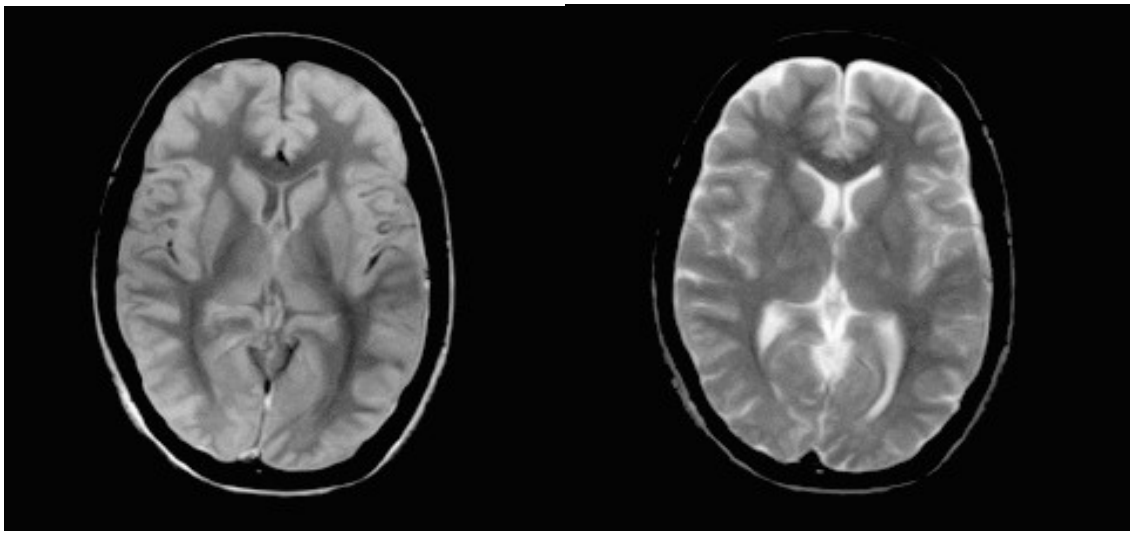


T1

IR

Figure (2.10) shows T1 and IR for anatomy

For pathology PD or T2W contrast is used.Most pathology produces water (edema) which shows bright on T2W images.



PD T2W

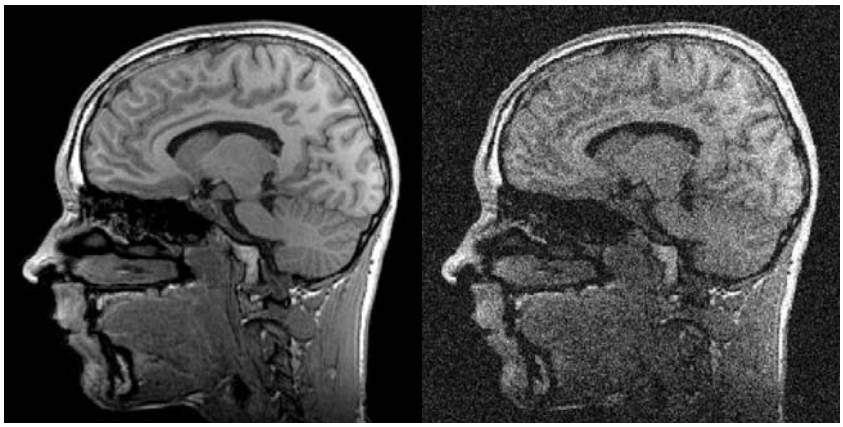
Figure (2.11) Shows PD and T2W for pathology.

https://www.google.com/search-examples of various mri images PD,T1,T2-biw,911-433-tbm.4/1/2014.

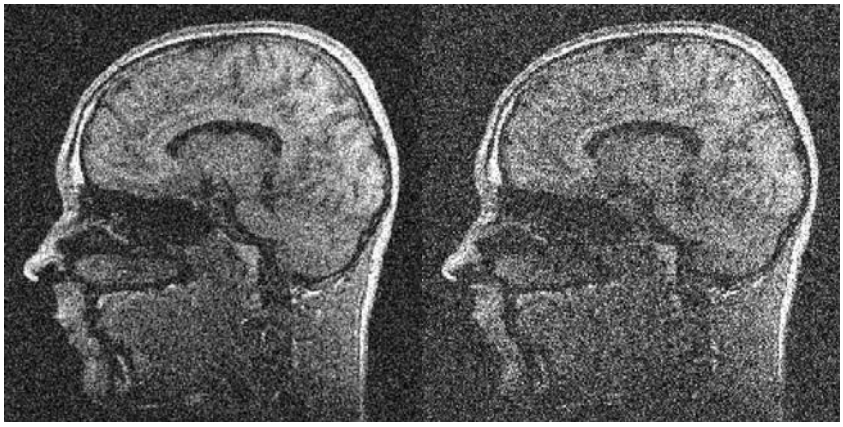
2.14 Signal and Noise:-

Image noise is present in practically all MR images and is one of the effects of the major limiting factors for MRI protocols.

Small low-contrast structures, such as in the cerebellum, become more difficult to differ- entire with increasing noise levels. The noise level is described by the noise standard deviation, and its statistical distribution. The visual impression of an MR image depends on the signal-to-noise ratio (SNR). (Shoenberg, 2003).



A B



C D

Figure.2.12

Illustration of image noise. The same MR image with increasing noise levels (from **A** to **d)** is shown. High noise levels reduce the visibility of small details and of low-contrast changes. (Dietrich (2003) Parallel imaging .

2.15 MRI of the brain:-

2.15.1 Equipment

Head coil (quadrature or phased array), Immobilization pads and strips,ear plugs, High performance gradients for EPI, diffusion and perfusion imaging. (Westbrook, 1999).

2.15.2 Patient positioning:-

The patient lies supine on the examination couch with their head within the head coil. The head is adjusted so that the interpupillary line is parallel to the couch and the head is straight. The patient is positioned so that the longitudinal alignment light lies in the midline, and the horizontal alignment light passes through the nasion.straps and foam pads are used for immobilization. (Westbrook, 1999).

2.16 Protocols

2.16.1 Sagittal FSE/GEE T1

Medium slices /gap are prescribed on either side of the longitudinal alignment light from one temporal lobe to the other.

The area from the foramen magnum to the top of the head is included in the image (Westbrook, 1999).

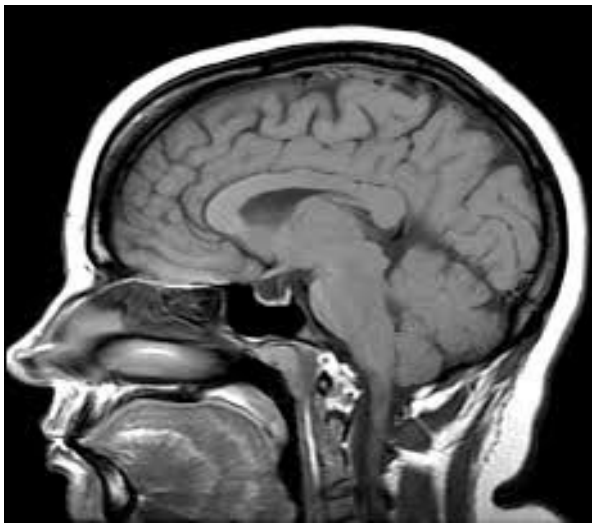
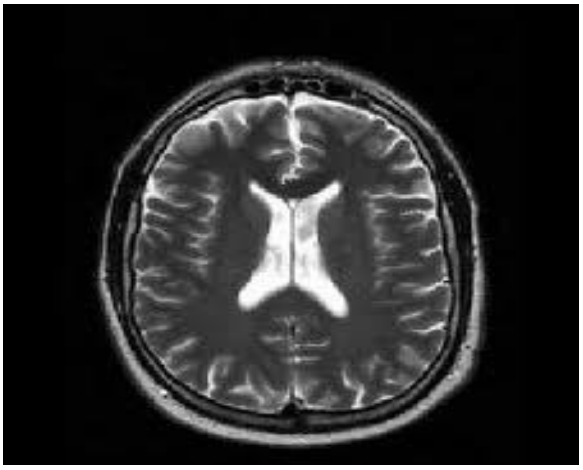


Figure (2.13) sagittal T1

http://emedicine.medscape.com/article/2105033.technique.

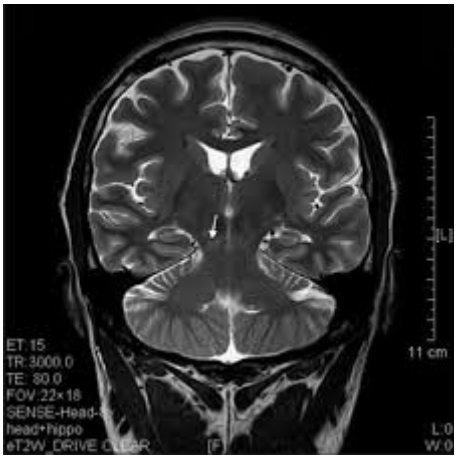
2.16.2 Axial/oblique FSE/PD/T2:- Medium slices/gap are prescribed from the foramen magnum to the superior surface of the brain.slice may be angled so that they are parallel to the anterior posterior comissure axis.this enables precise location of leisons. (Westbrook, 1999).



Figure(2.14)Axial MRI T2W

2.16.3 Coronal FSE/PD/T2

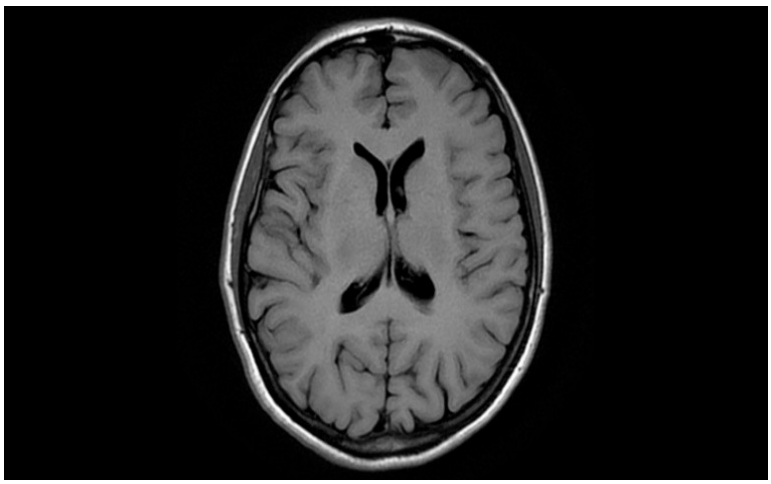
As for axial T2 except that, the prescribed slices from the cerebelum to the frontal lobe.



Figure(2.15)CoronalT2https://www.google.com/search-coronalt2image-tbm/ biw=911-433.

2.16.4 Axial/oblique/ IR/T1

Slice prescribed as for axial/oblique/T2.this sequence is usefull in imaging the paediatric brain.white matter does not fully myelinate untill approximately 5 years of age,therefor in the very young patient,gray matter and white matter havbe very similar T1 relaxation times,and the CNR between these tissues is small on T1 sequences.



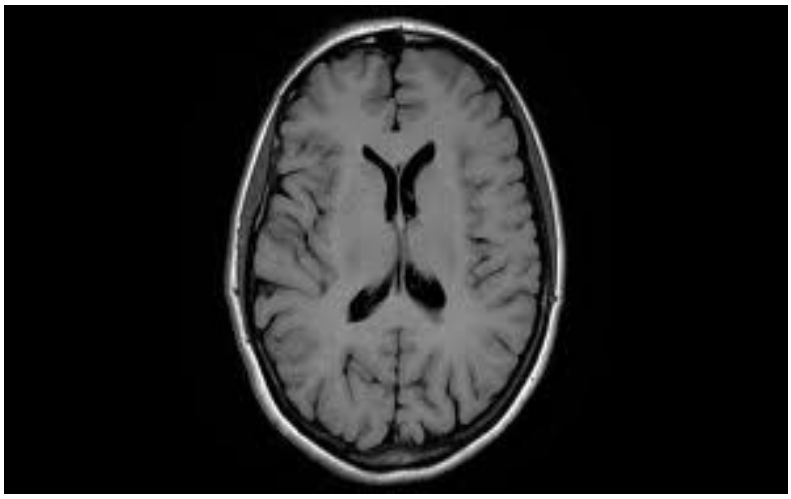
Figure(2.16)Axial/T1/IR(http://emedicine.medscape.com/article/2105033-technique).

2.16.5 Axial/oblique/Flair

Slice prescription as for axial/oblique/T2.This sequence provides a rapid acquisition with suppression of CSF signal. It may be useful when examining preventricular or cord lesions such as MS plaque.

2.16.6 Axial/oblique SE/FSE/T1

Slice prescribes as for axial oblique/ T1.Pre and post contrast scans are common especially for tumor assessment. Short TR and short TE used.

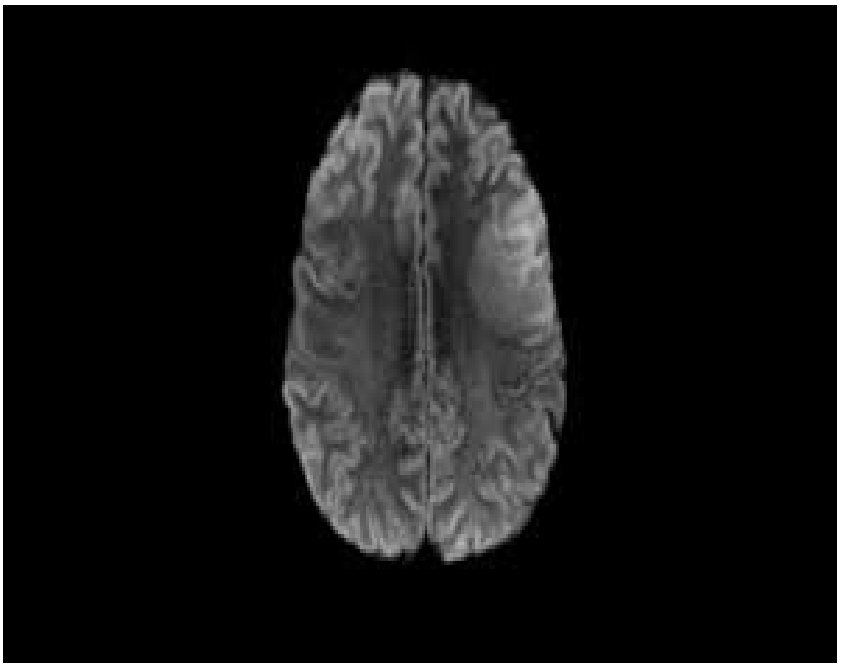


Figure(2.17)Axial T1 http://emedicine.medscape.com/article/2105033-technique

2.16.7 Axial /DWI

Demonstrate areas with restricted diffusion of extracellular water such as infarct tissues DWI are most effectively acquired by combining a rapid sequence such as EPI or GRE with two bipolar gradients. The gradient pulses are designed to cancel out the phase shift of stationary spins, whilst moving spins experience a phase shift. Therefore signal attenuation occurs in normal tissue with random motion, and high signal appears in tissue with restricted diffusion.

Slice prescription as for Axial/oblique T2.this sequence is important in the investigation of early stroke. It is also utilized in pediatric patients to investigate the effects of hypoxia and myelination pattern. A b-value of 800-1000 s/mm is selected (the higher the b-value the more diffusion weighting. (Westbrook,1999).

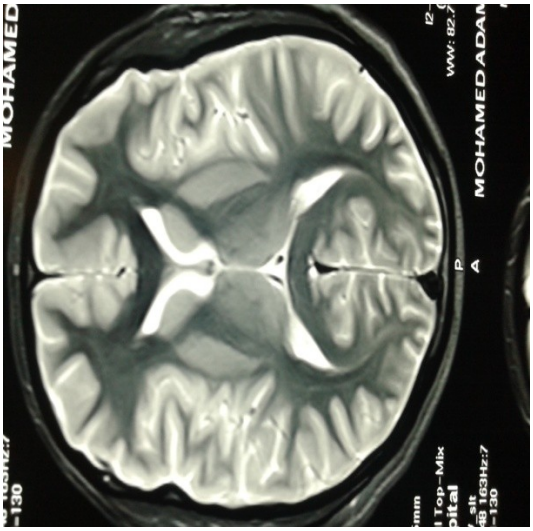


Figure(2.18)Axial/DWI

https://www.google.com/search-DWIaxialimage-tbm/biw=911-433-3.436.16044.

2.16.8 STIR:- The inversion recovery sequences are spin echo sequences with a 180° preparation pulse to flip the longitudinal magnetization into the opposite direction (i.e. spins are flipped to the 180° position). Transverse magnetization remains equal to zero therefore we do not receive any an MR signal. During the recovery, the negative longitudinal magnetization decays to zero

and then begins to rise. Because transverse magnetization is not possible, no signal is measured. To generate an MR signal, the longitudinal magnetization is then converted to transverse magnetization through the application of a 90° pulse. The interval between the 180° pulse and the 90° stimulation pulse is known as inversion time (TI). As the spins relax back to their equilibrium configuration the signal for each spin group will evolve from a negative signal which is zero (null point) to a positive. The easiest way to identify STIR images is to look for fat and fluid filled space in the body (e.g. Cerebrospinal fluid in the brain ventricles and spinal canal, free fluid in the abdomen, fluid in the gall bladder and common bile duct, synovial fluid in joints, fluid in the urinary tract and urinary bladder, edema or any other pathological fluid collection in the body). (http//mri master.com/characterize images.html) 23/5/2014



Figure(2.19)(AxialSTIR)https://www.google.com/search-stir,imageof+brain biw=911 -433.

2.17 MR Imaging technique:-

2:17.1 T1 weighting

In a T1 weighted image, differences in the T1 relaxation times of tissues must be demonstrated. To achieve this TR is selected that is short enough to ensure that the NMV in neither fat nor water has had time to relax back to *B* before the application of the next excitation pulse. If the TR is long, the NMV in both fat and water recovers and their respective T1 relaxation times can no longer be distinguished.

AT1 weighted image is an image whose contrast is predominantly due to the differences in T1 recovery times of tissues.

For T1 weighting differences between the T1 times of tissues is exaggerated

And to achieve this TR must be short. To diminishT2 effects the TE must also be short.

In T1 weighted images, tissues with short T1 relaxation times such as fat, are

Bright (high signal), because they recover most of their longitudinal magnetization during the TR and therefore more magnetization is available to be flipped into the transverse plane by the next RF pulse.

Tissues with long T1 relaxation times such as water, are dark (low signal) because they do not recover much of their longitudinal magnetization during the TR. and therefore less magnetization is available to be flipped into the transverse plane by the next RF pulse. T1 weighted images best demonstrate anatomy but also

show pathology if used after contrast enhancement. (Westbrook, 2002).

2.17.2 T2 weighting

In a T2 weighted image the differences in the T2 relaxation times tissues must be demonstrated. To achieve this, a TE is selected that is long enough to ensure that the NMV in both fat and water have had time to decay. If the TE is too short, the NMV in neither fat nor water has had time to decay and their respective T2 times cannot be distinguished.

AT2 weighted image is an image whose contrast is predominantly due to the differences in the T2 decay times of tissues.

For T2 weighting the differences between the T2 times of tissues are exaggerated, therefore the TE must be long. T1 effects are diminished by selecting along TR.

Tissues with a short T2 decay time such as fat are dark (low signal) because they lose most of their coherent transverse magnetization during the TE period.

Tissues with a long T2 decay time such as water are bright (high signal), because they retain most of their transverse coherence during the TE period. T2 weighted images best demonstrate pathology as most pathology has increased water content and is therefore bright on T2 weighted images.

2.17.3 Flair :-(Fluid attenuation at inversion recovery):-

Suppress the signals generated by fluids in the body. Unwanted signals from cerebrospinal fluid in the brain, and darken the

portions of the images containing this fluid. Used in cerebral MRI for edema imaging.

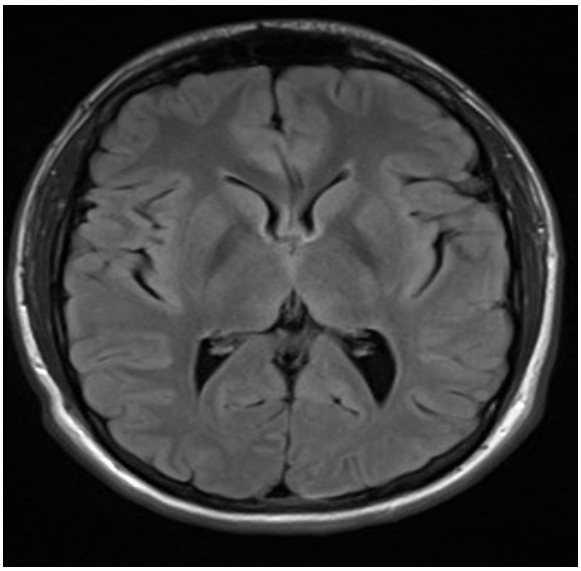


Figure (2.20) axial flair

https://www.google.com/search?hl=ar&site=imghp&tbm=isch&source=hp&bi.

2.18 Patient consideration:-

Claustrophobia is often troublesome because of the enclosing nature of the head coil. In addition neurological factors may increase likelihood of patient movement. Examples of these are epilepsy, Parkinson disease and reduced awareness or consciousness. Sedation or general anathesia is sometimes required. Due to a loud gradient noise associated with some sequence,ear plugs may always be provided to prevent hearing impairment(Westbrook ,1999).

2.19 MR imaging of substantia nigra:-

A number of optimizing steps needed to be implemented in order to develop an MR imaging protocol that could accurately demonstrate substantia nigra. Current study explored imaging parameters that included MR Sequence selection, slice orientation and positioning. Imaging slices positioned in the axial orientation with an oblique angle tilted towards the occipital cortex.

The positioning of the slice should be done to observe visual image quality (contras sensitivity) and immunity to image distortion, as well as CNR between structures (Figure 2.22).Thin slice thickness(2.2mm-1mm),slice gap (0-1mm),128x128,matrix 320x256 .

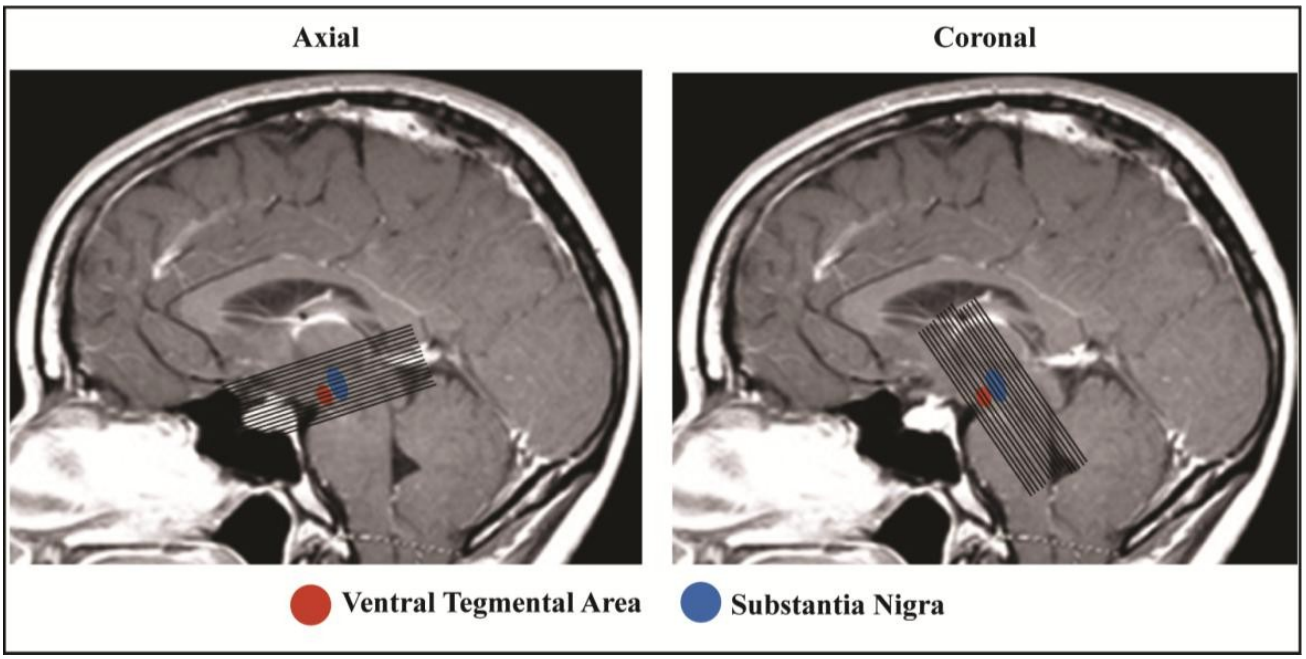


Figure (2.21) Slice positioning for anatomical midbrain imaging overlaid on mid sagittal MR images. The left panel shows slice coverage in the axial plane (horizontal slice slab) and the right panel shows the slice coverage in the coronal plane (vertical slice slab). The VTA and SN are represented as red and blue solid circles respectively underneath the slice stack. **A** denotes the anterior part of the brain. (Coster 2012).

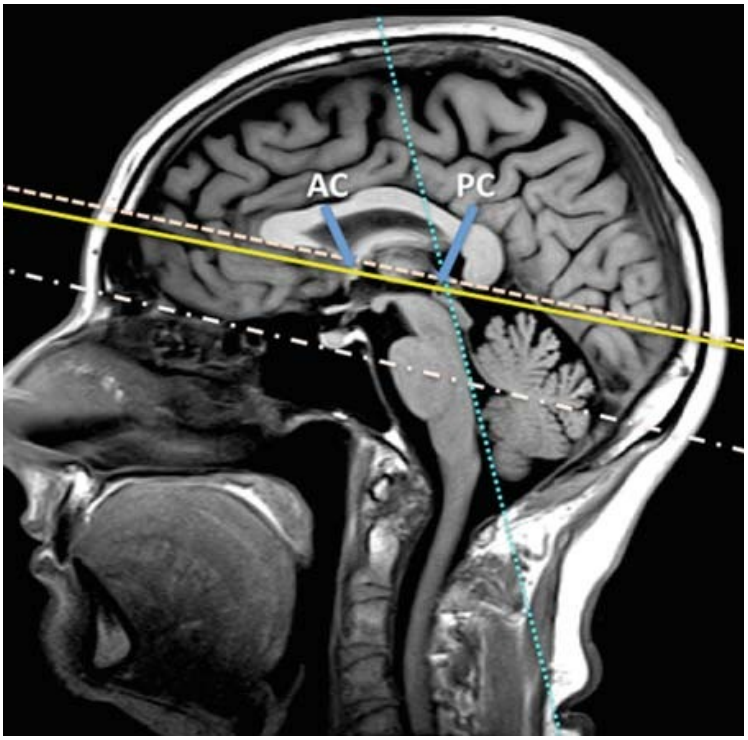


Figure (2.22) Sagittal MRI shows anatomic landmarks for positioning of axial slices. Axial slices should be positioned parallel to the bicommissural line, which links the anterior to the posterior commissure. Alternatively position slices parallel to a line linking the inferior borders of the genu and splenium of the corpus callosum

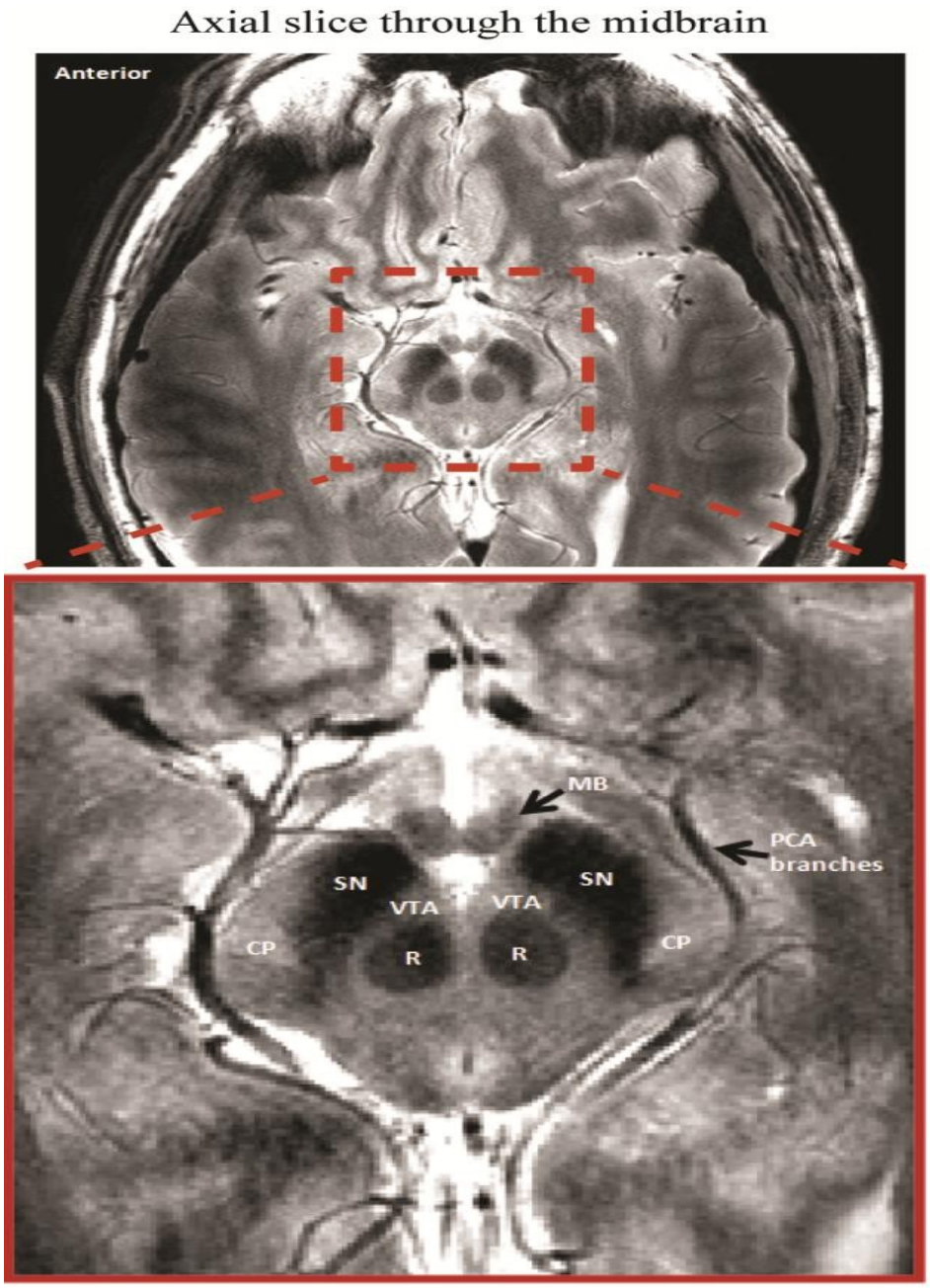


Figure (2.22) represent axial section through the mid brain.insert represent a zoom version of the image.legeng structure include: SN Substantia nigra: Ventral tegmental area. R red nucleus: CP

Cerepral pedunces: MB. Mamillary Boy,and PCA Posterior cerebral artery. (Coster 2012)

2.20 previous studies:-

According to Huseyin Tugrul Atasoy et al (2004) in their study using T2-weighted MRI in (PD), they study, 20 patients with PD (6 women, 14 men) from

The movement disorders, sixteen healthy subjects (5 men, 11 women) were taken as control group. The mean age of the patient group was 66.7± 8.5 and of the control group was 57.19± 9.46. PD patients had mean disease duration of 6.25±3.31 years. The width of Substantia nigra was measured. They concluded that, Substantia nigrawidth was lower in patients than in control subject.

L. Minati et al (2007) in their study about imaging Degeneration of the Substantia Nigra in Parkinson Disease with Inversion-Recovery MR imaging. They investigate the Potential role of area and T1 contrast measurements in differentiating patients from controls and their age-related changes. They stated that, Inversion-recoverySequences may provide a convenient way to visualize nigral degeneration.

Michael Hutchinson et al (2000) in their study about Structural Changes of the

Substantia Nigra in Parkinson’s disease as Revealed by MR Imaging, their study suggests that MR imaging is sensitive to

structural changes in even the earliest cases of Parkinson’s disease.

Michael Hutchinson et al (1999) Parkinson's disease concerning a novel MRI method for determining structural changes in the substantia nigra. Six patients with Parkinson’s disease were compared with six age matched control subjects. The subjects were imaged using a combination of pulse sequences. The images showed patterns of change in patients with Parkinson's disease. Highly significant differences between the patients and control population ($p<0.001$). They concluded that, the methodology Suggests the possibility of detecting presymptomatic disease in those judged to be at risk, and also in confirming the diagnosis in patients with early disease. Furthermore, the technique seems to hold promise as a means for staging the disease, and possibly differentiating other forms of Parkinson disease.

Andrew R. Gilbert et al 2001 in study of MRI structural findings in shizophernia revealed enlarged lateral ventricular volumes in schizophrenia patients as compare

With controls.

Sarah Jesse et al (2012) had studied Signal alterations of the basal ganglia in the differential diagnosis of Parkinson’s disease. T2-weighted scans were performed for substantia nigra in seventy control subjects and 38 patients with Parkinson disease.the result of the study shows that, In patients with PD, significant changes in signal intensities within the substantia nigra were observed compared to controls at $p < 0.001$, and they concluded

that, Signal alterations of substantia nigra in routine magnetic resonance imaging were useful to distinguish patients with PD from controls.

Haukvik et al (2012), they studied structural MRI of schizophrenia patients, they concluded that, in patients with schizophrenia, MR imaging shows a smaller total brain volume and enlarged ventricles. Specific subcortical regions are affected, and a reduction in cortical volume and thickness, most pronounced in the frontal and temporal lobes.

Donald. H. et al in studding (MR in Temporal Lobe Epilepsy).186 consecutive patients diagnosed as temporal lobe epilepsy underwent MRI examination. They concluded that, MR imaging is highly sensitive in detecting and locating abnormalities in the temporal lobe and the hippocampus.

In patients with temporal lobe epilepsy. Hippocampus Atrophy appears to correspond to the duration of seizure disorder.

Kalivinen R (2002) MRI volumetry in adults with partial epilepsy. The result shows hippocampal sclerosis is found in 60-70% of patients with intractable temporal lobe epilepsy. The data provide evidence that in some patients hippocampal damage may progress as a function of repeated seizures.

Martha J. Holmes et al 2013 stated study in Functional Networks in Temporal-Lobe Epilepsy using MRI.They concluded that, Temporal-lobe epilepsy (TLE) involves seizures that typically originate in the hippocampus. There is evidence that seizures involve

anatomically and functionally connected brain networks. A subset of hippocampus had significantly reduced.

Chapter Three

Material and Methods

3.1 Materials:-

3.1.1. Patients

A prospective study of 100 consecutive Sudanese patients previously diagnosed as

Parkinson, schizophrenia and epilepsy disease.
Parkinson's disease included 40 patients, 29 (72.5%) were males and 11 (27.5%) were females, 46 to 77 years old (mean age, 60.42±7.84 years) with a Mean duration of disease of 7.8±3.5 years (range, 2 to13) Year. Schizophrenia disease included18 patients, 14(77.8%) were males and 4(22.2%) were females, (mean age, 44.8 years) with a mean duration of disease of 7.8 years (range, 2 to13 years). epilepsy disease included 42 patients, 27(64.3%) were males and 15(35.7%) were females, (mean age, 43.4 years) with a mean duration of disease of 5.66 years. The control group consisted of 50 subjects 37 (74%) males and 13 (26%) females, 30 to 86 years old (mean age, 49.04±11.51 years) without neurologic insufficiency or abnormal findings on T1 or T 2 weighted brain MR images. Were enrolled in the study during the period from January 2013 to octoper2015.

They were referred to MRI centers in Military Hospital, Alamal and Modern Medical Center, and they were subjected to MRI brain.
The study was obtained using a 1.5-T superconductive system (SIGNA HDE; GE medical systems, and Philips medical system 1.5 T. Coil: - HD 8 channels (neurovascular array) and Toshiba. For T2 weighted sequences; images were obtained using:-TR: 5200 ms TE: 90 ms FOV: 25x22 cm slice thickness: 2.0 mm spacing: 1.0

mm. For T1 weighted sequence; images were obtained using: TR: 600ms TE: 20 ms FOV:-25x22cm slice thickness: 2mm spacing: 1.0mm. For FLAIR TR: 9000ms TE: 80, TI: 1700–2500 ms and ETL: 16.

3.1.2 Study Design:

This study was descriptive analytical study deal with MRI examination of brain for Parkinson, epilepsy, schizophrenia disease and control subject

3.2 Instrumentation: -

The study was obtained Using a 1.5-T superconductive system (SIGNA HDE; GE medical systems, and Philips medical system 1.5 T. Coil: - HD 8 channels (neurovascular array) and Toshiba medical system.

3.3 Methods:-

T1, T2 and FLAIR-weighted MR studies of the substantia nigra were obtained for Parkinson’s disease patients, and for control subjects who were examined at the Military hospital, Khartoum-Sudan during the period from 2013 up to 2016. The study protocol was approved by Research Ethical Committee -College of Medical Radiological Science-Sudan University of Science and Technology. Patients with tumor or Abnormal findings on T1 or T 2 weighted were excluded. The MRI is performed with the patent in a supine position, it is very important to ensure that there is no rotation or tilt of head in

order to demonstrate bilateral asymmetry. The protocol used for routine head with thin slices (1-2 mm) and gap (0-1mm).

The diagnosis of Parkinson's disease was based on clinical criteria, including the following neurologic signs: resting tremor, rigid muscles, bradykinesia, depression, disorder of postural reflex, gait disturbance, speech change. Patients with abnormal MR findings as abnormal high signal intensity on T2 weighted images were excluded from the study.

3.3.1 Data Collection

The data was collected using MRI examination and with the aid of data collection sheet. The data was collected from hundred patients (forty of Parkinson disease, forty two of epileptic patients, eighteen of schizophrenia and fifty control subjects.

The groups consist of male and female and they are subjected to MRI examination.

3.3.2. Measurement of the Substantia Nigra:-

The patient lies supine on the examination couch with their head within the head coil. The head is adjusted so that the interpupillary line is parallel to the couch and the head is straight. The patient is positioned so that the longitudinal alignment light lies in the midline, and the horizontal alignment light passes through the nasion.straps and foam pads are used for

immobilization. (Cathrine.Westbrook, 1999). Axial images of the brain, which included the mammillary body and red nucleus, were obtained in all control subjects and patients. At this plane where the mid- brain appeared, the substantia nigra become visible so we measured the width of the substantia nigra axis and then the length at the same view , the measurements were taken in (mm).

3.3.3 Measurement of the lateral ventricle and temporal lobes:-

Axial images of the brain, which included the lateral ventricle,basal ganglia,caudate nucleus ,lentiform nucleus putamen, globus pallidus and thalamus, were obtained in all control subjects and patients. At this plane we measured the width of the lateral ventricles and temporal lobes of brain and then the length at the same view, the measurements were taken in (mm).Frontal horn of lateral ventricle (at level of foramen of Monro) considered as the transverse (width for right and left ventricle) and from anterior horn to posterior horn for the length of lateral ventricle

3.3.4 Data Analysis Method:-

The data obtained was analyzed statistically by computing descriptive statistics like mean ± SD values and percentages.

Statistical tests were performed by using the Statistical Package for the Social Sciences, Version 16.0 (SPSS, Chicago, Illinois).

The correlation between age and width between the right and left substantia nigra was tested in the control group using Excel programme, Statistical tests were

Performed by using the Statistical Package for the Social Sciences, Version 16.0 (SPSS, Chicago, Illinois).

Statistical comparisons of the width and length of the right and left substantia nigra between the control and(Parkinson's schizophrenia,epilepsy) disease groups were based on results of an unpaired Student's *t*-test. *P*- Values less than0.005 were considered to indicate a significant difference. Also the correlation between age and width of the right and left substantia nigra was tested in the diseased group using Excel programme.

3.3.5 Data Storage Method

Data in correspondence with the thesis procedures were storage safely in personal computer (PC), and patient questionnaire was kept safely and responsibly.

3.3.6 Ethical Issue:

Permission from MRI centers and patients arise at the area of the study was taken to Use the patients' data.

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Chapter Four

Results

Table (4.1): Distribution of the study sample according to patients and control groups

Group	Frequency	Percent (%)
Control	50	33.3
Parkinson	40	26.7
Epilepsy	42	28.0
Schizophrenia	18	12.0
Total	*150*	*100.0*

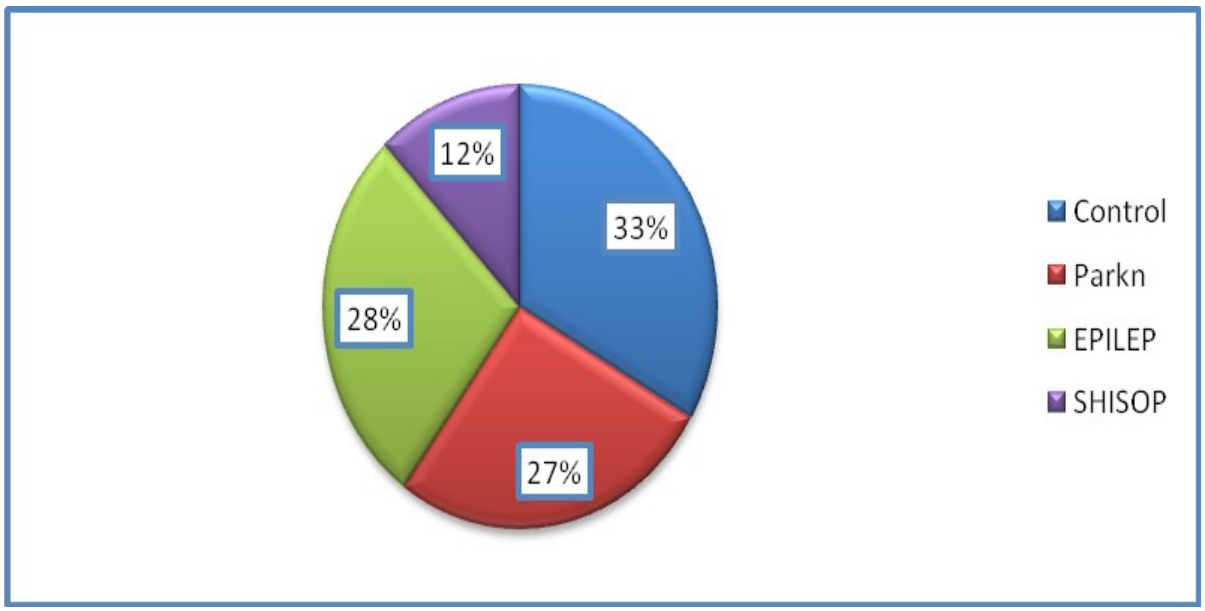


Figure (4.1): Distribution of the study sample according to patients and control groups

Table (4.2): Distribution of the study sample of patients and control groups

according to (Gender)

Gender	***Frequency***	***Percent (%)***
Male	**107**	**71.3**
Female	**43**	**28.7**
Total	***150***	***100.0***

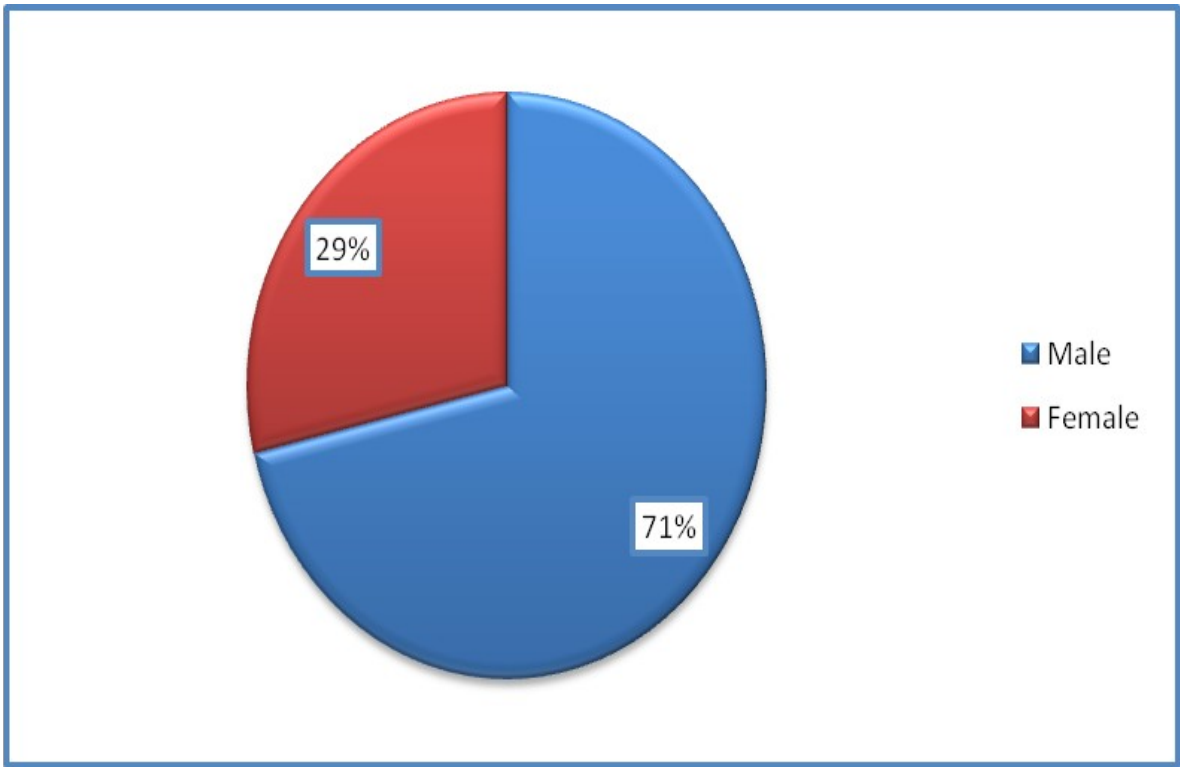


Figure (4.2): Distribution of the study sample of patients and control groups

according *to (Gender)*

Table (4.3): Distribution of the study sample of patients and control groups

According *to (Age)*

Age	Frequency	Percent (%)

27-36	**20**	**13.3**
37-46	**32**	**21.3**
47-56	**58**	**38.7**
57-66	**29**	**19.3**
67 >	**11**	**7.3**
Total	***150***	***100.0***

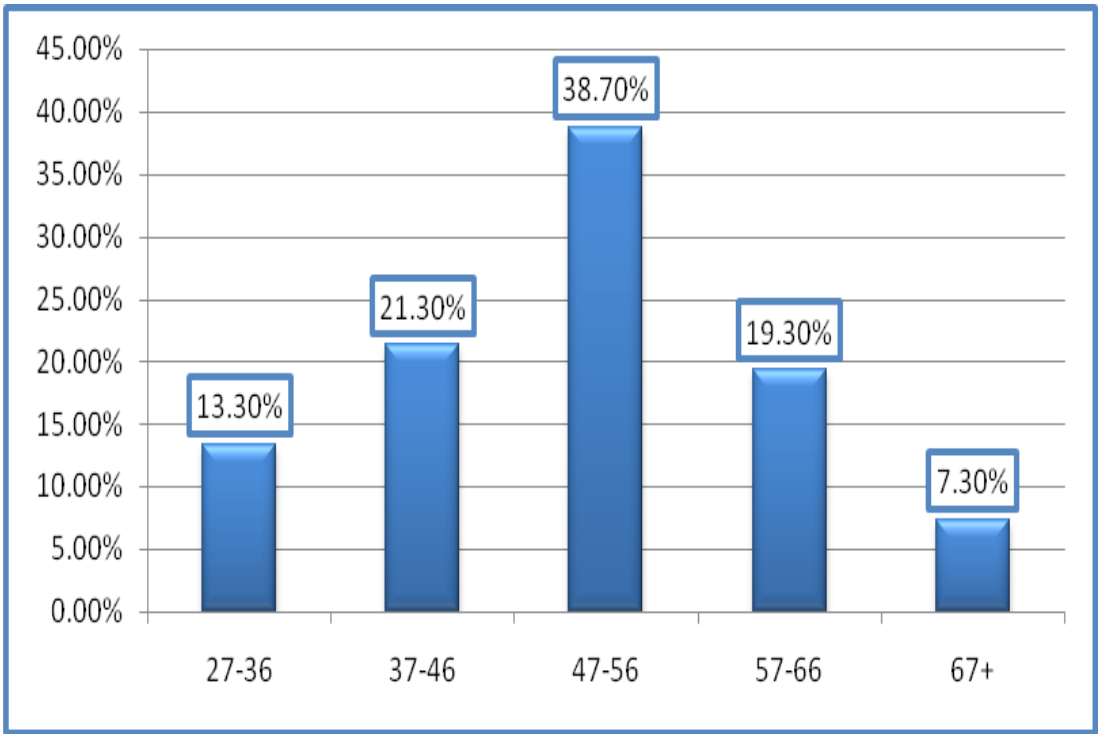


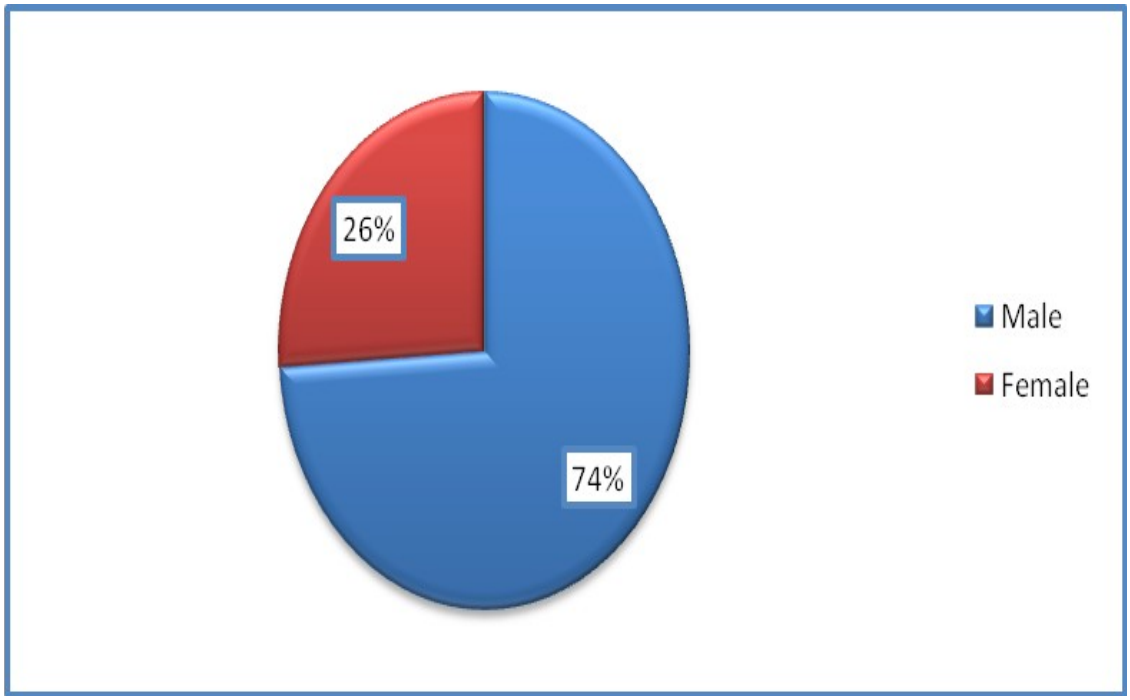
Figure (4.3): Distribution of the study sample of patients and control groups

according *to (Age)*

Table (4.4): Distribution of the study sample of control group according to (Gender)

Gender	Frequenc	Percent

	y	(%)
Male	**37**	**74.0**
Female	**13**	**26.0**
Total	***50***	***100.0***



Figure(4.4): Distribution of the study sample of control group according to (Gender)

Table (4.5): Distribution of the study sample of control group according to (Age)

Age	Frequency	Percent (%)
27-36	7	14.0
37-46	10	20.0
47-56	23	46.0
57-66	7	14.0
67+	3	6.0
Total	50	100.0

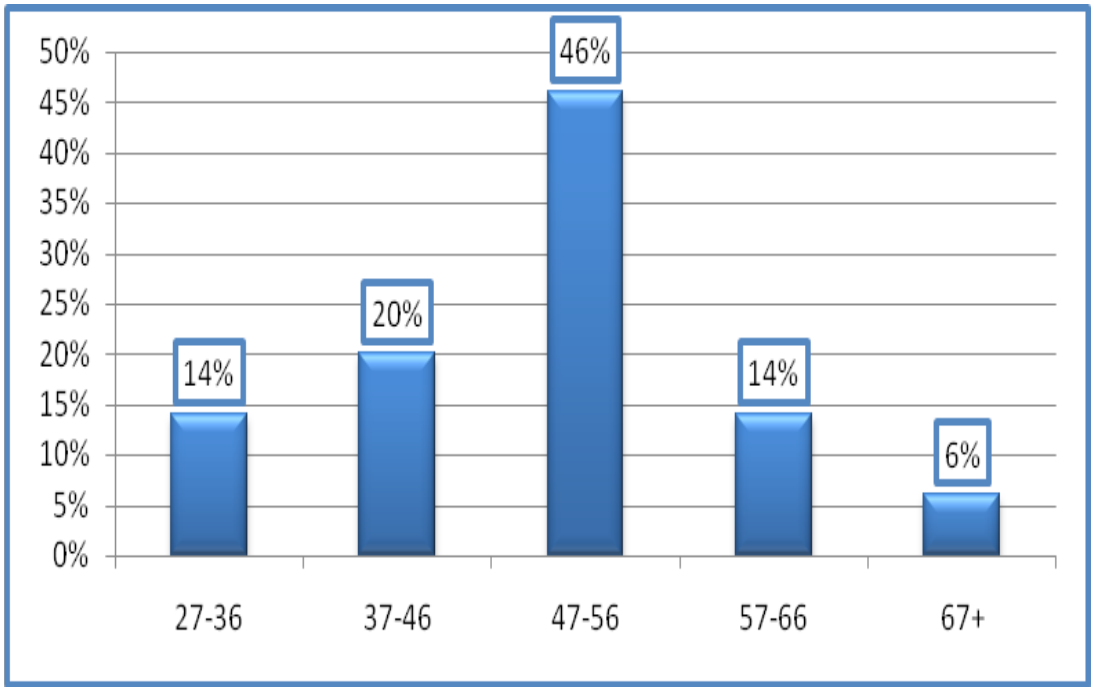


Figure (4.5): Distribution of the study sample of control group according to (age)

Table (4.6): Distribution of the parkinson disease group according to (Gender)

Gender	Frequency	Percent (%)
Male	29	72.5
Female	11	27.5
Total	40	100.0

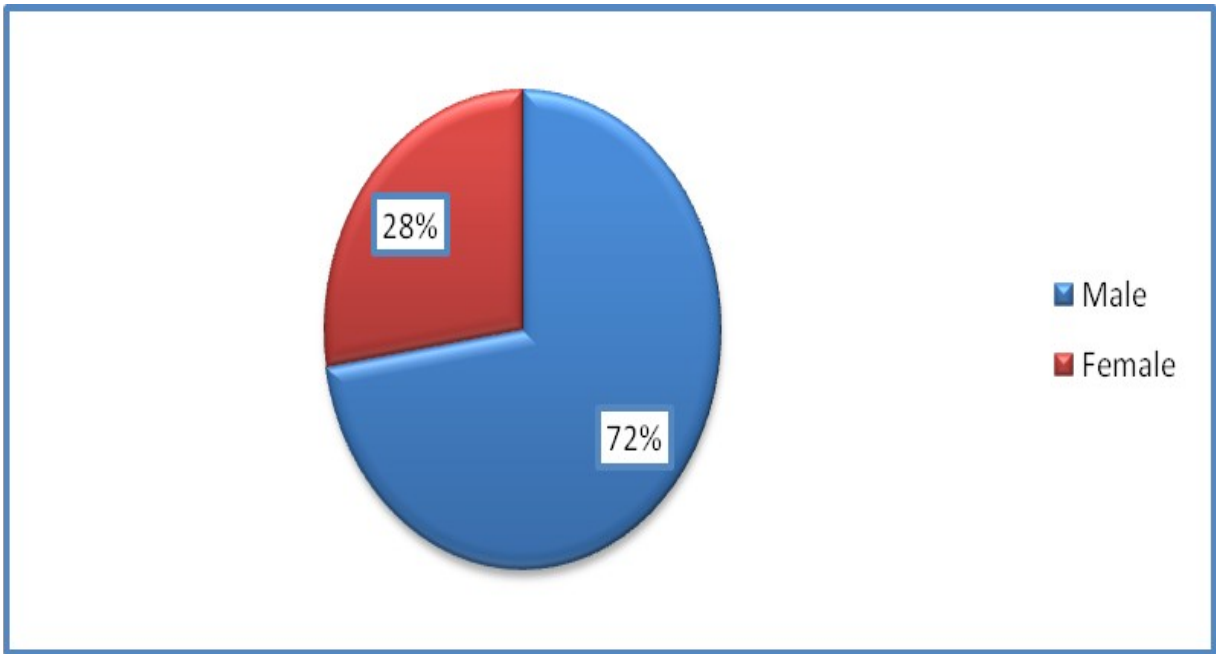


Figure (4.6): **Distribution of the Parkinson disease group according to (Gender)**

Table (4.7): Distribution of the parkinson disease group according to (age)

Age	Frequency	Percent (%)
37-46	1	2.5
47-56	11	27.5
57-66	20	50.0
67+	8	20.0
Total	40	100.0

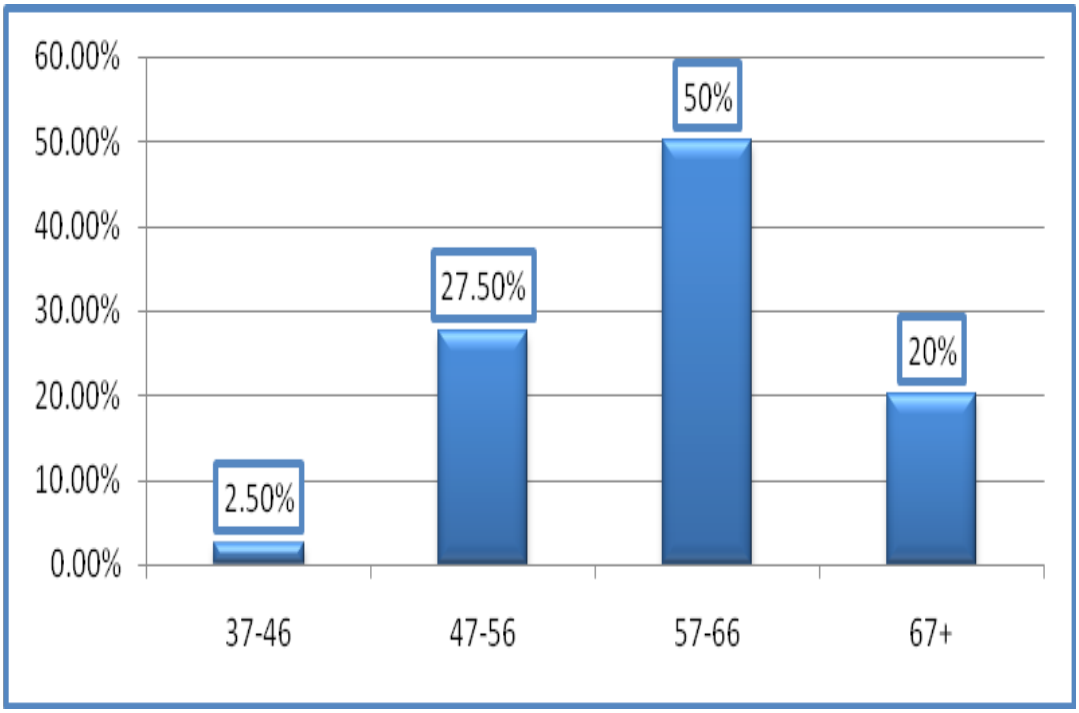


Figure (4.7): Distribution of the Parkinson disease group according to (age)

Table (4.8): Distribution of the epilepsy patients sample according to (Gender)

Gender	Frequency	Percent (%)
Male	27	64.3
Female	15	35.7
Total	42	100.0

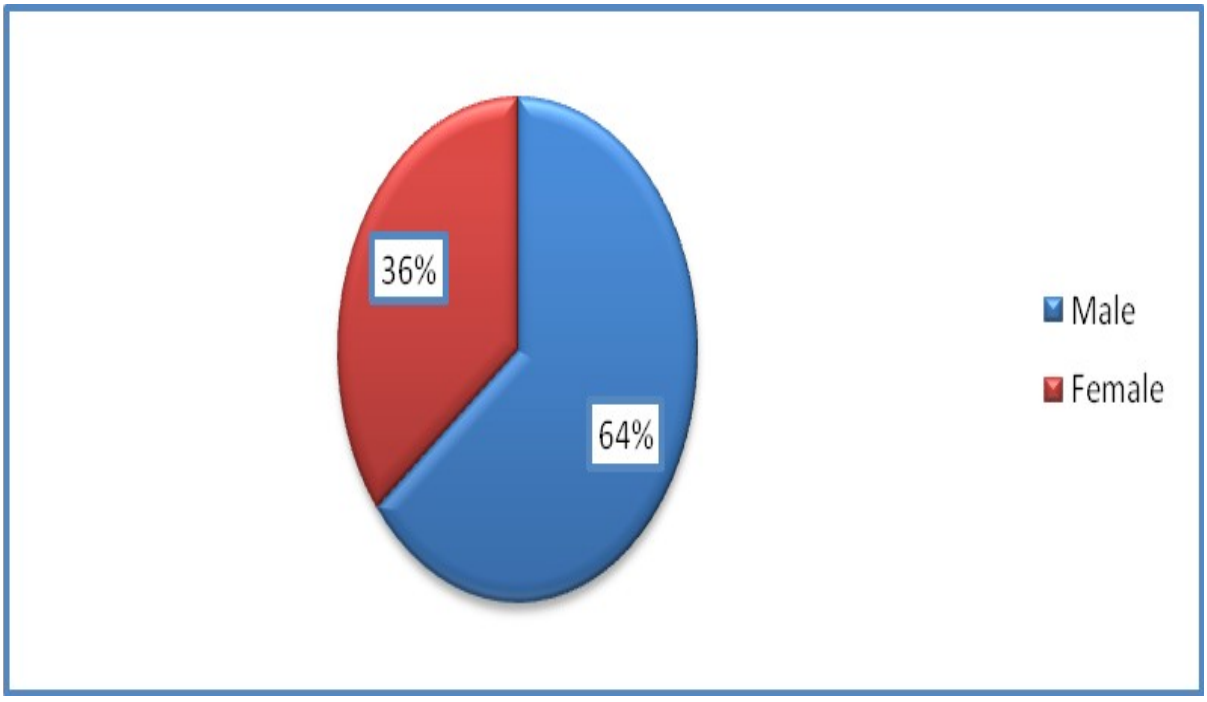


Figure (4.8): Distribution of the epilepsy patients sample according to (Gender)

Table (4.9): Distribution of the epilepsy patients sample according to (Age)

Age	Frequency	Percent (%)
27-36	10	23.8
37-46	15	35.7
47-56	15	35.7
57-66	2	4.8
Total	42	100.0

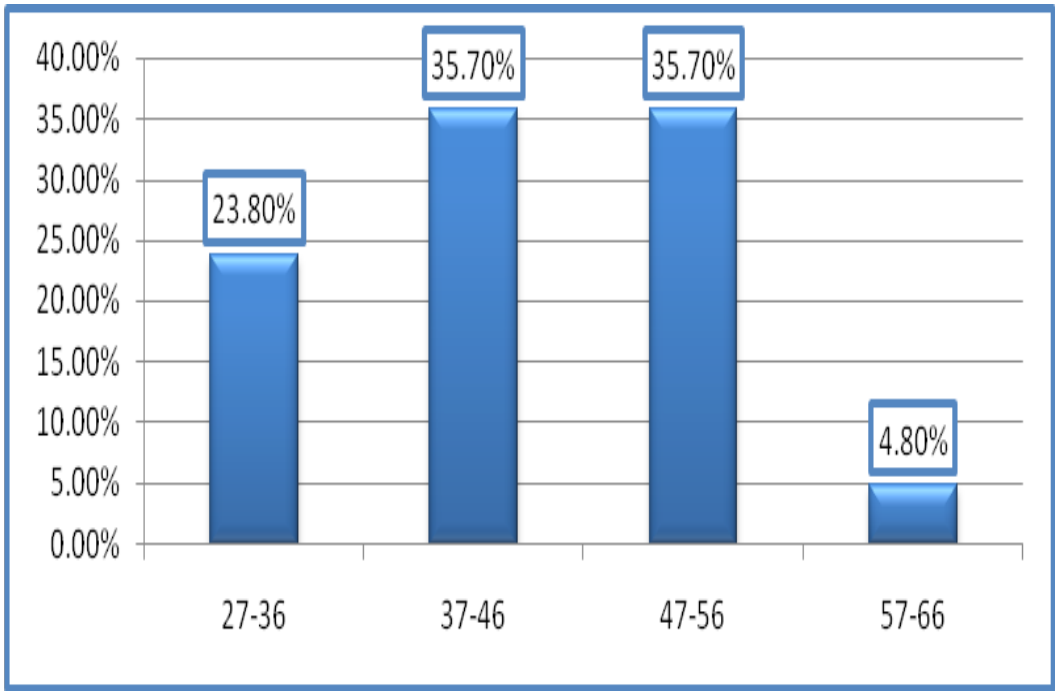


Figure (4.9): Distribution of the epilepsy patients sample according to (age)

Table (4.10): Distribution of the schizophrenia patients sample according to (Gender)

Gender	Frequency	Percent (%)
Male	14	77.8
Female	4	22.2
Total	18	100.0

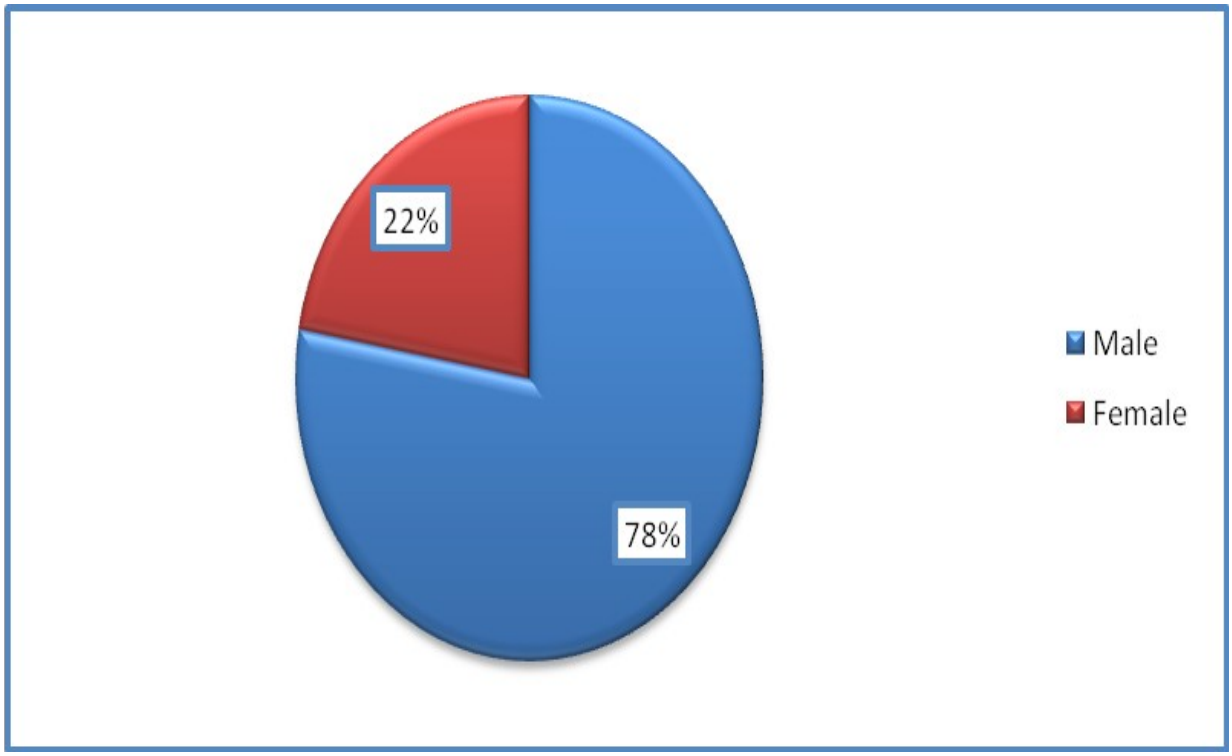


Figure (4.10): Distribution of the schizophrenia patients sample according to (Gender)

Table (4.11) Distribution of the schizophrenia patients sample according to (age)

Age	Frequency	Percent (%)

27-36	**3**	**16.7**
37-46	**6**	**33.3**
47-56	**9**	**50.0**
Total	**18**	**100.0**

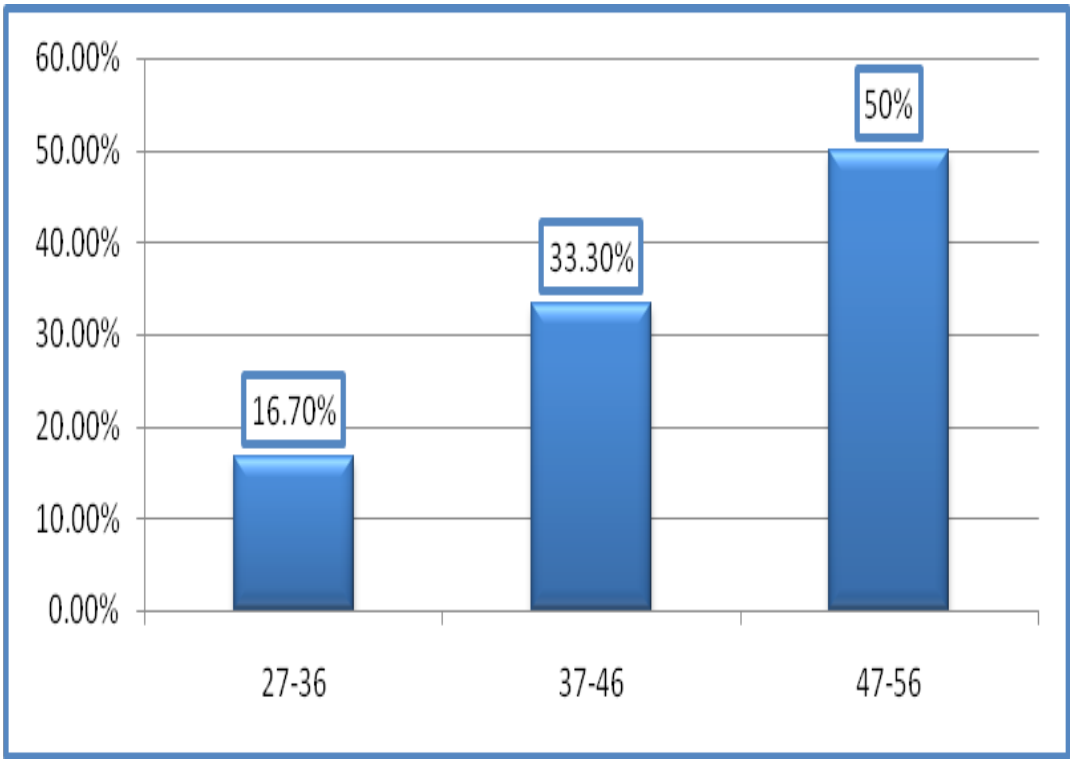


Figure (4.11): Distribution of the schizophrenia patients sample according to (age)

4.1 Result of Parkinson disease:

Table (4.12) Mean and standard deviation (SD) Minimum and Maximum values of the Age, right and left Nigra length and width measured for the control group.

	Age	Rt nigra width (mm)	Rt nigra length (mm)	Lt nigra width (mm)	Lt nigra length (mm)
N Valid	50	50	50	50	50
Mean	49.o4	3.88	11.65	3.51	11.44
S.D	11.51	0.31	0.65	0.32	0.62
Minimum	30.00	3.02	10.21	3.00	10.18
Maximum	86.00	4.27	12.82	4.16	12.93

Table (4.13) *Mean* and standard deviation (SD) Minimum and Maximum values of The Age, right and left Nigra length and width measured for the Parkinson diseae group.

	Age	Rt nigra width (mm)	Rt nigra length (mm)	Lt nigra width (mm)	Lt nigra length (mm)
N Valid	40	40	40	40	40
Mean	60.42	3.31	*11.37*	*2.92*	10.42
S.D	7.844	0.39	*0.23*	*0.314*	0.25
Minimum	46.00	2.24	10.03	3.13	10.05
Maximum	77.00	3.90	10 .89	3.59	11.00

Table (4.14) mean and standard deviation (SD) values of the Age, the right and Left Nigra length and width measured and classified according to Gender for the Control group.

	Gender	N	Mean	Std.deviation	Std.error mean
Age	Male	37	49.11	12.29	2.02
	Female	13	48.85	9.37	2.60
Rt nigra width	Male	37	3.91	0.31	0.51
	Female	13	3.83	0.33	0.09
RT nigra Length	Male	37	11.90	0.70	0.12
	Female	13	11.86	0.43	0.12
Lnigra width	Male	37	3.56	0.34	0.06
	Female	13	3.39	0.25	0.07
L nigra length	Male	37	11.35	0.66	0.11
	Female	13	11.70	0.44	0.12

Table (4.15) Mean and standard deviation (SD) of the Age, the right and left Nigra length and width measured and classified according to gender. For the Parkinson disease group.

	Gender	N	Mean	Std.deviation	Std.error mean
Age p=.0746	male	29	60.17	7.68	1.43
	female	11	61.09	8.61	2.60
RT NIGRA (Width) P=0.730	male	29	3.32	0.36	0.07
	female	11	3.28	0.48	0.15
RT NIGRA (Length) P=0.971	male	29	10.37	0.23	0.04
	female	11	10.37	0.24	0.07

LT NIGRA (Width) P=0.663	**male**	**29**	**2.90**	**0.35**	**0.06**
	female	**11**	**2.95**	**0.21**	**0.06**
LT NIGRA (Length) P=0.516	**male**	**29**	**10.44**	**0.24**	**0.05**
	female	**11**	**10.39**	**0.28**	**0.08**

Independent Samples Test t-test for Equality of Means, significant when P value is less than 0.005

Table (4.16) multiple comparisons between the right and left Nigra length and width measured for the Control and Parkinson disease groups.

Multiple Comparisons

Dependant Variable	**Control**	**parkinson**	**Mean difference Control-parkinson**	**Std.error**	**sig**	**95%confidence interval**

						Lower upper Bound	Bound
Rt nigra width	**Control**	**parkinson**	**0.58**	**0.66**	**000**	**0.44**	**0.71**
Rt nigra length	**Control**	**parkinson**	**1.28**	**0.10**	**000**	**1.09**	**1.48**
Lt nigra width	**Control**	**parkinson**	**0.59**	**0.07**	**000**	**0.46**	**0.72**
Lt nigra length	**Control**	**parkinson**	**1.01**	**0.09**	**000**	**0.82**	**1.21**

The differences are significant between the control Group and Diseased Group p=0.005

Table (4.17) Coefficient between the right and left Nigra length and width measured for the Parkinson disease group with the disease duration.

Coefficient Model	Un-standardized coefficients		standardized coefficients	T	Sig
	B	Std.error	Beta		
Constant	6.10	43.99		.14	0.89
Rt Nigra Width	5.81	1.85	.74	3.15	0.00
Rt Nigra length	2.76	2.87	.55	.96	0.35
Lt Nigra Width	4.90	2.08	.69	2.36	0.00
Lt Nigra length	5.37	2.95	.98	1.81	0.08

Dependent Variable: Duration of Parkinson disease,*Significant at p=0.00

A

B

Figure (4.12) A scatter plot diagram shows a linear relationship between the age (Parkinson group) and the width of RT substantia nigra. As the age increases, the width decreases by 0.029/year starting from, 5.07mm. R^2 =0.337.the age has an effect of 58% on the RT nigra width. For the disease group(B) a linear relationship between the age(Control group)and the width of RT nigra,as the age increases, the width decreases by 0.017/year starting from 4.0761mm. R^2 =0.425.the age has an effect of 65% on the RT nigra width for the normal population .

A

B

Figure(4.13) A scatter plot diagram shows a linear relationship between the age(Parkinson group)and the width of LT substantia nigra. As the age increases, the width decreases by 0.017/year

starting from 3.956mm. R^2 =0.184.the age has an effect of 43% on the LT nigra width. For the disease group(B) a linear relationship between the age(Control group)and the width of LT nigra,as the age increases, the width decreases by 0.018/year starting from 4.4061mmR^2 =0.419. The age has an effect of 65% on the LT nigra width for the normal population.

Table (4.18) Mean and standard deviation (SD) Minimum and Maximum values of the Age, right and left Putamen length and width measured for the control group.

	Age	RT Putamen Width control	RT Putamen Length control	LT Putamen (Width control	LT Putamen Length control
N Valid	50	50	50	50	50
Mean	49.04	10.81	37.46	10.76	37.40
S. D	11.51	.809	1.684	.803	1.693
Minimum	30.00	8.44	33.01	8.72	33.18
Maximum	86.00	12.34	40.65	12.32	41.5

Table (4.19) Mean and standard deviation (SD) Minimum and Maximum values of the Age, right and left Putamen length and width measured for the Parkinson group.

	Age	RT Putamen Width Control)	RT Putamen Length control)	LT Putamen Width Control	LT Putamen Length control)
N Valid	40	40	40	40	40
Mean	60.42	9.70	35.55	9.74	35.53
S. D	7.844	.73	1.27	.86	1.45
Minimum	46.00	7.84	32.43	7.92	32.63
Maximum	77.00	10.80	37.70	10.86	37.63

Table (4.20) Mean and standard deviation (SD) values of the Age, the right and left put amen length and width measured and classified according to Gender for The control group

	Gender	N	Mean	Std.deviation	Std.error
RT Putamen	Female	13	10.80	.85	.14

(Width Control)	Male	37	10.86	.69	.19
RT Putamen Length (Control)	Female	13	37.40	1.79	.29
	Male	37	37.64	1.38	.38
LT Putamen (Width Control)	Female	13	10.77	.83	.14
	Male	37	10.75	.75	.21
LT Putamen Length (Control)	Female	13	37.37	1.74	.29
	Male	37	37.50	1.63	.45

Table (4.21) multiple comparisons between the right and left putamen length and width measured for the Control and Parkinson disease groups

Dependant Variable	Control	parkinson	Mean difference Control-parkinson	Std.error	sig	95%confidence interval Lower Bound	upper Bound
Rt putamen width	Control	parkinson	1.11	.16	.00	1.41	.80
Rt putamen length	Control	parkinson	1.91	.319	.00	2.54	1.28
Lt putamen width	Control	parkinson	1.02	.16	.00	.69	1.34

Lt putamen length	**Control**	**parkinson**	**1.87**	**.33**	**.00**	**1.22**	**2.52**

The differences are significant between the control Group and Diseased Group p=0.005

4.2 Result of schizophrenia:

Table (4.22): Distribution of the schizophrenia patient according to Residence

Residence	Frequency	Percentages%
Khartoum(Capital)	**9**	**50**
Western Sudan	**4**	**22**

Central Sudan (blue Nile)	**3**	**17**
North Sudan	**2**	**11**
Total	**18**	**100%**

Table (4.23): Distribution of the schizophrenic patients according to race

Race	Frequency	Percentages%
Gali	1	5.5
Nuba	4	22
Shaigi	3	16.5
Hmag	2	12
Hlfawi	1	5.5
Foor	1	5.5
Barno	1	5.5
Rbatab	1	5.5
Malia	1	5.5
Hamar	1	5.5
Flati	1	5.5

Msairi	**1**	**5.5**
Total	**18**	**100**

Table (4.24): Mean And Standard Deviation (SD) Minimum And Maximum Values of The Age, Right And Left Nigra Length And Width Measured For The Control Group.

	Age /year	RT Nigra Width A (mm)	RT Nigra Length (mm)	LT Nigra width (mm)	LT Nigra Length (mm
N	**50**	**50**	**50**	**50**	**50**
Mean	**49.04**	**3.88**	**11.65**	**3.51**	**11.44**
SD	**±11.51**	**±0.314**	**±0.650**	**±0.324**	**±0.623**
Minimum	**30.00**	**3.02**	**10.21**	**3.00**	**10.18**
Maximum	**86.00**	**4.27**	**12.82**	**4.16**	**12.93**

Table (4.25): Mean And Standard Deviation (SD) Minimum And Maximum Values Of The Age, Right And Left Nigra

Length And Width Measured For The Schizophrenia Disease Group.

	Age	RT Nigra Width (mm)	RT Nigra Length (mm)	LT Nigra Width (mm)	LT Nigra Length (mm)
Valid	18	18	18	18	18
Mean	44.77	4.10	11.96	3.91	11.87
SD	±7.78	±0.14	±0.30	±0.27	±0.25
Minimum	29.00	3.73	11.26	3.35	11.27
Maximum	55.00	4.26	12.34	4.22	12.16

Table (4.26): Mean and Standard Deviation (SD) Minimum and Maximum Values of the Right and Left Temporal Lobe Length And Width Measured For The Control Group

	RT Temoral Lobe Width (mm)	RT Temoral Lobe Length (mm)	LT Temoral Lobe Width (mm)	LT Temoral Lobe Length (mm)
Valid	50	50	50	50

Mean SD	**40.49±4.43**	**78.99±5.01**	**40.90±3.18**	**77.45±5.33**
Minimum	**30.39**	**68.68**	**32.16**	**65.74**
Maximum	**46.47**	**86.56**	**45.80**	**86.11**

Table (4.27): Mean and Standard Deviation (SD) Minimum And Maximum Values Of The Right And Left Temporal Lobe Length And Width Measured For The Schizophrenia Group

	RT Temoral Lobe Width	RT Temoral Lobe Length (mm)	LT Temoral Lobe Width (mm)	LT Temoral Lobe Length (mm)

	(mm)			
Valid	18	18	18	18
Mean SD	40.35±3.003	78.98±3.29	40.72±3.01	77.84±3.8
Minimum	34.18	75.44	34.43	74.30
Maximum	45.85	84.62	45.80	85.70

Table (4.28): Mean and Standard Deviation (SD) Minimum and Maximum Values of the Right and Left Lateral Ventricles Length and Width Measured For the Control Group

	RT lateral ventricle (Width)	RT lateral ventricle (Length)	LT lateral ventricle (Width)	LT lateral ventricle (Length)

	(mm)	(mm)	(mm)	(mm)
Valid	50	50	50	50
Mean	11.79	68.21	11.38	66.57
SD	±2.197	±4.38	±1.95	±8.70
Minimum	6.58	55.11	6.58	11.14
Maximum	16.74	73.90	16.42	73.65

Table (4.29): Mean and Standard Deviation (SD) Minimum and Maximum Values of the Right and Left Lateral Ventricles Length and Width Measured For the Schizophrenia Group

	RT lateral ventricle	RT lateral ventricle	LT lateral ventricle	LT lateral ventricle

	Width (mm)	Length (mm)	Width (mm)	Length (mm)
Valid	18	18	18	18
Mean	11.85	68.21	12.29	67.63
SD	±1.25	±3.09	±1.40	±2.93
Minimum	10.02	57.70	10.44	57.23
Maximum	14.06	71.10	15.14	70.00

Table (4.30): Multiple Comparison of the Right and Left Nigra Length and Width between control and Schizophrenia Group

Dependent Variable	*Group (1)*	*Group (2)*	Mean Difference	*Std Error*	*Sig*	*95%Confedence*	
						Lower Bound	*Upper Bound*
RT Nigra Width	Control	Schizophrenia	.22	.08	0.01	.39	.06
RT Nigra length	Control	Schizophrenia	.30	.13	0.02	.56	.04
LT Nigra Width	Control	Schizophrenia	.40	.09	0.00	.57	.23
LT Nigra length	Control	Schizophrenia	.43	.13	0.00	.69	.18

the mean difference is significant at the 0.05 level

Table (4.31): Multiple Comparison of the Right and Left temporal lobes length and width between control group and Schizophrenia patients.

Dependent Variable	*Group (1)*	*Group (2)*	Mean Difference	*Std Error*	*Sig*	*95%Confedence*	
						Lower Bound	*Upper Bound*
RT Temporal Lobe Width	Control	Schizophrenia	.15	1.00	.89	2.12	1.83
RT Temporal Lobe Length	Control	Schizophrenia	.013	1.21	.99	2.37	2.40
LT Temporal Lobe Width	Control	Schizophrenia	.18	.82	.83	1.45	1.81

LT Temporal Lobe Length	Control	Schizophrenia	.39	1.27	.76	2.89	2.11

the mean difference is significant at the 0.05 level

Table (4.32): Multiple Comparison of the Right and Left Lateral Ventricles Length and Width between control and Schizophrenia Group

Dependent Variable	Group (1)	Group (2)	Mean Difference	Std Error	Sig	95% Confedence	
						Lower Bound	Upper Bound
RT	Control	Schizophrenia	1.11	.16	.	.80	1.41

Lateral ventricle (Width)	ol	nia			00		
RT Lateral ventricle (Length)	Control	Schizophrenia	.43	.41	.31	1.24	.39
LT Lateral ventricle (Width)	Control	Schizophrenia	1.02	.16	.00	.69	1.34
LT Lateral ventricle (Length)	Control	Schizophrenia	.35	.42	.41	1.19	.49

the mean difference is significant at the 0.05level

Table(4.33)shows MRI signsl intensity in different sequences in schizophrenia.

Region	T1W	T2W	FLAIR
Supstantia nigra	Isointense	Dark	Dark
Putamen	Isointense	Grey	Grey
Temporal lobe	Grey	Grey	Grey

Ventricles	**Dark**	**Bright**	**Dark**

Figure (4.14) Scatter plot diagram between disease duration and RT nigra width in schizophrenia group R^2 =0.002

Figure (4.15) Scatter plot diagram between drug duration and RT nigra length in schizophrenia group R^2=0.003

Figure (4.16) Scatter plot diagram between disease duration and LT nigra width in schizophrenia group R^2=0.015.By increasing the disease duration, the left nigra width decreases by 0.007mm starting from3.98mm.The reduction was for each 5 years duration.

Figure (4.17) Scatter plot diagram between disease duration and LT nigra length in schizophrenia group R^2=0.027. By increasing the disease duration, the left nigra length increased by 0.01mm starting from 11.79 mm.The elevation was for each 5 years duration.

4.3 Result of epilepsy:-

The following tables and figures represent the data obtained from 42 Sudanese patients. All the 42 patients were clinically diagnosed as (epilepsy).

Table(4.34) Mean and standard deviation (SD) Minimum and Maximum values of the Age, right and left Nigra length and width measured for the control.

	Age	Rt Nigra width	Rt Nigra length	Lt Nigra width	Lt Nigra length
N Valid	50	50	50	50	50
Mean	49.04	3.88	11.65	3.51	11.44
S.D	11.51	0.31	0.65	0.32	0.62
Minimum	30.00	3.02	10.21	3.00	10.18
Maximum	86.00	4.27	12.82	4.16	12.93

Table (4.35) Mean and standard deviation (SD) Minimum and Maximum values of the Age, right and left Nigra length and width measured for epilepsy.

		Age	RT NIGRA Width control	RT NIGRA Length Control	LT NIGRA Width control	LT NIGR Length Contro
N	Valid	42	42	42	42	42
Mean		43.47	3.91	11.74	3.64	11.49
S. D		8.79	.26	.46	.30	.47
Minimum		27.00	3.34	10.70	3.02	10.62
Maximum		60.00	4.24	12.93	4.15	12.24

Table (4.36) Mean and standard deviation (SD) values of the Age, right and left Nigra length and width measured and classified according to gender for the control group.

	Gender	N	Mean	Std.deviation	Std.error mean
Age	Male	37	49.11	12.29	2.02
	Female	13	48.85	9.37	2.60
Rt Nigra width	Male	37	3.91	0.31	0.05
	Female	13	3.83	0.33	0.09
Rt Nigra	Male	37	11.59	0.70	0.12
	Female	13	11.85	0.44	0.12

length					
Lt Nigra width	**Male**	**37**	**3.56**	**0.34**	**0.06**
	Female	**13**	**3.39**	**0.25**	**0.09**
LTNigra length	**Male**	**37**	**11.35**	**0.76**	**0.11**
	Female	**13**	**11.70**	**0.44**	**0.12**

Table (4.37) Mean and standard deviation (SD) of the Age, the right and left Nigra length and width measured and classified according to gender for the epilepsy disease group.

	Gender	N	Mean	Std. Deviation	Std. Error
Age	**Male**	**27**	**44.33**	**8.29**	**1.60**

	Female	15	41.93	9.72	2.51
RT NIGRA (Width)	Male	27	3.99	.21	.04
	Female	15	3.76	.27	.07
RT NIGRA (Length)	Male	27	11.72	.42	.081
	Female	15	11.79	.52	.13
LT NIGRA (Width)	Male	27	3.68	.30	.06
	Female	15	3.59	.31	.08
LT NIGRA (Length)	Male	27	11.55	.49	.10
	Female	15	11.39	.42	.11

Table (4.38) multiple comparisons between the right and left Nigra length and width measured for the Control and epilepsy disease groups.

Dependant Variable	control	epilepsy	Mean difference	Std.error	sig	95%confidence interval
			Control-			Lower

		epilepsy				upper Bound	Bound
Rt Nigra width	control	epilepsy	.022	.06	.72	.15	.10
Rt Nigra length	control	epilepsy	.08	1.00	.41	.12	.28
Lt Nigra width	control	epilepsy	.13	.06	.05	.26	.55
Lt Nigra length	control	epilepsy	.05	.97	.59	.14	.24

The differences are not significant between the controls Group and Diseased Group

Table (4.39) multiple comparisons between of the right and left Temporal lobe length and width measured for the Control and epilepsy disease groups

Dependant Variable	control	epilepsy	Mean difference Control-	Std.error	sig	95%confidence interval Lower

			epilepsy				upper Bound Bound
Rt Temporal lobe width	**control**	**epilepsy**	1.06	.76	.16	2.57	.44
Rt Temporal lobe Lenngth	**control**	**epilepsy**	2.65	.92	.00	.84	4.52
LT Temporal lobe width	**control**	**epilepsy**	1.19	.63	.06	2.43	.05
LT Temporal lobe Length	**control**	**epilepsy**	2.14	.97	.02	.23	4.05

Table (4.40) Multiple Comparisons

Right Nigra width Control and the disease groups

Dependant variable	I Group	J Group	Mean difference Control-epilepsy	Std.error	sig	95%confidence interval Lower Bound upper Bound
RT NIGRA Width Control	control	Parkinson	.58	.07	.00	.45 .71
		Epilepsy	.02	.06	.72	.15 .10
		Schizophrenia	.22	.08	.01	.39 .05

Table (4.41) Multiple Comparisons

Right Nigra Length Control and the disease groups

Dependant variable	I Group	J Group	Mean difference Control-	Std.error	sig	95%confidence interval Lower upper Bound

			epilepsy			Bound	
RT NIGRA Length Control	control	Parkinson	1.28	.10	.00	1.09	1.48
		Epilepsy	.08	1.00	.40	.28	.11
		Schizophrenia	.30	.13	.02	.56	.04

Table (4.42) Multiple Comparisons

Left Nigra width Control and the disease groups

Dependant variable	lGroup	J Group	Mean difference Control - epilepsy	Std.error	sig	95%confidence interval	
						upper Bound	Lower Bound
LTNIGRA Width	control	Parkinson	.59	.07	.00	.46	.72
		Epilepsy	.13	.06	.	.26	.00

Control		Schizophrenia	.40	.09	.09 .00	.59	.23

Table (4.43) Multiple Comparisons

Left Nigra Length Control and the disease groups

Dependant variable	I Group	J Group	Mean difference Control - epilepsy	Std.error	sig	95%confidence interval Lower Bound upper Bound	
LT NIGRA Length Control	control	Parkinson	1.01	.09	.00	.82	1.21
		Epilepsy	.05	1.00	.59	.24	.140
		Schizophrenia	.43	.13	.00	.69	.18

Chapter five

Discussion, Conclusion and Recommendations

5.1 Discussion:

Tables from (4.1) to (4.11) revealed the demographic data of patients previously diagnosed as epilepsy,schizophrenia,parkinson disease and control subjects.

Characterization of the substantia nigra (SN) in Parkinson's disease (PD) by

MR imaging procedures has been an advantageous practice.

We obtained T1, T2 and FLAIR (Fluid attenuation at inversion Recovery). Studied and observed T2 signal changes of both the (SN) in the right and left side,

For the length and width; this was useful to support the diagnosis of PD; whereas

Controls did not show these features.

Tables (4.12) and (4.13) showed the measurements taken for both control and disease group. The gender was also taken into our consideration in the measurements. No significant differences were detected between the two genders in controlAnd diseased group. This was noticed in tables (4.14), and (4.15).

Table (4.16) presented the difference between the control group and the diseased

Group regarding the Nigral measurements. It significantly differs, p=0.000.

Similar findings were studied by (Minati et al., 2007) who mentioned that, the

nigral area measured was significantly different between Parkinson patients and controls. The changes in intracellular compartment and in iron deposition were both being acknowledged factors for these differences. (Hutchinson et al. 2003, Vymazal et al, 1999).

The study shows low signal intensity In patients with Parkinson's disease in the putamen, globus pallidus, and substantia nigra onT2 weighted images. Similar findings has been reported resulting from the accumulation of iron (Gorell et al., 1995).

The causes of the measurement reduction and restoration of signal may be

Justified by the fact that in the dorsal lateral substantia nigra, a depletion of iron

Due to increased cellular metabolic activity) or local cell death, result in an

Expansion of the extracellular space, as mentioned by (Rutledge et al , 1997).

When the SN is known to have high iron content and has been shown to be correlated with decreased signal intensity (associated with decreasedT2relaxation times). (Drayer et a., 1996), the justification is that the SN contains neuromelanin. (Yelnik et al, 1997) and iron can be stored in neuromelanin by the iron-storage protein ferritin(Zecca et al. 1994).

Iron alters the magnetic field uniformity in tissues and causes MR signal intensity within tissues to decrease (Tosk et al.1992).

Therefore the MR imaging_related signal intensity effects observed in the SN,

SN could be attributed to the paramagnetic neuromelanin or intracellular iron stores.

A characteristic signal-intensity difference in the SN, showing demarcation of this region with imaging using T2 weighted sequences at 1.5T was observed (Duguid et al. 1996).

The duration of the disease was also tested as one of the factors that may

Contribute In the nigra changes, table (4.17) showed that the substantia nigra width of the right and left sides were significantly reduced by the duration of disease. Measurements assessment proves that the substantia nigra degenerates from lateral to medial and in a rostral to caudal direction.

There is also thinning, and the structure takes on a mottled appearance compared with the normal subjects, (Moriwaka et al., 1992). This is why the width of SN was

reduced.Another study mentioned that in patients with Parkinsonism of long duration, the striatonigral pathway could be damaged and the whole volume of the substantia nigra was reduced (Adachi et al., 1999).

The selected age classes were similar in both control and diseased group. It has

been shown that the high frequencies of patients who were affected with Parkinson

Lie in the ages between 57-66 years old, with mean duration of disease of 7.8±3.5

Years (range, 2 to13 years). Figures (4.12) and (4.13) showed the relations between the age and right and left nigral width in both normal and diseased groups.

Magnetic resonance imaging showed that changes in nigra due to Parkinson

Could be predicted when it is associated with clinical neurological signs or changes according to advancing age.

As it was mentioned previously, MR imaging benefits include the detection of

presymptomatic and staging of disease especially in the inherited disorder which

Would allow the protection and early treatments of those determined to be at risk, and hence interventions in both presymptomatic and symptomatic patients (Brooks et al, 1998).

Prediction of the changes that may happen in the SN for the known age of Parkinson diseased patients can be described by the following equations:-

RT Nigra Width= 5.075-0.029X patient’s age

LT Nigra width=3.956- 0.017X patient’s age

In the normal group the changes of the nigral width regarding age can also

Be estimated for the known subjects’ ages:-

RT Nigra Width=4.761-0.017X subject’s age

LT Nigra Width=4.406-0.018X subject’s age

Table (4.18, 4.19) shows the Mean and standard deviation (SD) Minimum and Maximum values of the Age, the right and left putamen length and width measured for the control group and parkinson groups.

Table (4.20) shows the mean and standard deviation (SD) values of the Age, the right and left putamen length and width measured and classified according to Gender for The control group. Table (4.21) shows MRI signal intensity in different sequences.

Table (4.21) shows multiple comparisons between the right and left put amen length and width measured for the Control and Parkinson disease groups, presented the difference between the control group and the diseased group regarding the Nigral measurements. It significantly differs, p=0.000.

The purpose of this study was to elucidate the characteristics of substentia nigra, temporal lobes and lateral ventricle in patients affected with schizophrenia with mean duration of disease of 5.66 years (range: 1 to 11 years)using magnetic resonance imaging (MRI) and compared the findings with healthy control subjects. The present study provides the largest set of MRI findings in patients with schizophrenia. The patients’ characteristics including their residence and race distribution were presented in tables (4.22) and (4.23).

These results demonstrate SN signal intensity changes of patients with schizophrenia and this supports the dopamine hypothesis for

schizophrenia, Howers et al (2013) reported the same results using a post-mortem study, which revealed that tyrosine hydroxylase staining scores were significantly greater in the schizophrenia group at substantia nigra compared to in healthy controls. It has been reported that T_1-weighted MRI with 3T can indicate T_1-shortening tissues containing neuromelanin at SN. We are aware of only two previous reports on neuromelanin imaging in patients with schizophrenia. Shibata et al and Sasaki et al described signal changes in the SN among patients with schizophrenia. These two previous reports indicate the signal changes in the SN in patients with schizophrenia is higher than that in controls, and our study showed also signal intensity changes but we believe that, this results may be not accurately evaluated or generalizes due to the small sample size and large variations as well as the subjectivity of the evaluation. We performed a similar comparison in our study by measuring the length and width of SN.The mean measured values were significantly higher in patients with schizophrenia than in healthy controls, Tables (4.24) and (4.25) and table (4.30).It is reported that neuromelanin levels in the SN can increase with disease. Regarding that issue we reveal our results to that the deposited melanin in the SN reflects the measured values to be varied, and the difference between patients and healthy controls was found to be more prominent.

These results showed that the patient group had smaller temporal lobes than healthy subjects but the differences were not

significant.Tables (4.26), (4.27) and (4.31).On the hand subtle reductions on the order of 10–15% have been reported in the overall size of the temporal lobe ((Dauphinais et al., 1990), in temporal lobe gray matter ((Suddath et al., 1999) and in specific mesial and lateral temporal lobe structures in patients with schizophrenia (shenton et al. 1992)

According to these results, lateral ventricles were enlarged in patients as compared with healthy subjects Tables (4.28 and 4.29) .The difference between the healthy and diseased patients was found to be significant table, (2.32) .Similar results were originated and it should be pointed out that patients with schizophrenia might reflect progressive ventricular enlargement, possibly related to the excitotoxic effect of repeated psychotic episodes, or might reflect an early onset non progressive developmental process . Also justify and referred the findings to these causes.

Regarding the duration of the diseases our study revealed that the duration of illness affected the nigra dimensions, however ventriculomegaly and reduction of the temporal lobe dimensions appear to have linear relations as illness duration increases these findings were illustrated in the graphs (4.14, 4.15, 4.16, 4.17) and table (4.27),(4.29). But adverse results were mentioned by the study done by Marsh et al. this observation suggests a neuro-pathological condition. Temporal lobe abnormalities on MRI have been linked to a greater degree of auditory hallucinations, thought disorder, and negative symptoms. (Stephen E et al 2006).

Our patients complain of the schizophrenia symptoms as 16(89%) with Delusion and 18(100%) with Hallucination and patients with other different symptoms including 6(33%). but our study didn’t correlate the temporal lobe changes with neither the patients symptoms nor the treatment used.

There are several limitations to our study: is that we didn’t consider the treatment type and duration .The use of a sample including patients with a long-term exposure to drug treatment, might also limit the generalizability of the findings. Our results showed that the number of participants in this study was not enough and further study is needed .Third, we used 1.5 T magnetic fields and our acquisition time is shorter than that used in previous studies, and this short acquisition might make lower signal to noise ratio and large signal variability. Future studies are needed to complement the present findings by investigating, in both patient groups and in healthy subjects, different segments of the lateral ventricles, and different subregions within the cingulate gyri, the hippocampi, and the temporal lobes.

5.1.3 Table (4.34) and (4.35) shows the measurement taken for both control subject group and epilepsy disease group.

Table (4.36) and (4.37) shows the mean and standard deviation (SD) values of the Age, the right and left Nigra length and width measured and classified according to Gender for The control

group and epilepsy disease group, There were no significant differences were detected between the two genders in control and diseased group. This was noticed in tables (4.38).

Table (4.39) shows comparisons between the right and left Temporal lobe length and width measured for the Control and epilepsy disease groups.

We justify our finding to that, epilepsy has a relation with the hippocampus and not with substantia nigra.It has been reported that, Temporal-lobe epilepsy (TLE) involves seizures that typically originate in the hippocampus. subset of hippocampus had significantly reduced(Martha J. Holmes et al 2013).

Table (4.40, 4.41, 4.42 and 4.43) shows multiple comparisons between the control, RT nigra and left nigra width and length ,it represent significance difference between control and substantia nigra in Parkinson and schizophrenia while no significance difference in epilepsy disease.

5.2 Conclusion:-

T2weighted imaging is acknowledged for depicting the change in the width and length of the substantia nigra in Parkinson disease patients. New equations were established to predict the changes in substantia nigra in normal subjects and patients with Parkinson disease.

This study was in agreement with earlier studies done; hence it showed changes of the substantia nigra in Parkinson disease.

The measurements of the subsatntia nigra are valuable in studding some disease
Like Parkinson disease with high significant difference between Parkinson patients and control were observed. The mean measured values were significantly higher in patient with schizophrenia than in healthy control.
This study finding may be considered as a reference for Sudanese.
Visualizing with MR imaging and obtaining quantitative indices of degeneration of the substantia nigra in Parkinson disease has been extended- required goals.

MRI technology has enabled studies of brain anatomy in patients with schizophrenia aimed at understanding more about the substantia nigra, lateral ventricles temporal lobes in schizophrenia disease.

In conclusion, this study has demonstrated that, magnetic resonance imaging is, accurate, and reliable in the assessment of the substantia nigra changes.

5.3 Recommendation:-

Future research is needed to further confirm the results acquired with this study for substantia nigra.

More research is recommended for substantia nigra measurement, in different Sudanese states.

Future studies are needed to complement the present findings by investigating, in both patient groups and in healthy subjects, different segments of the lateral ventricles, and different subregions within the cingulate gyri, the hippocampi, and the temporal lobes in schizophrenia disease.

More research is recommended to use the magnetic resonance imaging measurements of substantia nigra as indicator for associated pathology.

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APPENDIX

APPENDIX: A

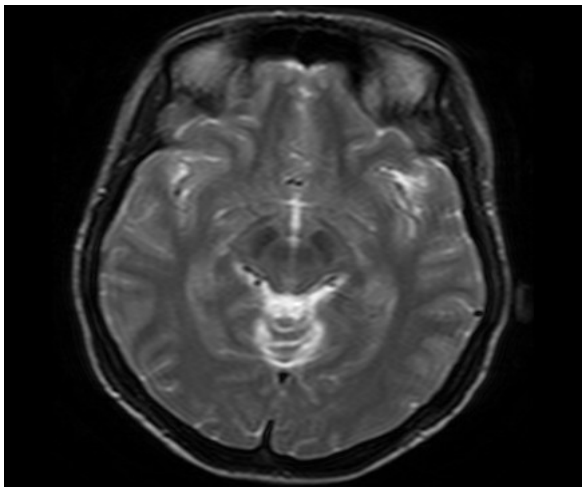


Image1: Shows a Normal substantia nigra in a Normal subject

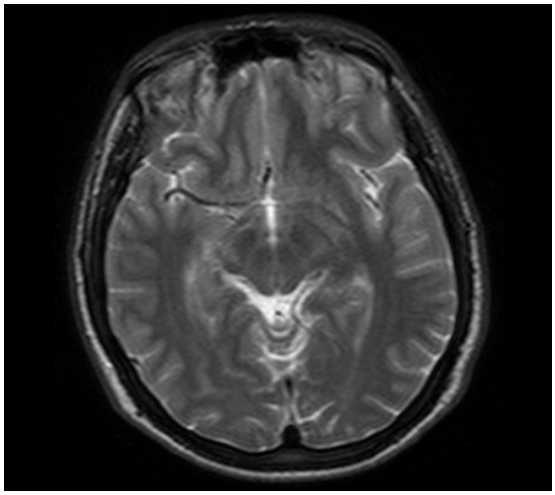


Image2: Shows substantia nigra in epileptic patient

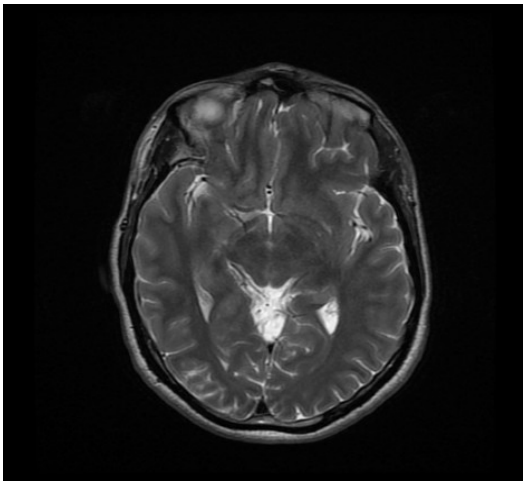


Image3: Shows substantia nigra in Parkinson disease

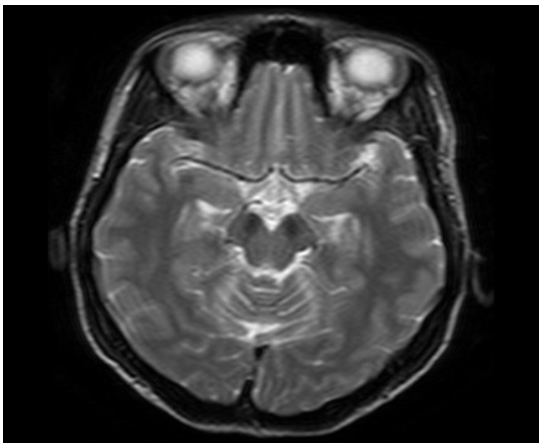


Image4: Shows substantia nigra in Schizophrenia disease

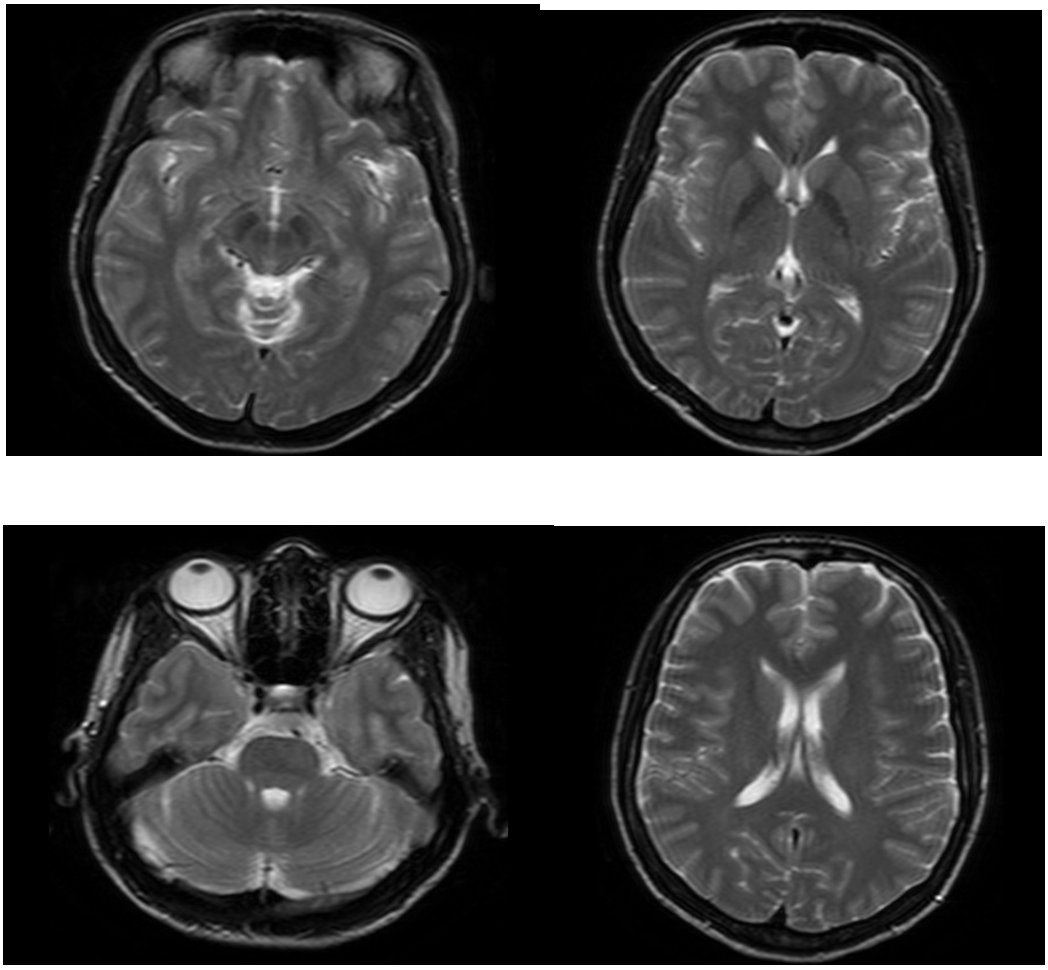


Image 5: 1.5 T Axial T2 images of substantia nigra, put amen, temporal lobes and lateral ventricle in a healthy 36 years old female.

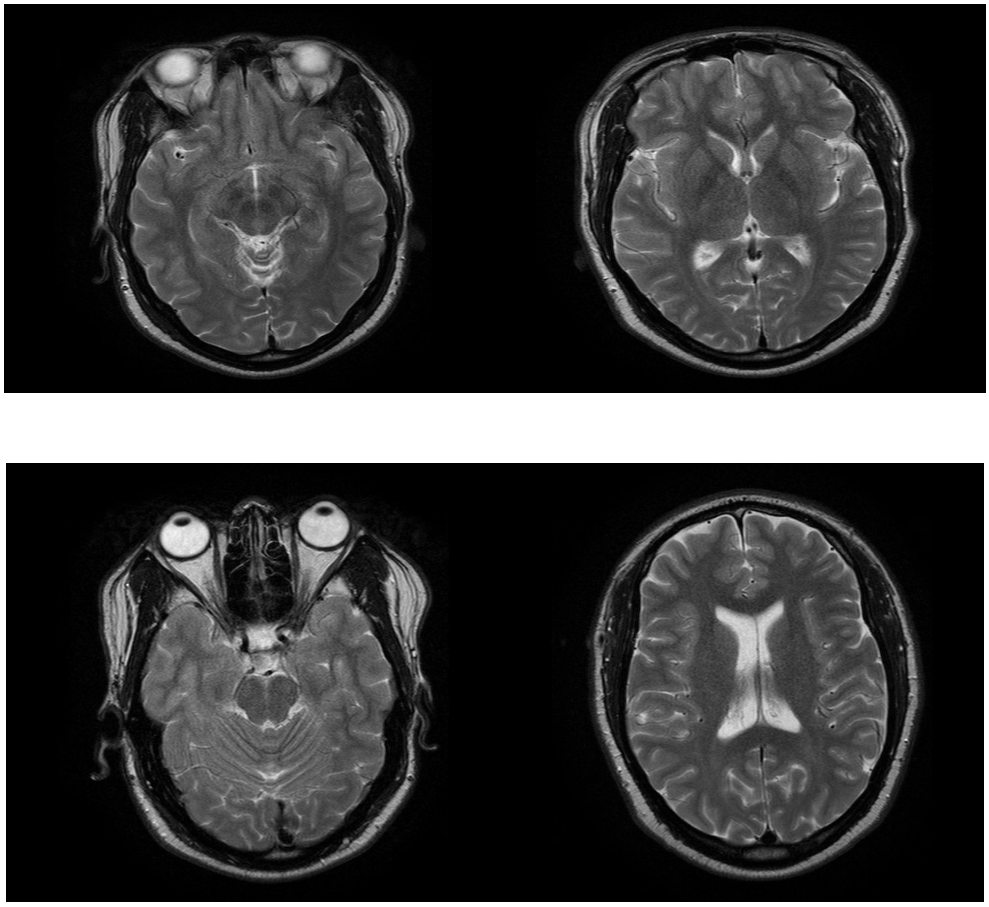


Image 6: Shows Axial T2w of substantia nigra, put amen, temporal lobes and ventricles in a 43 years old male previously diagnosed as epilepsy.

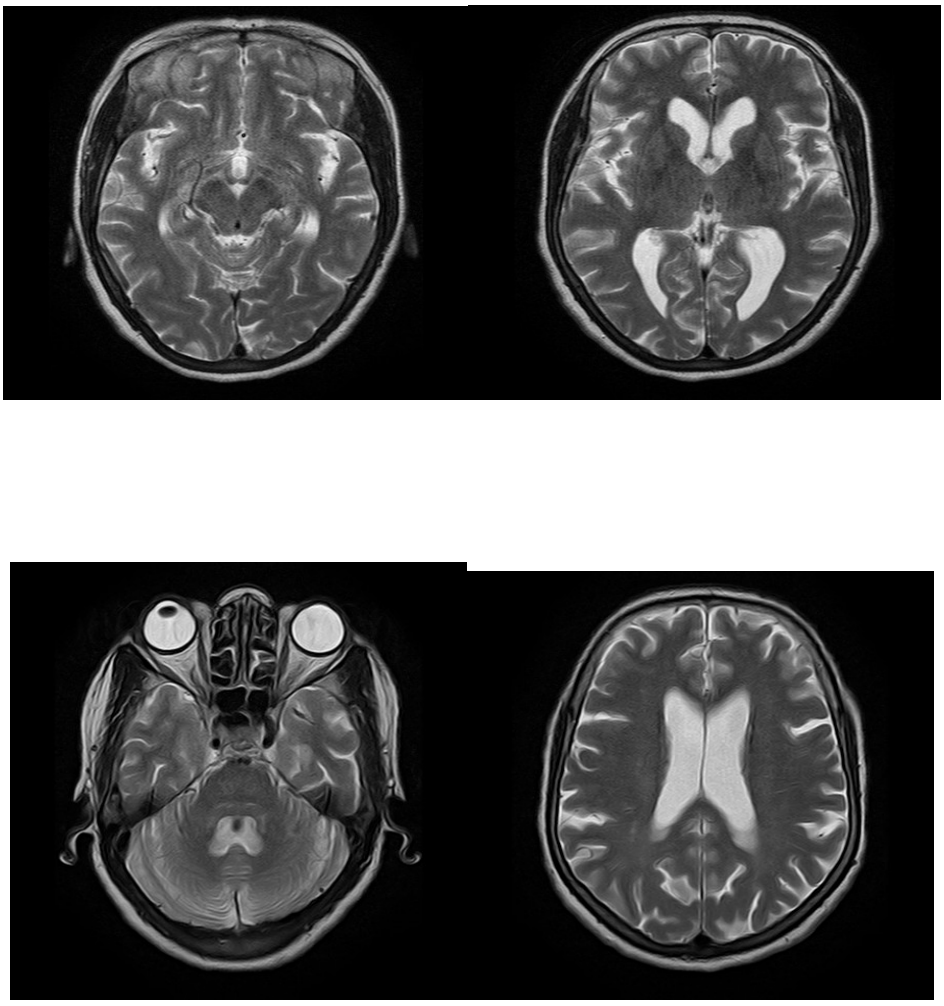


Image 7: Shows substantia nigra, put amen, temporal lobes and ventricles in a 58 years old male diagnosed previously as Parkinson disease .

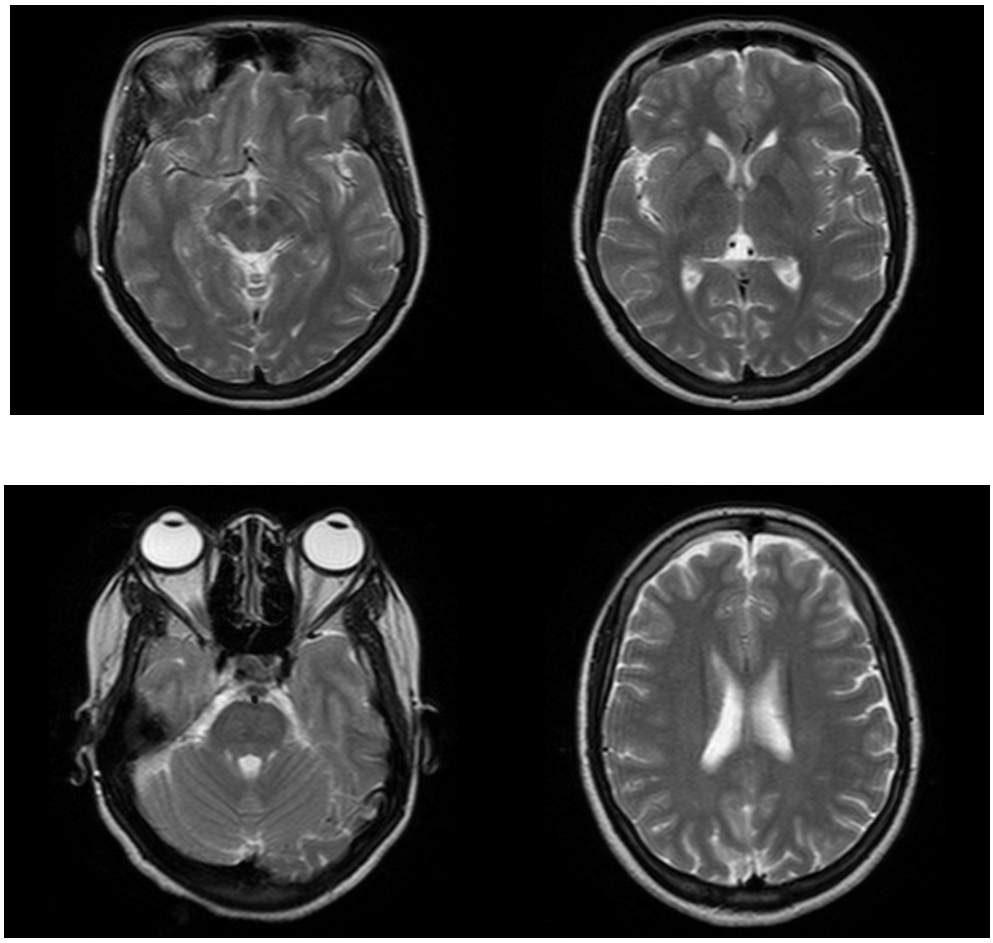
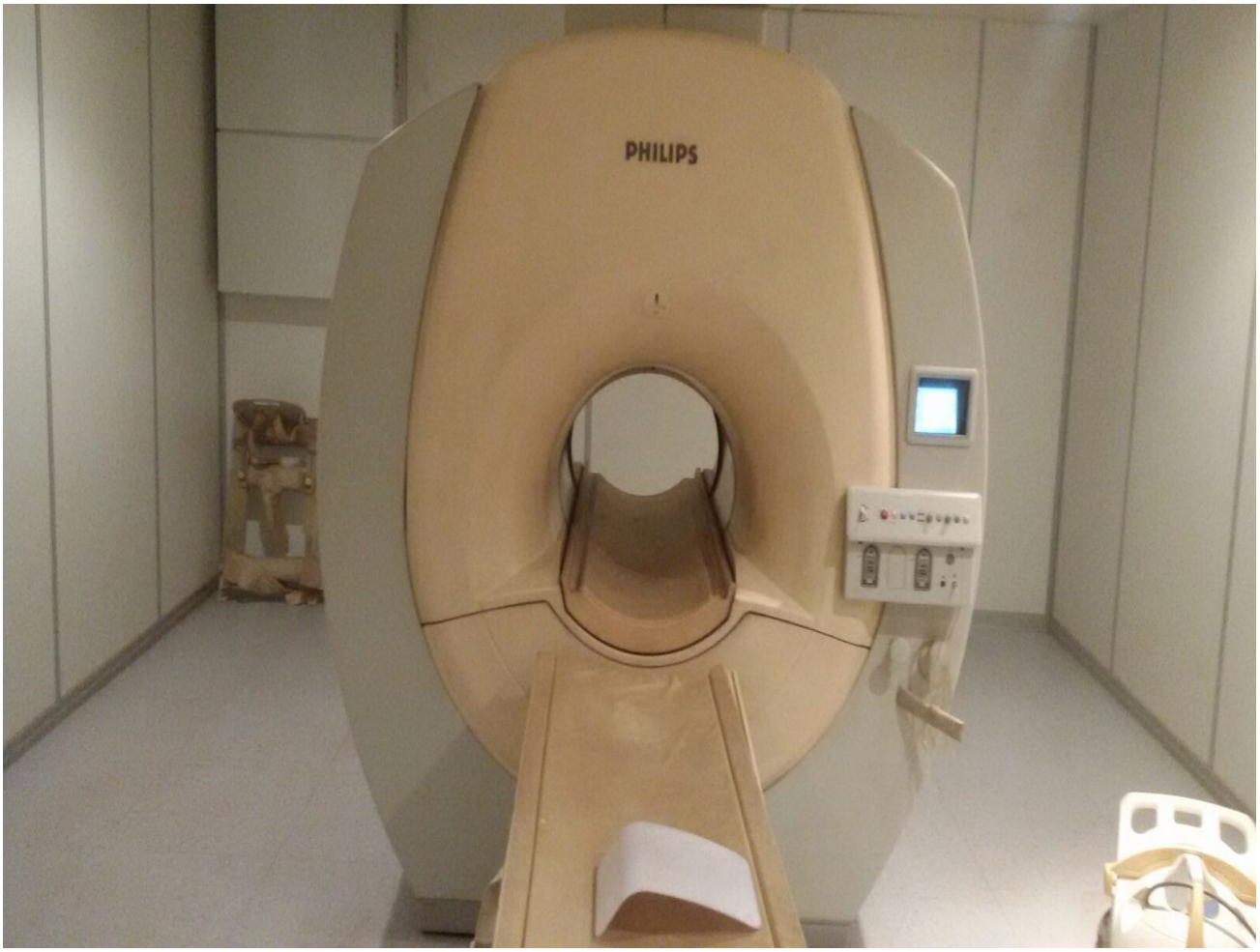
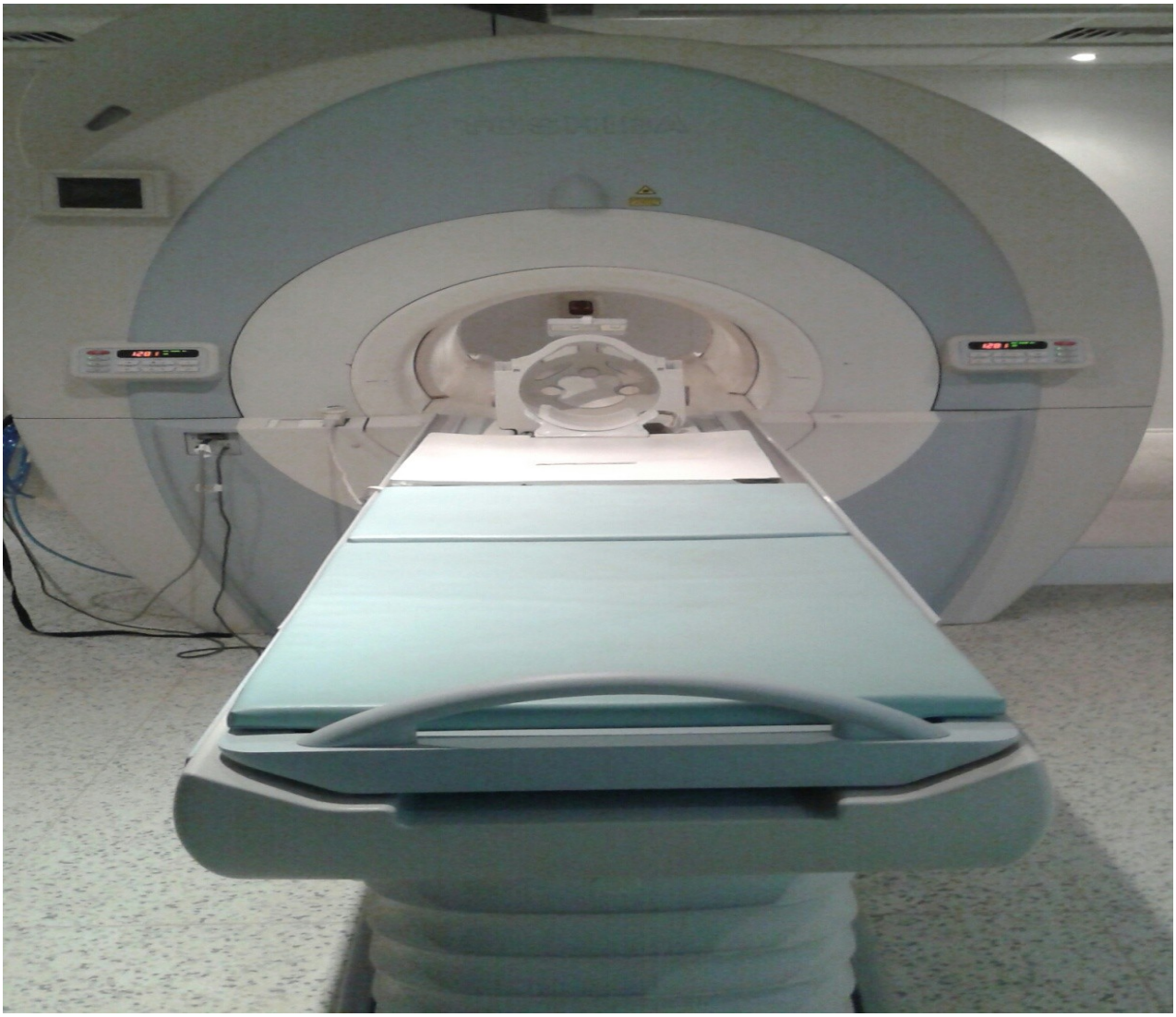


Image 8: Shows substantia nigra, put amen, temporal lobes and ventricles in a 44 years old male diagnosed as Schizophrenia .



MRI machine 1.5 T (Philips, Alamal Hospital)



MRI machine 1.5T (TOSHIBA, Military Hospital)

Appendix B

Data Collection Sheet

Sudan University of science and technology

College of graduate studies

Study of characterization of substantia nigra using Mri

PhD degree in medical radiologic technology

Patient data:-

Age: - Gender Area Area Race

Clinical symptoms:-Parkinson

Bradykinesia Tremor Rigid muscles Others

Family history

Mri finding:-

(1) Pons:-

Measurement: - length width

Signal intensity: -

T1 T2 Flair Stir Diffusion

(2)Substantia nigra:-

Measurement: Length Width

Rt

RT

LT

Signal intensity: -

T1 T2 Flair Stir Diffusion

(3)Put amen:-

Measurement: Length Width

RT

LT

Signal intensity: -

T1 T2 Flair Stir Diffusion

(4)Temporal lobe:-

Measurement: Length Width

RT

LT

Signal intensity: -

T1 T2 Flair Stir Diffusion

(5)Hippocampus:-

Measurement: Length Width

RT

LT

Signal intensity: -

T1 T2 Flair Stir Diffusion

(6)Lateral v ventricles:-

Measurement: Length Width

RT

LT

Signal intensity: -

T1 T2 Flair Stir Diffusion

(7)3D Ventricle:-

Measurement: Length Width

Signal intensity: -

T1 T2 Flair Stir Diffusion

(8) 4TH Ventricle:-

Measurement: - Length width

Signal intensity: -

T1 T2 Flair Stir Diffusion

Diagnosis Treatment Duration

Sudan University of science and technology

College of graduate studies

Study of characterization of substantia nigra using Mri

PhD degree in medical radiologic technology

Patient data:-

Age: - Gender Area Area Race

Clinical symptoms:-Epilepcy

Repeated seizure Unconsciousness Muscle jerking others

Family history

MRI finding:-

(1) Pons:-

Measurement: - length width

Signal intensity: -

T1 T2 Flair Stir Diffusion

(2)Substantia nigra:-

Measurement: Length Width

RT

It

Accomplishment

Two papers were published:

1-Tag Alsir Altayeb Beshier Ahmed, Caroline Edward Ayad, Hussein Ahmed Hassan, Elsafi Ahmed Abdalla, Characterization of Substantia Nigra in Parkinson disease using MR Imaging. Global Advanced Research Journal of Medicine and Medical Science (ISSN: 2315-5159) Vol. 4(1) pp. 010-015, January, 2015. Available online http://garj.org /garjmms/index.htm Copyright © 2015 Global Advanced Research Journals.

2-Tag Alsir Altayeb Beshier Ahmed, Caroline Edward Ayad, Hussein Ahmed Hassan, Elsafi Ahmed Abdalla, Morphometric analyses of Substantia Nigra Pars Compacta, temporal lobes and lateral ventricles in Schizophrenia Disease: MRI Study. Global Advanced Research Journal of Medicine and Medical Science (ISSN: 2315-5159) Vol. 4(12) pp. 562-570, December, 2015 Special Issue. Available online http://garj.