

## Neuroimaging and Psychiatric disorders: a literature review

Javed Ather Siddiqui<sup>1</sup>, Shazia Farheen Qureshi<sup>2</sup>, Ahmed Mohammed Dahlawi<sup>3</sup>,

<sup>1</sup>Psychiatrist, Department Of Psychiatry, Mental Health Hospital, Taif, Kingdom Of Saudi Arabia

<sup>2</sup>Psychiatrist, Department Of Psychiatry, Mental Health Hospital, Taif, Kingdom Of Saudi Arabia

<sup>3</sup>Radiologist, Department Of Radiology, Mental Health Hospital, Taif, Saudi Arabia

**Corresponding author:** Javed Ather Siddiqui

**Email** – javedsiddiqui2000@gmail.com

### ABSTRACT

The aim of this review is to estimate the rate of organic brain abnormalities in patients who present with psychiatric disorders. The literature overview was composed using database including Research Gate, Psyc Info, PubMed, Scopus, Science Direct, and Google Scholar to conduct a thorough search. There are a variety of neuroimaging techniques that can provide insight into the pathophysiology, and abnormalities of the brain in patients with psychiatric disorders. Computed tomography scans show mild enlargement of the ventricles and sulci, as well as reversed asymmetry of the Sylvian fissure. A Magnetic resonance imaging study generally shows grey matter reduction, primarily in the frontal and temporal limbic regions, along with gross abnormalities of the brain like deviated sulcogyral patterns. There is a reduction in fractional anisotropy and white matter in diffusion tensor imaging scan, and in positron emission tomography studies, there is a reduction in dopamine transporter density. Neuroimaging is a technique that studies the structure and function of the nervous system using imaging technology, where images of the brain are obtained non-invasively. The Psychiatric disorders are also associated with abnormalities in the nervous system so neuroimaging plays an important role in psychiatric disorders. We have discussed the importance of neuroimaging in the workup and evaluation of psychiatric disorders. This review provides physicians with primary knowledge on the neurobiology of psychosis based on a collection of in vivo brain imaging studies, as well as insight into future operations in neuroimaging.

**Keywords:** Neuroimaging techniques, psychiatric disorders, magnetic resonance imaging.

*(Paper received – 23<sup>rd</sup> December 2022, Peer review completed – 15<sup>th</sup> March 2023)*

*(Accepted – 19<sup>th</sup> March 2023)*

### INTRODUCTION

In psychiatric disorders, neuroimaging has been used since computed tomography was introduced, and now new forms of imaging are commonly used as technology is advances. Currently, neuroimaging techniques such as magnetic resonance imaging, magnetic resonance spectroscopy, diffusion tensor imaging, functional magnetic resonance imaging, and radionuclide imaging are used. Schizophrenia is a psychiatric disorder characterized by hallucinations such as hearing voices, delusions, disorganized behaviour [1], and thought interference in the acute phase, and social withdrawal, apathy, and slowness of activity in the chronic phase [2]. Currently, there is no clear protocol or guidelines for the use of neuroimaging in psychiatry [3]. In clinical practice, neuroimaging might be helpful in certain cases, including unusual or new-onset psychotic and mixed presentations, treatment resistance, cognitive or intellectual disability or change in cognitive capacity with comorbid neurological disorders or neurological abnormalities on physical examination, history of head trauma, including the central nervous system, older age and, delirium [4]. According to neuroimaging studies, hallucinations and delusions are correlated with the left medial temporal lobe and the cingulate cortex, whereas disorganized thought and behavioural patterns are correlated with the anterior cingulate, bilateral parietal cortex, and ventral frontal cortex. The activity of the frontal cortex is reduced in psychomotor poverty, on the other hand [5].

In this context, neuroimaging studies are not solely conducted to identify the aetiology of schizophrenia. Additionally, neuroimaging may assist in ruling out organic pathologies, predicting response to treatment, and estimating prognosis, identifying high-risk individuals, and developing drug development processes, as well as evaluating accompanying neurodevelopmental pathologies. A major objective of this paper is to provide clinicians with basic physics information about various neuroimaging techniques used during the diagnosis and treatment of schizophrenia, with an emphasis on current and future clinical applications [6]. Additionally, to neuropsychological and functional assessments, brain imaging can also be helpful in diagnosing and treating mental disorders. Specialized imaging techniques might also play an important role in diagnosing and treating psychiatric disorders [7]. Organic disease is responsible for both the early and late onset of psychosis symptoms. These organic causes of psychosis should be identified early, as the primary disease may require urgent treatment. Magnetic resonance imaging (MRI) can detect some of these underlying organic disorders. It remains controversial whether all psychotic patients should undergo routine MRI scans or in some specific cases, whether doing an MRI scan with contrast is mandatory.

### **Neuroimaging in Psychotic Disorders**

#### **A computed tomography Scan (CT scan)**

A highly collimated x-ray beam is used in computed tomography (CT). Psychiatric patients are increasingly requesting these tests because they are convenient, quick, and sensitive imaging tests for most brain lesions. According to some clinicians, all patients with psychotic illness should have a computed tomography scan of their brain to rule out infection, tumours, abscesses, Huntington's disease, and encephalitis [8-9]. Additionally, it is useful for assessing cerebral volume loss, hydrocephalus, and traumatic sequel [10], and the diagnostic value of this non-invasive technique in examining intracranial contents was quickly recognized. It is a valuable tool in psychiatric research studies to dig deeper into the aetiology as well as the long-term structural abnormalities in the brains of persons with schizophrenia, mood disorders, metabolic disorders, or neurological disorders. Nevertheless, CT plays a less clear role in clinical psychiatry. Psychiatric symptoms may initially manifest in patients with neurological disorders caused by trauma, intracranial haemorrhage, tumours, and vascular abnormalities. If a CT scan of the brain is not performed, it is very likely that untreatable causes will be missed, as these symptoms may be incorrectly diagnosed as psychiatric disorders. A CT scan is helping aid or tool to rule out any organic abnormality of the brain.

CT is not conclusively used in psychiatry as a diagnostic tool, according to the current literature. As reported by international and local studies, CT is indicated for patients with confusion or dementia, the first episode of psychosis of unknown cause, a movement disorder of unknown cause, prolonged catatonia, the first episode of major affective disorder, personality changes after 50 years of age, and cognitive decline. Some psychiatrists recommend CT for all first admissions to the hospital [11-13]. Some researchers [14-15] recommend that CT is eligible for only mentally ill patients with neurological abnormalities like focal signs, seizures, head injuries, and abnormal special investigations such as EEG, and blood tests. Psychiatric patients with first-episode psychosis showed a significant number of abnormalities on a CT scan. In schizophrenia, there is a large cavum and pellucidum seen, but this is not considered to be a causal factor [16]. Patients with schizophrenia are more likely to have a large cavum and septum pellucidum, but this is not considered a causal factor. Schizophrenia may be attributed to aberrant neurodevelopmental processes, and pathophysiological changes [17]. In schizophrenia patients, ventricular hypertrophy and cortical atrophy are also more common, but these symptoms are not secondary to chronic antipsychotic medication use. It is shown that ventricular hypertrophy is associated with age, a decline in cognitive functioning, and a decreased response to treatment [18-19]. In one case study a CT scan showed left temporal cerebrospinal fluid leading to compression on the temporal lobe and likely arachnoid cyst, and it presented symptoms of psychosis [20].

#### **Magnetic resonance imaging (MRI)**

Magnetic resonance imaging (MRI) is becoming a widely used tool for investigating cerebral abnormalities associated with mental health disorders. The use of MRI to investigate psychiatric illness has several advantages over computed tomography. Recent research has shown that MRI can help study neurologic deficits in schizophrenia, affective disorders, dementia, and anxiety disorders. New investigational

techniques like magnetic resonance spectroscopy add functional information to structural changes detected by standard MRI scans. The contrast resolution of magnetic resonance imaging (MRI) is four times higher than that of computed tomography [21].

The MRI should be recommended when patients present for psychosis for the first time, especially if the presentation is unusual, if psychosis develops rapidly or atypically, if there is dementia, or if focal neurologic deficits occur. This type of imaging is particularly useful to rule out possible underlying diseases like epilepsy, multiple sclerosis, certain tumours, and vasculitis. The volume of grey matter is reported to be reduced by four percent in schizophrenia, while the volume of white matter is unaffected. From the moment of the first attack, structural changes are evident. However, the relationship between volume loss and disease duration is still controversial [22]. There was a 3 percent decline in frontal lobe volumes, a 5 to 6 percent decrease in temporal lobe volumes, a 4 percent decrease in hippocampal volumes, and a 10 percent decrease in para hippocampal volumes, which are all associated with declines in executive function and cognitive decline [23-24]. There is a correlation between auditory hallucinations and volume loss in the superior temporal gyrus, and negative symptoms are associated with volume loss in the prefrontal lobe [25].

Anatomical information about brain structures is provided by structural MRI, along with detailed information on how disorders affect those structures. Major depressive disorder (MDD) and many other neurological disorders are also associated with structural brain changes. MRI revealed lateral ventricular enlargement in MDD patients, along with increased cerebrospinal fluid (CSF) volume compared with healthy controls. Additionally, patients with MDD have structural alterations in their parietal lobes. Cortical thickening and volumetric changes of gray matter are the most consistent findings [26]. It has been observed that patients with schizophrenia and MDD have asymmetric occipital lobes [27].

### **Magnetic resonance Spectroscopy (MRS)**

Based on the chemical shift phenomenon, magnetic resonance spectroscopy (MRS) relies on changes in the magnetic field created by protons in the presence of electrons. In vivo, magnetic resonance spectroscopy allows us to analyse chemical concentrations by analysing the precession frequency of bound protons. In MRS studies, N-acetyl aspartate, creatinine, choline, myo-inositol, and glutamate- glutamine are frequently analysed markers [28]. A low concentration of N-acetyl aspartate in vivo indicates neuronal damage or axonal injuries in disease states including multiple sclerosis, Huntington's disease, Alzheimer's disease, and encephalitis.

### **Functional Magnetic Resonance Imaging (fMRI)**

In patients with psychotic disorders, functional magnetic resonance imaging (fMRI) has been widely used to identify neurobiological substrates for cognitive impairments associated with the illness, with its excellent spatial resolution and non-invasive accessibility contributing to its popularity. According to functional magnetic resonance imaging (fMRI), areas of the brain that are active during a given task experience increased cerebral blood flow. Schizophrenia patients can undergo functional MRI studies to study executive and cognitive functions such as attention, memory, psychomotor function, and basic stimulus processing. Functional MRI showed that loss of superior temporal gyrus volume and functionality is associated with such symptoms. In psychotic symptoms, auditory hallucinations are studied extensively. These symptoms are associated with a loss of superior temporal gyrus volume and functionality, as shown by functional MRI. The results of functional MRI studies revealed that schizophrenia patients suffer from diffuse functional disorders throughout the body [29].

### **Diffusion Tensor Imaging (DTI)**

The diffusion tensor imaging (DTI) technique provides precise details on the microstructure of tissue, making it a popular tool to evaluate abnormalities in the cerebral white matter. As part of general neuroimaging, diffusion tensor imaging is used to visualize white matter associations, projections, and commissural fibres, to demonstrate white matter degeneration and myelin breakdown in demyelinating disorders, and to visualize axonal tracts to plan the extent of resection before tumour surgery and to demonstrate the extent of tumour infiltration. The diffusion tensor imaging technique is also used to visualize white matter tracts in coloured three-dimensional images and this method is known as tractography

[29]. DTI (diffusion tensor imaging) is a magnetic resonance imaging technique increasingly used for the non-invasive and quantitative evaluation of cerebral white matter (WM) and fractional anisotropy (FA) in psychiatric disorders. Some examples include schizophrenia, major depression, anxiety disorders, obsessive compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), autism, personality disorders, post-traumatic stress disorder (PTSD), and anxiety disorders.

Researchers found a significant amount of heterogeneity in chronic schizophrenia patients. There was a reduction in fractional anisotropy (FA) of the cingulate, corpus callosum, and frontal lobes associated with illness duration rather than medication. These studies and their results can also be affected by factors such as age, gender, and hand dominance among the subjects [30]. Among young adults with major depressive disorder, FA is decreased in the right middle frontal gyrus, the left occipitotemporal gyrus, the right parietal lobe subgyral and angular gyrus, the left anterior limb of the internal capsule, the right parahippocampal gyrus, and the left posterior cingulate cortex. Major depressive disorder in older individuals is characterized by decreased FA in the dorsolateral prefrontal cortex and anterior cingulate, as well as the diffuse frontal and temporal regions. A decrease or increase in FA in the cingulum bundle is observed in anxiety disorders. It has been shown that in OCD, the right cingulum has decreased FA, whereas in PTSD, the left cingulum has reduced FA. There have been widespread reductions in FA in autistic individuals leading to more focal findings in the temporal lobe WM.

### **Single-Photon emission computed Tomography (SPECT) and positron emission tomography (PET)**

Single photon emission computed tomography (SPECT) and positron emission tomography (PET) are radionuclide neuroimaging techniques. The SPECT detects radionuclide-emitted gamma rays. In positron emission tomography, images are constructed using positrons. Two types of radionuclide studies are performed on schizophrenia patients: blood flow-glucose metabolism studies and neuro receptor studies. Blood flow abnormalities in the temporal limbic tracts are highly correlated with disorders that inhibit subcortical dopamine release as well as positive symptoms of Parkinson's. There is an association between auditory hallucinations and increased blood flow to the limbic system and medial temporal lobe [31]. In schizophrenia patients, radionuclide studies showed increased levels of dopamine in synapses. PET and SPECT can be used to determine the receptor affinities of antipsychotic drugs. When compared with first-generation antipsychotics, second-generation drugs have a greater affinity for dopamine receptors and are more reversible when binding to receptors.

SPECT and PET studies have revealed dysregulation of the dopamine system in schizophrenia patients and varying losses of monoamines in depression patients. Antipsychotic responses have been linked to the blockade of dopamine D2 receptors, and antidepressant responses have been linked to the blockade of serotonin transporter receptors. The use of PET and SPECT as diagnostic procedures for dementia has been extensively evaluated. The development of radio ligands that bind to amyloid deposits in the brain has made significant progress, providing new opportunities for early diagnosis and treatment monitoring of different disorders. PET and SPECT imaging advances have provided new insights into the biology and treatment of major psychiatric disorders. These imaging techniques will become increasingly important for the treatment of psychiatric disorders in the future [32-33]. A recently published PET study found that decreased dopamine transporter density (DAT) was seen in manic patients [34].

### **CONCLUSION**

The use of neuroimaging techniques can provide insight into the pathophysiology of mental illnesses. Psychosis-related brain changes might be targeted for early intervention. Future studies are needed to revise therapeutic strategies to prevent or mitigate these active brain changes before psychosis begins. On CT scans, psychosis is characterized by mild enlargement of the ventricles and sulci, as well as reverses asymmetry of the Sylvian fissure. It was reported in 1927 that patients with schizophrenia had enlarged ventricles. In schizophrenia patients, grey matter volume has been shown to be decreased in multiple brain regions. In many studies, white matter disruption in schizophrenia patients has been reported, despite grey matter deficits receiving most of the attention.

In schizophrenia, magnetic resonance imaging (MRI) studies generally show grey matter reduction, primarily in the frontal and temporal limbic regions, along with gross abnormalities of the brain like deviated sulcogyral patterns. Active brain changes remain a mystery due to unknown pathological mechanisms. Functional MRI revealed a reduction in the volume of the superior temporal gyrus in psychosis. Diffusion tensor Imaging (DTI) in chronic schizophrenia patients shows reduction in the fractional anisotropy (FA) of the cingulate, corpus callosum, and frontal lobes, and also a reduction in white matter. The receptor affinities of antipsychotic drugs can be determined using PET and SPECT. In PET studies, a decreased concentration of dopamine transporter density was seen in people suffering from acute mania. Additionally, diffusion tensor imaging is used to visualize white matter tracts in colored three-dimensional images.

## REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5 (5th ed). Arlington, VA: American Psychiatric Association. 2013.
2. Owen MJ, Sawa A, Mortensen PB. Schizophrenia. *The Lancet* 2016;388(10039):86–97.
3. Stern T, Fava M, Wilens T, Rosenbaum J. Massachusetts General Hospital Comprehensive Clinical Psychiatry. Elsevier; 2015.
4. Camprodon JA, Stern TA. Selecting neuroimaging techniques. *Prim Care Companion CNS Disord* 2013;15(4)
5. Hill K, Mann L, Laws KR, Stephenson CM, Nimmo-Smith I, McKenna PJ. Hypofrontality in schizophrenia: a meta-analysis of functional imaging studies. *Acta Psychiatr Scand* 2004;110(4):243-56.
6. Yildirim A, Turelib D. Schizophrenia: A review of neuroimaging techniques and findings. *East. J. Med.* 2015;20:1-6
7. Power BD, Nguyen T, Hayhow B, Looi JCL. Neuroimaging in psychiatry: an update on neuroimaging in the clinical setting. *Australasian Psychiatry* 2016;24(2):157–63.
8. Gewirtz G, Squires-Wheeler E, Sharif Z, Honer WG. Results of computerised tomography during first admission for psychosis. *Br J Psychiatry* 1994;164(6):789-95.
9. Battaglia J, Spector IC: Utility of the CAT scan in a first psychotic episode. *Gen Hosp Psychiatry* 1988;10:398-401.
10. Wooley J, McGuire P. Neuroimaging in schizophrenia: What does it tell the clinician? *Adv Psychiatr Treat* 2005;11:195- 202.
11. Weinberger DR. Brain disease and psychiatric illness: when should a psychiatrist order a CAT scan? *Am J Psychiatry* 1984;141:1521-7.
12. Hollister LE, Boutros N. Clinical use of CT and MR scans in psychiatric patients. *J Psychiatry Neurosci* 1991; 16:194-8.
13. Berk M. Indications for computed tomographic brain scanning in psychiatric inpatients. *S Afr Med J.* 1992; 82:338-40.
14. McClellan RL, Eisenberg RL, Giyanani VL. Routine CT screening of psychiatric inpatients. *Radiology.* 1988; 169:99-100.
15. Tsai I, Tsuang MT. How can we avoid unnecessary CT scanning for psychiatric patients? *J Clin Psychiatry* 1981;42:452-4.
16. Kasai K, McCarley RW, Salisbury DF, Onitsuka T, Demeo S, Yurgelun-Todd D, Kikinis R, Jolesz FA, Shenton ME. Cavum septi pellucidi in first-episode schizophrenia and first-episode affective psychosis: an MRI study. *Schizophr Res* 2004;71(1):65-76.
17. Lubman DI, Velakoulis D, McGorry PD, Smith DJ, Brewer W, Stuart G, Desmond P, Tress B, Pantelis C. Incidental radiological findings on brain magnetic resonance imaging in first-episode psychosis and chronic schizophrenia. *Acta Psychiatr Scand* 2002;106(5):331-6.
18. Smith GN, Flynn SW, Kopala LC, Bassett AS, Lapointe JS, Falkai P, Honer WG. A comprehensive method of assessing routine CT scans in schizophrenia. *Acta Psychiatr Scand* 1997;96(5):395-401.
19. Andreasen NC, Olsen S. Negative and positive schizophrenia. Definition and validation. *Arch. Gen. Psychiatry* 1982;39:789-94.
20. Siddiqui JA, Qureshi SF, Alzahrani A. Left Temporal Lobe Arachnoid Cyst Presenting with Symptoms of Psychosis. *Psychosom Med Res* 2021;3(4):196-9.
21. Bushong SC. Magnetic Resonance Imaging: Physical and Biological Principles (3rd ed). St.Louis: Mosby, 2003
22. Kasai K, Shenton ME, Salisbury DF, Hirayasu Y, Lee CU, Ciszewski AA, Yurgelun-Todd D, Kikinis R, Jolesz FA, McCarley RW. Progressive decrease of left superior temporal gyrus gray matter volume in patients with first-episode schizophrenia. *Am J Psychiatry* 2003;160(1):156-64.
23. Nestor PG, O'Donnell BF, McCarley RW. A new statistical method of testing hypotheses of neuropsychological / MRI relationships in schizophrenia: partial least squares analysis. *Schizophrenia Res* 2002;53:57-66.
24. Gur RE, Turetsky BI, Cowell PE, Finkelman C, Maany V, Grossman RI, Arnold SE, Bilker WB, Gur RC. Temporo-limbic volume reductions in schizophrenia. *Arch Gen Psychiatry* 2000;57(8):769-75.
25. Rajarethinam R, DeQuardo JR, Miedler J. Hippocampus and amygdala in schizophrenia: assessment of the relationship of neuroanatomy to psychopathology. *Psychiatry Res* 2001;108:79-87.

26. Zhang FF, Peng W, Sweeney JA, Jia ZY, Gong QY. Brain structure alterations in depression: Psychoradiological evidence. *CNS Neurosci Ther* 2018;24:994–1003.
27. Falkai, P., Schneider, T., Greve, B., Klieser, E. & Bogerts, B. Reduced frontal and occipital lobe asymmetry on the CT-scans of schizophrenic patients. Its specificity and clinical significance. *J. Neural Transm. Gen Sect* 1995;99:63–77.
28. Thermenos HW, Keshavan MS, Juelich RJ, Molokotos E, Whitfield-Gabrieli S, Brent BK, Makris N, Seidman LJ. A review of neuroimaging studies of young relatives of individuals with schizophrenia: a developmental perspective from schizotaxia to schizophrenia. *Am J Med Genetics Part B: Neuropsychiatr Genet* 2013;162(7):604-35.
29. Grossman RI, Yousem DM. *Neuroradiology: The Requisites* (2nd ed). India: Mosby, 2009.
30. Kanaan RA, Kim JS, Kaufmann WE, Pearlson GD, Barker GJ, McGuire PK. Diffusion tensor imaging in schizophrenia. *Biol Psychiatry* 2005;58(12):921-9.
31. Erritzoe D, Talbot P, Frankel WG. Positron emission tomography and single photon emission CT molecular imaging in schizophrenia. *Neuroimag Clin North Am* 2003;13:817-32.
32. Abi-Dargham A, Laruelle M. Mechanism of action of second-generation antipsychotic drugs in schizophrenia: insights from brain imaging studies. *Eur Psychiatry* 2005;20:15-27.
33. Grossman RI, Yousem DM. *Neuroradiology: The Requisites* (2nd ed). India: Mosby, 2009.
34. Zipursky RB, Meyer JH, Verhoeff NP. PET and SPECT imaging in psychiatric disorders. *Can J Psychiatry* 2007;52:146-57.
35. Yatham LN, Liddle PF, Gonzalez M, Saraf G, Vafai N, Lam RW, Sossi V. A Positron Emission Tomography Study of Dopamine Transporter Density in Patients with Bipolar Disorder with Current Mania and Those With Recently Remitted Mania. *JAMA Psychiatry* 2022;79(12):1217-24.

\*\*\*\*\*

Acknowledgements – Nil

Conflict of Interest – Nil

Funding – Nil