

# Magnetic resonance imaging in schizophrenia: Luxury or necessity? (Review)

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**Abstract.** Schizophrenia, one of the most common psychiatric disorders, with a worldwide annual incidence rate of approximately 0.3-0.7%, known to affect the population below 25 years of age, is persistent throughout lifetime and includes people from all layers of society. With recent technological progress that allows better imaging techniques, such as the ones provided by computed tomography and particularly magnetic resonance imaging (MRI), research on schizophrenia imaging has grown considerably. The purpose of this review is to establish the importance of using imaging techniques in the early detection of brain abnormalities in patients diagnosed with schizophrenia. We reviewed all articles which reported on MRI imaging in schizophrenia. In order to do this, we used the PubMed database, using as search words 'MRI' and 'schizophrenia'. MRI studies of first episode patients and chronic patients, suggest reduction of the whole brain volume. Enlargement of lateral ventricles was described as positive in 15 studies out of 19 and was similar to findings in chronic patients. Moreover, for the first episode patients, all data collected point to important changes in medial temporal lobe structures, diminished hippocampal volume, the whole frontal lobe, asymmetry in prefrontal cortex, diminished volume in

cingulate, corpus callosum, and cavum septum pellucidum reported abnormalities. MRI is recommended as an important tool in the follow-up process of patients with schizophrenia. Yet, it is still under debate whether the abnormalities described in this condition are able to be used as diagnostic biomarkers.

## Contents

1. Introduction
2. Scope of the review
3. Literature search methods
4. Results
5. First episode patient data
6. Chronic patient data
7. Conclusions

## 1. Introduction

Schizophrenia, one of the most common psychiatric disorders, with a worldwide annual incidence rate of approximately 0.3-0.7%, known to affect the population below 25 years of age, is persistent throughout lifetime and includes people from all layers of society (1). The main signs and symptoms may differ among patients as well as the debut period and can include perceptual abnormalities, delusions, deterioration of cognitive function and emotional impairment. It affects both patients and their families, manifesting in poor care and social exclusion because of the widespread ignorance about the disorder (2). Although schizophrenia has been studied for more than a century, the neuropathology of schizophrenia is still unknown, with no single set of causes that can be pinned down as an underlying mechanism for this condition (2-5). Najjar and Pearlman described, in a review of 15 studies that involved 792 patients, that schizophrenia is strongly related with white matter abnormalities and it could lead to structural

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and functional dysconnectivity, even in an early development of psychosis (6).

With recent technological progress that allows better imaging techniques, such as the ones provided by computed tomography (CT) and particularly magnetic resonance imaging (MRI), research on schizophrenia imaging has grown considerably. Multiple neuroimaging studies have identified substantial evidence of structural and functional brain alterations in schizophrenia. There is no specific region in which these alterations occur, but they are frequently found in the association cortex and subcortical (limbic, striatal) brain regions. These findings still do not have diagnostic value (7-9).

In the 19th and 20th century, there were numerous attempts to identify brain abnormalities that led to discouraging results because of the lack of technology. Although the benefits of using CT to discover brain abnormalities *in vivo* were important, using the newer technique of MRI, allowed researchers to better analyze different regions of the brain due to an improved picture of the gray matter (10).

## 2. Scope of the review

The main method of diagnosing schizophrenia is based on clinical diagnostic criteria, psychiatric history and mental examination of the patient, with imaging techniques being used for differential diagnosis with other disorders that could cause psychosis. The purpose of this review was to establish the importance of using imaging techniques in the early detection of brain abnormalities in patients diagnosed with schizophrenia.

## 3. Literature search methods

We reviewed all articles which reported on MRI imaging in schizophrenia. In order to do this, we used PubMed database, using as search words 'MRI' and 'schizophrenia'. Only articles indexed in PubMed, written in English and published between 1988 to 2020 were reviewed for this study.

A total of 197 articles were reviewed. From these we selected 84 articles which offered information about significant brain structures mainly linked with schizophrenia: Lateral ventricles, third ventricle, fourth ventricle, temporal lobe, frontal lobe, parietal lobe, occipital lobe, cerebellum, basal ganglia structures, thalamus, corpus callosum and septum pellucidum.

## 4. Results

Although large individual variations in brain size in the general population such as gender, age, economic and social status, perinatal factors and potential nutritional deficits are reported, there are no statistically eloquent differences in MRI studies between patients diagnosed with schizophrenia and normal controls (10).

In the review conducted by Shenton *et al* concerning 55 MRI studies in patients with schizophrenia, 44 reported structural modifications such as enlarged lateral ventricles (10). While lateral ventricle enlargement was not always identified in some studies, enlargement of the temporal horn portion, which is commonly found on the left sided ventricle, has been mentioned (11-20).

In 33 MRI studies of the third ventricle, 24 (73%) describe an enlargement of this area, and 9 (27%) report negative findings (10,21-23).

The fourth ventricle was investigated in 5 MRI studies, and only one of them reported positive findings, representing 20%; the remaining 4 studies were negative (10,24,25).

Of 51 MRI studies evaluating the volume of temporal lobe, 31 (61%) reported smaller temporal lobe volume, while 20 (39%) reported negative findings (10,26-29).

MRI findings of frontal lobe abnormalities in schizophrenia are vague. From 50 MRI studies, 30 (60%) reported volumetric reduction, while 20 (40%) reported negative findings (10,30-33).

An important brain region involved in processes that are altered in schizophrenia, such as attention (34), spatial working memory (35) and language (36) is the parietal lobe. In 15 studies regarding the MRI of the parietal lobe, only 9 (60%) describe abnormalities in this region (7,10,37,38).

Four of the studies that describe the occipital lobe, representing 44%, showed a reduction in the volume of patients diagnosed with schizophrenia (8,9,39,40).

Four (31%) out of 13 MRI studies of the cerebellum in schizophrenia, reported positive findings, while 9 (69%) reported negative findings (41,42). Nopoulos and coworkers (43) reported negative findings, but they did report a reduction in volume in the anterior lobe of the vermis and Rossi and coworkers (44) showed a decrease in vermal-to-brain ratio in male patients with schizophrenia compared to female patients with schizophrenia.

From 25 studies involving the basal ganglia structures, 17 of them, representing 68%, described increased volume (45-47) and 8 reporting negative results (48,49). Recent studies describe that the enlargement of the basal ganglia is rather caused by neuroleptic medication (10,47).

The thalamus, although an important relay station in the brain, which is involved in modulating the input from various levels such as the cortical areas, limbic system and reticular activating system, has been little scanned, mainly because this area fades from gray matter to white matter. From 12 MRI studies, 5 (42%) describe a reduction in the volume and 7 (58%) reported no discrepancy between the control group and the patients with schizophrenia (50-53).

Corpus callosum, a brain structure composed of white matter, has been reviewed in 27 MRI studies, 17 (63%) of them reporting reduction in thickness all along its structures (10,54-57).

One of the most important findings in literature is related to MRI studies of septum pellucidum, 11 (92%) describing an enlargement of this region in schizophrenia (10).

Akhtar *et al* conducted an MRI study of 66 subjects (33 with schizophrenia and 33 control test) and found that brain atrophy was present only in 13 patients with schizophrenia (39.4%) and none of the control group. The presence of prominent cavum septum pellucidum was described in 10 cases of schizophrenia representing 30% and none in the control. Prominent Virchow Robin spaces were significantly associated with schizophrenia (30.3%) as compared to the control group. Enlargement of ventricles was reported only in 4 cases (12%) and 2 (6%) of the control group (58).

## 5. First episode patient data

MRI studies of first episode patients are quite comparable with those of chronic patients, especially in data regarding the reduction of the whole brain volume. Enlargement of lateral ventricles was described as positive in 15 studies out of 19 and is similar to the findings of chronic patients (59-61). Also, several researchers note the increase in volume of the left temporal horn of the lateral ventricles which is comparable with data gathered from chronic patients (10,62,63).

Five out of 6 studies regarding medial temporal lobe structures report positive data for schizophrenic patients (10), in comparison with 5 out of 11 MRI studies that examined the whole temporal lobe volume (45,64). When investigating the hippocampus and amygdala independently, 8 out of 10 studies report a diminished hippocampal volume and only 1 out of 5 studies report a decreased amygdala volume (29,64,65).

Regarding the whole frontal lobe, 7 out of 10 MRI studies showed abnormalities, one of them noted asymmetry in the prefrontal cortex (9) and another one a diminished volume in the cingulate, while the other study reported negative findings (65).

For other brain regions, MRIs also gathered important data. From 4 studies of corpus callosum, 3 reported abnormalities; 7 out of 10 basal ganglia studies, and 3 out of 3 studies of cavum septum pellucidum reported abnormalities (10,47,65-68).

## 6. Chronic patient data

The inception reports (45,66,69) noted that there were no differences between the patients with first episode and the control group regarding the volume of ventricles. Previous studies revealed increased volume of lateral ventricles as the subject sample grew larger (66,70).

In a 4-year study, DeLisi and coworkers (66) noted that there were no modifications in temporal lobe volume or in the amygdala-hippocampal complex.

## 7. Conclusions

Summarizing all of these studies regarding MRI imaging in patients with schizophrenia, the most frequent findings are enlargement of lateral ventricles, cortical atrophy, affecting mostly temporal and frontal lobes, and white matter abnormalities.

MRI findings thus demonstrate that brain abnormalities are present at first episode of the illness, and that the brain regions involved are the same brain regions observed in more chronic patients. There are some anomalies which progress over time, such as reduction in the volume of frontal and parietal lobes, superior temporal gyrus and lateral ventricles (10).

The changes in the volume of the basal ganglia seem to be related rather to the type and duration of neuroleptic treatment, whereas the volume of amygdala-hippocamp appears not to change over time.

It is still under debate whether the abnormalities described in this condition could be used as a biomarker for diagnosis. Hopefully, the new MRI technique with a higher resolution will offer new data regarding the brain anomalies in schizophrenia with a better understanding of the

innermost pathogenic mechanism of this devastating disease, subsequently impacting the therapeutic interventions in these patients.

These data recommend MRI investigation as an important tool in the follow-up process of patients with schizophrenia.

In conclusion, regarding the continuous evolution of technology, MRI investigation may be considered a necessity and no longer a luxury in early schizophrenia diagnosis.

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## Availability of data and materials

All information included in this Review is documented by relevant references.

## Authors' contributions

FPI analyzed and collected data regarding the MRI findings. MCM analyzed and collected data regarding the MRI findings. MB was involved in revising the review critically for important intellectual content. AMC was involved in revising the review critically for important intellectual content. MM critically revised the manuscript. All authors read and approved the final manuscript for publication.

## Ethics approval and consent to participate

Not applicable.

## Patient consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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