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# Neuroanatomical alterations in brain disorder: A magnetic resonance imaging analysis

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## Abstract

**Background**: Bipolar disorder is a serious mental disorder caused by strong mood fluctuations, affecting 2% of the world's population. People with bipolar disorder experience both manic and depressive episodes, which can lead to suicidal thoughts and changes in appetite, activity, and focus. There are different subtypes of bipolar disorder, with cyclothymic disorder being the milder of the two. Bipolar I is characterized by manic periods, while bipolar II is marked by hypomanic and significant depressive episodes. Bipolar disorder is a biological, genetic, and environmental condition that can affect anyone at any age.

**Methods**: In this study, we enrolled a total of 49 bipolar disorder (BD) participants to 44 healthy control (HC) subjects. Bipolar disorder patients were enlisted with their consent using web portals, medical facilities, and local marketing. MRI contraindications, medical history, self-reported using a mood-altering medication, inadequate vision, and left-handedness were among the exclusion criteria. The various tissue structures which are: the gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) were examined using voxel-based morphometry (VBM) to ascertain these changes. We employed statistical parametric mapping (SPM) for both image processing and statistical analysis.

**Results**: Our findings demonstrate that individuals with bipolar disorder showed a substantial volume decrease in both gray matter (GM) and white matter (WM), with gray matter (GM) and white matter (WM) volume decreases being more noticeable in the frontal, temporal, parietal, and occipital lobes. Additionally, individuals with bipolar disorder showed no CSF volume in any of the brain regions.

**Conclusion**: Our VBM research backs up earlier studies that link changes in brain structure, particularly gray matter and white matter, to bipolar disorder. These discoveries shed more information on the neurology of bipolar disorder and could guide the creation of more potent diagnostic and treatment modalities.

**Keywords:** Bipolar disorder; Voxel-Based Morphometry; Gray Matter; White Matter; Cerebrospinal Fluid; Magnetic Resonance Imaging; Statistical Parametric Mapping (SPM12)

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## 1. Introduction

Bipolar disorder, sometimes referred to as a form of manic depression, are symptoms of significant fluctuations in mood and energy. It impacts 1% of the world's population and is distinguished by mood swings between melancholy and mania (1). Each individual with bipolar disorder has their own manic-depressive episodes, which can be accompanied by thoughts of suicide and may persist anywhere from months to days (2). There is evidence to suggest that damages to particular neuroanatomical areas of the brain, such as brain tumors or strokes, could result in the emergence of further mental illnesses (3).

Genetic factors account for 80% of the causes of BD, which is primarily inherited. The disorder may begin as a result of stressful life events like a job loss, trauma, having a kid, or a death (2). An estimated 10% of children of bipolar parents will develop bipolar disorder (BD), which is a mental health condition which is likely to run in family. It is linked to anatomical and functional modifications of the brain, including chemical alterations and the shrinking of particular brain regions (4). Different symptoms might result from abnormalities in specific neurotransmitters, such as serotonin, dopamine, and noradrenaline. Furthermore, the amygdala and other brain regions may experience structural and functional alterations (5). The heritability of bipolar disorder is a measurement of the degree to which the variability of the trait may be attributed to genetic factors. There is a sizable heritable factor for mental disorders, ranging between 60% and 80% (6). Although predictions that members of the second-degree relatives had an increased risk in depression, an additional study has shown the risk of unipolar disorder in second-degree relatives is comparable with that of the population as a whole (7). To ascertain whether a variation in genetics is more common in affected close relatives than in healthy relatives, the transmission disequilibrium test (TDT) and family-based association test (FBAT) are utilized (8).

Bipolar I and bipolar II disorders are the two main classifications for bipolar disorder employed in the DSM-5 (9). A comprehensive evaluation by a psychologist, which must include a clinical interview, is necessary to detect bipolar disease (10). In order to diagnose whether bipolar illness has been detected, mental health specialists look at thoughts, emotional state, symptoms, and activities. To filter other physical conditions, laboratory tests could be required. To examine symptoms, mental health professionals employ assessment methods and questionnaires (11). Bipolar disorder is diagnosed using DSM-5 criteria (12). As a result of symptoms which seem similar to those of various mental diseases, lack of understanding, restricted access to resources, miscommunication, and stigma, bipolar disorder is frequently misdiagnosed (13). Whereas reverse neurovegetative symptoms like irritation of emotion and anger are indicative of bipolar disorders, studies have indicated that observable symptoms could be equally helpful to assessments in evaluating an individual with bipolar illness (14). Bipolar disorder is also predicated by motor retardation and hypersomnia (15). Bipolar disorder is the sixth-leading type of illness, with a lifetime prevalence of 1.4–6.4% and high economic costs (16). Only an accredited psychologist is capable of making the diagnosis, and a proper diagnosis is necessary to guarantee that patients receive the best possible treatment and aid.

Bipolar disorder is treated with therapy and medication (10), while valproic acid, and lithium, among others, becoming the two most frequently administered medications for regulating mood. In addition, psychosis and mania symptoms are managed using atypical antipsychotics (17). A mood stimulant called lithium is prescribed for treating bipolar disorder. By bringing the amounts of particular chemicals in the brain into balance, it aids in lowering the severity and frequency of manic and depressive episodes (18). It can result in shaking, gaining weight, diarrhea, and nausea (19). Psychiatrist John Cade from Australia first identified lithium in 1948 (20), and the 1950s and 1960s saw a rise in its use (21). Lithium was initially approved as a mania treatment by the US FDA in 1970 (22). The activation of CA1 cell pyramids was raised after a 4-week lithium treatment (23), and the hippocampal formation's plasticity of synapses was boosted. Suicide risk was also decreased (24). In addition to medication, psychotherapy is employed for the treatment of bipolar disorder, particularly CBT and IPSRT concentrating at recognizing and changing insufficient thought processes (25). In order to avoid recurrence and enhance quality of living, maintenance therapy entails maintaining treatment regardless of whether symptoms have subsided (24).

Throughout the earlier decade, numerous studies employing VBM are being carried out to examine the structural changes in individuals experiencing brain (26,27). According to a study, bipolar individuals have less gray matter in their prefrontal cortex, anterior cingulate cortex, insula, and amygdala. White matter volume did not significantly differ between bipolar patients and healthy controls, either (28). In comparison to people having first-episode bipolar disease, chronic bipolar individuals showed a greater reduction in grey matter volume, according to the study (29). Another study discovered that individuals with BD had no differences in their white matter volume, but have decreased gray matter volume in specific regions of the brain (30). According to VBM investigations (31,32), people with BD had reduced gray matter volume in the prefrontal cortex, amygdala, hippocampus, and thalamus. The volume of white matter (31) did not differ noticeably. Bipolar disorder patients altered functional connectivity and structural

dysconnectivity were studied by (5), who hypothesized that the striatum may be crucial for the pathophysiology of the condition (33). Bipolar disorder persons experienced greater diffusivity radial within the white matter course of the superior longitudinal fasciculus, genu and body, spleen, cingulum bundle, and thalamic radiation, according to research by Benedetti F. et al., whereas no areas of the brain in the control group of participants displayed less diffusivity values or greater FA (33).

The structure and function of the brain can be studied using the effective imaging method known as MRI. A whole-brain, voxel-wise analytic method called voxel-based morphometry (VBM) evaluates variations in gray matter volume or concentration among groups of people over a period of time (34). Voxel-wise changes in the volume of gray matter or concentration among groups or situations can be found using the VBM approach, which is utilized to preprocessing T1-weighted MRI images. The distribution of structural differences can be shown spatially by superimposing the outcomes of statistical parametric maps into the brain model. It continues to be used in numerous study fields and has given important insights on alterations in structure of the brain linked to various illnesses and ailments (35). By analysing voxel-based morphometry (VBM) data, this research examines the anatomical variations in the brains of bipolar illness sufferers and healthy controls. This work seeks to advance the area through the use of more participants and standard methods in contrast to earlier VBM investigations, which were constrained by limited sample numbers or experimental variations. The study also takes into account the volumes of gray matter, white matter, and CSF.

The purpose of the study aims to employ VBM analysis to shed light on the cognitive deficiencies that underlie different types of bipolar disorder. Grey matter, white matter, and cerebrospinal fluid are the 3 primary elements that comprise the VBM process in brains of 44 healthy controls and 49 bipolar disorder persons among the available data. As the VBM has been pre-processed, the scans shall be subjected to statistical evaluation. Pre-processing procedures are performed before statistical evaluation on SPM12 in order to increase the correctness of the set of data that has been set forth. The results may have consequences for how bipolar disorder is understood and treated, and they could help with the creation of more focused therapy. Furthermore, the standard techniques employed in this experiment could be used as a guide in another research.

## 2. Materials and Methods

### 2.1. Participants

**Table 1** Information on the primary diagnosis and participant characteristics for those with bipolar disorder (BD).

| Diagnosis (DSM code) | Number |
|---|---|
| BP I, most recent episode hypomanic (296.40) | 4 |
| BP I, most recent episode manic, mild (296.41) | 2 |
| BP I, most recent episode moderate (296.42) | 1 |
| BP I, most recent episode manic, in partial remission (296.45) | 3 |
| BP I, most recent episode manic, in full remission (296.46) | 6 |
| BP I, most recent episode depressed, mild (296.51) | 2 |
| BP I, most recent episode depressed, moderate (296.52) | 4 |
| BP I, most recent episode depressed, severe without psychotic features (296.53) | 5 |
| BP I, most recent episode depressed, in partial remission (296.55) | 8 |
| BP I, most recent episode depressed, in full remission (296.56) | 5 |
| BP I, most recent episode mixed, moderate (296.62) | 1 |
| BP I, most recent episode mixed, severe with psychotic features (296.64) | 3 |
| BP I, most recent episode unspecified (296.70) | 5 |

DSM, Diagnostic and statistical manual of mental disorders

Healthy individuals were enlisted for the research from the Los Angeles region. An outreach program to nearby medical facilities as well as the internet sites was used to find subjects suffering from bipolar disorder. Those with long-term

diagnosis of bipolar I or II disorder, were not allowed to participate in the group of healthy individuals. A total of 44 healthy control volunteers and 49 bipolar disorder patients, who had been selected for gender, age, and educational attainment, participated in the research. Before participating in the study, each participant gave explicit permission and received payment to the time they spent.

The diagnoses were made using the Diagnostic and Statistical Manual of Mental Disorders. Left-handedness, insufficient vision to perceive task stimuli, MRI contraindications, Significant medical history, self-reported use of mood-altering medication on the scan day, or additional causes for which they weren't eligible to be examined have been omitted from the research. The parent study was used to find qualified English-speaking volunteers among the age range of 21 and 50. Tables 1 and 2 contain information on participant demographics, significant diagnoses in bipolar disorder patients, and medication. (36)

**Table 2** Patients with bipolar disorder (BD) by medication table**.**

| **Medication table** | **Number** |
|---|---|
| Anticonvulsant-mood stabilizer | 30 |
| Psychostimulant | 4 |
| Antidepressant | 15 |
| Antipsychotic | 22 |
| Sedative-Hypnotic | 3 |
| Analgesic | 2 |
| Hormone | 2 |
| Anxiolytic | 6 |
| Antiparkinsonia | 1 |
| Anticholinergic | 0 |
| Other | 4 |

### 2.2. MRI acquisition

Data for neuroimaging were collected using a 3T Siemens Trio scanner. The T2-weighted echoplanar imaging (EPI) sequence was used to acquire the functional MRI data, and the following settings were used: slice thickness = 4 mm, 34 slices, TR = 2 s, TE = 30 ms, flip angle = 90, matrix = 64 x 64, and FOV = 192 mm. Using the following settings, a T1-weighted high-resolution anatomical scan (MPRAGE) was collected: 250 mm FOV, 176 slices, 1 mm slice thickness, TR of 1.9 s, TE of 2.26 ms, matrix of 256 x 256.

Voxel-based morphometry

Image Preprocessing

MATLAB and the CAT12 toolbox (37,38) were used to evaluate voxel-based morphometry (VBM). Gray matter, white matter, and cerebrospinal fluid tissues were identified in 3D T1-weighted Neuroimaging Informatics Technology Initiative (NIFTI) MR scans applying the DARTEL technique with the default parameters of 1.5 mm cubic resolution in MNI space. The Jacobian determinant maps have been altered so they maintained the gray matter volumes in native space, and the normalized images had been smoothed with an 8-mm FWHM Gaussian kernel. The covariate total intracranial volume (TIV) has been employed.

### 2.3. Data analysis

The two-tailed test was then created using a 0.05 p-value and the family-wise error (FWE) correction. Then, the collected voxel regions of the brain utilizing significant differences, activation intensity (statistically evaluated using a t-test and reported as T value; T value is proportional to intensity), and activation volume (cluster), were examined employing the xjview (39) toolbox for MATLAB. The extent threshold of 100 voxels was selected. The VBM analysis process is graphically illustrated in Figure 1.

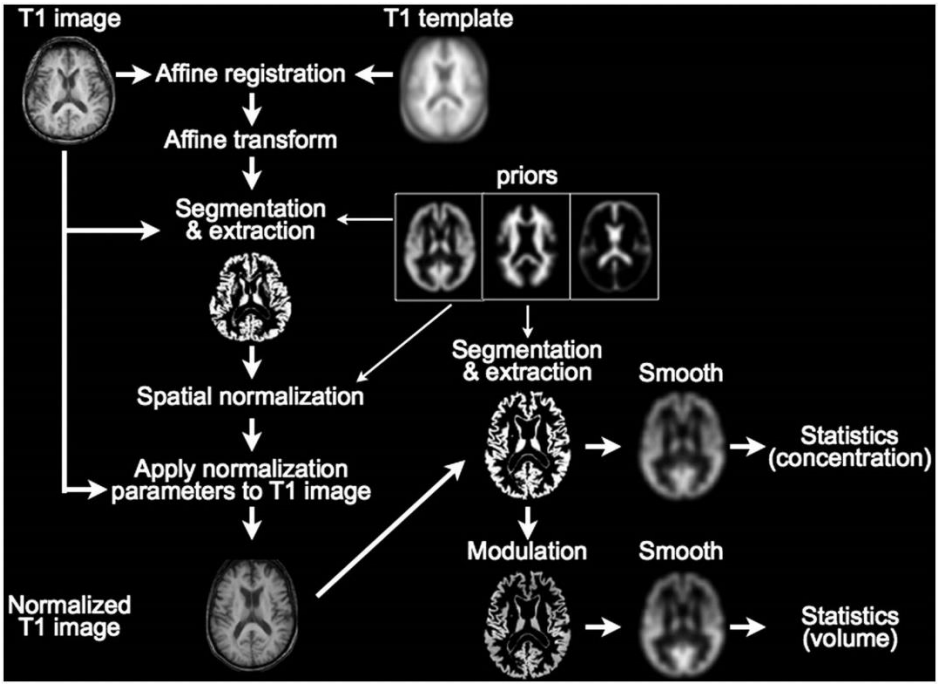


**Figure 1** The processing model for voxel-based morphometry (VBM).

### 2.4. Demographic and Neuropsychological Characterization of Participants

There are no obvious differences between the two groups upon the grounds of sex or ages ($p>0.05$) in the medical records of individuals and the medication consumed among the bipolar disorder category participants presented in Tables 1 and 2. The chi-square test was used to assess gender, and the t-test for independent samples were used to analyze the other parameters.

#### *2.4.1. Voxel-based morphometry analysis*

A voxel-by-voxel analytic method was used in the research for comparing the volumes of the white matter, cerebrospinal fluid, and gray matter among bipolar disorder individuals and healthy controls. The significance level in a t test with an extent threshold of K = 100 was set at $p<0.05$. The right superior frontal gyrus, left medial frontal gyrus, left inferior frontal gyrus, right superior frontal gyrus, right middle frontal gyrus, right superior temporal gyrus, right cuneus, and left postcentral gyrus, left inferior frontal gyrus, right precuneus, right inferior occipital gyrus, left precentral gyrus, and right precentral gyrus, all showed major decreases in gray matter (GM) volume when compared to healthy controls (Table 3, Figure 2, Figure 3, Figure 4, Figure 5 and Figure 6).

**Table 3** Evidence of gray matter alteration detected by voxel-based morphometry

| **Contrast** | **Regions** | **L/R** | **Voxels Size** | **Clusters Number** | **MNI coordinates(mm)** | | | **Voxel level** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | X | Y | Z | T-value | Z-value | P FWE corrected | P FDR corrected |
| BD < HC | Inferior Frontal Gyrus | L | 2603 | 2 | -44.60 | 34.64 | 15 | 5.13 | 5.03 | 0.008 | 0.005 |
| | Middle Frontal Gyrus | R | 512 | 23 | 40.73 | 51.34 | 15 | 4.29 | 4.15 | 0.244 | 0.012 |
| | Superior Frontal Gyrus | R | 697 | 25 | 8.40 | 51.34 | 28.99 | 4.97 | 4.89 | 0.535 | 0.016 |
| | Precentral Gyrus | L | 432 | 5 | -20.04 | -19.28 | 70.36 | 4.54 | 4.32 | 0.689 | 0.009 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Precentral Gyrus | R | 402 | 18 | 22.63 | -16.72 | 70.36 | 4.37 | 4.26 | 0.472 | 0.015 |
| | Medial Frontal Gyrus | L | 556 | 20 | -17.45 | 66.75 | 8.30 | 3.99 | 3.86 | 0.259 | 0.048 |
| | Superior Temporal Gyrus | R | 167 | 9 | 42.02 | -32.12 | 15 | 3.43 | 3.36 | 0.975 | 0.038 |
| | Precuneus | R | 27 | 7 | 13.57 | -53.95 | 54.85 | 3.48 | 3.35 | 0.962 | 0.039 |
| | Postcentral Gyrus | L | 8 | 16 | -51.07 | -18 | 44.5 | 3.35 | 3.26 | 0.992 | 0.041 |
| | Inferior Occipital Gyrus | R | 24 | 7 | 26.50 | -100.58 | -14.97 | 3.29 | 3.22 | 0.995 | 0.041 |
| | Cuneus | R | 15 | 23 | 7.11 | -78.35 | 8.30 | 3.11 | 3.02 | 0.921 | 0.046 |
| BD > HC | - | - | - | - | - | - | - | - | - | - | - |

White matter (WM) levels in the left lingual gyrus, right sub-gyral, left superior temporal gyrus, right middle occipital gyrus, left lingual gyrus, left sub-gyral, left superior parietal lobule, right precentral gyrus, right middle occipital gyrus, left inferior frontal gyrus, and left supramarginal gyrus, were all significantly lower among individuals with bipolar disorder (Table 4, Figure 7, Figure 8, Figure 9, and Figure 10). White matter is crucial because it facilitates information among various parts of the brain and connects them. In comparison to the controls, the BD class of patients showed no CSF volume in every area of the brain.

**Table 4** Evidence of white matter alteration detected by voxel-based morphometry

| **Contrast** | **Regions** | **L/R** | **Voxels Size** | **Clusters Number** | **MNI coordinates(mm)** | | | **Voxel level** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | X | Y | Z | T-value | Z-value | $P_{FWE\ corrected}$ | $P_{FDR\ corrected}$ |
| BD < HC | Inferior Frontal Gyrus | L | 392 | 13 | -52,50 | 31.50 | 15 | 4.16 | 4.03 | 0.361 | 0.013 |
| | Precentral Gyrus | R | 168 | 5 | 26.50 | -20.57 | 76.82 | 3.86 | 3.76 | 0.676 | 0.024 |
| | Superior Temporal Gyrus | L | 65 | 2 | -45.90 | -37.26 | 15 | 3.56 | 3.34 | 0.995 | 0.042 |
| | Sub-gyral | R | 162 | 6 | 39.43 | -59.09 | -4.63 | 3.51 | 3.30 | 0.677 | 0.028 |
| | Middle Occipital Gyrus | R | 2,953 | 5 | 39.43 | -83.49 | 7.01 | 4.37 | 4.21 | 0.193 | 0.012 |
| | Lingual Gyrus | L | 10 | 3 | -17.45 | -97.61 | -9.80 | 3.45 | 3.28 | 0.246 | 0.009 |
| | Supramarginal Gyrus | L | 34 | 7 | -31.68 | -53.95 | 35.45 | 3.39 | 3.21 | 0.743 | 0.038 |
| | Sub-gyral | L | 154 | 6 | -32.97 | -53.95 | 40.63 | 3.32 | 3.17 | 0.931 | 0.033 |
| | Superior Parietal Lobule | L | 487 | 27 | -30.32 | -59.09 | 44.50 | 3.21 | 3.08 | 0.981 | 0.046 |
| BD > HC | - | - | - | - | - | - | - | - | - | - | - |

## 3. Discussion

This research used voxel-by-voxel evaluation and the family-wise error correction approach to examine variations volume in the brain among individuals suffering from bipolar disorder and healthy controls. The right superior frontal gyrus, left medial frontal gyrus, left inferior frontal gyrus, right superior frontal gyrus, right middle frontal gyrus, right superior temporal gyrus, right cuneus, and left postcentral gyrus, left inferior frontal gyrus, right precuneus, right inferior occipital gyrus, left precentral gyrus, and right precentral gyrus, all showed major decreases in gray matter (GM) volume when compared to healthy controls. Moreover, white matter (WM) levels in the left lingual gyrus, right sub-gyral, left superior temporal gyrus, right middle occipital gyrus, left lingual gyrus, left sub-gyral, left superior parietal lobule, right precentral gyrus, right middle occipital gyrus, left inferior frontal gyrus, and left supramarginal gyrus, were all significantly lower among individuals with bipolar disorder. Furthermore, White matter is crucial because it facilitates information among various parts of the brain and connects them. In comparison to the controls, the BD class of patients showed no CSF volume in every area of the brain.

### 3.1. Gray and white matter reduction in frontal lobe

The frontal lobe has an impact on problem-solving, memory, spontaneity, initiation, planning, judgement, social behavior, working memory, and decision-making (40). The inferior frontal gyrus (IFG) plays a crucial role in the creation of speech, the understanding and use of language, as well as processing semantics (41). The precentral gyrus is crucial for more sophisticated brain functions like and decision-making, working memory, and attention (42).

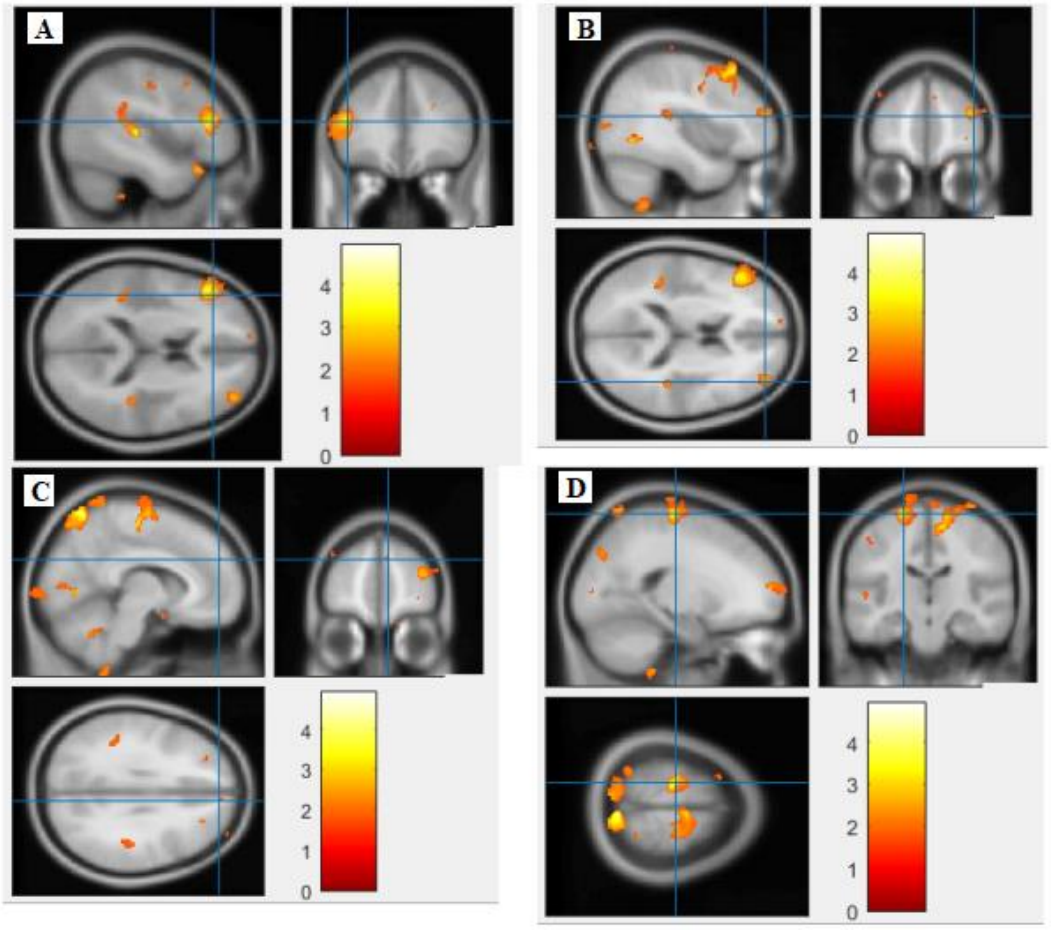


**Figure 2** Voxel-based morphometric analyses identified gray matter (GM) alterations in the Left inferior frontal gyrus (A), Right middle frontal gyrus (B), Right superior frontal gyrus (C), and left precentral gyrus (D), with statistical significance at $p<0.05$ and an extent threshold of $K = 100$ when BD<HC.

The inferior frontal gyrus and precentral gyrus of the frontal lobe have decreased gray matter and white matter, providing proof of the illness's neurological foundations. Decreased gray matter was also found in earlier studies. The studies are consistent with other studies for instance, white matter impairment, notably in the frontal lobes, was found

in adolescents with bipolar disorder in research using diffusion tensor imaging. In a comparison with healthy controls, their findings revealed significant white matter changes (43). Additionally, a study found less gray matter volume in the inferior frontal gyrus (44). However, other studies are inconsistent with this study, for instance, a study employing VBM results suggests that bipolar disorder individuals have more gray matter in their precentral gyrus (45).

The superior frontal gyrus affects difficult cognitive functions like problem-solving, working memory, attention, and decision-making (46). The middle frontal gyrus is situated beneath the superior frontal gyrus and plays a role in the processing of language (47). The medial frontal gyrus which is on top the corpus callosum and is connected to both cognitive and affective functions (48). The precentral gyrus is found in the primary motor cortex of the brain. In a different study (49), less white matter but no gray matter was discovered in the superior frontal gyrus. The results, however, differ from those of previous research. For example, bipolar patients had less gray matter in the left precentral gyrus than healthy subjects who were not related (50). Moreover, a voxel-wise meta-analysis research found patients with bipolar illness have gray matter anomalies in the medial frontal gyrus and other parts of the brain (51). In patients with MDD, a VBM investigation discovered gray matter volume in the superior frontal gyrus and medial frontal gyrus (52). Additionally, another study revealed that the superior frontal gyrus along with additional parts of the brain had less gray matter (53).

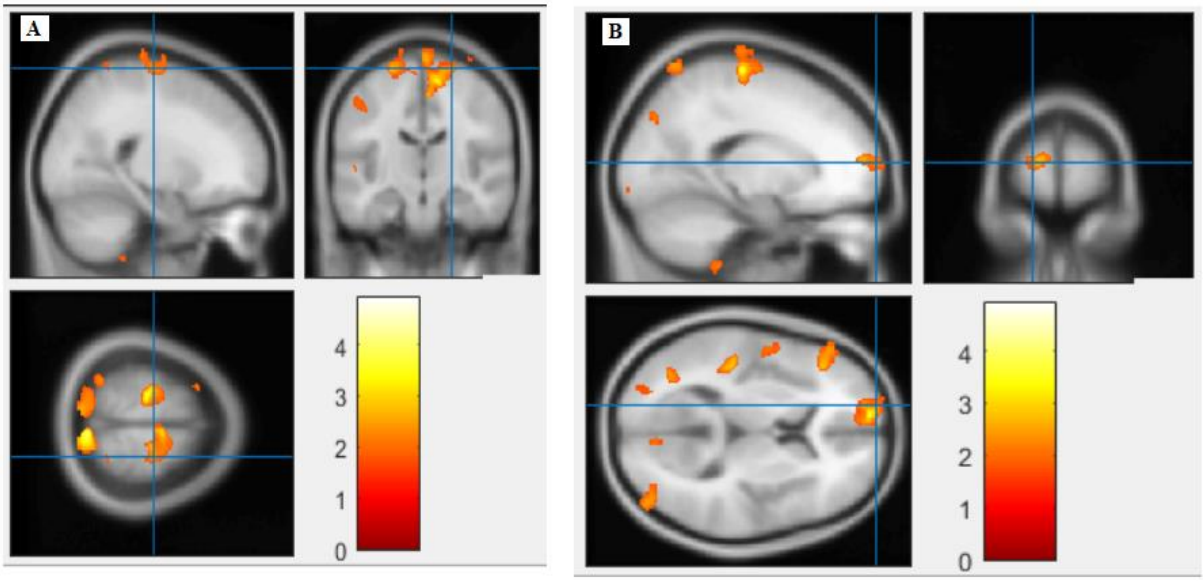


**Figure 3** Voxel-based morphometric analyses identified gray matter (GM) alterations in the Right precentral gyrus (A), and left medial frontal gyrus (B), with statistical significance at $p<0.05$ and an extent threshold of K =100 when BD<HC.

### 3.2. Gray and white matter reduction in the temporal lobe

The temporal lobe is a part of the brain that manages and stores emotions, language, hearing, and long-term memory (54). The superior temporal gyrus has Numerous functions in language processing, auditory perception, memory, attention, social cognition, and other activities. Receptive aphasia may develop as a result of harm to the superior temporal gyrus (55). Additionally, abnormalities in the superior temporal gyrus have been found in bipolar illness individuals in earlier studies. One study found less gray matter volume in the superior temporal gyrus was reported in a different investigation employing voxel-based morphometry analysis, which was connected with mental impairments (48). According to another study's findings, bipolar illness type II patients had significantly lower gray matter volumes in the left superior temporal gyrus (56). Furthermore, according to the research's outcomes, bipolar disorder patients have a reduced amount of gray matter volume than healthy people in the left superior temporal gyrus along with various areas of the brain (57).

The sub-gyral is crucial in spatial processing, memory, and emotion, which are all performed by a part of the temporal lobe. It consists of the entorhinal cortex, perirhinal cortex, fusiform gyrus, amygdala, basal temporal cortex, and inferotemporal cortex (58). It also contains the hippocampus, amygdala, parahippocampal gyrus, and amygdala. There may be cognitive anomalies and deficits as a result of harm caused to such regions (58). One study using diffusion tensor imaging (DTI) identified white matter anomalies in the sub-gyral area compared to earlier research (41). Additionally,

the outcome conflicts with findings from various studies, such as a study showed the sub-gyral and right superior temporal gyrus both had significantly decreased GMV in CSVD patients with sleep disruption (59).

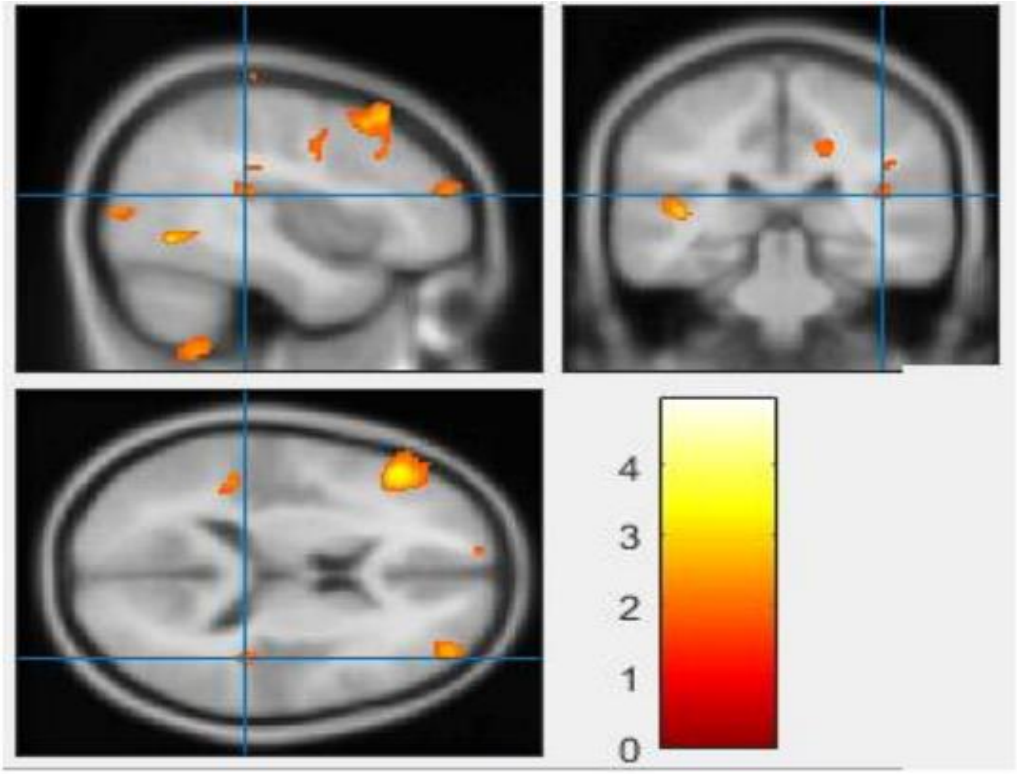


**Figure 4** Voxel-based morphometric analyses identified gray matter (GM) alterations in the Right superior temporal gyrus with statistical significance at p<0.05 and an extent threshold of K =100 when BD<HC.

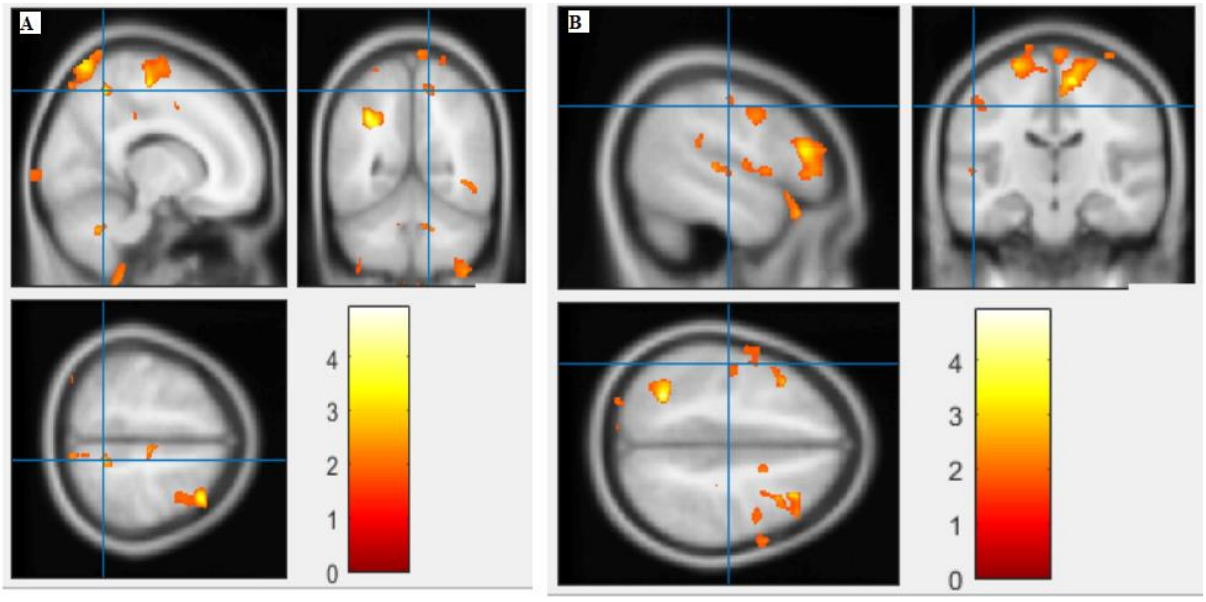


**Figure 5** Voxel-based morphometric analyses identified gray matter (GM) alterations in the Right precuneus (A), and left postcentral gyrus (B), with statistical significance at p<0.05 and an extent threshold of K =100 when BD<HC.

### 3.3. Gray and White Matter Reduction in Parietal Lobe

The parietal lobe is in charge of interpreting sensory information like pain, pressure, temperature, and touch (59). The parietal lobe's postcentral gyrus is where sensory information is processed (60). The precuneus, which is located in the medial parietal lobe along the middle line, is in charge of cognitive functions like self-awareness, memory, perception,

and consciousness. The precuneus has been associated with neurological and behavioral issues (61). Patients with bipolar disorder have less gray matter in the precuneus and postcentral gyrus compared to a number of research. A study showed compared to healthy controls, patients have significantly reduced gray matter volumes in the postcentral gyrus (62). Further, according to another study, in comparison with healthy controls, methadone maintenance patients exhibited less gray matter volume in the postcentral gyrus along with various regions of the brain (59). Also, a reduction in postcentral gyrus gray matter volume was discovered by another investigation (60). The results obtained here demonstrate that our findings are consistent with past studies.

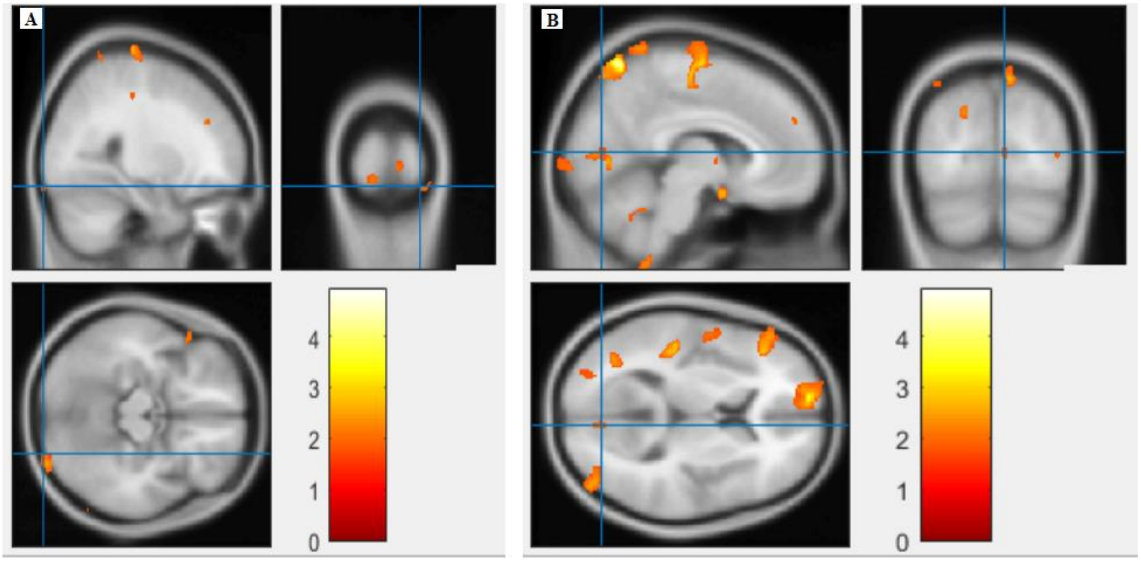


**Figure 6** Voxel-based morphometric analyses identified gray matter (GM) alterations in the Right inferior occipital gyrus (A), and Right cuneus (B), with statistical significance at p<0.05 and an extent threshold of K =100 when BD<HC.

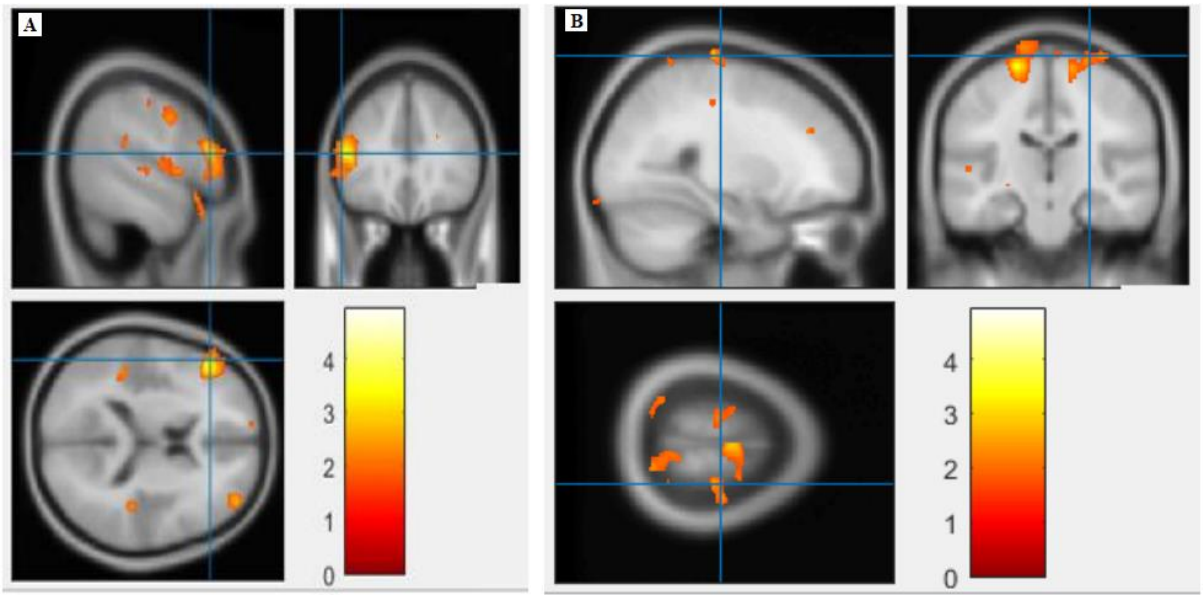


**Figure 7** Voxel-based morphometric analyses identified white matter (WM) alterations in the Left inferior frontal gyrus (A), and right precentral gyrus (B), with statistical significance at p<0.05 and an extent threshold of K =100 when BD<HC.

The supramarginal gyrus is crucial for perception, social cognition, and language, and the superior parietal lobule supports perception of space (61). the superior parietal lobule (SPL) is used in order to create a cohesive perception of the surroundings, and combined sensory data (62). The parietal lobe sub-gyral region is crucial for a variety of cognitive functions, including attention, perception, spatial awareness, and sensory processing (63). Bipolar disorder has been linked to reduced white matter volume in the superior parietal lobule, sub-gyral, and supramarginal gyrus. One study

found reduced gray matter and no changes to the white matter were observed in the superior parietal lobule along with various brain areas (64). Moreover, the supramarginal gyrus and other particular brain regions with psychotic symptoms and bipolar disorder have decreased gray matter volumes, according to the study (65). Here, the outcome is conflicting with previous research.

### 3.4. Gray and White Matter Reduction in Occipital Lobe

The occipital lobe constitutes one among the primary lobes of the brain and is in charge of analysing visual data (66). Visual issues such as hallucinations, blindness, or difficulty recognizing people and things can result from injuries to the occipital lobe (67). The inferior occipital gyrus handles visual information linked to object recognition and perception (68). The cuneus, an area of the occipital lobe which resembles a wedge, manages the analysis of basic visual stimuli, regulates attention to visuals, and takes role in complex cognitive processes (69). One study showed individuals with bipolar disorder show less gray matter in the cuneus, inferior occipital gyrus, and various regions of the brain (64). Additionally, individuals with bipolar disorder who struggle with episodic memory have less gray matter in the cuneus according to a different study (70). Here, evidence from earlier investigations supported our conclusions.

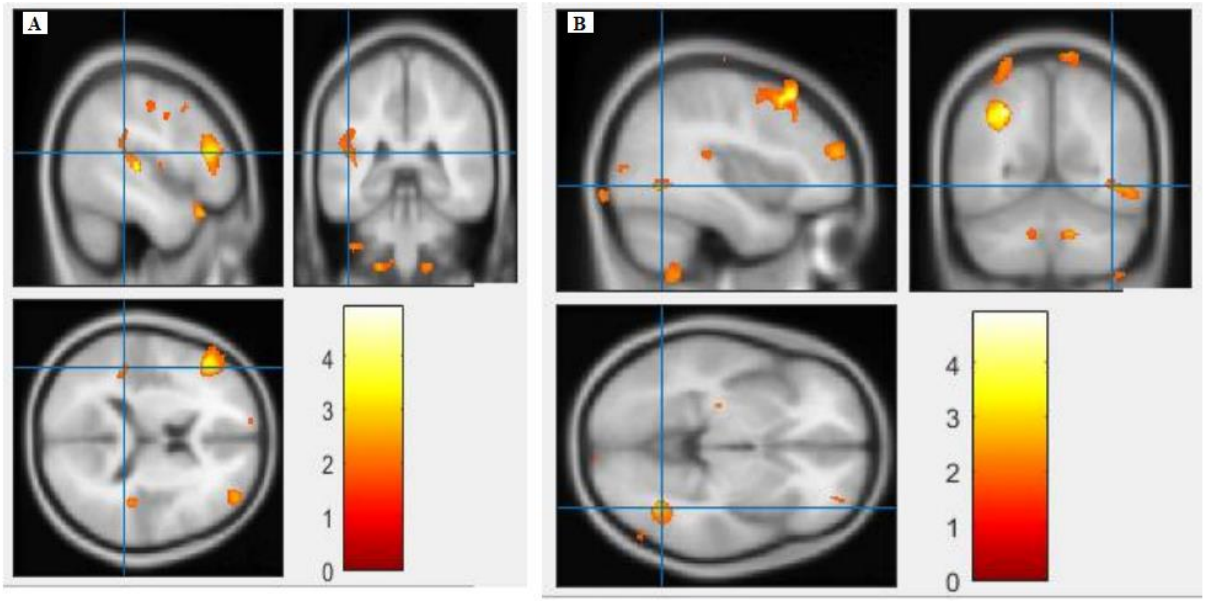


**Figure 8** Voxel-based morphometric analyses identified white matter (WM) alterations in the Left superior temporal gyrus (A), and right sub-gyral (B), with statistical significance at $p<0.05$ and an extent threshold of K =100 when BD<HC.

The middle occipital gyrus is crucial for handling visual information related to depth perception, motion, and object recognition (67). The lingual gyrus plays a crucial role in interpreting visual information related to shape perception and color as well as memory of visuals (71). A study found the lingual gyrus as well as various areas of the brain showed a reduction in gray matter in the study's bipolar disorder I participants compared the healthy families, but there were no changes to the white matter in accordance with the research using a combination of voxel-based morphometry (VBM) and source-based morphometry (SBM), Euthymic kids who have bipolar disorder had drastically different white and gray matter volumes in multiple areas of the brain, including the lingual gyrus, and middle occipital gyrus in comparison with healthy controls (72). However, another study found reduced gray matter in the lingual gyrus and the middle occipital gyrus including various regions of the brain (64).

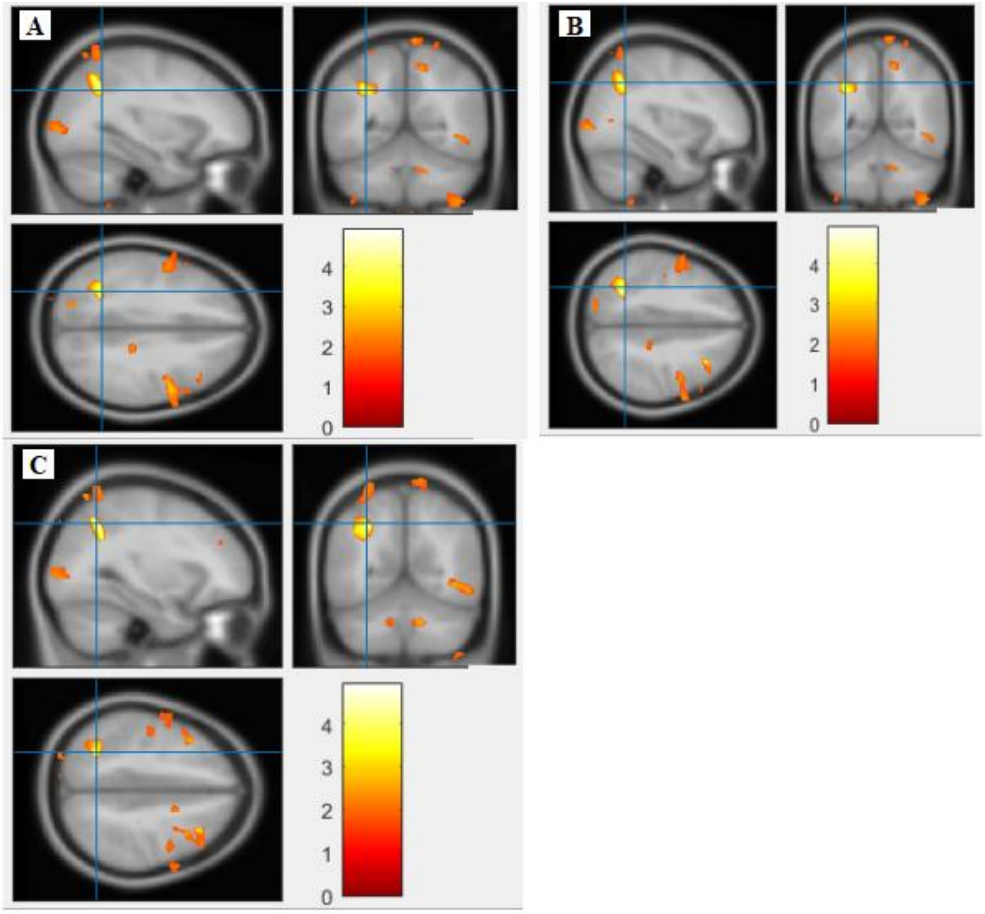


**Figure 9** Voxel-based morphometric analyses identified white matter (WM) alterations in the Left supramarginal gyrus (A), Left sub-gyral (B), and left superior parietal lobule (C), with statistical significance at p<0.05 and an extent threshold of K =100 when BD<HC.

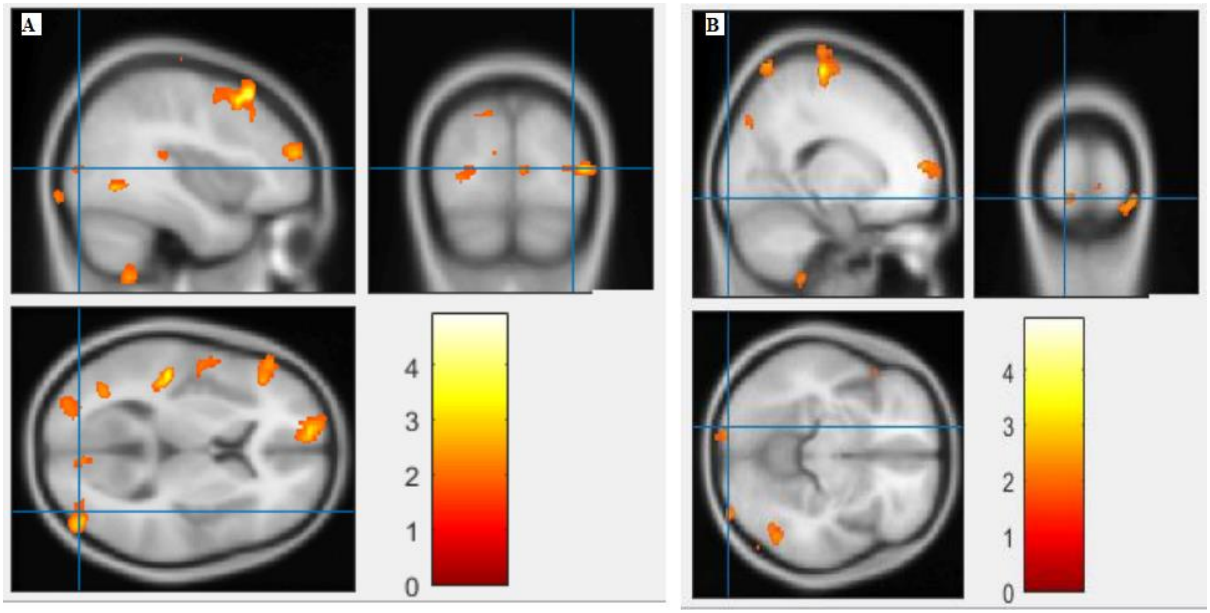


**Figure 10** Voxel-based morphometric analyses identified white matter (WM) alterations in the Right middle occipital gyrus (A), and left lingual gyrus (B), with statistical significance at p<0.05 and an extent threshold of K =100 when BD<HC.

### *Limitations and Future Directions*

The cross-sectional anatomy of the brain limits the ability to establish a causal connection among the structural defects of the brain that have been found with bipolar disorder. Long-term investigations are necessary to determine if these alterations are brought on by the illness or show a previously existing dependability.

This research examined structural anomalies in people with bipolar illness however did not examine whether such alterations relate to specific medical signs or mental health issues. In order to assess possible variations in brain structure among bipolar illness subgroups as well as to determine the generality of the results, more sample numbers are required.

Lastly, the research depended mainly on structural magnetic resonance imaging (MRI) records, thus unlikely to shed light on other possible aspects such as metabolism in the brain, connection, or activity related to function. Future studies must take into account using a comprehensive strategy to look at the relationship between brain shape, function, as well as medical signs in bipolar illness patients.

## 4. Conclusion

This study compared the brain anatomy of 44 healthy individuals and 49 individuals who had bipolar disorder. Bipolar disorder individuals showed reduced gray matter and white matter volumes in comparison with controls, especially in the parietal, temporal, occipital, and frontal lobes, with no changes in cerebrospinal fluid. The results of this study might lead to the development of more specific and effective bipolar disorder medications. It showed how important brain areas involved in cognitive suffered neuroanatomical change in bipolar disorder. The study emphasizes the requirement on additional investigation to completely comprehend the practical consequences of those aberrations and the possible consequences on the disorder's medication and diagnosis.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest was declared by the Authors.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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