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Article *in* Neurosciences · July 2015

DOI: 10.17712/nsj.2015.3.20140757 · Source: PubMed

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Alterations of the occipital lobe in schizophrenia

Hassaan Tohid, *MBBS,* ***Muhammad Faizan,*** *MBBS,* ***Uzma Faizan,*** *MBBS.*

ABSTRACT

إن العلاقة بين الفص القذالي من الدماغ مع مرض انفصام الشخصية لم يدرس جيداً، ولكن يعتبر هذا الموضوع أساسياً بين الأطباء والعلماء. أجرينا هذه المراجعة المنهجية لإيضاح العلاقة بشكل أعمق. وجدنا أن معظم مرضى الفصام يظهر التشريح القذالي بشكل طبيعي وعلم وظائف الأعضاء أظهرت أقلية تضاءل القيم وبعض من وظائفه والهيكلة. النتائج التي توصل إليها شاقة كي تدرج ضمن نماذج المرض الواحد الذي يقدم مشاركة الفص القذالي في مرض الفصام. تقدم مرض الفصام سريرياً في منتصف العشرينات والثلاثينات والتنبؤ بها غير كافية. التغيرات في حجم والمادة الرمادية والمادة البيضاء في الفص القذالي واضحة تماماً، ولكن آلية هذه المشاركة ليست مفهومة تماماً حتى الآن. ولذلك، فإننا نوصي بمزيد من البحث لاستكشاف وظائف الفص القذالي وأحجامه عبر مراحل مختلفة من الفصام.

The relationship of the occipital lobe of the brain with schizophrenia is not commonly studied; however, this topic is considered an essential subject matter among clinicians and scientists. We conducted this systematic review to elaborate the relationship in depth. We found that most schizophrenic patients show normal occipital anatomy and physiology, a minority showed dwindled values, and some demonstrated augmented function and structure. The findings are laborious to incorporate within single disease models that present the involvement of the occipital lobe in schizophrenia. Schizophrenia progresses clinically in the mid-twenties and thirties and its prognosis is inadequate. Changes in the volume, the gray matter, and the white matter in the occipital lobe are quite evident; however, the mechanism behind this involvement is not yet fully understood. Therefore, we recommend further research to explore the occipital lobe functions and volumes across the different stages of schizophrenia.

Neurosciences 2015; Vol. 20 (3): 213-224
doi: 10.17712/nsj.2015.3.20140757

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Schizophrenia was first studied by a German psychiatrist named Dr. Emil Kraepelin in the year 1887. He believed that it was an organic brain disease. However, it was another scientist named Alzheimer who studied the neuropathological aspects of schizophrenia in far more detail and brought an explanatory clarification of the disorder to surface.[1,2] In this introduction, we briefly describe what schizophrenia is, what parts of the brain it affects, what is known and unknown of the association of the occipital lobe with schizophrenia. Schizophrenia is a severe chronic mental disorder that consists of positive and negative symptoms. The positive symptoms comprise hallucinations, delusions, disorganized speech, and behavior. While the negative symptoms consist of flat affect, alogia, and avolition, in addition, it also causes significant social and occupational dysfunction.[3] The disorder can develop as early as the age of 5; however, it is extremely rare in early childhood. Most men become ill between the ages of 16 and 25 whereas most women start showing symptoms between the ages of 25 and 30. Despite the age differences in the development between men and women, the risk for schizophrenia remains equal in both genders. What causes schizophrenia is still a topic of debate. However, it is commonly believed to be an amalgamation of multiple factors including genetics, some pre-natal viruses, and brain damage early in life leading to neurotransmitter problems in the brain.[4] The fragments of the brain most commonly known to be affected in schizophrenia are the forebrain, hindbrain, and the limbic system. It is believed that schizophrenia may be caused by a disruption in some of the functional

Disclosure. The authors declare no conflicting interests, support or funding from any drug company.

circuits in the brain, rather than a single abnormality in one part of the brain. However, complete knowledge about the areas of the brain involved is yet to be acquired. Therefore, it is estimated that the temporal lobe, limbic system (specifically the cingulate gyrus, the amygdala, and the hippocampus), frontal lobe, and the thalamus could be involved. The cerebellum is also thought to be affected in people suffering from schizophrenia. Moreover, various structural changes are seen in the schizophrenic patient's brain on structural MRI. Most of these changes are observed in the forebrain. Some other interesting structural and functional MRI (fMRI) findings in schizophrenic patients are; decreased volume of gray matter (frontal lobe), and reduced activity, and brain volume. The ventricles and the basal nuclei in the brain of a schizophrenic patient are frequently found to be larger than normal. While the hippocampus and amygdala are often smaller in size as compared to people not suffering from schizophrenia. The disorder is also found to be associated with changes in blood flow to certain parts of the human brain.[5] It is also believed that the occipital lobe is likely to be involved in schizophrenia, since the increased knowledge of the role of γ-amino butyric acid (GABA) receptors in vision and N-Methyl-D-aspartate (NMDA) is brought to surface in the recent scientific literature.[6,7] Schizophrenia has been associated with altered structure and function of the occipital cortex. Proper knowledge of any brain changes in schizophrenic patients may provide a deeper understanding of the alterations in brain development linked with the onset or progression of the illness.[8] Schizophrenia affects almost all parts of the brain; however, in this article our primary focus is the relevance of schizophrenia with the occipital lobe.

Little is known about the association of schizophrenia with the occipital lobe. The association of visual hallucination with occipital lobe damage in schizophrenia is already known, however, whether the visual symptoms exacerbate if the occipital lobe is severely damaged is not yet known. Whether the whole occipital lobe is involved in schizophrenia or just some part of it is involved also remains an unsolved mystery. If all lobes are involved, then what is the sequence of damage (is the occipital lobe damaged before the other lobes or after the involvement of other lobes of the brain). Can we prevent the occipital lobe involvement in schizophrenia or not? Whether there are specific kinds of neurons that are damaged or affected in the occipital lobe of a schizophrenic patient, is also not known.

We conducted this systematic review that reports results of people with schizophrenia and its relevance to the occipital lobe. Reviews on the occipital lobe in schizophrenia were conducted in PubMed, MEDLINE, PubMed Central, Journal of Neural Transmission, Oxford Journal, Psych Central, PsycINFO, Schizophrenia library, Cochrane library, and various newspapers. Cross checking of references led to the identification of additional relevant references. The decision to include or exclude reviews and data extraction was completed by the authors, and any disagreements were settled by discussion. The articles with real human patient data were included. Articles with patients of schizophrenia, psychosis, and schizoaffective disorder were thoroughly searched and later the articles focusing mostly on schizophrenia were included. While the reviews with high possibility of bias and the studies with blurred/mixed and confusing data was excluded. Any studies published in non-popular journals were also excluded to maintain the high standard of the review. Moreover, the animal data studies were also excluded to maintain the study totally human brain focused. A total of 773 articles were initially reviewed and 82 were included based on their relevance to schizophrenia and its association with the occipital lobe. Keywords included but were not limited to schizophrenia, the occipital lobe, schizophrenia and the occipital lobe, visual cortex damage, vision science, neuro imaging (CT, MRI), the occipital lobe asymmetries and schizophrenia, the occipital psychosis, schizo-occipital psychosis and the brain lobes and schizophrenia.

The occipital lobe and schizophrenia. The anatomical structure. The occipital lobe is popularly known to be associated with the sense of vision. This triangular shaped part of the brain is situated posterior to the parietal lobe. It is delineated on the medial side by the parieto-occipital (PO) sulcus. The lateral side is delineated by an imaginary line that connects the PO sulcus to the pre-occipital notch (known as the parieto-temporal lateral line). The inferior tentorial surface is delineated by a line connecting the pre-occipital notch to the beginning of the PO sulcus, at this point it manifests from the calcarine sulcus. Three Brodmann areas (areas: 17, 18, and 19) are also situated in the occipital lobe. On its medial surface, there is the cuneus, a gyrus localized between the calcarine sulcus and the PO sulcus. The lingual gyrus is present, in the tentorial surface of the occipital lobe (inferior to the calcarine sulcus); this lingual gyrus is separated from the fusiform gyrus by the collateral sulcus. The fusiform gyrus is delineated laterally by the occipitotemporal sulcus.[9]

Occipital lobe lesions and their neuro psychiatric manifestations. Occipital lobe epilepsy. Occipital epilepsy is not as common as other kinds of epilepsies. It is not commonly known amongst the clinical and non-clinical

fraternity, mostly because of its rarity with a prevalence of around 1.2-2.6% cases among the overall cases of epilepsy.[10] The hallmark of the occipital seizures are the visual hallucinations, however, they are not present in every case of occipital seizures. Hallucinations usually initiate in the visual field contralateral to the affected visual cortex, and later disseminate to encompass the whole visual field. Transient visual symptoms that may be either the more commonly seen positive symptoms (like phosphenes and flashes) or negative symptoms like (amaurosis, hemianopia, and scotoma) are commonly felt by the patients. Static or mobile flashes, which are the positive symptoms could be considered as the distinctive feature of occipital lobe involvement. The visual hallucinations become colorful and complex, if there is an involvement of the occipito-temporal cortex, with scenes of varying complexity.[11,12]

Occipital lobe infarction. In comparison with infarctions of other areas of the brain, the occipital lobe infarctions differ in etiology, risk factors, and prognosis.[13] Patients with infarctions exclusive to the occipital lobe generally have no other neurological loss besides visual-field loss, and are relatively facile to handle than the patients who have numerous infarctions or have infarctions to other areas of the brain. Visual-field loss from the occipital lobe damage can be managed propitiously and aptly with the optical systems and/or visual rehabilitation. The extent and location of the visual field damage, functional visual needs, and health concerns including personal concerns of the patient are commonly known management factors.[14]

Dream loss in stroke patients linked to occipital damage. Waknine in 2004[15] reported that patients with deep bilateral occipital lobe damage complain of total dream loss. This happens in normal sleep (REM). Moreover, the 'minimal lesion extension,' which is obligatory for ensuing Charcot-Wilbrand Syndrome (CWS), may be represented by deep bilateral occipital lobe damage with the right inferior lingual gyrus. This study advocated that CWS can depict a discrete and secluded neuropsychological symptom of deep occipital lobe damage, and may occur even in the absence of measurable REM sleep aberrations and other cognitive deficits.

Early visual processing. In the context of social perception, visual social information proceeds through the ventral stream during the early visual processing, and then is sent to regions such as the prefrontal cortex when higher order cognitive processing is necessary. It is reported that face processing transpires in the ventral stream, and position of activation is contingent upon task, indicating a hierarchical arrangement of the ventral stream.[16] Categorically, the thalamus may be turned on by the faces, temporo-occipital cortex, fusiform, para cingulate gyrus and lingual gyrus,[17] while face and body stimuli also actuate the superior temporal sulcus and middle occipital gyrus.[18] The ventral stream may also be linked in the perception of emotional stimuli, via significant connectivity with the amygdala.[19] Along these lines, in the ambience of early visual processing, emotional and social information is processed in the ventral stream, in conjunction with the thalamus, temporal, and occipital lobes.

The occipital lobe in schizophrenia. Schizophrenia as already known, consists of delusions, hallucinations, disorganized speech and behavior, and other symptoms, which lead to serious social and occupational problems.[20] Presently, here is no lab test to diagnose schizophrenia. However, we believe that the structural MRI and functional MRI could be the future diagnostic modality for the accurate diagnosis of schizophrenia in the 21st century. According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (DSM-V),[21] in order to be diagnosed with schizophrenia, the patient must have experienced at least 2 of the following symptoms: delusions, hallucinations, disorganized speech, disorganized or catatonic behavior, negative symptoms. At least one of the symptoms must be the presence of delusions, hallucinations, or disorganized speech. Uninterrupted manifestations of the distress must persist for a minimum of 6 months. During this phase the patient must experience at least one month of active symptoms, with social and/or occupational problems occurring over a notable period of time. These problems, however, must not be attributable to any other condition. Schizophrenia subtypes like residual, catatonic, undifferentiated, and paranoid schizophrenia were removed from the DSM-V by the American Psychiatric Association (APA) because they did not appear to be helpful for providing better treatment or predicting treatment response.[22]

Structural imaging studies with occipital lobe involvement in schizophrenia. There is enough evidence to support the notion of a reduction in the overall volume of the occipital lobe in schizophrenic patients.[23-25] Seven axial MRI sections were used by Zipursky and his team for segmentation.[26] They noticed reduction in the volume of gray matter in the occipital lobe in the participating patients. While, another group of scientist reported no group differences between the schizophrenic patients and controls in the occipital lobe.[27] Moreover, decreased gray matter in the areas associated with the occipital lobe in schizophrenic patients is also reported in voxel based morphometric studies[28] and various other

studies.[29] There is a lack of extensive previous studies on occipital bone depth. However, later in the 20th century Daniel et al,[30] measured occipital bone depth and the occipito median angle in patients with chronic schizophrenia and medical controls. Cranial asymmetry measures among the medical controls and the schizophrenic patients were almost equal. Nonetheless, in right-handed participants with homolateral sighting dominance, a debilitating progression was noticed for more symmetrical tilting along the sagittal suture in the patients suffering from schizophrenia. Cranial asymmetry was able to prophesize increased prefrontal markings in the patients of schizophrenia.[30]

Phillips et al[31] used high-resolution structural and diffusion tensor images and cortical pattern matching methods to juxtapose general and local variations in exterior white matter fractional anisotropy between schizophrenic patients and their relatives, and community comparison subjects and their relatives. Schizophrenic patients showed reduced external white matter fractional anisotropy dispersed crosswise in each hemisphere, especially in the left temporal and bilateral occipital lobes, as compared with control subjects. Additionally, patient relatives, and control subjects, by modeling biological risk for schizophrenia in participants, fractional anisotropy was shown to differ in accordance with relatedness to a patient in both hemispheres and in the occipital and temporal areas. Nevertheless, correction procedures were not survived by the effects, for 2 group comparisons between control subjects and patient relatives.[31]

A comparison of microstructural diffusion related parameters by whole brain voxel wise map between schizophrenia into its deficit (SZD) and non-deficit (SZND) subtypes indicated that the radial diffusivity was higher in the left forceps minor of SZD patients, in the left internal capsule of SZND patients, and in the right inferior fronto-occipital fasciculus in the whole schizophrenia group. Mean diffusivity was increased from healthy controls to SZD patients to SZND patients in the right occipital lobe.[32]

Another study revealed that the long duration of untreated psychosis was associated with the temporal and occipitotemporal gray matter volume decrease in treatment naive (treated for the first time) schizophrenia.[33] It is also found that the schizophrenic patients have remarkably lower fractional anisotropy in the temporal (superior temporal and parahippocampal) and occipital (superior and middle the occipital) white matter compared with patients with bipolar disorder and healthy volunteers. The temporal and occipital lobe white matter shortfall can also exacerbate the chances of acquiring schizophrenia.[34] In some schizophrenic patients, gray matter density increase in the left occipital lobe and basal ganglia exists.[35] Fujimoto et al[36] studied the imaginary coherence of gamma frequency oscillations with male schizophrenic participants. They found a positive correlation of auditory hallucination and the left occipital and right frontoparietal lobe areas.

In a study involving the first episode schizophrenia patients,[37] diffusion tensor imaging (DTI) with voxel-wised analysis of the fractional anisotropy (FA) indicated aberrations in white matter. Cingulum bundle, the left inferior fronto-occipital fasciculus, the left inferior longitudinal fasciculus and the interhemispheric fibers running through the corpus callosum were shown to be involved by fiber tracking.

Wei and his team in 2012[38] investigated the roles of DTI of white matter at an early stage of the disorder. They found a noteworthy decrease of regional white matter functional anisotropy values in the right anterior and right middle occipital lobe. The study concluded that the decreased white matter in the right anterior cingulated and middle occipital lobe may help in an early diagnosis. It is also reported that the schizophrenic patients with a more serious and debilitating disease possess larger ventricles, smaller prefrontal, temporal and occipital cortices, and smaller subcortical regions.[39] The modified white matter solidarity of the left precentral gyrus, cerebellum anterior lobe and occipital lobe could be associated in the neural process of impetuous behaviors in schizophrenia.[40] Notable reductions of gray matter are seen in first episode drug naive schizophrenia in bilateral temporal lobe, bilateral occipital lobe, left insula, left frontal lobe superior frontal gyrus, and right lentiform nucleus medial globus pallidus. The unaffected siblings of the same schizophrenic patients, showed remarkable decreases of gray matter especially in the right temporal lobe, bilateral the occipital lobe, and left insula. Studies like these supported the genetic linkage of the mental disorder.[41] However, the reduction was mostly evident in the lateral occipital cortex (in the ventral stream) according to another imaging study.[42]

According to Chan et al,[43] first episode schizophrenic patients have lower white matter volume (right temporo-occipital region). Diffusion anisotropy in the right temporo-occipital region disclosed lower planar anisotropy, and higher linear anisotropy (p=0.012) in schizophrenics. Moreover, the facial emotion recognition subtask demonstrated a noteworthy relationship with FA reductions in the left occipital white matter and left posterior callosal area.[44]

A gradual reduction of gray matter volume in the frontal, temporal, parietal, and occipital lobes of

schizophrenic patients was demonstrated. The study suggested that an earlier onset of psychosis especially in schizophrenic patients is associated with an earlier disease related disruption of anatomical brain growth.[45] Another important structural imagining study revealed a significant reduction in FA in schizophrenics. This is observed in most major white matter (WM) tracts (corpus callosum, superior and inferior longitudinal fasciculi, inferior fronto-occipital fasciculus, and posterior thalamic radiation).[46]

Functional occipital lobe abnormalities in schizophrenia (fMRI). Evidence demonstrates that the population suffering from schizophrenia has decreased activity in the middle occipital gyrus during decision-making assignments. Moderate quality evidence shows decreased functional activity in the right lingual gyrus during episodic memory encoding, and decreased activation of the fusiform gyrus during episodic memory recovery in the patients suffering from schizophrenia as compared with control groups. In addition, moderate quality evidence advocates that schizophrenic patients demonstrate reduced activation during emotion processing tasks in the lentiform, fusiform, and middle occipital gyri. During unequivocal emotional tasks, schizophrenic patients exhibit decreased activation in fusiform gyrus, while implicit emotion was associated with decreased volume in the middle occipital gyri.[47-50] Complete brain inspection in patients has also demonstrated subsequent memory activation in the occipital pole, lateral occipital cortex, left inferior temporal gyrus, and fusiform cortex.[51]

Temporo-occipital and parietal region hyper-activations were also later found by a group of researchers in schizophrenic patients.[52] During processing of task-irrelevant aversive pictures relative to neutral pictures, the familial risk group demonstrated less activation of the anterior cingulate cortex, with reduced age related engagement of the inferior prefrontal and occipital parts of the brain. Furthermore, age-related adjustment in enrolment of the frontal, insular, thalamic, and other temporal and occipital parts of the brain could reveal growth changes in the operation of these circuits in people in jeopardy of acquiring schizophrenia.[53] Loss in facial emotion recognition is linked with temporo-occipital gray matter volume decrease,[54] while in some patients decreased overall occipital activation volume is seen.[55]

Decreased coupling was most noticeable between fronto-parietal cortical regions and subcortical structures, and between the frontal and occipital regions. Moreover, an increased bond was found among the limbic and frontal zones, and for temporo-occipital coupling.[56] While, there have been no variance in temporal, posterior parietal, or occipito-cortex connectivity with the thalamus.[57] A study with mapping statistics divulged that the delusion misattribution was linked with thickness in the orbitofrontal cortex (Brodmann's area [BA] 11/47). On the other hand, delusion, flat affect, and asociality misattribution was associated with cortical thinness in the dorsolateral prefrontal cortex (BA 9/46).[58]

Hoptman et al,[59] studied functional connectivity between homotopic points in the brain using voxel-mirrored homotopic connectivity (VMHC). They performed VMHC research on resting state fMRI data. They found notable reductions in VMHC in patients in the occipital lobe, thalamus, and cerebellum. Early onset schizophrenia patients demonstrate atypical reduction in the connection of the dorsolateral prefrontal cortex with the anterior cingulate cortex, inferior parietal lobule, and middle occipital gyrus.[60]

Fujimoto T et al[61] conducted a research on schizophrenic patients. They collected some images in functional map of event-related desynchronization (ERD) and synchronization (ERS) in theta, lower alpha (8-10 Hz), upper alpha (10-13 Hz), and beta bands. The ERD/ERS changes were noted in the left temporal pole and midline frontal and anterior cingulate cortex in theta ERS, occipital lobe in alpha ERS, and right temporal-frontal-parietal, midline frontal, and anterior cingulate cortex in beta ERD.[61] In some other imaging studies, all night sleep data was analyzed by period amplitude analysis. Delta waves during sleep in the bilateral frontal, central, parietal, and occipital areas of the brain were studied. It was observed that the patients had lower total delta wave counts during all-night sleep.[62] A psychophysiological interaction analysis of the dorsal anterior cingulate cortex revealed that the activity in the occipital cortex is related to bad social adjustment and impaired social cognition.[63] Furthermore, it is also studied that fMRI showed 3 brain networks interrupted in children and adolescents with schizophrenia. These networks included the anterior cingulate and the temporal lobes, cerebellum with subcortical regions, and occipital lobe and the cerebellum. Early-onset schizophrenic patients showed abnormal functional connectivity in the networks involving the temporal lobe, limbic, cerebellum, and early visual processing streams.[64]

According to a research by Hartberg et al,[65] a positive relation was present between the frontal, temporal, and occipital areas and tests for verbal intelligence quotient (IQ), verbal learning, and various executive functions. Diagnostic synergy was observed for the alliance

between verbal IQ and the right temporo-occipital junction and left middle occipital gyrus. Another study[66] revealed an increase in activation in the left middle and superior occipital lobe. Furthermore, altered prefronto-hippocampal and parieto-occipital connectivity was found to be linked with positive symptoms, which can be helpful in describing the pathophysiology of these symptoms.[67]

Zhou et al[68] indicated that patients suffering from schizophrenia demonstrate remarkably high resting-state functional connectivity density (rsFCD) in the bilateral striatum and hippocampus and significantly lower rsFCD in the right occipital cortex and bilateral sensorimotor cortices. While in another study, Wende et al[69] studied that the left inferior frontal gyrus interconnectivity with bilateral occipital cortex is decreased in schizophrenic patients. These kinds of studies could yield primary understanding into the neural correlates of abnormal causal judgements in schizophrenia.[69]

Metabolic changes involving the occipital lobe in schizophrenia. A systematic review was carried out by Steen et al.[70] The whole brain comparison of metabolic N-acetyl aspartate activity (measured by magnetic resonance spectroscopy) in white and gray matter areas in schizophrenia patients versus healthy controls was conducted. Low to moderate quality evidence suggested no differences in N-acetylaspartate (NAA) levels in schizophrenics compared with controls.[70] However, another study indicated that the levels of N-acetylaspartate to creatine ratio (NAA/Cr) in the left basal ganglia (p=0.0065) and parieto-occipital lobe (p=0.00498), were remarkably lower in patients with first-episode schizophrenia psychosis than in control subjects.[71] Pro-oxidant xanthine oxidase (XO), which is found to play an integral role in purine/adenosine metabolism has decreased activity of XO in the occipital cortex and thalamus of patients with psychosis.[72]

The results of this comprehensive review indicate that the 82 studies included show that the patients with schizophrenia show structural changes (CT, MRI) in the occipital lobe and some show functional changes (fMRI, PET). On the other hand, some patients show metabolic changes in the occipital lobe (**Table 1**). Moderate quality evidence (due to large sample size and no consistency and precision) found that the white matter integrity is reduced in the occipital cortex as compared with healthy individuals, moderate to low quality evidence (inconsistent, imprecise) suggests that there is higher frequency of abnormal (reversed) asymmetry in the occipital lobe in schizophrenia as compared with controls. Progressive changes in gray matter volume were reported across longitudinal MRI scans. Significantly greater reductions were reported over time in schizophrenia compared with controls (the occipital gray matter: 69.9%, while the occipital white matter: 45.9%.)

Evidence (moderate quality) also advocates that during executive function tasks, schizophrenic patients demonstrate reduced activity in the middle occipital gyrus. Moderate quality evidence (due to large sample size and inconsistency) suggests reduced activity in the right lingual gyrus during episodic memory encoding, and reduced activation in the fusiform gyrus and right cuneus during episodic memory retrieval in schizophrenia patients compared with controls. Moderate quality evidence suggests that people with schizophrenia show decreased activation during emotion processing tasks in the fusiform, lentiform, and middle occipital gyri. Schizophrenia sufferers showed reduced activation in the fusiform gyrus, while implicit emotion was related with reduction in the middle occipital gyri, during explicit emotional tasks. (**Table 2**)

Overall results indicated that there was no significant metabolic changes in the brains of the schizophrenic patients. The nature and timing of pathological processes underlying structural, functional, and metabolic changes in schizophrenia remain unclear. Our review provides a selection of studies indicating that the occipital lobe is related to schizophrenia and the occipital lobe abnormalities could be important for schizophrenia and related disorders. Structural brain irregularities in the parietal lobe were found in imaging studies in childhood onset schizophrenia suggesting that gray matter abnormalities commence in the parietal and occipital lobes and continue in a dynamic wave to frontal cortices.[73,74] Thus, structural alterations in the occipital lobe may occur early in the course of the illness and point to genetic influences as yet to be determined.[75] A study demonstrated that disruptions in neural connectivity in gray and white matter pathways in the occipital lobe are associated with schizophrenia and might indicate a genetic predisposition for the disorder.[30] In a post-mortem study of individuals with schizophrenia, Selemon et al[76] showed abnormally high neuronal density in the prefrontal and occipital cortices. In the past, neuronal cell death was attributed to be the cause of decreased cortical gray matter volume.[77] However, Selemon and Goldman-Rakic[78] associated the increased density of cells, in the context of reduced volume, with the loss of neutrophil, or interconnections between the neurons, which could be the result of excessive pruning.

There are studies indicating structural occipital lobe abnormalities in schizophrenia some of them are

Table 1 - Relevant studies showing the association of the occipital lobe in the brain of schizophrenic patients.

Author/ publication year	Country	Study design	Population	Sample size	Diagnostic criteria	Main findings
Spalletta G et al, 2015[32]	Italy USA	Cross-sectional study	21 schizophrenia into its deficit (SZD) patients, 21 schizophrenia into its non-deficit (SZND) patients, and 21 healthy controls	63	DSM-IV-TR	Radial diffusivity was found to be higher in the left forceps minor of schizophrenia into its deficit (SZD) patients, in the left internal capsule of schizophrenia into its non-deficit (SZND) patients, and in the right inferior fronto-occipital fasciculus in the whole schizophrenia group. Mean diffusivity increased from healthy controls to SZD patients to SZND patients in the right occipital lobe
Guo X et al, 2013[33]	China USA	Cross-sectional study	57 patients (27 short DUP * and 30 long DUP*) and 30 healthy controls *Duration of untreated psychosis	87	The structured clinical interview for DSM-IV Axis I Disorders–Clinician Version administered by clinicians (QL and YS)	Long DUP was found to be linked with temporal and occipitotemporal gray matter volume reduction in treatment naive schizophrenia.
Anderson D et al, 2013[34]	USA	Cross-sectional study	Fifty-five patients with a diagnosis of schizophrenia or bipolar I disorder	55	Clinical interview using the SCID for DSM-IV Disorders	Schizophrenic patients have lower fractional anisotropy in temporal (superior temporal and parahippocampal) and occipital (superior and middle occipital) white matter compared to patients with bipolar disorder and healthy volunteers
Nieuwenhuis M 2012, et al[35]	The Netherlands	Cross-sectional study	239 subjects (128 patients and 111 healthy controls) independent sample of 277 subjects (155 patients and 122 healthy controls)	516	Patient=DSM-IV-TR Healthy participants=never been mentally ill	Gray matter density was found to be increased in the left occipital lobe and the basal ganglia
Fujimoto T et al, 2013[36]	Japan	Cross-sectional study	10 right-handed male schizophrenia patients and 10 healthy controls	20	DSM-IV-TR criteria	A positive correlation of auditory hallucination and left occipital and right frontoparietal lobe areas was found
Yao L et al, 2013[37]	China	Meta-analysis (DTI)	271 first episode schizophrenia patients and 297 healthy controls	568	Inclusion exclusion criteria by keywords	White matter changes in the left inferior fronto-occipital fasciculus was found
Plomp G et al, 2013[42]	Switzerland	Cross-sectional study	20 schizophrenic patients (14 patients were inpatients; 8 were outpatients) 20 controls	40	(DSM-IV) criteria, based on SCID-CV	Activity reduction was mostly seen in lateraloccipital cortex (in the ventral stream)
Chan WY et al, 2010[43]	Singapore	Cross-sectional study	103 individuals comprising of 39 patients with first-episode schizophrenia and 64 healthy controls	103	DSM-IV	First episode schizophrenic patient have lower white matter volume (right temporal-occipital region) diffusion anisotropy in the right temporal-occipital region revealed lower planar anisotropy, and higher linear anisotropy
Miyata J et al, 2010[44]	Japan	Cross-sectional study	26 schizophrenia patients and 27 healthy controls	53	Patient edition of the Structural Clinical Interview for DSM-IV Axis – 1 Disorder	Facial emotion recognition subtask demonstrated a noteworthy relationship with fractional anisotropy reductions in the left occipital white matter
Gutierrez D et al, 2015[45]	Spain Germany	Cross-Sectional study	101 first-episode psychosis patients (FEP) and 69 healthy volunteers	170	DSM-IV	Gradual reduction of gray matter volume in the frontal, temporal, parietal and occipital lobes of schizophrenic patients was found.

Table 1 - Relevant studies showing the association of the occipital lobe in the brain of Schizophrenic patients. (continued)

Author/ publication year	Country	Study design	Population	Sample size	Diagnostic criteria	Main findings
Pirnia T et al, 2015[52]	USA	Cross-sectional study	26 schizophrenia patients (mean age: 33, 19m/7f), 30 controls (mean age: 29, 24m/6f), and 14 unaffected relatives of patients (mean age: 40, 5m/9f).	70	DSM-IV-Patient Version(SCID-1/P) and informant information	Temporo-occipital and parietal region hyper-activations were observed
Hart SJ et al, 2013[53]	USA	Cross-sectional study	21 children with a first-degree family member with schizophrenia and 21 controls without FHR	42	DSM IV Disorders for adults and the Washington University Kiddie Schedule for Affective Disorders and Schizophrenia for children	It was found that during emotional processing, the FHR group showed reduced anterior cingulate activation, with reduced age-related recruitment of inferior frontal, parietal and occipital areas
Rigucci S et al, 2013[54]	Italy	Cross-sectional study	19 patients with first episode of non-affective psychosis and 18 controls	37	DSM-IV-TR criteria	Loss in facial emotion recognition was found to be linked with temporo-occipital gray matter volume reduction
Calderone DJ et al, 2013[55]	USA	Cross-sectional study	15 schizophrenic patients and 15 healthy volunteers	30	Structured Clinical Interview for DSM-IV (SCID) and available clinical information	Occipital activation volume reduction was observed
Collin G et al, 2013[56]	The Netherlands	Cross-sectional study	146 schizophrenia patients and 122 healthy comparison subjects	268	DSM-IV	Reduced coupling was most prominent between fronto-parietal cortical regions and subcortical structures, and between frontal and occipital regions. Moreover, a marked association was found among frontal and limbic regions, and for temporo-occipital connections
Woodward ND et al, 2012[57]	USA	Cross-sectional study	62 patients with schizophrenia and 77 healthy subjects	139	The Structured Clinical Interview for Diagnosing DSM-IV Disorders (SCID: 19)	There was no difference in temporal, posterior parietal, or occipito-cortex connectivity with the thalamus
Hoptman MJ et al, 2012[59]	USA	Cross-sectional study	23 healthy controls 25 patients	48	Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Patient version (SCID-I/P)	Notable reductions in VMHC in patients in the occipital lobe, the thalamus, and the cerebellum
Fujimoto T et al, 2012[61]	Japan	Cross-sectional study	10 right-handed male schizophrenia patients	10	DSM-IV-TR criteria	ERD and ERS changes were found in the left temporal pole and midline frontal and anterior cingulate cortex in theta ERS, occipital lobe in alpha ERS, and right temporal-frontal-parietal, midline frontal, and anterior cingulate cortex in beta ERD

DSM-IV-TR - Diagnostic and Statistical Manual of Mental Disorders, SZD - deficit, SZND - non-deficit, FHR - Familial High Risk, VMHC - voxel-mirrored homotopic connectivity, ERD - event-related desynchronization, ERS - synchronization, DTI - diffusion tensor imaging, DUP - duration of untreated psychosis, SCID - Structured Clinical Interview for DSM-IV, SCIM - scanlan collaborative interview method, M - male, F - female

Table 2 - Structural, functional, and metabolic changes in the occipital lobe summary of the study by Steen et al.[70]

Changes in the occipital lobe	Evidence for occipital alterations in schizophrenia
Structural changes	Reduction in the white matter integrity of the occipital cortex and fusiform gyrus in schizophrenia as compared to controls A higher frequency of reverse asymmetry in the occipital lobe in schizophrenics No significant change in occipital lobe volume over time in schizophrenia compared to controls
Functional changes	Moderate evidence suggests people with schizophrenia demonstrate reduced activity in the middle occipital gyrus during executive function tasks Moderate quality evidence shows decreased functional activity in the fusiform gyrus and right lingual gyrus during memory encoding, and memory retrieval in schizophrenic patients compared to controls Moderate quality evidence shows that schizophrenic patients show decreased activation during emotion processing tasks in the fusiform, lentiform and middle occipital gyri
Metabolic changes	Metabolic changes considering N-Acetyl Aspartate were found in the occipital lobe in schizophrenic patients

shown in **Table 1**. A quantitative MRI study[79] suggests that patients with schizophrenia have relative intact gray matter volumes in the primary visual area (PVA), and reduced bilateral volumes of gray matter in visual association areas (VAA), which may be the substrate of some deficits observed in early visual processing. Excessive occipital lobe gray matter loss in several patients is studied,[80] moreover a subgroup exists that demonstrates severe perceptual impairments, this shows a primary role for occipital lobe dysfunction in visual stimulus assembly failures in schizophrenic patients.

Evidence regarding functional occipital lobe abnormalities remains unclear as to the direction of the changes in functional activity in the occipital cortex during cognitive tasks in individuals with first episode schizophrenia.[34] Another study[35] suggests that people with schizophrenia demonstrate reduced activation during emotion processing tasks in the fusiform, lentiform, and middle occipital gyri. During explicit emotional tasks, people with schizophrenia showed decreased activation in the fusiform gyrus, while implicit emotion was associated with decreases in the middle occipital gyri. No measure of consistency or precision in the results was mentioned. According to Ragland et al[81] moderate quality evidence (large sample, direct, unable to assess precision or consistency) suggests activity during episodic encoding is reduced in the right lingual gyrus, and reduced in the right cuneus during episodic retrieval in schizophrenia patients compared with controls.

Occipital lobe asymmetries in schizophrenic patients have also been found to be reduced.[82] More research is needed to explore occipital lobe functions and volumes across different stages of schizophrenia. More extensive data are necessary from the earliest phase of schizophrenia, to conclude the understanding of the alterations of the occipital lobe in schizophrenia. A better understanding of the time course of structural and functional brain changes will not only help us to differentiate between individuals at risk for schizophrenia and associated mental disorders like psychosis and bipolar disorder, it will further expand our knowledge and understanding regarding the advanced modalities of diagnosis of this severe mental enigma.

In conclusion, with all the above-mentioned studies and results in mind, schizophrenia is associated with the occipital lobe (gray matter and white matter) changes. The volume changes of the occipital lobe are also associated with schizophrenia. The conclusions emerging from this systematic review are useful to initiate new questions and recommendations for further studies, specifically on changes in the occipital lobe in the schizophrenic patient's brain. The questions like whether the occipital lobe damage (or changes) in schizophrenic patients is confined to just the occipital lobe or does it involve nearby areas. Does involvement of the occipital lobe with nearby areas bring about some related physical symptoms? Or it brings a combination of some psychiatric illnesses with physical symptoms, or if other areas of the brain are also involved besides the occipital lobe, then what is the sequence of the involvement. Therefore, further studies are required to better understand how the progressive brain changes affect the structural, functional, and metabolic activities of the occipital lobe in schizophrenia and the presence of associated physical or psychiatric disorders or symptoms with occipital lobe involvement.

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