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Subcortical Volume Changes in Schizophrenia and Bipolar Disorder: A Quantitative MRI Study

Cambios en el Volumen Subcortical en la Esquizofrenia y el Trastorno Bipolar: Un Estudio Cuantitativo de Resonancia Magnética

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SUMMARY: Volume abnormalities in subcortical structures, including the hippocampus, amygdala, thalamus, caudate, putamen, and globus pallidus have been observed in schizophrenia (SZ) and bipolar disorder (BD), not all individuals with these disorders exhibit such changes. In addition, the specific patterns and severity of volume changes may vary between individuals and at different stages of the disease. The study aims to compare the volumes of these subcortical structures between healthy subjects and individuals diagnosed with SZ or BD. Volumetric measurements of lateral ventricle, globus palllidus, caudate, putamen, hippocampus, and amygdale were made by MRI in 52 healthy subjects (HS), 33 patients with SZ, and 46 patients with BD. Automatic segmentation methods were used to analyze the MR images with VolBrain and MRICloud. Hippocampus, amygdala and lateral ventricle increased in schizophrenia and bipolar disorder patients in comparison with control subjects using MRIcloud. Globus pallidus and caudate volume increased in patients with schizophrenia and bipolar disorder compared control subjects using Volbrain. We suggested that our results will contribute in schizophrenia and bipolar disorder patients that assessment of the sub-cortical progression, pathology, and anomalies of subcortical brain compositions. In patients with psychiatric disorders, VolBrain and MRICloud can detect subtle structural differences in the brain.

KEY WORDS: MRI; Bipolar disorder; Schizophrenia; MRIcloud; Volbrain.

INTRODUCTION

Bipolar disorder (BD) is an inheritable psychiatric disorder characterized by recurrent (hypo) manic and depressive episodes. Schizophrenia (SZ) is a chronic and debilitating mental health disorder typically associated with positive (psychotic symptoms such as delusions, hallucinations), negative (anhedonia, social withdrawal, etc.), and cognitive symptoms. Bipolar disorder and schizophrenia are disorders that involve specific functional and structural brain abnormalities that can cause symptoms in cognitive and emotional domains (Ellison-Wright & Bullmore, 2010). It has become possible to understand the mechanisms of mental disorders using neuroimaging methods. It is believed that subcortical structures in bipolar and schizophrenia patients are inadequate in controlling emotions (Singh & Rose, 2009). In both SZ and BD, Dobri *et al*. (2022), indicated cortical and subcortical gray matter abnormalities using MRI. Adriano *et al*. (2012) and van Erp *et al*. (2016) stated that smaller hippocampus, amygdala, thalamus and nucleus accumbens, and determined intracranial volume reduction. Rimol *et al*. (2010) found expanded lateral ventricles and enlarged putamen, and pallidum according to meta-analysis. Hibar *et al*. (2016), determined that the volumes of the amygdala, hippocampus and thalamus were smaller and the ventricular volumes were larger in BD patients with comparison of healthy control (HC).

Segmenting subcortical compositions has recently become a popular area of brain research. For automatic or semi-automatic segmentation of subcortical compositions, various techniques are used (Kocaman *et al*., 2019). Using

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magnetic resonance imaging (MRI), FSL (Jenkinson *et al*., 2012), AFNI (Cox, 2012), BrainVoyager (Goebel, 2012), FreeSurfer (Fischl, 2012), and SPM (Sato *et al*., 2021) have been used to evaluate the structural properties of the human brain. In recent years, using web-based cloud systems have become more popular in these studies. VolBrain and MRICloud are the most used cloud-based systems. These systems allow MRI data to be easily uploaded to the website. The validity and reliability of these methods have been tested and approved. Based on literature, there is no study available that calculates the subcortical structure volumes of both bipolar and schizophrenia patients using these two web-based methods (either individually or together).

The study aims to compare subcortical structures volumes in BD and SZ patients with those of control group using MRICloud and VolBrain methods.

MATERIAL AND METHOD

Ethics. The ethical approval was taken from the Kahramanmaras Sütcü Imam University Non-Interventional Scientific Research Ethics Committee of Medicine Faculty. All subjects gave written informed consent for participation in this research.

Study Design. This cross-sectional study was retrospectively conducted on BP and SZ patients. Magnetic Resonance images (MRI) were scanned by specialists for suitable. MRI were analyzed retrospectively by radiologist.

Participants. The research was conducted with 33 patients with SZ (11 female and 22 male), 46 BD patients (27 female and 19 male), and 52 healthy controls (31 female and 21 male) referred from outpatient clinics and community centers to the Psychiatry Department of Medicine Faculty, of Kahramanmaras Sütcü Imam University from 2020 January to 2023 May. All participants were applied the Structured Clinical Interview for DSM-IV (SCID-I) based on American Psychiatric Association diagnostic criteria (1994).SZ patients constitute 25.2 % of the participants, individuals with BD constitute 35.1 %, and individuals in the control group constitute 39.7 %. Male individuals make up 47.3 % of the participants, and female individuals make up 52.7 %. Employed individuals constitute 26.0 % of the participants, while unemployed individuals constitute 74.0 %. Illiterate individuals make up 9.2 % of the participants, individuals with primary-secondary school education make up 37.4 %, those with high school education make up 23.7 %, and individuals with university education make up 29.8 %. 96.2 % of the participants have paranoid schizophrenia, while 3.8 % have catatonic schizophrenia. 97.0 % of the participants are right-handed individuals, and 3.0 % are left-handed individuals (Table I). Statistically significant difference ($p<0.05$) is seen in gender and employment variables among groups. In male individuals, the percentage of the SZ group is higher than the percentages of the BD and control groups. In female individuals, the percentage of the schizophrenia group is lower than the percentages of the bipolar and control groups. Among employed individuals, the percentage of the SZ group is lower than the percentages of the bipolar and control groups. Among unemployed individuals, the percentage of the schizophrenia group is lower than the percentages of the bipolar and control groups (Table II). The variables of age, number of children, onset age, treatment initiation age, illness duration, number of hospitalizations, and education level do not create a statistically significant difference among the groups ($p>0.05$).

Table I. Descriptive statistics of the variables of the study data.

Variables	Descriptive statistics
Group	
Schizophrenic	33(25.2)
Bipolar	46(35.1)
Control	52(39.7)
Sex	
Male	62(47.3)
Female	69(52.7)
Job	
Yes	34(26.0)
No	97(74.0)
Education Level	
Illiterate	12(9.2)
Primary School-Middle	49(37.4)
High School	31(23.7)
University	39(29.8)
Schizophrenic Type	
Paranoid	75(96.2)
Catatonic	3(3.8)
Dominant Side	
Right Hand	32(97.0)
Left Hand	1(3.0)
Data are expressed as n (%) and median (1st quartile-3rd quartile).	

Criteria for Exclusion

1- Other DSM-IV comorbidity
2- First-degree relatives diagnosed with mood disorders
3- Neurological disorders, including dementia, or any current medical condition, especially those affecting brain volume or mental function.

Table II. Comparison results of the variables of the study data according to the groups

Variables	Groups			*p*
	Schizophrenic (n=33)	Bipolar (n=46)	Control (n=52)	
Age	39.73±10.21	36.26±12.85	40.21±16.59	0.335
Number of children	3.0(2.0-3.0)	2.0(2.0-3.0)	3.0(2.0-3.0)	0.422
Disease Onset Age	23.0(19.0-33.0)	20.0(18.0-27.0)	-	0.114
Treatment Onset Age	25.0(20.5-35.0)	23.0(19.0-28.0)	-	0.111
Disease Duration	12.0(6.0-20.0)	10.0(5.0-20.0)	-	0.479
Number of Hospitalizations	3.0(1.0-3.0)	2.0(1.0-3.0)	-	0.229
		Sex		
Male	22(66.7)	19(41.3)	21(40.4)	0.036
Female	11(33.3)	27(58.7)	31(59.6)	
		Job		
Yes	2(6.1)	12(26.1)	20(38.5)	0.004
No	31(93.9)	34(73.9)	32(61.5)	
		Education Level		
Illiterate	1(3.0)	5(10.9)	6(11.5)	0.810
Primary School-Middle School	13(39.4)	16(34.8)	20(38.5)	
High School	10(30.3)	11(23.9)	10(19.2)	
University	9(27.3)	14(30.4)	16(30.8)	

Data are expressed as mean±standard deviation and median (1st quartile-3rd quartile). The same letters on the same line indicate the similarity between the groups, and different letters indicate the difference.

Data Acquisition for Magnetic Resonance Imaging. A 1.5 T unit (Philips Gyroscan Intera, Best, the Netherlands) with a 20-channel head coil was used to perform MRI on the adult participants. The MRI protocol included 3D T1 and 3D brain flair weighted imaging sequences. Sagittal T1-weighted images were used for volumetric assessment. The imaging parameters of T1-weighted Magnetization Prepared Rapid Acquisition Gradient Echo (MPRAGE) sequence were as follows: repetition time (TR): 2400 ms, echo time (TE): 3.54 ms, field of view (FOV): 240 mm, slice thickness: 1 mm, voxel size: 1.3 × 1.3 × 1 mm. Mricron software was used to convert the MRI data into an analysis format (http://www.sph.sc.edu/comd/rorden). The converted data were uploaded to the volBrain and MRICloud web sites.

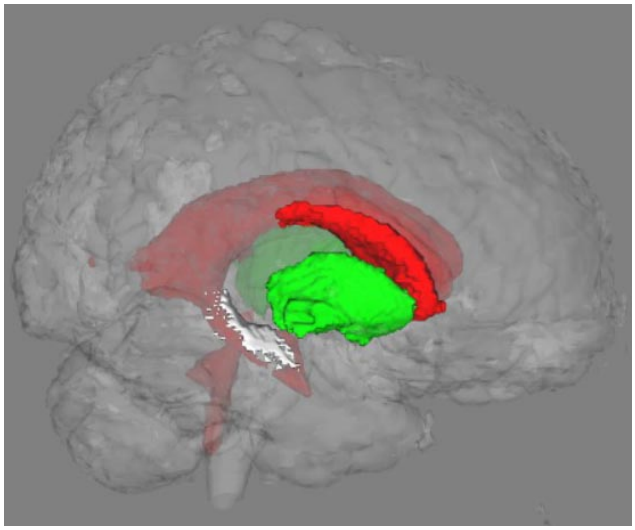

Fig. 1. Parcellation of MPRAGE images, based on the MultipleAtlas Likelihood Fusion algorithm.

Automatic Segmentation. Below is a brief overview of the methods used for automatic segmentation: MRICloud and volBrain.

MRICloud. A fully-automated cloud service is provided with MRICloud for brain parcellation of MPRAGE images, based on the MultipleAtlas Likelihood Fusion algorithm, JHU multi-atlas inventories with a total of 286 defined structures, and an Ontology Level Control technology (https://MRICloud.org) (Hannoun *et al.*, 2019). The adult_286labels_ 11atlases_V5L was the atlas used to process our data was (Fig. 1).

The sum of the telencephalon, diencephalon, mesencephalon, metencephalon, myelencephalon, and CSF volumes were added as total brain volume. We got 10 (cerebellum, accumbens, amygdala, caudate, hippocampus, pallidum, putamen, and thalamus etc.) volume measurements as subcortical structures (right and left).

VolBrain. VolBrain 1.0 (v.1.0, http://volbr ain.upv.es) and lesion brain pipeline were used to process magnetic resonance imaging data and perform volumetric analyses of subcortical structures. We used T1-weighted sequences for patients. VolBrain, a free and online MRI brain volumetry system, a fully-automated segmentation method of which the algorithm is based on multi-atlas, patch-based label fusion segmentation technology (Manjón & Coupé, 2016).

Within 10 minutes, automatic segmentation of subcortical structures and associated volumes and label maps were performed. ITKSNAP software was used for all visualizations (http://www.itksnap.org) (Fig. 2).

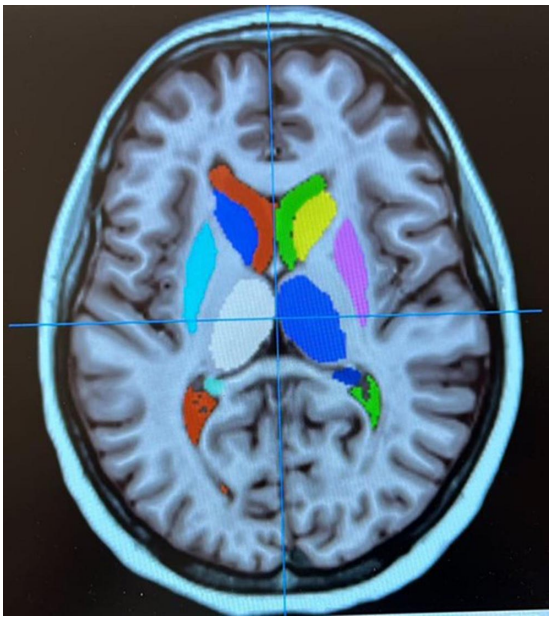

Fig. 2. Automatic segmentation of subcortical structures and associated volumes and label maps.

Statistical analysis. Normality of the data was assessed using histograms, Q-Q plots, and the Shapiro-Wilk test. Homogeneity of variance was tested using the Levene test. For comparisons between more than two groups, one-way analysis of variance (ANOVA) and Kruskal-Wallis tests were used. Multiple comparisons were performed using Tukey, Tamhane, and Dunn-Bonferroni tests. Data analysis was conducted using R 4.3.0 program (www.r-project.org). Moreover, $p<0.05$ was accepted as the level of significance.

RESULTS

In the schizophrenia group, the average value of CSF variable is higher than the average value of control group. In the bipolar group, the mean value of the nucleus caudatus variable is higher than the mean value of control group. In the SZ and BD, the mean value of the globus pallidus variable is greater than the mean value of the control group. In VolBrain measurements, no statistically significant difference ($p>0.05$) is seen between the groups in the variables of putamen, thalamus, hippocampus, amygdala, nucleus accumbens, and lateral ventricle (Table III).

In MRICloud measurements, a statistically significant difference ($p<0.05$) is observed among the groups in the variables of globus pallidus, hippocampus, amygdala, and lateral ventricle. In the SZ group, the mean value of the globus pallidus variable is greater than the mean value of the BD group. In the SZ group, the mean value of the hippocampus variable is higher than the mean value of the control group. In the SZ and BD groups, the mean values of the amygdala variable are higher than the mean value of the control group. In the SZ group, the mean value of the lateral ventricle variable is greater than the average value of the control group. In MRICloud measurements, there is no statistically significant difference ($p>0.05$) between the groups in the variables of CSF (cerebrospinal fluid), brainstem, nucleus caudatus, putamen, thalamus, and nucleus accumbens (Table IV).

Table III. Comparison results of various variables according to groups in VolBrain measurement.

Parameters	Groups			*p*
	Schizophrenic (n=33)	Bipolar (n=46)	Control (n=52)	
Nucleus Caudatus	6.89±0.74^{ab}	6.92±0.67^{b}	6.52±0.82^{a}	0.015
Putamen	7.71±0.96	7.63±1.01	7.31±0.8	0.093
Thalamus	10.22±1.04	10.04±0.99	9.95±1.09	0.489
Globus Pallidus	2.14±0.32^{a}	2.02±0.37^{ab}	1.93±0.29^{b}	0.021
Hippocampus	7.33±0.58	7.42±0.58	7.45±0.75	0.686
Amygdala	1.16±0.24	1.27±0.2	1.2±0.24	0.117
Nucleus Accumbens	0.56±0.14	0.53±0.08	0.56±0.14	0.456
Lateral Ventricle	16.5(9.9-23.2)	17.7(12.2-21.7)	17.2(13.5-21.5)	0.897

Data are expressed as mean±standard deviation and median (1st quartile-3rd quartile). The same letters on the same line indicate the similarity between the groups, and different letters indicate the difference.

Table IV. Comparison results of various variables according to groups in MRICloud measurement.

Parameters	Groups			*p*
	Schizophrenic (n=33)	Bipolar (n=46)	Control (n=52)	
Nucleus Caudatus	6.24±0.98	6.35±0.82	6.26±1.19	0.878
Putamen	6.95±1.26	7.12±0.91	6.84±0.98	0.400
Thalamus	10.72±0.74	10.23±0.87	10.55±1.37	0.121
Globus Pallidus	3.17±0.46^{a}	2.87±0.35^{b}	3.02±0.38^{ab}	0.004
Hippocampus	7.47±1.17^{a}	7.10±0.59^{ab}	6.89±0.63^{b}	0.005
Amygdala	3.32±0.41^{b}	3.23±0.31^{b}	3.03±0.33^{a}	<0.001
Nucleus Accumbens	1.38±0.24	1.35±0.18	1.32±0.14	0.334
Lateral Ventricle	27.3(17.7-33.0)^{a}	24.0(18.9-29.7)^{ab}	18.1(14.3-28.4)^{b}	0.021

Data are expressed as mean±standard deviation and median (1st quartile-3rd quartile). The same letters on the same line indicate the similarity between the groups, and different letters indicate the difference.

Finally, hippocampus, amygdala and lateral ventricle increased in patients with SZ and BD with comparison of control subjects using MRIcloud. Globus pallidus and caudate volumes increased in patients with SZ and BD compared control subjects using Volbrain.

DISCUSSION

It was determined that hippocampus, amygdala and lateral ventricle volumes increased in patients with SZ and BD compared control subjects using MRIcloud. Globus pallidus and caudate volume increased in patients with SZ and BD compared control subjects using Volbrain.

The use of web-based cloud systems such as VolBrain and MRICloud has become increasingly popular in recent years in studies of subcortical brain volumes in psychiatric disorders such as BD and SZ. While several studies have used these methods separately, to our knowledge there is no study that has used both VolBrain and MRICloud to compare the volume of the subcortical brain volumes in bipolar disorder and schizophrenia. Evaluation studies often include comparing the measurements obtained from VolBrain and MRICloud to reference standards or expert manual segmentations. This allows researchers to identify the level of agreement or discrepancy among the automated measurements and the ground truth. The VolBrain is a web-based platform that provides automated neuroimaging analysis for brain MRI scans. It uses advanced algorithms to segment and quantify various brain structures, including the cerebral cortex, subcortical nuclei, and cerebellum. The platform is designed to be user-friendly and does not require any programming or advanced technical knowledge. It is useful for researchers, clinicians, and radiologists who want to obtain accurate and reliable measurements of brain structures from MRI scans. The VolBrain offers a wide range of features, including quality control, image registration, and volume measurement (Manjón & Coupé, 2016).It is used in a wide range of clinical and research settings to study brain disorders like Alzheimer's disease, multiple sclerosis, and traumatic brain injury. Also, MRICloud is a web-based platform that provides a range of tools for processing and analyzing MRI data. It enables researchers and clinicians to upload their MRI images and use a variety of processing pipelines for tasks such as image segmentation, registration, and visualization. MRICloud is designed to be user-friendly, with a simple and intuitive interface, and it can be accessed from any device with an internet connection. The platform is also designed to be scalable, so it can handle large datasets and complex analyses. Sakamoto *et al*. (2019) utilized MRICloud for brain segmentation and volume measurements in patients with Alzheimer's disease. Additionally, Pérez *et al*. (2021) used MRICloud for brain volumetry in patients with multiple sclerosis. These studies demonstrate the utility and validity of MRICloud as a tool for neuroimaging analysis. There have been lots of studies using freesurfer and machine learning approach to investigate volumetric changes in the brains of individuals with BD (Sartori *et al*., 2018; Ohi *et al*., 2022). Sartori *et al*. (2018) used 49 participants and 59 HC underwent clinical and functioning evaluations, as well as structural MRI. They used a machine learning approach for bipolar disorder. Ohi *et al*. (2022) used Fressurfer for volumetric analysis in patients with BD and schizophrenia. Significantly smaller volumes in the left thalamus, bilateral hippocampi and left amygdala were determined in patients with SZ had according to the control group. When the comparison with controls was done, patients with BD had bilateral reductions in hippocampal volume only. Yousef *et al*. (2020) used both VolBrain and voxel-based morphometry to compare brain volume measurements in 16 patients with BD and 16 healthy patients. They determined that significantly larger right globus pallidus and right lateral ventricle. Erbay & Kartalcı (2020) used 23 male SZ patients and age-matched 25 healthy male subjects. They found that volumes of both the left and the right insula were significantly lower in the patient group vs. the control group. Dobri *et al.* (2022) stated cortical and subcortical gray matter anomalies in BD and SZ using MRI studies. And, some studies found that smaller hippocampus (Adriano *et al*., 2012; van Erp *et al*., 2016), amygdala, thalamus, and nucleus accumbens. Reduced intracranial volumes (Rimol *et al*., 2010; van Erp *et al*., 2016); bigger lateral ventricles (Rimol *et al*., 2010); and increased putamen and pallidum according to meta-analysis. Reduced whole brain volume and lateral ventricular enlargement were found in SZ patients compared to controls by Wright *et al*. (2000). Huhtaniska *et al*. (2017) used VolBrain for schizophrenia patients and found volume increase in lateral ventricles and decrease in the caudate nucleus, hippocampal and amygdalae volume. Dobri *et al*. (2022) stated that both regional reduces in gray matter and a widespread reduce in cortical gray matter volume looks to be more consistently related with SZ than with BD. Goghari *et al*. (2014) used freesurfer to analyze brain MRI data from 30 SZ patients, and 30 healthy patients. The study determined that patients with SZ had smaller volumes in several brain regions compared to controls, while patients with BD had smaller volumes in the prefrontal cortex compared to controls. Finally, we found that in schizophrenia and BD, as the ventricles in the brain expand, the volumes of subcortical structures also decrease.

CONCLUSION

VolBrain and MRICloud are used by researchers, clinicians, and educators in the field of neuroimaging to process and analyze MRI data for a range of applications,

including diagnosis, research, and education. To investigate the structural changes in brain MRI of BD and SZ and to identify disease-specific biological markers, longitudinal follow-up studies are needed in larger patient groups, including children and adolescents, healthy individuals at risk for the disease, patients who have never taken medication and those in their first episode, where structural imaging techniques are integrated with functional imaging methods.

DEMIR, M.; FINDıKLI, E.; TUNCEL, D.; ATAY, E.; BAYKARA, M.; ACER, N. & DOGANER, A. Cambios en el volumen subcortical en la esquizofrenia y el trastorno bipolar: un estudio cuantitativo de resonancia magnética. *Int. J. Morphol., 42(2)*:503-509, 2024.

RESUMEN: Se han observado anomalías de volumen en las estructuras subcorticales, incluidos el hipocampo, la amígdala, el tálamo, el núcleo caudado, el putamen y el globo pálido, en la esquizofrenia (SZ) y el trastorno bipolar (BD); no todos los individuos con estos trastornos presentan tales cambios. Además, los patrones específicos y la gravedad de los cambios de volumen pueden variar entre individuos y en diferentes etapas de la enfermedad. El estudio tuvo como objetivo comparar los volúmenes de estas estructuras subcorticales entre sujetos sanos e individuos diagnosticados con SZ o BD. Se realizaron mediciones volumétricas del ventrículo lateral, globo pálido, núcleo caudado, putamen, hipocampo y amígdala mediante resonancia magnética en 52 sujetos sanos (HS), 33 pacientes con SZ y 46 pacientes con BD. Se utilizaron métodos de segmentación automática para analizar las imágenes de resonancia magnética con VolBrain y MRICloud. El hipocampo, la amígdala y el ventrículo lateral aumentaron en pacientes con esquizofrenia y trastorno bipolar en comparación con sujetos de control que utilizaron MRIcloud. El globo pálido y el núcleo caudado aumentaron en pacientes con esquizofrenia y trastorno bipolar en comparación con los sujetos control que utilizaron Volbrain. Sugerimos que en pacientes con esquizofrenia y trastorno bipolar, nuestros resultados contribuirán a la evaluación de la progresión subcortical, la patología y las anomalías de las composiciones cerebrales subcorticales. En pacientes con trastornos psiquiátricos, VolBrain y MRICloud pueden detectar diferencias estructurales sutiles en el cerebro.

PALABRAS CLAVE: RMN; Trastorno bipolar; Esquizofrenia; MRICloud; VolCerebro.

REFERENCES

Adriano, F.; Caltagirone, C. & Spalletta, G. Hippocampal volume reduction in first-episode and chronic schizophrenia: a review and meta-analysis. *Neuroscientist, 18(2)*:180-200, 2012.

Cox, R. W. AFNI: What a long strange trip it's been. *NeuroImage, 62(2)*:743-47, 2012.

Dobri, M. L.; Diaz, A. P.; Selvaraj, S.; Quevedo, J.; Walss-Bass, C.; Soares, J. C. & Sanches, M. The limits between schizophrenia and bipolar disorder: what do magnetic resonance findings tell us? *Behav. Sci. (Basel), 12(3)*:78, 2022.

Ellison-Wright, I. & Bullmore, E. Anatomy of bipolar disorder and schizophrenia: A meta-analysis. *Schizophr. Res., 117(1)*:1-12, 2010.

Erbay, M. F. & Kartalcı, S¸. Insular volume reduction in young male schizophrenia patients. Anadolu Psikiyatri Derg., 21(6):579-84, 2020.

Fischl, B. FreeSurfer. *Neuroimage, 62(2)*:774-81, 2012.

Goebel, R. BrainVoyager — Past, present, future. *Neuroimage, 62(2)*:748-56, 2012.

Goghari, V. M.; Macdonald 3rd, A. W. & Sponheim, S. R. Relationship between prefrontal gray matter volumes and working memory performance in schizophrenia: a family study. *Schizophr. Res., 153(1-3)*:113-21, 2014.

Hannoun, S.; Tutunji, R.; El Homsi, M.; Saaybi, S. & Hourani, R. Automatic thalamus segmentation on unenhanced 3D T1 weighted ımages: comparison of publicly available segmentation methods in a pediatric population. *Neuroinformatics, 17(3)*:443-50, 2019.

Hibar, D. P.; Westlye, L. T.; van Erp, T. G. M.; Rasmussen, J.; Leonardo, C. D., Faskowitz J.; Haukvik, U. K.; Hartberg, C. B.; Doan, N. T.; Agartz, I.; *et al*. Subcortical volumetric abnormalities in bipolar disorder. M*ol. Psychiatry, 21(12)*:1710-6, 2016.

Huhtaniska, S.; Jaaskelainen, E.; Heikka, T.; Moilanen, J. S.; Lehtiniemi, H.; Tohka, J.; Manjon, J. V.; Coupe, P.; Bjornholm, L.; Koponen, H.; *et al*. Long-term antipsychotic and benzodiazepine use and brain volume changes in schizophrenia: The Northern Finland Birth Cohort 1966 study. *Psychiatry Res. Neuroimaging, 266*:73-82, 2017.

Jenkinson, M.; Beckmann, C. F.; Behrens, T. E. J.; Woolrich, M. W. & Smith, S. M. FSL. *Neuroimage, 62(2)*:782-90, 2012.

Kocaman, H.; Acer, N.; Köseoglu, E.; Gültekin, M. & Dönmez, H. Evaluation of intracerebral ventricles volume of patients with Parkinson's disease using the atlas-based method: A methodological study. *J. Chem. Neuroanat., 98*:124-30, 2019.

Manjón, J. V. & Coupé, P. volBrain: an online Mrı brain volumetry system. *Front. Neuroinform., 10*:30, 2016.

Ohi, K.; Ishibashi, M.; Torii, K.; Hashimoto, M.; Yano, Y. & Shioiri, T. Differences in subcortical brain volumes among patients with schizophrenia and bipolar disorder and healthy controls. *J. Psychiatry Neurosci., 47(2)*:E77-E85, 2022.

Pérez, C. A.; Salehbeiki, A.; Zhu, L.; Wolinsky, J. S. & Lincoln, J. A. Assessment of Racial/Ethnic Disparities in Volumetric MRI Correlates of Clinical Disability in Multiple Sclerosis: A Preliminary Study. *J. Neuroimaging, 31(1)*:115-23, 2021.

Rimol, L. M.; Hartberg, C. B.; Nesvåg, R.; Fennema-Notestine, C.; Hagler Jr., D. J.; Pung, C. J.; Jennings, R. G.; Haukvik, U. K.; Lange, E.; Nakstad, P. H.; *et al*. Cortical thickness and subcortical volumes in schizophrenia and bipolar disorder. *Biol. Psychiatry, 68(1)*:41-50, 2010.

Sakamoto, R.; Marano, C.; Miller, M.I.; Lyketsos, C.G.; Li, Y.; Mori, S.; Oishi, K. & Adni ADNI. Cloud-based brain magnetic resonance image segmentation and parcellation system for ındividualized prediction of cognitive worsening, *J. Healthc. Eng., 2019*:9507193, 2019.

Sartori, J. M.; Reckziegel, R.; Passos, I. C.; Czepielewski, L. S.; Fijtman, A.; Sodré, L. A.; Massuda, R.; Goi, P. D.; Vianna-Sulzbach, M.; Cardoso, T. A.; *et al*. Volumetric brain magnetic resonance imaging predicts functioning in bipolar disorder: A machine learning approach. *J. Psychiatr. Res., 103*:237-43, 2018.

Sato, J.; Hirano, Y.; Hirakawa, N.; Takahashi, J.; Oribe, N.; Kuga, H.; Nakamura, I.; Hirano, S.; Ueno. T.; Togao, O.; *et al*. Lower hippocampal volume in patients with schizophrenia and bipolar disorder: a quantitative MRI study. *J. Pers. Med., 11(2)*:121, 2021.

Singh, I. & Rose, N. Biomarkers in psychiatry. *Nature, 460(7252)*:202-7, 2009.

van Erp, T. G.; Hibar, D. P.; Rasmussen, J. M.; Glahn, D. C.; Pearlson, G. D.; Andreassen, O. A.; Agartz, I.; Westlye, L. T.; Haukvik, U. K.; Dale, A. M.; *et al*. Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium. *Mol. Psychiatry, 21(4)*:547-53, 2016.

Wright, I. C.; Rabe-Hesketh, S.; Woodruff, P. W.; David, A. S.; Murray, R. M. & Bullmore, E. T. Meta-analysis of regional brain volumes in schizophrenia. *Am. J. Psychiatry, 157(1)*:16-25, 2000.

Yousef, H. A.; ElSerogy, Y. M. B. E.; Abdelal, S. M. & Abdel-Rahman, S. R. Voxel-based morphometry in patients with mood disorder bipolar I mania in comparison to normal controls. *Egypt. J. Radiol. Nucl. Med., 51*:9, 2020.

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