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Review Paper

Role of MR spectroscopy and Structural MRI in MDD and BPAD

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ABSTRACT

BACKGROUND:

Major (Unipolar) depressive disorder (MDD) and Bipolar Associative disorder (BPAD) are both major health issues associated with increased morbidity and mortality rates. There is an overlapping symptomatic spectrum between both these conditions, especially during the depressive phase of BPAD. Apt and early diagnosis of the condition can help prevent misdiagnosis and ensure that the patient receives the appropriate treatment mandated for the condition. Studies have shown that neuro imaging and monitoring of brain metabolites using functional MRI (MRS) could be used as a potential tool for understanding the pathophysiology of depression and prove as a diagnostic tool in differentiating unipolar and bipolar depression.[2] This study combines the role of structural imaging: hippocampal volumetry and white matter changes, with the biochemical concentration of metabolites using MR spectroscopy, in the differentiation of both these conditions.

AIMS &OBJECTIVES OF THE STUDY: To utilize MRI to evaluate structural and metabolic changes in the anterior cingulate, medial prefrontal cortex, parietal cortex, and posterior cingulate cortex [using MR spectroscopy] in patients diagnosed with depressive disorder. To differentiate between unipolar depressive disorder and bipolar disorder presenting in the depressive phase, using the above structural and metabolic changes.

MATERIALS AND METHODS: Written informed consent was taken from all the subjects included in the study. The study was conducted after approval from the ethics committee.

METHOD OF EVALUATION: Patients clinically diagnosed with major depressive and bipolar affective disorder and referred from the Department of Psychiatry at Vydehi Institute of Medical Sciences and Research Centre from January 2019 to June 2020. Patients who met the inclusion and exclusion criteria were recruited after written informed consent is taken for the study. All the MRI was performed on a 1.5 T full body system (Achieva, Phillips, The Netherlands) with the use of a standard eight-channel head coil. MR volumetry was performed for bilateral hippocampi, and total hippocampal volume was generated in both cases and controls for comparison among cases and controls. Multi voxel PRESS (Spin – echo point resolved) spectroscopy (Repetition time TR = 1750 ms, echo time [TE = 24 ms], matrix = 320x 224,, field of view : 240 x 240 , number of excitation = 8) with chemical - shift selective saturation (CHESS) water suppression will be used for proton MR spectra.

RESULT: Patients with Bipolar Affective Disorder showed significantly higher levels of Choline,Phospho Creatine, Glutamic acid/ Glutamine in their anterior cingulate cortex, lower Myo Inositol, and N- Acetyl Aspartate in their Posterior cingulate cortex, and lower N- Acety lAspartate , Myo Inositol in their medial pre-frontal cortex, compared to healthy controls, Patients with Major depressive disorder presented significantly lower Phosphocreatine andN-acetyl aspartate levels in their Posterior cingulate cortex and lower Glutamic acid/ Glutamine in their medial pre-frontal cortex. Mean hippocampal volumetry was found to be reduced in patients with major depressive disorder compared to those with bipolar affective disorder and the control group. The occurrence of white matter changes in all three groups was inconclusive.

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CONCLUSION: MRI has a significant advantage over other imaging modalities in the differentiation ofunipolar and bipolar affective disorder. MR-based hippocampal volumetry combined with H1 MRS has a significant role in enablingearly differentiation between these conditions

OBSERVATIONS AND RESULTS

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi- square test** was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. **ANOVA (Analysis of Variance)** was the test of significance to identify the mean difference between more than two groups for quantitative data.

Graphical representation of data: MS Excel and MS word was used to obtain various typesof graphs such as bar diagram. **p value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. **Statistical software:** MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Results:

Table 1: Age distribution comparison between three groups

		Age		P value
		Mean	SD	
Group	BPAD	36.13	8.77	0.741
	MDD	36.73	12.72	
	Control	33.80	10.95	
	Total	35.56	10.76	

In the study there was no significant difference in age distribution between three groups.

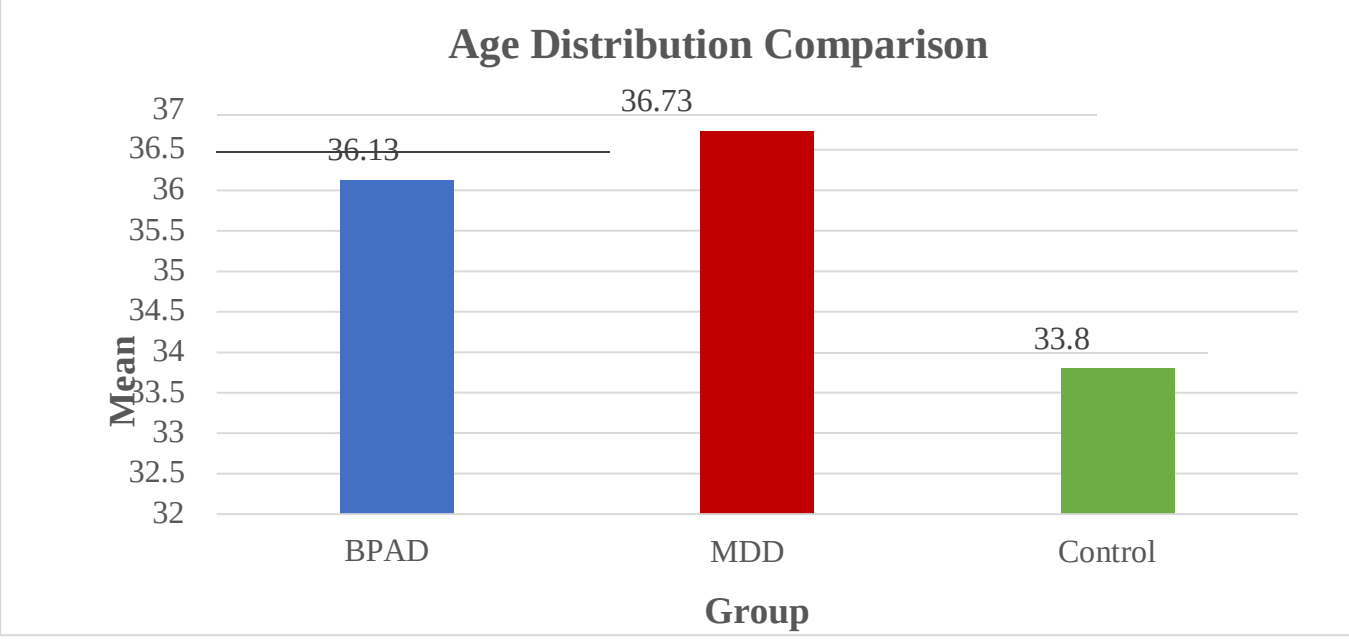

Figure 1: Bar diagram showing Age distribution comparison between three groups

Table 2: Sex distribution comparison between three groups

		Group					
		BPAD		MDD		Control	
		Count	%	Count	%	Count	%
Sex	Female	5	33.3%	6	40.0%	4	26.7%
	Male	10	66.7%	9	60.0%	11	73.3%
	Total	15	100.0%	15	100.0%	15	100.0%

χ 2 =0.600, df =2, p =0.741

In all the three groups majority of subjects were males. There was no significant difference ingender distribution between three groups.

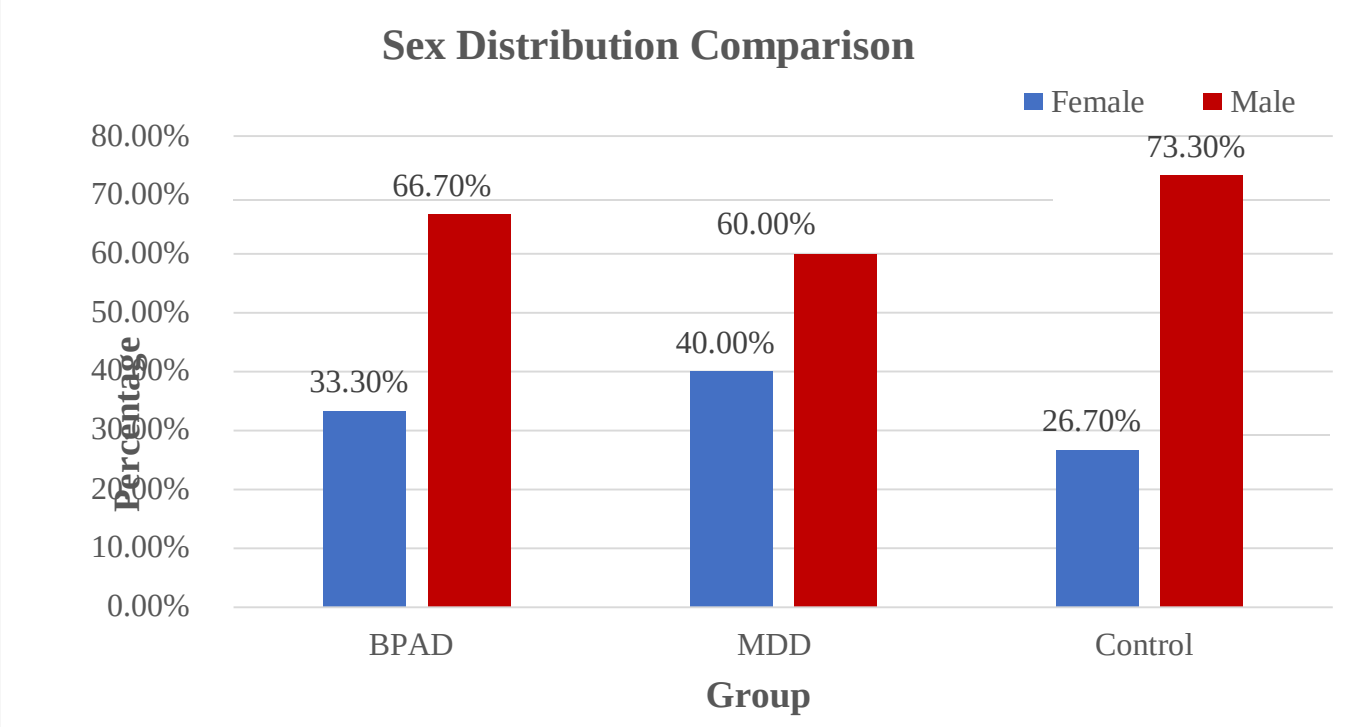

Figure 2: Bar diagram showing Sex distribution comparison between three groups.

MRS BRAIN METABOLITES mmol/L

Table 3: ACC parameters comparison between three groups

ACC	Group								P valueb/w 3 groups
	BPAD		MDD		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	

Cho	2.46	0.30	2.05	0.16	2.08	0.17	2.20	0.29	<0.001*
Cr	7.19	0.25	6.45	0.34	6.61	0.29	6.75	0.43	<0.001*
Glx	12.51	0.73	11.60	0.47	11.85	0.42	11.99	0.67	<0.001*
MI	6.87	0.19	7.13	0.38	6.64	0.37	6.88	0.38	<0.001*
NAA	7.10	0.33	7.62	0.44	7.09	0.36	7.27	0.45	<0.001*

In the study there was significant difference in mean ACC parameters between three groups.Mean Cho, Cr, Glx, was significantly high in BPAD group compared to other two groups.

Mean MI and NAA was significantly high in MDD group compared to other two groups.

ACC	BPAD vs MDD	BPAD vs Control	MDD vs Control
Cho	<0.001*	<0.001*	1.000
Cr	<0.001*	<0.001*	0.434
Glx	<0.001*	0.008*	0.669
MI	0.102	0.181	0.001*
NAA	0.001*	1.000	0.001*

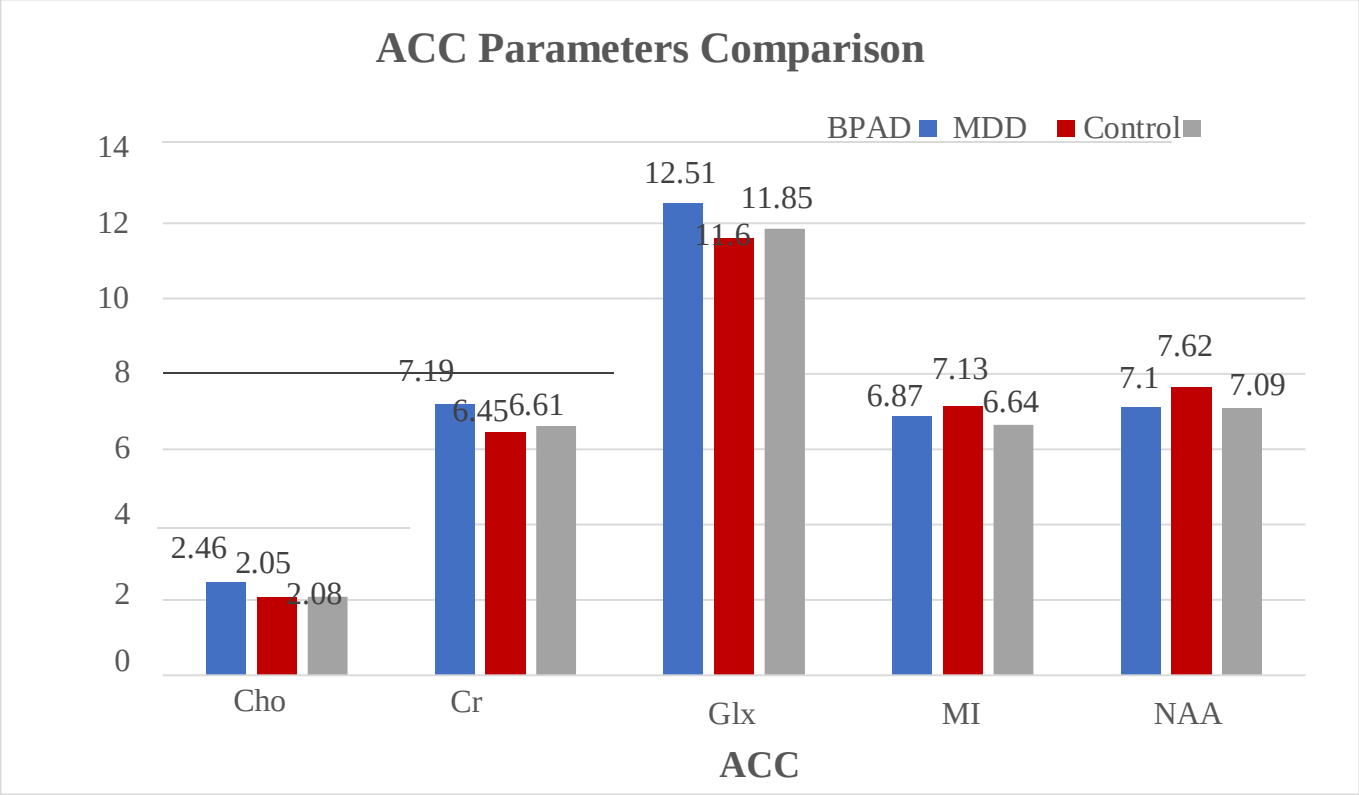

Figure 3: Bar diagram showing ACC parameters comparison between three groups

Table 4: MPFC parameters comparison between three groups

MPFC	Group								P value
	BPAD		MDD		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean		
Cho	1.61	0.14	1.72	0.17	1.57	0.21	1.64	0.18	0.065
Cr	5.51	0.22	5.46	0.26	5.62	0.08	5.53	0.21	0.086
Glx	9.42	0.48	8.87	0.65	11.25	0.60	9.85	1.18	<0.001*
MI	5.34	0.36	5.38	0.39	5.81	0.44	5.51	0.45	0.004*
NAA	4.74	0.38	5.06	0.62	5.86	0.52	5.22	0.69	<0.001*

In the study there was significant difference in mean MPFC parameters such as GLX, MI and NAA between three groups. Mean Glx, MI and NAA was high in Control group compared toother groups.

mPFC	BPAD vs MDD	BPAD vs Control	MDD vs Control
Cho	0.260	1.000	0.076
Cr	1.000	0.407	0.093
Glx	0.039*	<0.001*	<0.001*
MI	1.000	0.007*	0.015*
NAA	0.282	<0.001*	<0.001*

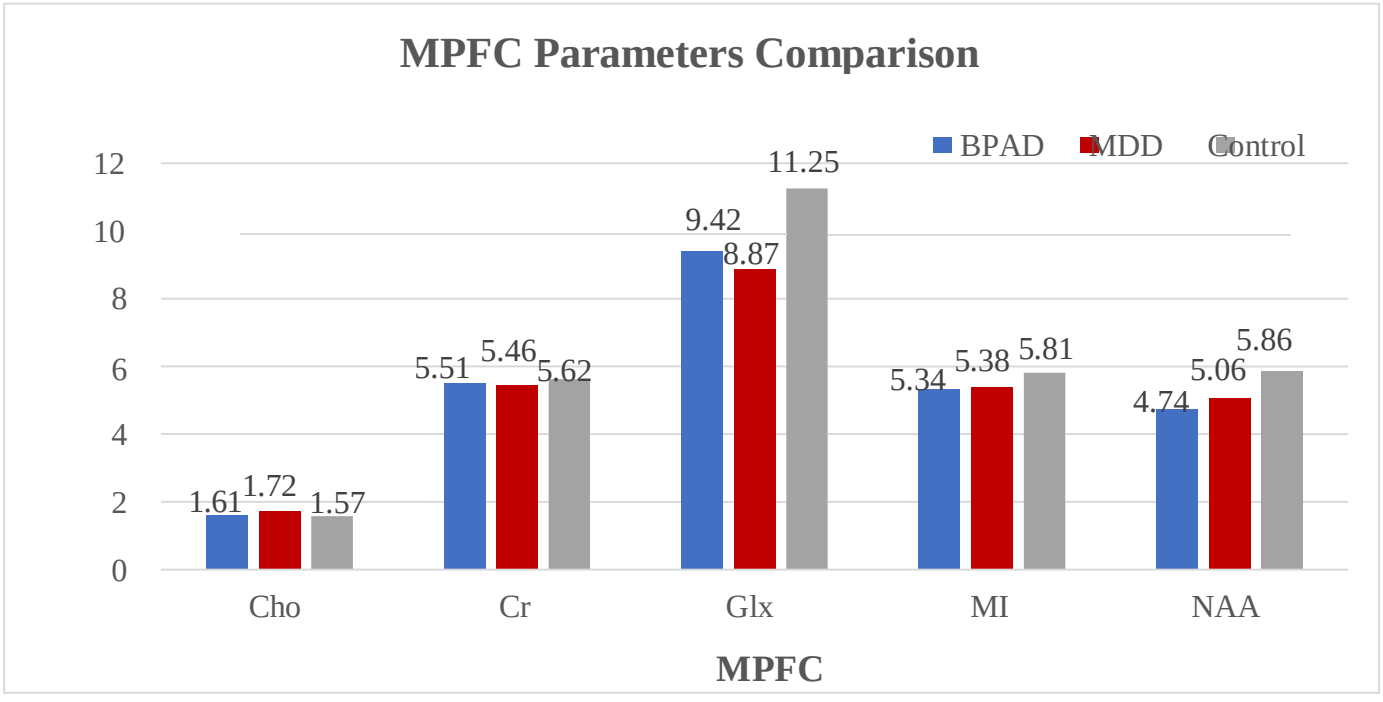

Figure 4: Bar diagram showing MPFC parameters comparison between three groups

Table 5: PC parameters comparison between three groups

PC	Group								P value
	BPAD		MDD		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Cho	0.68	0.13	0.99	0.17	**1.12**	0.17	0.93	0.24	<0.001*
Cr	4.26	0.46	4.83	0.71	**6.23**	0.48	5.10	1.00	<0.001*
Glx	8.01	0.88	9.06	0.63	**9.31**	0.76	8.79	0.94	<0.001*
MI	2.90	0.39	3.79	0.34	**4.86**	0.68	3.85	0.94	<0.001*
NAA	7.92	1.41	8.80	0.66	**9.37**	0.58	8.70	1.11	0.001*

In the study there was significant difference in mean PC parameters between three groups. Mean Cho, Cr, Glx,MI and NAA was significantly high in Control group compared to other two groups.

PC	BPAD vs MDD	BPAD vs Control	MDD vs Control
Cho	<0.001*	<0.001*	0.09
Cr	0.024*	<0.001*	<0.001*
Glx	0.001*	<0.001*	1.000
MI	<0.001*	<0.001*	<0.001*
NAA	0.05	<0.001*	0.326

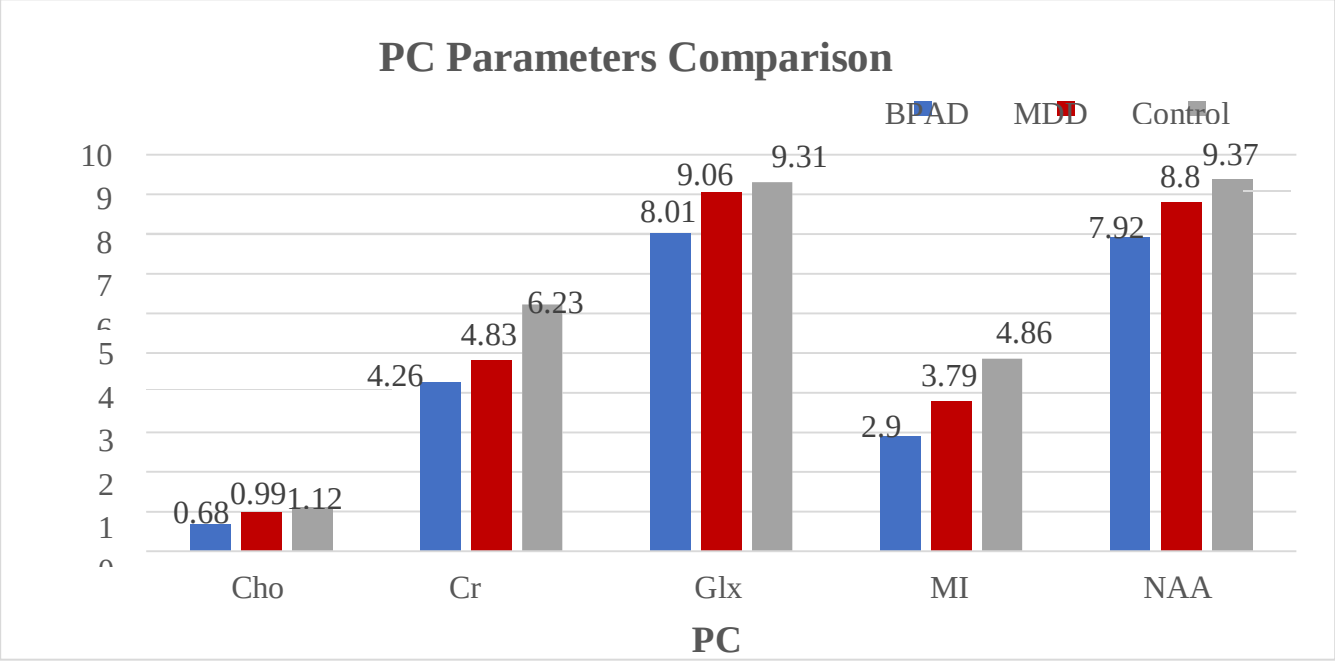

Figure 5: Bar diagram showing PC parameters comparison between three group

Table 6: PCC parameters comparison between three groups

PCC	Group								P value
	BPAD		MDD		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Cho	1.21	0.16	1.23	0.17	**1.36**	0.16	1.27	0.17	0.031*
Cr	6.99	0.62	6.79	0.53	**7.62**	0.33	7.13	0.61	<0.001*
Glx	12.21	0.91	13.02	1.15	**14.22**	0.95	13.15	1.30	<0.001*
MI	5.78	0.54	6.34	0.44	**6.59**	0.46	6.24	0.58	<0.001*
NAA	9.66	0.57	8.94	0.43	**10.68**	0.64	9.76	0.90	<0.001*

In the study there was significant difference in mean PCC parameters between three groups. Mean Cho, Cr, Glx, MI and NAA was significantly high in Control group compared to othertwo groups.

PCC	BPAD vs MDD	BPAD vs Control	MDD vs Control
Cho	1.000	0.045*	0.106
Cr	0.806	0.005*	<0.001*
Glx	0.096	<0.001*	0.007*
MI	0.008*	<0.001*	0.468
NAA	0.003*	<0.001*	<0.001*

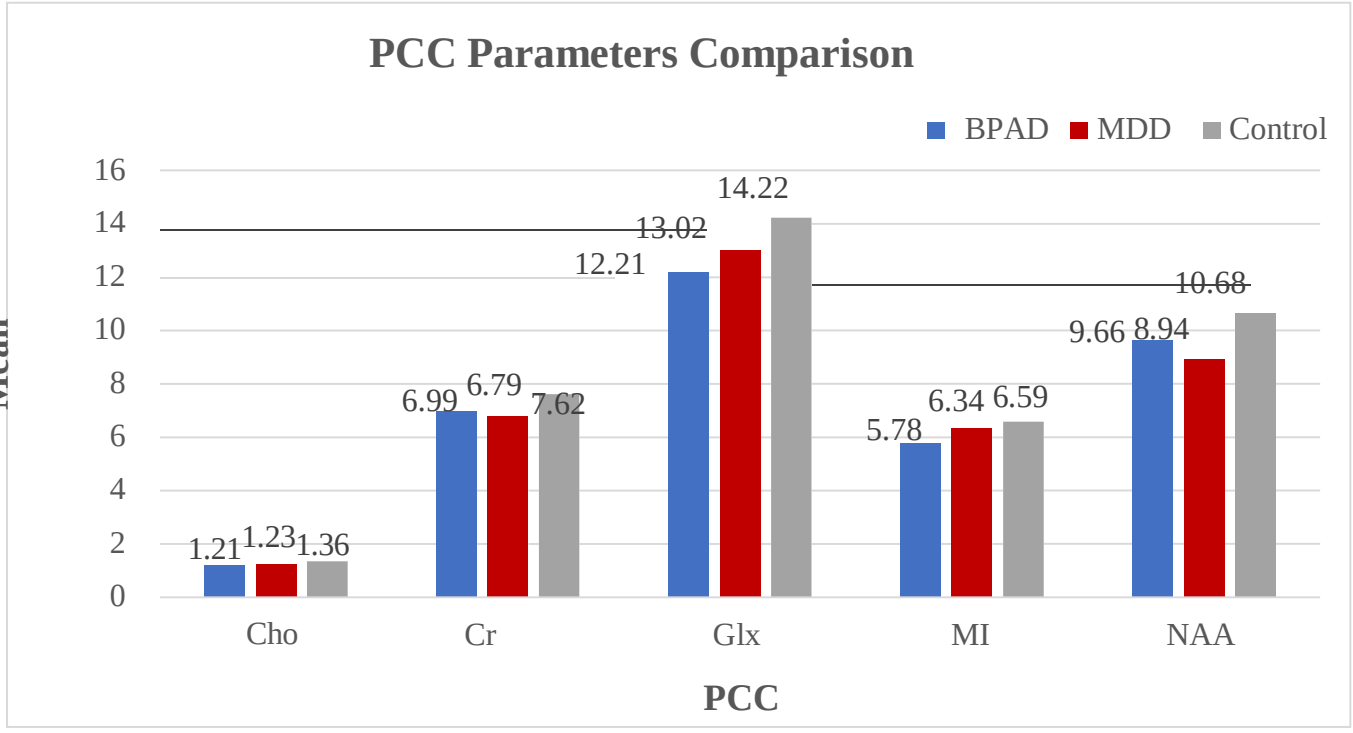

Figure 6: Bar diagram showing PCC parameters comparison between three groups

Table 7: Hippocampal Volumetry comparison between three groups

	Group								P value
	BPAD		MDD		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Right Lobe	2.51	0.15	2.14	0.23	2.56	0.15	2.40	0.26	<0.001*
Left Lobe	2.52	0.17	2.18	0.23	2.58	0.13	2.43	0.25	<0.001*

In the study there was significant difference in Hippocampal Volumetry between three groups on right and left lobe. Mean Hippocampal Volumetry was low in MDD compared to BPAD and Control group.

Hippocampal Volumetry	BPAD vs MDD	BPAD vs Control	MDD vs Control
Right Lobe	<0.001*	1.000	<0.001*
Left Lobe	<0.001*	1.000	<0.001*

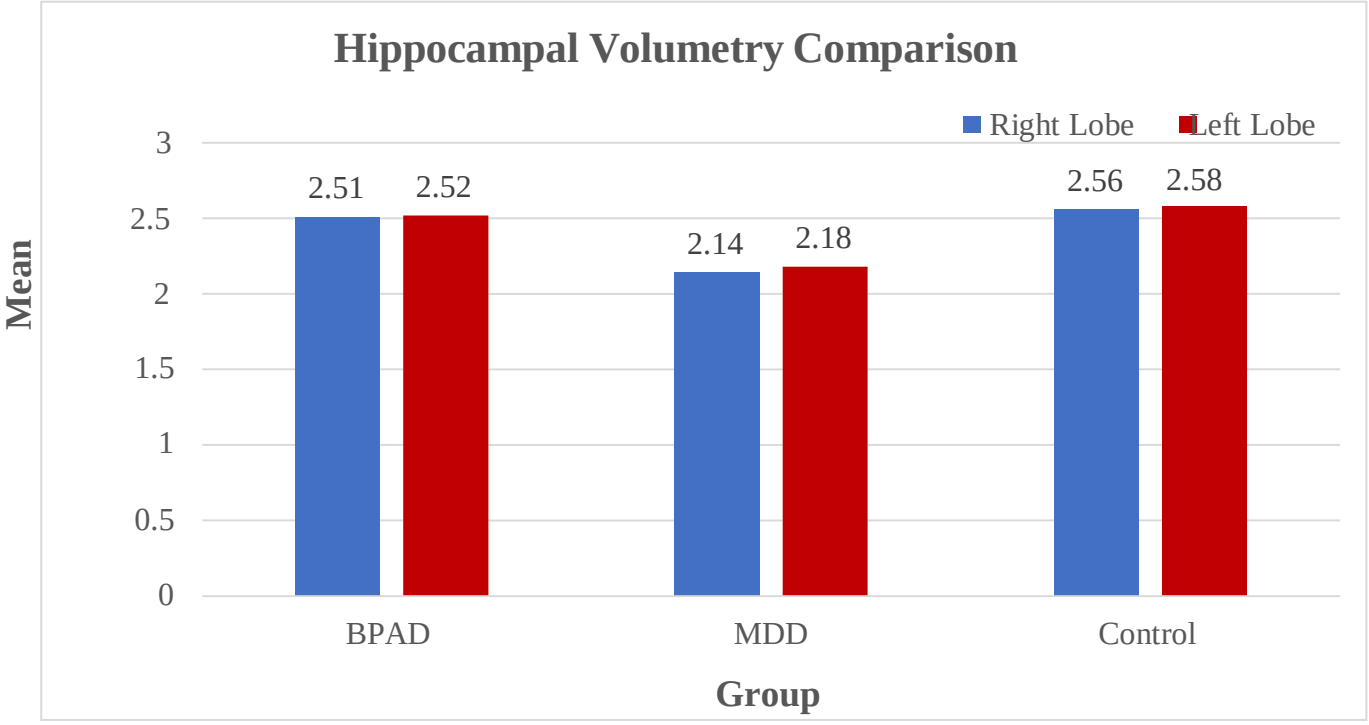

Figure 7: Bar diagram showing Hippocampal Volumetry comparison between three groups

Table 8: Total Volume comparison between three groups

		Total Volume		P value b/w 3 groups	BPAD vs MDD	BPAD vs Control	MDD vs Control
		Mean	SD				
Group	BPAD	5.03	0.32	<0.001*	<0.001*	1.000	<0.001*
	MDD	4.32	0.45				
	Control	5.14	0.27				
	Total	4.83	0.51				

In the study there was significant difference in mean Total Volume between three groups.Mean Total volume was high in Control group and low in MDD group.

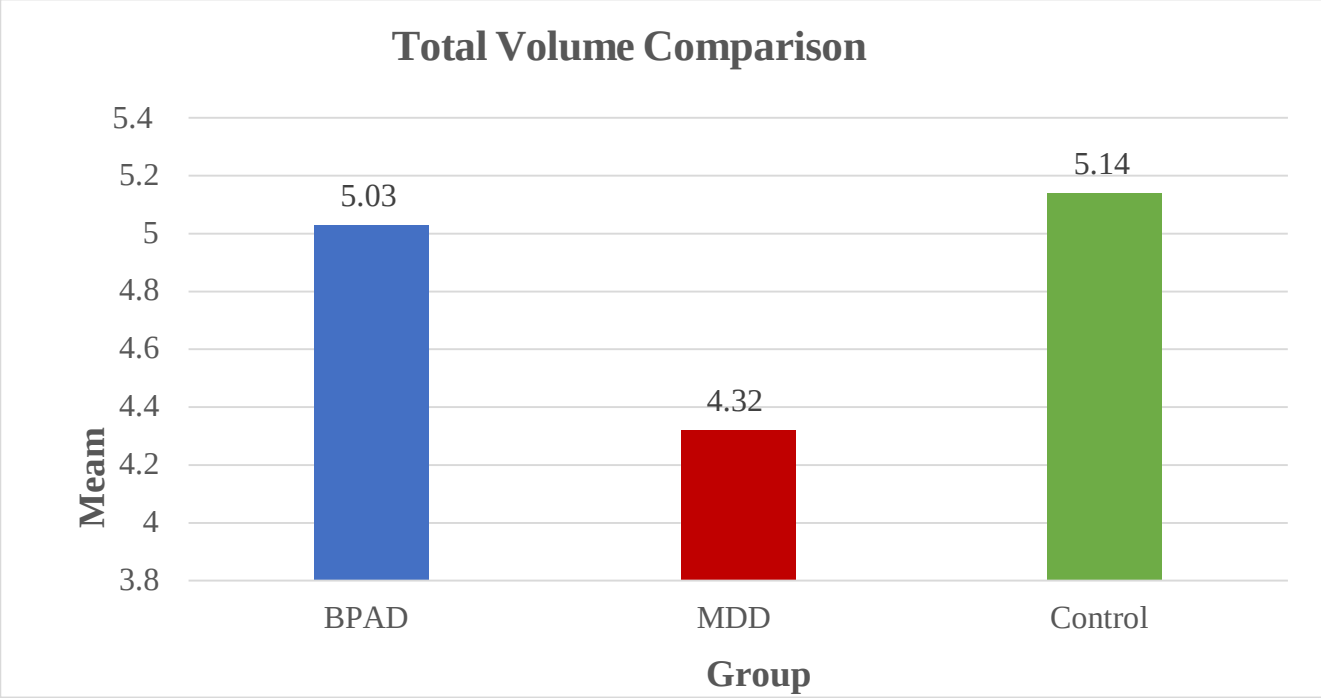

Figure 8: Bar diagram showing Total Volume comparison between three groups

Table 9: White Matter Changes comparison between three groups

		Group							
		BPAD		MDD		Control		Total	
		Count	%	Count	%	Count	%	Count	%
White Matter Changes	Absent	11	73.3%	13	86.7%	15	100.0%	39	86.7%
	Present	4	26.7%	2	13.3%	0	0.0%	6	13.3%
	Total	15	100.0%	15	100.0%	15	100.0%	45	100.0%

$\chi 2 = 4.615$, df =2, p =0.099

Among BPAD subjects, 26.7 had white matter changes, among MDD subjects 13.3% had white

matter changes and among control group, 0% had white matter changes. There was nosignificant difference in white matter changes between three groups.

Figure 9: Bar diagram showing White Matter Changes comparison between three groups

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