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Assessment of regional cerebral blood flow using dual energy multi detector computed tomography perfusion in patients of depression

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Abstract
Background: Major depressive disorder (MDD) involves a wide variety of psychobiological syndromes with the central characteristics of depressed mood and/or lack of interest associated with cognitive and somatic conditions, resulting in severe deterioration of function. Established correlation between depression and Regional cerebral hypoperfusion in specific areas by several SPECT studies. Aimed to assess changes In Regional Cerebral Blood Flow by CT Perfusion In patients of Depression.
Material and Method: This prospective follow-up study conducted for duration of 18 months at Department of Radiodiagnosis, Era's Lucknow Medical University, and Lucknow. Included all the patients aged between 18-40ys with newly diagnosed major depression fulfilling the ICD-10 criteria. Selected patients to undergo rCBF assessment before and after treatment by SIEMENS Somatom Force 384 Slice MDCT. The depression score was measured using questionnaire based with HAMD.
Result: Total of 40 patients who met the inclusion criteria were included in present study after obtaining the informed consent from all. Majority of the patients were in age group of 18-30yrs of age. Majority of the patients were female than male. The depression score (HAMD) was significantly reduced at the 2nd visit (14.01±1.63) compared to the 1st visit (16.12±2.10). There was a significant improvement in the mean cerebral blood flow at 2nd visit compared to the 1st visit in various regions included as ACA, MCA and PCA of right and left side.
Conclusion: The patients with depression are characterized by a wide range of cerebral blood flow impairments and there appear to be more prominent changes. The 384 slice MDCT appears to be a potentially useful tool for measuring rCBF, with advantages over existing instruments. This technique could be employed in psychiatric settings for biomarker, diagnostic and treatment response purposes.

Keywords: MDCT, Cerebral blood flow, HAM-D score, major depression

Introduction
Depressive disorders are known as mood disorders, which are characterized by the absence of depressive episodes from bipolar disorders. Depressive disorders include MDD, according to the American Psychiatric Association (APA) Diagnostic and Statistical Manual of Mental Illnesses, 4th edition, Text Revision (DSM-IV-TR), Dysthymic illness (low-grade persistent depression for 50 percent of days for at least 2 years) and low-grade depression (minimum 2 depressive symptoms for at least 2 weeks) [1]. Established correlation between depression and Regional cerebral hypoperfusion in specific areas by several SPECT studies,[2–4] fMRI[5] and MR with Arterial Spin studies [6, 7] and its improvement by antidepressants,[8] Electroconvulsive therapy and Cognitive Behaviour Therapy [9, 10]. Lack of conclusive studies by PET in Depressed patient for monitoring Brain Glucose Metabolism.
Many studies suggest that there is a potential relationship between depressive episode and altered Regional Cerebral Blood Flow(rCBF), most studies are subject to limitations including their use of semi-quantitative measurement that do not objectively reflect rCBF changes. CT Perfusion being cost effective and available compared to other and short duration scan than other established modalities. Dual Energy MDCT Perfusion – allows the acquisition of data pertaining to brain blood circulation and perfusion maps, including unenhanced, enhanced, delayed patterns, and assessment of arterial and venous diagrams in the same phase. This study aimed to assess changes In Regional Cerebral Blood Flow by CT Perfusion in patients of Depression, and correlate changes in perfusion with treatment and

clinical scoring.

Material and Method

This prospective follow-up study conducted for duration of 18 months at Department of Radiodiagnosis, Era's Lucknow Medical University, and Lucknow. Included all the patients aged between 18-40ys with newly diagnosed major depression fulfilling the ICD-10 criteria. Patients with past history of depression or associated psychotic features, disease of nervous system aneurysms involving the aortic vessels or chronic cerebral venous insufficiency and somatic diseases like diabetes, hypertension, coronary heart disease and atherosclerosis, also patients who are defaulters were excluded from the present study.

Selected patients to under-go CBF assessment by SIEMENS Somatom Force 384 Slice MDCT before and after treatment. The steps followed for rCBF measurement were; after iodine allergy testing, Nonionic contrast agent 40 ml was administered and Scan parameters were as follows: At 70kv, 120 mA and 120kv, 200mA, total scan time 40 sec. Each inspection obtained a total of 784 images (each volume data=0.5 min, total time=9.5 min). Perfusion image analysis was done by Syngo. Via software. The depression score was measured using questionnaire based with HAMD.

Statistical analysis: All the patient data were collected in excel sheet and analysed using the SPSS v21 operating on windows 10. The categorical variables are presented as frequency and percentage; the continuous variables are presented as mean ±SD. The follow-up data of the cerebral blood flow variables are analysed of mean difference using paired t-test. A p-value <0.05 was considered statistically significant.

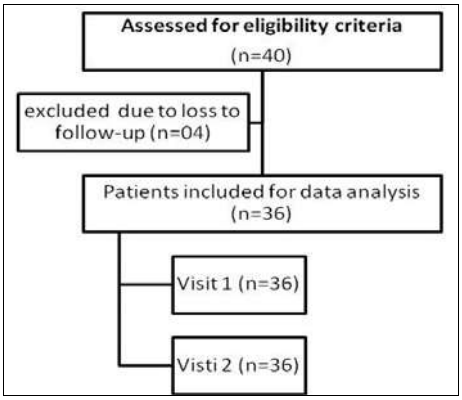

Fig 1: Study Design

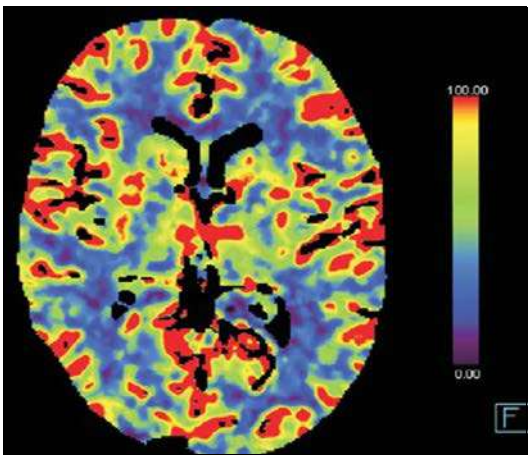

Fig 2: Cerebral Blood flow (d) CBFD/(ml/100ml/min)

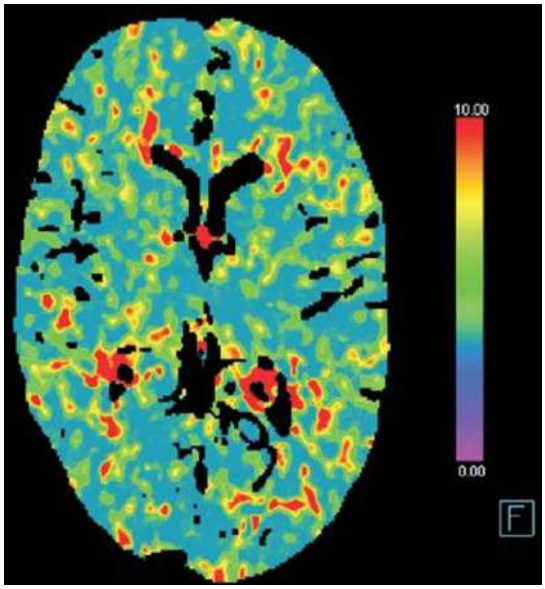

Fig 3: Mean Transit time (d) MTTD/S

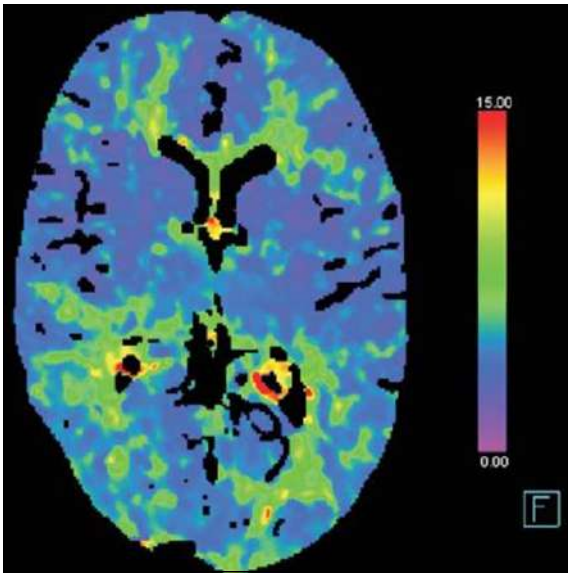

Fig 4: Time to drain TTDD/s

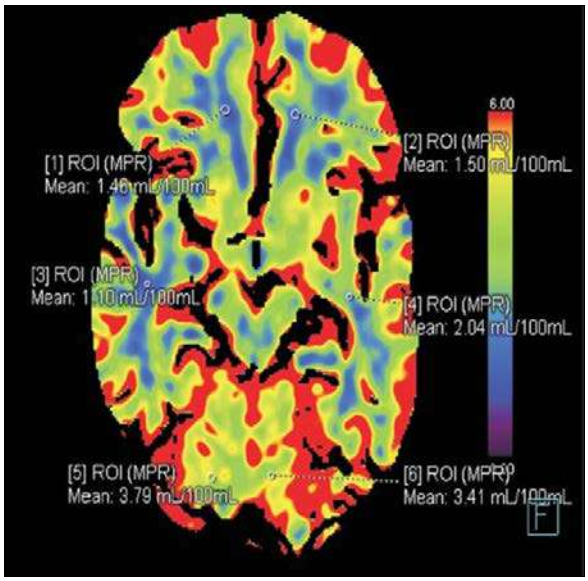

Fig 5: (Pt. 1)-Cross sectional cerebral hemispheres showing various CBR measurement ROIs in ACA, MCA & PCA territories

on first visit

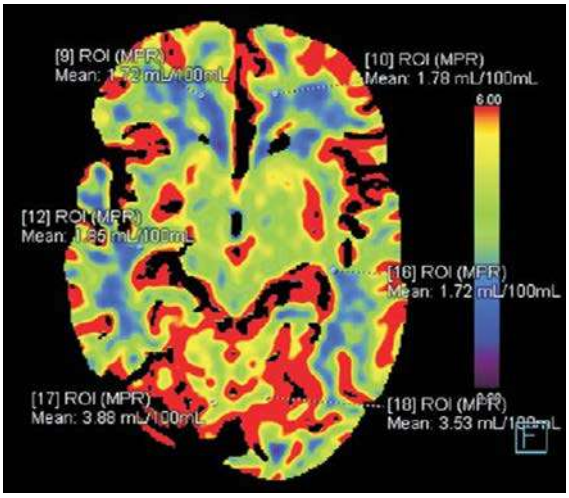

Fig 6: (Pt. 1)-Cross sectional cerebral hemispheres showing various CBR measurement ROIs in ACA, MCA & PCA territories on second visit

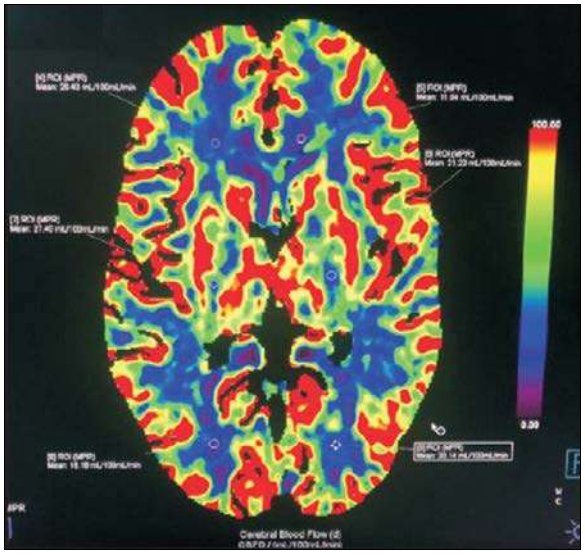

Fig 7: (Pt. 2)-Cross sectional cerebral hemispheres showing various CBR measurement ROIs in ACA, MCA & PCA territories on first visit

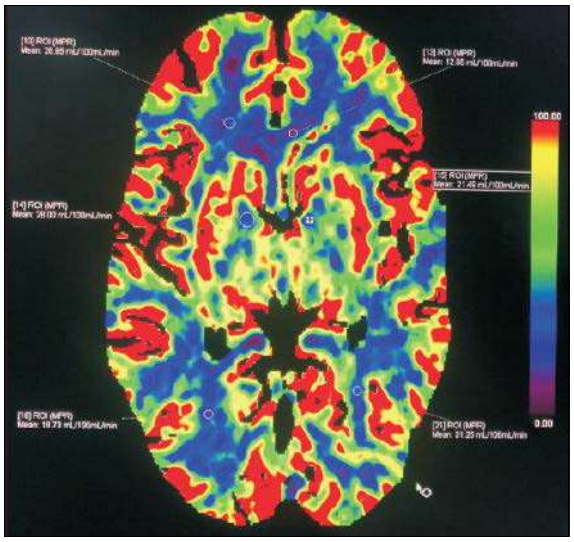

Fig 8: (Pt. 2)-Cross sectional cerebral hemispheres showing various CBR measurement ROIs in ACA, MCA & PCA territories on second visit

Result

Total of 36 patients fulfilling inclusion criteria who consented to be part of the study were included. The mean age of the patients was 35.18yrs with female preponderance.

Table 1: Age distribution of patients

		No. of Patients	Percent
Age in years	18-30	15	41.6
	31-40	12	33.3
	41-50	10	27.7
Gender	Male	15	42.5
	Female	21	57.5

There was a significant improvement in the regional cerebral blood flow in all the regions in present study with treatment. There was improvement in the rCBF in anterior cerebral artery, middle cerebral artery and posterior cerebral artery blood supply to the brain regions, this finding was statistically significant ($p<0.05$).

Table 2: Comparison of ACA region cerebral blood flow between visit 1 and visit 2.

Blood flow region		VISIT	Mean	SD	Paired t-test (p-value)
Anterior Cerebral Artery (ACA)	Right	1st visit	39.95	9.85	0.028*
		2nd visit	40.54	9.54	
	Left	1st visit	40.48	9.05	0.01*
		2nd visit	41.61	8.34	
Middle Cerebral Artery (MCA)	Right	1st visit	40.77	6.38	0.01*
		2nd visit	41.49	6.22	
	Left	1st visit	41.55	5.68	0.03*
		2nd visit	42.38	5.46	
Posterior Cerebral Artery (PCA)	Right	1st visit	43.35	7.56	0.049*
		2nd visit	43.92	7.14	
	Left	1st visit	42.86	5.87	0.01*
		2nd visit	43.77	5.89	

*$p<0.05$ is statistically significant, **$p<0.001$ is statistically highly significant.

Table 3: Comparison of depression (HAMD) score between visit 1 and visit 2

	VISIT	Mean	SD	Paired t-test (p-value)
Hamilton Depression Rating Scale (HAMD)	1st visit	16.12	2.10	0.045*
	2nd visit	14.01	1.63	

*$p<0.05$ is statistically significant, **$p<0.001$ is statistically highly significant.

In present study, there was a significant improvement in the

HAMD scores among the patients on the second visit compared to the first visit ($p<0.05$)

Discussion

The current conceptual framework indicates a functional discrepancy in particular neuro circuits that are centrally involved in mental and emotional behaviour regulation, cognitive processes, and default network operation [11]. The corresponding biological pathology of this hypothesised functional imbalance is complex. Chemical imbalances in neurotransmitter systems, neuroendocrine abnormalities and inflammatory mechanisms have all been suggested as role players in this shift away from functional homeostasis.[12]The hippocampus is mainly known for its function in learning and memory, but it also plays a significant role in general cognition, mood control and stress response.[13]

Majority of the patients were in age group of 18-30yrs of age (42.4%), with mean age of 35.18±8.74yrs. Majority of the patients were female compared to male. There is a changes in the regional blood flow in all the patients with depression and other disorders. The improvements in the regional blood flow have shown to reduce the symptoms in many studies. Su liang *et al*., [14] proposed that elderly depressive patients with cognitive impairment exhibited decreased local glucose meta bolism in the caudate nucleus bilaterally, the inferior frontal gyrus, left cingulate and anterior central gyrus regions, and the decline in both executive function and memory function was related to low local glucose metabolism in the caudate nucleus bilaterally, the frontal lobe, temporal lobe, the left central gyrus and limbic brain regions of deep white matter. Indeed, our results were concordant with this study.

ACA right showed a significant improvement in the blood flow at 2nd visit (40.54±9.54) compared to 1st visit (39.95±9.85). ACA left side showed a significant improvement in the blood flow at 2nd visit (41.61±8.34) compared to 1st visit (40.48±9.03). MCA right side showed a significant improvement in the blood flow at 2nd visit (41.49±6.22) compared to 1st visit (40.77±6.38). MCA left side showed a significant improvement in the blood flow at 2nd visit (42.38±5.46) compared to 1st visit (41.55±5.68). PCA right side showed a significant improvement in the blood flow at 2nd visit (43.92±7.14) compared to 1st visit (43.35±7.56). PCA left side showed a significant improvement in the blood flow at 2nd visit (43.77±5.89) compared to 1st visit (42.86±5.87).

Similar to present study, Takano *et al*., found improvement in the cerebral blood flow in patients at follow-up with treatment for major depression. They suggested that depressive patients have decreased CBF in the frontal and limbic region and medial frontal region playing a crucial role in ECT and recovery from depression [8]. In contrast, the study by Navarro V *et al*., assessed the brain perfusion alteration in depression patient, found no significant difference in 2 subgroups of patients for follow-up period of 12 months. The long-term evolution of frontal perfusion in elderly major depressives who respond to antidepressant biological treatment is essentially the same in those who receive electroconvulsive therapy and in those who receive medication [15].

Regional blood flow findings in patients with MDD indicate hyperactivity in VMPFC and LOPFC and hypoactivity in DLFPC relative to controls.[16] Given the functions of these areas, as mentioned above, this irregular pattern of behaviour may be responsible for the manifestations of symptoms associated with MDD [12]. Within the anatomical networks implicated in emotional processing by other types of evidence, these blood flow and metabolic data demonstrate that major depression is associated with reversible, mood state-dependent, neurophysiological abnormalities in some structures and irreversible, trait-like abnormalities in other structures [16]. With the treatment of depression by ECT, patients VBF showed a significant improvement in study by Nordanskog P *et al*. [17]

Previous studies have suggested reduced rCBF in MDD, illustrated by hypoperfusion in the frontal lobe, temporal lobe, and in the limbic system [18, 19]. Previous studies on functional imaging during depression have presented a diverseand complex picture [11]. Although many inconsistencies exist, acommon finding across studies is a decrease in cerebral blood flow (CBF) or cerebralmetabolic rate (CMR) during depression, especially in the frontal and prefrontal regions [3, 8, 15, 20, 21]. A more novel method for understanding neuronal activity during depression is functional resting state MRI (fMRI). Although studies are sparse, evidence of disturbed connectivity in subcortical neuro circuits during depression[22]support the suggested pathophysiological concept of depressionas a functional imbalance in specific neuro circuits.

In a study by Wang Y *et al*., found that there was decreased rCBFV in the majority of cerebral arteries in depressive patients, for example, Vs and Vm differed in the bilateral ACA, CA, TICA, VA and BA regions, while Vd differed in the left ACA and right TICA regions [23]. Also observed that the whole blood viscosity and hematocrit were significantly increased in the depressed patients [23]. Blood viscosity is a measure of the thickness and stickiness of blood, and increased levels of blood viscosity has been associated with arterial disease including myocardial infarction and stroke [24, 25]. It has been suggested that stress is associated with hemo-concentration of the cerebral hemispheres in patients with MDD [26].

The Hamilton Depression Rating Scale (HAM-D), the oldest, most widely used and validated instrument, has numerous versions, both clinician-rated and self-reported, as well as a computer-administered version. The depression score (HAMD) was significantly reduced at the 2nd visit (14.01±1.63) compared to the 1st visit (16.12±2.10).

Conclusion

The people with depression are characterized by a wide range of cerebral blood flow impairments. Patients responded to the treatment led to both improvement in Hamilton score and the CT rCBF volume changes. The 384 slice MDCT appears to be a potentially useful tool for measuring rCBF, with advantages over existing instruments. This technique could be employed in psychiatric settings for biomarker, diagnostic and treatment response purposes. Future studies should replicate this study in a larger sample, acquiring additional data to determine the factors influencing blood supply to the region of the brain of patients affected in those with depression. The relationship to treatment response in particular needs to be explored.

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