

ORIGINAL RESEARCH

**ROLE OF SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY
SCAN IN AFFECTIVE DISORDERS**

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ABSTRACT

Background: Depression is a common psychiatric illness affecting all age groups with high life time prevalence. Recurrent depressive disorder is diagnosed from the time of second episode of depression. Psychiatry specialty has started searching for a biological basis of illness with recent advances in functional imaging techniques, like Single Photon Emission Computed Tomography to identify changes in cerebral perfusion pattern associated with psychiatric illness

Aim and objectives: To study cerebral perfusion changes in Recurrent Depressive Disorder subjects in different regions of brain using SPECT scan during depressive episode and during clinical remission.

Methods: Prospective, observational study at a tertiary care center with institutional ethics committee approval.

Results: Increased cerebral perfusion was observed in Right Frontal region, Temporal and Caudate nucleus and decreased perfusion in Left Parietal region following successful treatment was observed in this study with eleven subjects. There has been regional perfusion pattern changes with treatment in different brain regions, no significant difference in regional blood flow was noticed between pre and post treatment groups (p value > 0.05) in all cerebral regions measured.

Conclusion: There are multiple regional variations in perfusion pattern in different Cerebral regions, but there does not exist significant differences in cerebral perfusion before and after successful treatment with oral anti depressant medications.

Keywords: **Recurrent Depressive Disorder, Single Photon Emission Computed Tomography, regional Cerebral Blood Flow, Ethyl Cysteine Dimer**

INTRODUCTION

Depression is a common psychiatric illness affecting both genders and all age groups with a life time prevalence of 5-17 %^[1]. Neuropsychiatric conditions are the most important causes of disability, accounting for around one third of Years Lost due to Disability among adults aged 15

years and over. Depression is the leading cause for disability both in males and females, the burden of depression is 50% higher for females than males.^[2] Brain imaging has become an important area of psychiatric research and is beginning to influence how we understand psychiatric illness and how it should be treated. Imaging techniques such as SPECT have this potential – the challenge is to identify the clinically relevant variables significantly associated with SPECT pattern. Brain SPECT is a well-established and reliable method for evaluating brain function through measurement of regional cerebral blood flow (rCBF).^[3] Recurrent depressive disorder is a common clinical condition where still diagnosis and management are dependent solely on clinical history. After a single episode of major depression, around 85% experience recurrent episodes. While the first episode of major depression is often provoked by a negative life event, subsequent episodes are often not precipitated by a stressor. Depressive episodes typically increase in frequency and duration as they return. Early functional neuroimaging studies comparing healthy and depressed subjects reported decrease in regional cerebral blood flow (rCBF) and metabolism typically in the frontal and prefrontal regions, but also in temporal, parietal and limbic-subcortical structures. The role of functional imaging like SPECT has been instrumental in current research on biological basis of depression. rCBF alterations in depression generally normalize after a response to treatment with medication.

MATERIALS & METHOD

Study Subjects

The study population consisted of 11 subjects suffering from Recurrent Depressive Disorder current episode Mild or Moderate Depressive episode recruited from the outpatient/inpatient population who fulfilled the DSM IV TR criteria. The study protocol was approved by the Institutional Ethics Committee of Sri Venkateswara Medical College. Informed written consent was obtained from the patient and Legally Associated Relative before enrolling into the study and confidentiality of individuals and results were maintained. Selection of Cases Individuals suffering from Recurrent Depressive Disorder currently Mild or Moderate depression were identified and diagnosis confirmed by DSMIV TR. Severity of depressive episode is evaluated by administering Hamilton Rating Scale of Depression (HAM-D). All the subjects who underwent SPECT acquisition during depressive phase were followed up on monthly basis. A repeat SPECT was performed after the patient attained clinical remission within three months duration.

Inclusion Criteria

1. Both Genders between the ages of 18 to 45 years.
2. Subjects who have signed a valid written consent along with Legally associated Relative
3. Subjects having a diagnosis of Major Depressive Disorder, Recurrent fulfilling criteria of DSM IV TR.
4. Subjects currently in a depressive episode, HAM-D score >7 and <8 .

Exclusion Criteria

1. Meeting DSM IV TR criteria for any other co morbid psychiatric diagnosis or other Axis I disorder
2. Associated abuse or dependence of drugs during the past three years

Procedure:

The SPECT study was performed in the above subjects with 740 MBq (20 mCi) of Tc99m Ethyl Cysteinate Dimer (ECD) injected intravenously into the antecubital vein that was cannulated 10 min before. The metabolic process of deesterification accounts for hydrophilic conversion of 99m Tc-ECD, a perfusion-metabolic (deesterification) coupling is needed in case of 99m Tc-ECD to be trapped within Nerve cell. Thus, 99m Tc-ECD would have a predominant cellular-metabolic

uptake.^[4] The patient lied in the dorsal decubitus position in a room with ambient noise and light under control and patient is instructed not to sleep. No environmental stimuli were allowed to distract the patient. Thirty minutes after the injection, brain SPECT images were gathered. Radioactive urine excreted by the subject following acquisition of SPECT was disposed as any radioactive hazardous waste for the next 24 hours.

Preparation of the patient

Before arrival, patients were instructed to avoid, caffeine, alcohol, or any other drugs known to affect cerebral blood flow (CBF). Brain perfusion is sensitive to neuronal activities, hence, tracer injection is administered in a quiet room and no interaction with patients at this time is desirable, to avoid any sensorial and cognitive stimuli.

Image Processing:

The Acquisition is tri dimensionally reconstructed with iterative reconstruction using Ordered Subset Expectation Maximum 2-D technique applying Gaussian filter with an intrinsic resolution of camera of 4.2 mm Full Width Half Maximum and with attenuation correction factors were applied using Chang's attenuation correction having 0.15 attenuation coefficient.

Data Analysis

For interpretation of SPECT scan of subjects, a Semi Quantitative analysis using Neurogam analysis software was performed by the mean counts per pixel in each region were measured and exported into a personal computer running a statistical analysis software package (Stat View v.4.02). The mean counts per pixel in each region, including Frontal, Temporal, Parietal, Occipital, Caudate nucleus and Thalamus regions, were compared to the mean activity per pixel in the entire cortex (whole brain).

DSM IV TR (Diagnostic and Statistical Manual IV TR)

DSM IV TR is designed for use in both clinical diagnosis and research. The diagnosis of Major Depressive Disorder requires the presence of at least five of nine symptom criteria for at least 2 weeks, one of which is depressed mood or loss of interest.

Hamilton Rating Scale for Depression

The HAM-D was developed to monitor the severity of depressive episode, the version in most common use has 17 items. Items on the HAM-D are scored from 0 to 2 or from 0 to 4, with total score ranging from 0 to 50. Scores of 7 or less may be considered normal; 8 to 13, mild; 14 to 18, moderate; 19 to 22, severe; and 23 and above, very severe. The ratings can be completed in 15 to 20 minutes. Reliability is good to excellent, particularly when the structured interview version is used.

RESULTS

Visual Inspection of the Images

A review of the images did not reveal any occult brain disease. We observed mild asymmetry with decreased radioactivity in several regions of the cortex. However, no specific, consistent abnormalities in ECD activity were observed on any of the sagittal, coronal or transaxial images.

Table 1: Depression Subjects - Clinical Profile

S.No	Gender	Positive Family History	Age of Onset	Total Duration of Illness	No of Episodes	HAM-D (Score) Pre Treatment	HAM-D (Score) Post Treatment
1	Female	Present	31	4	4	18	3
2	Female	Absent	28	2	2	18	5
3	Female	Absent	25	3	2	15	2
4	Male	Present	27	8	3	16	1
5	Male	Absent	24	2	2	11	2
6	Female	Absent	33	3	2	14	4
7	Male	Present	32	8	3	121	2
8	Female	Absent	24	2	2	10	1
9	Male	Absent	35	7	4	9	3
10	Female	Absent	29	5	3	17	2
11	Female	Absent	35	8	3	17	4

Table 2: Treatment Details Of Patients Participated In The Study

MEDICATION	N
ANTI DEPRESSANTS	
FLUOXETINE	10
DOTHIEPIN	04
BENZODIAZEPINES	
Clonazepam max (2 mg)	10

Table 3 : t-Test : PRE TREATMENT PHASE VS POST TREAT PHASE

	Groups	N	Mean	Std. Deviation	Std. Error Mean	t-value	P value
Frontal Right	Pre Treat	11	48.855	4.186	1.262	0.620	0.543
	Post Treat	11	47.627	5.064	1.527		
Frontal Left	Pre Treat	11	47.336	4.581	1.381	-0.135	0.894
	Post Treat	11	47.582	3.891	1.173		
Parietal Right	Pre Treat	11	52.955	4.885	1.473	1.200	0.244
	Post Treat	11	50.600	4.301	1.297		
Parietal Left	Pre Treat	11	53.446	4.484	1.352	0.676	0.507
	Post Treat	11	52.227	3.956	1.193		
Temporal Right	Pre Treat	11	37.291	8.117	2.448	-0.366	0.719
	Post Treat	11	38.382	5.664	1.708		
Temporal Left	Pre Treat	11	31.191	10.707	3.228	-0.998	0.330
	Post Treat	11	35.109	7.402	2.232		
	Pre Treat	11	55.091	5.359	1.616	0.612	0.547

Occipital Right	Post Treat	11	53.755	4.870	1.469		
Occipital Left	Pre Treat	11	55.955	5.953	1.795	0.423	0.677
	Post Treat	11	55.027	4.176	1.259		
Caudate Nucleus Right	Pre Treat	11	42.346	8.005	2.414	0.016	0.987
	Post Treat	11	42.300	4.742	1.430		
Caudate Nucleus Left	Pre Treat	11	41.855	6.436	1.940	0.973	0.342
	Post Treat	11	39.700	3.543	1.068		
Thalamus Right	Pre Treat	11	44.746	15.722	4.740	-0.234	0.817
	Post Treat	11	45.909	4.928	1.486		
Thalamus Left	Pre Treat	11	48.627	8.166	2.462	0.989	0.335
	Post Treat	11	45.464	6.779	2.044		

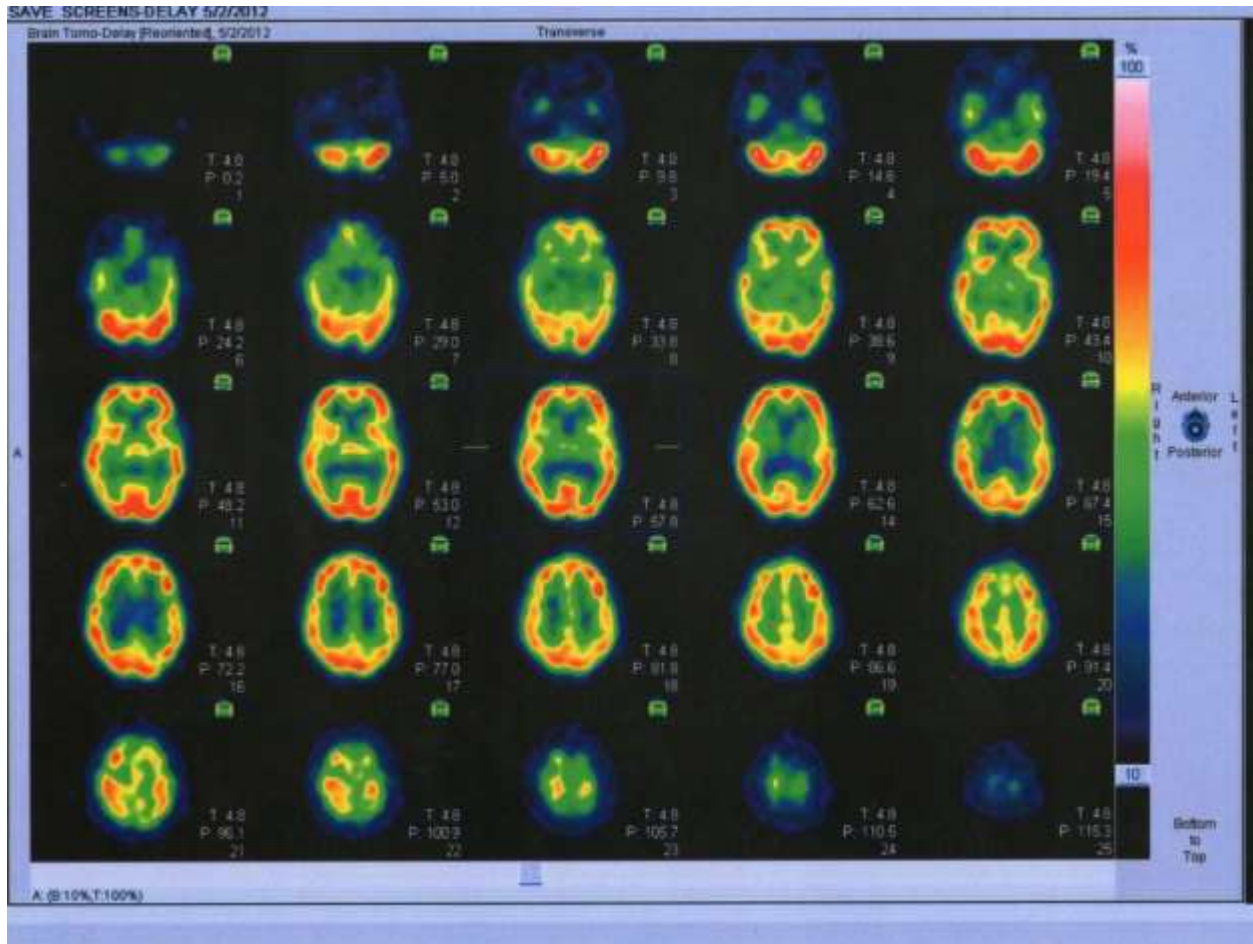


Image 1 :SPECT findings of female Subject during Depressive Episode

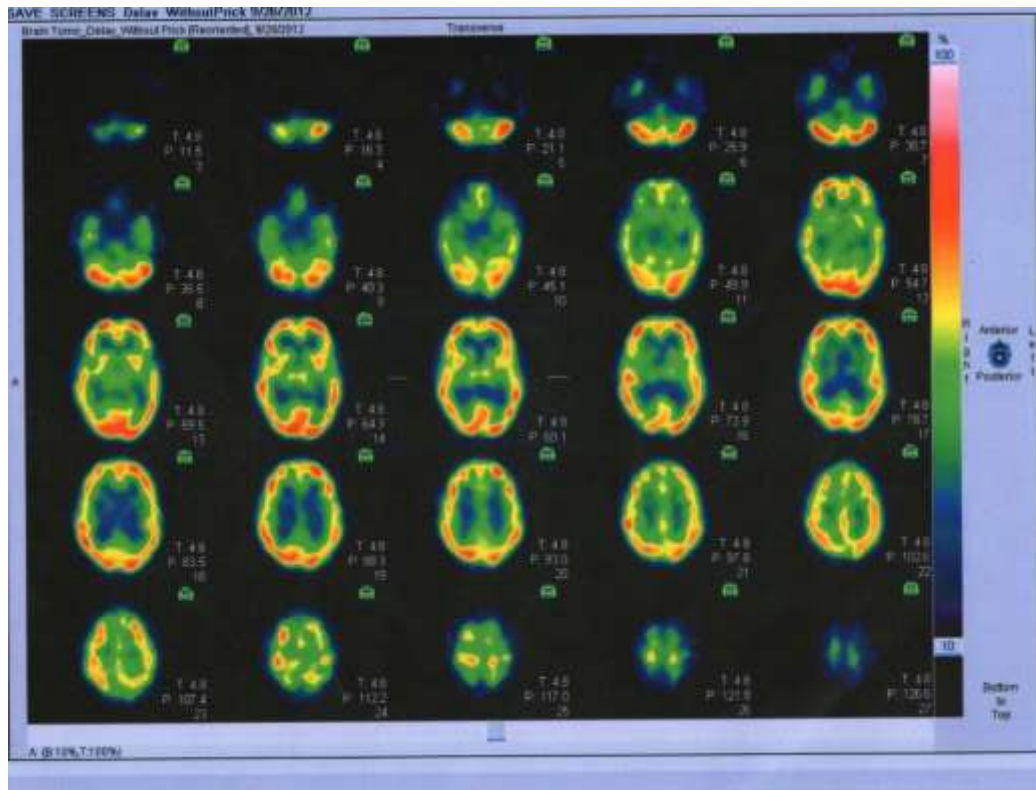


Image 2 :SPECT findings of female Subject during Clinical Remission

DISCUSSION

The present prospective, observational study revealed the pattern of regional cerebral blood flow changes in subjects with Recurrent Depressive Disorder currently Mild or Moderate depressive episode using SPECT scan. The available literature with regard to SPECT imaging and Depressive episode consists of studies in different clinical settings with varying severity and magnitude of depressive episode. There are conflicting observations across all over these studies with some studies reporting an increased perfusion and other studies reporting a decreased perfusion with inconsistent results. More over there is paucity of literature particularly in the Indian population. Socio demographic data of subjects included in the present study was, 63.63% Subjects were female and 36.37% were male subjects, all the subjects were married and their educational status was primary education (54.54%), secondary education (18.18%), Intermediate qualification (18.18%) and Graduation (9.09%). Socio economic status was Low in 72.73% and Middle in 27.27% study population. Locality of individuals belonging to urban was 36.36% and Rural was 63.63%. In the present study, subjects with Major Depressive Disorder, Recurrent were examined both during depressive episode and follow up after attaining clinical remission. This helps to observe any change in regional cerebral blood flow differences that could be attributed to present depressive episode. Subjects were included in the study only after confirmation of diagnosis by thorough clinical evaluation and confirmation of previous depressive episode i.e Recurrent Depressive Disorder currently Mild or Moderate Depressive Episode fulfilling diagnostic criteria according to DSM-IV TR. Severity was assessed using Hamilton Rating Scale for Depression (HAM-D) during Depressive episode and after attaining clinical remission. Both the genders were included in the present study with seven female subjects and four male subjects. Positive family history of Depressive episode was observed in three subjects (one female and two male). Eight

individuals were not having significant family history of any psychiatric illness. Five subjects were suffering from second episode of Depression, whereas four subjects were suffering from third episode and two of them were suffering from fourth depressive episode.

The salient features of the present study

- 1) Mean age of the sample was 34.09 years
- 2) Mean age of onset of illness was 29.36 years
- 3) Mean number of depressive episodes were 2.7
- 4) Family history of Mood disorder was found in 27.27 % of sample population
- 5) Gender differences were noted in cerebral perfusion pattern, with higher perfusion observed in Female subjects when compared to Male subjects in right parietal, right caudate, left parietal, left occipital and left caudate nucleus regions.

However, in our study we did observe greater variability in regional ECD activity in depressed patients. No significant differences were observed in patients during depressive episode and after attaining clinical remission. Few studies with Brain SPECT with perfusion agents in patients free of medication has shown hypoperfusion of the following areas: The Prefrontal area and Temporal lobes, Cingulate gyrus, and Left Caudate nucleus.^{[5][6][7]} Where as in the present study, when Perfusion pattern was compared between Right and Left brain regions, higher perfusion values were observed in patients in Right Frontal, Temporal and Caudate Nucleus compared with Left Frontal, Temporal and Caudate Nucleus during pretreatment phase. Following successful treatment, decreased cerebral perfusion was restored in Right Frontal and Caudate Nucleus regions with no significant difference on both sides during post treatment phase. In Left Temporal region though perfusion has increased on post treatment significantly, there was difference in perfusion on both sides of brain regions even in post treatment phase. In contrast higher perfusion changes were observed during pre treatment phase on both sides of brain.

In the Parietal region of brain, after successful treatment it has shown decreased perfusion values in post treatment phase bilaterally. In thalamic region, perfusion has increased following treatment on Right side and decreased following treatment on left side. While some investigators have reported specific abnormalities in regional brain activity during depression^{[8][9][10][11]}. Maes et al. failed to detect any abnormalities in the distribution of HMPAO (hexamethylpropyleneamine oxime) in depressed patients compared to control groups^[12] Discrete rCBF abnormalities with HMPAO have included older patients who normally show more frequent rCBF disturbances^[13]. Investigations with Xenon-133 SPECT suggest that there may be an interaction of age with depressive subtype for both global and rCBF^[14]. Significant effect of normal aging on the distribution of HMPAO in healthy subjects has been demonstrated^[15]. In contrast, in the present study the patients were relatively young and without any significant effects of ageing on ECD activity. No significant interactions were observed between the mean HMPAO activity ratios in any brain region and age or gender^[16]. Severity of depression has also been found to be positively correlated with changes in rCBF^[17]. In a study using IMP (iofetamine) SPECT, right temporal lobe perfusion related asymmetry which was observed in depressed patients compared to medically ill controls.^[8] There is evidence of prefrontal, limbic, and paralimbic hypoperfusion in both unipolar and bipolar depression^[18] and the lateral frontal area involvement in acute depression in the elderly.^[19] Hypo frontal perfusion changes were associated with severe negative or cognitive symptoms rCBF in depressed patients before treatment was lower than in healthy controls, and a response to oral medication associated with an increase in cerebral perfusion.^[20] Though there has been perfusion changes between pre-treatment and post treatment groups, in the present study we were unable to find statistically significant difference between these two groups. ECD is a sensitive chemical agent for detecting abnormalities characterized by neuronal necrosis, the present study

suggests that it is less sensitive as a brain tracer for identifying the subtle abnormalities of functional psychiatric disorders than PET scan

CONCLUSION

Recurrent depressive disorder is a common psychiatric disorder affecting any age groups where the exact etiology of the condition is still poorly understood. SPECT scan is been explored in the field of psychiatry to find association between cerebral perfusion and the Depressive disorders. In the present study though cerebral perfusion changes were observed between depressive episode and post treatment, it was not statistically significant to define a specific association between the severity of depression episode and cerebral perfusion pattern of the individual.

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