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CEREBRAL PERFUSION CHANGES IN DEPRESSION SUBJECTS USING SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY

Psychiatry

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ABSTRACT

Background : Depression is a common psychiatric illness affecting all age groups with high life time prevalence. Psychiatry has started searching for a biological basis with recent advances in functional imaging techniques, like Single Photon Emission Computed Tomography to identify changes in cerebral perfusion associated with psychiatric illness

Aim and objectives: To study cerebral perfusion changes in Recurrent Depressive Disorder subjects in different locations of brain using SPECT scan during depressive episode and comparing with normal subjects

Material and Methods: Cross sectional, comparative and observational study at a tertiary care center with institutional ethics committee approval

Results:. Significant difference in perfusion was noted only in left temporal region (p value < 0.03) in depression population when compared to control population

Conclusion : Brain perfusion changes were observed in multiple brain regions, but significant only in Left Temporal region showing that perfusion pattern of brain has an association with depressive episode

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 one of the leading cause for disability in both genders, the burden of depression is 50% higher for females than males.[2]

Brain single photon emission computed tomography (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.

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. rCBF alterations in depression generally normalize after a response to treatment with medication.

Materials and Methods:

Study subjects:

The study population consisted of eleven subjects suffering from Recurrent Depressive Disorder current episode Mild or Moderate Depressive who fulfilled the DSM IV TR criteria and compared with ten normal subjects.

Selection of Cases:

Individuals suffering from Recurrent Depressive Disorder currently Mild or Moderate depressive episode were identified and diagnosis confirmed by DSM-IV TR.

Selection of Controls

The control group consisted of five men and five women who consented to participate in the study. All were subjectively healthy without a lifetime history of any psychiatric disorder. The results of their semi-structured histories, physical examinations, and laboratory screening studies were normal.

Inclusion Criteria :

1. Subjects between the ages of 18 to 45 years.
2. Subjects having a diagnosis of Major Depressive Disorder, Recurrent as defined by DSM IV TR.
3. Subjects experiencing Mild or Moderate depressive episode, HAM-D score >7 and <19

Exclusion Criteria:

1. Co morbid other psychiatric illnesses
2. Female subjects who are pregnant or breast feeding.

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 patient lied in the dorsal decubitus position in a room with ambient noise and light under control.

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[4]

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. 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 (years)	No. of Episodes	HAM-D score
1	Female	Present	31	4	4	18
2	Female	Absent	28	2	2	18
3	Female	Absent	25	3	2	15
4	Male	Present	27	8	3	16
5	Male	Absent	24	2	2	11
6	Female	Absent	33	3	2	14
7	Male	Present	32	8	3	11
8	Female	Absent	24	2	2	10
9	Male	Absent	35	7	4	9
10	Female	Absent	29	5	3	17
11	Female	Absent	35	8	3	17

Table 02 : t-test : Depression Subjects VS Control Subjects

Brain Region	Groups	N	Mean	Std. Deviation	Std. Error Mean	t-value	p value
Right Frontal	Depression	11	48.855	4.186	1.262	0.042	0.967
	Control	10	48.780	3.890	1.230		
Left Frontal	Depression	11	47.336	4.581	1.381	-1.535	0.141
	Control	10	50.400	4.557	1.441		
Right Parietal	Depression	11	52.955	4.885	1.473	0.104	0.918
	Control	10	52.740	4.549	1.438		
Left Parietal	Depression	11	53.446	4.484	1.352	-0.185	0.855
	Control	10	53.860	5.749	1.818		
Right Temporal	Depression	11	37.291	8.117	2.448	-1.485	0.154
	Control	10	41.530	4.118	1.302		
Left Temporal	Depression	11	31.191	10.707	3.228	-2.259	0.036
	Control	10	39.690	5.394	1.706		
Right Occipital	Depression	11	55.091	5.359	1.616	0.703	0.490
	Control	10	53.500	4.966	1.570		
Left Occipital	Depression	11	55.955	5.953	1.795	0.315	0.756
	Control	10	55.160	5.577	1.764		
Right Caudate Nucleus	Depression	11	42.346	8.005	2.414	-0.441	0.664
	Control	10	43.760	6.530	2.065		
Left Caudate Nucleus	Depression	11	41.855	6.436	1.940	0.075	0.941
	Control	10	41.640	6.740	2.131		
Right Thalamus	Depression	11	44.746	15.722	4.740	-0.653	0.522
	Control	10	48.270	6.890	2.179		
Left Thalamus	Depression	11	48.627	8.166	2.462	-0.302	0.766
	Control	10	49.560	5.629	1.780		

Significant difference in cerebral perfusion was observed only in left temporal region (p value < 0.03)

DISCUSSION

The present cross sectional, observational study evaluated the pattern of regional cerebral blood flow in subjects with Recurrent Depressive Disorder currently Mild or Moderate depressive episode patients and comparing them with control population using SPECT. The available literature with regard to SPECT and depression consists of studies which included patients in different clinical setting with varying severity of depressive episode. There are conflicting observations across these studies with some studies reporting an increased perfusion and other studies reporting a decreased perfusion. Moreover there is paucity of literature in the Indian context.

Socio demographic profile of Depressive subjects included in the study was, 63.63% subjects were female and 36.37% were male subjects, all the subjects were married. Socio economic status was Low in 72.73% and Middle in 27.27% study population, no subjects belonged to upper socio economic status. Locality of individuals belonging to urban was 36.36% and Rural was 63.63%.

Socio demographic profile of control subjects included in the study was 50% were females and 50% were males, 80% of subjects were married and 20% were unmarried, Socio economic status was high in 10%, middle in 40 % and Low in 50% .Urban was 60% and Rural was 40%Severity of depressive episode was assessed by HAM-D. Both the genders were included in the study with seven female subjects and four male subjects among patient group and five each in control group. Positive family history of Depressive illness was noticed in three subjects (one female and two males).

However, in our study we did observe greater variability in regional ECD activity in depressed patients.

Significant difference in cerebral perfusion pattern was observed in patients during depressive episode in Left Temporal region when compared to control group (p value <0.03) 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] 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 controls[12]

Clinical Correlates of SPECT Findings

Several clinical and technical reasons might explain the divergent observations in various SPECT studies in depression. For example, some studies reporting 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 age 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 positively correlate with changes in rCBF [17]. Interestingly, in a study using IMP (iofetamine) SPECT, right temporal lobe asymmetry was observed in depressed patients compared to medically ill controls.[8]

ECD is a sensitive agent for detecting abnormalities characterized by neuronal necrosis, the present study suggests that it is less sensitive as a tracer for identifying the more subtle abnormalities of functional psychiatric disorders when compared with PET scan

CONCLUSIONS

Recurrent depressive disorder is a common psychiatric disorder affecting all age groups. SPECT scan is being explored in the field of psychiatry to find association between cerebral perfusion and the depressive disorders. In our study though there were differences in cerebral perfusion pattern between depression population and control population, significant difference was observed only in Left Temporal region (p value <0.03)

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