CEREBRAL BLOOD FLOW PATTERNS USING SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY IN PATIENTS WITH DISSOCIATIVE DISORDERS AND HEALTHY CONTROLS

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ABSTRACT

Objective: To compare the cerebral blood flow (CBF) changes in patients diagnosed to have Dissociative Disorder with healthy controls.

Study Design: Cross Sectional Comparative study

Place and Duration of Study: The study was done in the Department of Psychiatry Military Hospital Rawalpindi in collaboration with Nuclear Medical Centre (NMC) Armed Forces Institute of Pathology (AFIP), a tertiary care centre of Pakistan Armed Forces from Dec 2004 to May 2005.

Patients and Methods: This cross sectional comparative study was done at Dept of Psychiatry Military Hospital Rawalpindi in collaboration with nuclear Medical Centre (NMC), at Armed Forces Institute of Pathology (AFIP) which is a tertiary referral center. A sample of 30 patients diagnosed as having Dissociative Disorder was compared with 10 controls for brain perfusion changes using TC-99m HMPAO (Hexamethyl-propylene-amine-oxime) Tc-99m.

Results: In group 1 perfusion changes were observed in 27 (90%) cases whereas unremarkable and insignificant changes were noted in 3 (10%) cases but no perfusion were noted in controls (P<0.001) In patients who were suffering from different types of dissociative disorder marked cerebral hypoperfusion was observed in frontal, frontomotor, orbitofrontal and temporal regions whereas hyperperfusion was noted in frontal and orbitofrontal areas in few cases.

Conclusion: Cerebral blood flow changes in the fronto parietal brain are associated with symptomotology in dissociative disorders.

Key words: Dissociative disorders, SPECT, Tc-99m HMPAO, Cerebral Blood Perfusion.

INTRODUCTION

The term Hysteria owes its origin to the ancient myth of "Wandering Uterus" as unmarried women folk were observed to be the predominant sufferers of this malady; the oldest mention is found in writings by Hippocrates and Galen [1].

In the 19th century Austrian psychiatrist Sigmund Freud [2] first used the term conversion as a substitute for somatic manifestations encountered in hysteria. The term Dissociative Disorders is currently used for Hysteria. Traditionally it has been recognised as stress related disorder with a psychiatric basis. In the 1960s Eliot Slater [3] reported that 64% of patients with conversion disorder show evidence of an organic brain disorder, compared with 5% of control subjects. The idea of blood flow as one of the central regulators of brain function has been considered as forerunner of neuroimaging, for more than two decades [4,5]. Neuroimaging using Tc-99m HMPAO and Single Photon Emission Tomography is being increasingly used in the assessment of vascular status in various diseases of the brain both organic and psychiatric [6]. Functional neuroimaging has revealed selective decreases in the activity of frontal and sub cortical circuits involved in motor control during hysterical paralysis, decreases in somatosensory cortices during hysterical anesthesia, or decreases in visual cortex during hysterical blindness [7]. Sar and colleagues reported brain perfusion changes among patients with Dissociative Identity Disorder (DID) [8]. The rCBF ratio was decreased in orbito-frontal region bilaterally and increased in left (dominant hemisphere) lateral temporal region among patients with dissociative identity disorder when compared to the control group [9].

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In Pakistan, no studies have been undertaken so far to study the biological basis of dissociative disorders. These disorders are common in military setting as well; the military setting with its peculiar logistics has the advantage of reaching individuals affected by dissociative disorders for both genders relatively easily. In order to find whether a pathophysiological basis for this disorder exists in our population, this study has been proposed. This study is intended to help fill in the gap that exists in our understanding of the biological aspects of the disease.

MATERIALS AND METHODS

This Cross-sectional, Comparative study was done at Department Of Psychiatry Military Hospital Rawalpindi in collaboration with Nuclear Medical Centre (NMC), at Armed Forces Institute of Pathology (AFIP) which are tertiary referral centres. A total of 40 cases were included with age ranging between 15-55 years. Thirty patients diagnosed to be suffering from Dissociative Disorders fulfilling the ICD-10 Diagnostic Criteria have been included in the study using non probability, convenience sampling. Ten individuals matched for age, gender that reported to Nuclear Medical Centre (NMC) Armed Forces Institute of Pathology, Rawalpindi for neuroimaging for suspicion of disorders other than psychiatric disorder but found to have normal single photon emission computed tomography (SPECT) scans have served as healthy controls. Only 10 controls were taken because of the high cost and difficulties in availability of radiopharmaceutical TC-99m HMPAO. An informed written consent was taken from the patient before the procedure; Patient was also informed that this test may not have any direct bearing with his treatment. Patients suffering from primary or secondary, cardiovascular or neurological diseases, or taking drugs that cause cerebrovascular changes in the brain were excluded. Patients suffering from Dementia or other neuropsychiatric diseases which can affect cerebral perfusion status were also excluded. All the subjects were injected TC-99m HMPAO in a dose of 20mci (740 MBq) in a quite dimly lit and sound free room in supine position in a controlled environment after taking necessary precaution according to standard operative procedures. Patient was positioned comfortably on the SPECT table, and was asked not to move during the course of SPECT acquisition. Head of the patient was fastened with a soft belt to avoid motion. Clearance of camera head was made for patient's safety and orbit was kept as close to the patient as possible for better resolution. After 45 min, static images of the brain were taken using gamma camera with Siemens integrated Orbitor R system interfaced with Macintosh based power PC 8100/110 with ICON software version 6.0.3.SPECT acquisition after initiation took 35-40 minutes. Whole procedure was closely observed to monitor patient's head movement and in case it happened the scan was aborted and started a new. Parallel hole high-resolution collimator was used. Camera calibration Quality Control procedures were performed on camera to optimize and evaluate its performance. Image Processing Raw data acquired was processed through ICON software (version 6.0.3) provided by the gamma camera. The raw projection obtained was reconstructed using Butterworth filter at a cutoff value of 0.3 cycles per cm, order was 12. Chang's attenuation coefficient value of 0.12/cm was used having upper and lower window levels set at 95% and 0% respectively for reconstruction 3 pixel thick slices were obtained, and further processed with the help of the software. The blood flow patterns were observed and reported upon by consultant Nuclear Physician. The data collected through a structured Proforma, was entered in SPSS version 13. Descriptive statistics was used to describe the data. Mean + SD was used for numerical variables like age and duration of illness. Frequencies along with percentages were used for categorical variables like sex, education and perfusion changes. t' test was used to compare the difference of age between cases and controls. Chi Square test was used to establish statistical significance for the findings of categorical variables.

RESULTS

Thirty patients were included in Group I and 10 controls were included in group 2 age in each group was 25.4 + 3.34 and 26.2 + 5.65,

respectively. Male to Female result was 1:1.4 and 1:1.5 respectively. Both the groups were comparable with respect to age (P>0.05) and gender (P>0.05). The mean duration of illness of group 1 was 18.76 + 13.13 in days with minimum of 1 day duration and maximum of 45 days. Distribution of patients with various dissociative disorders in group 1 is given in table 1. Half of them had dissociative motor disorder and about 1/4th had dissociative amnesia.

According to SPECT scan results in group-I 27(90%) cases had perfusion changes where as 3(10%) cases had unremarkable and insignificant perfusion changes while in controls no perfusion changes were observed (P<0.001).

In dissociative amnesia hypoperfusion changes were noted in frontal, temporal and orbitofrontal areas (Fig.1), whereas in dissociative aneasthesia and sensory loss no hypoperfusion but hyperperfusion were observed in frontal, temporal and orbitofrontal region while perfusion in the frontomotor region was unaltered (Fig. 2). In dissociative disorders (Trans and possession state) hypoperfusion changes were noted in frontal, orbitofrontal and temporal region. In dissociative fugue hypoperfusion changes were in left frontal and both temporal regions. In Dissociative motor disorder bilateral hypoperfusion were observed in frontal, frontomotor and temporal area as well as hyperperfusion in orbitofrontal area (Fig.3). Bilateral temporal and right frontal hypoperfusion were observed in mixed dissociative disorders (Table-2).

DISCUSSION

The insight into evaluation of regional cerebral blood flow changes in patients of dissociative (conversion) disorders by utilizing functional neuroimaging techniques is presently an upcoming research concern, merging both fields of psychiatry and nuclear medicine. Recent studies have shown that dissociative disorders have their own specific etiological backgrounds and not merely a medical or psychiatric misdiagnosis [10,11].

Single photon emission computerized tomography using Tc-99m ECD revealed a consistent decrease of regional cerebral blood flow in the thalamus and basal ganglia contralateral to the deficit as studied by Vulleimer P et al [12].

Physicians and psychiatrists are quite handicapped in finding any cerebral lesion in dissociative disorders because there is no

Table-1: Distribution of Various Dissociative Disorders (n=30)

Dissociative Disorders (n=30)	No of Cases	Percentage
Dissociative amnesia	8	26.66%
Dissociative aneasthesia and sensory loss	2	6.66%
Dissociative disorders (trans and possession state)	1	3.33%
Dissociative fugue	3	10%
Dissociative motor disorder	15	50%
Mixed dissociative disorders	1	3.33%

Table-2: Distribution of Perfusion Changes of Different Areas of the Brain in Various Dissociative Disorders n=30

Dissociative Disorders (n=30)	Frontal	Frontomotor	Orbitofrontal	Temporal	Parietal
Dissociative amnesia	Hypoperfusion	-	Hypoperfusion	Hypoperfusion	-
Dissociative aneasthesia and sensory loss	Hyperperfusion	-	Hyperperfusion	Hyperperfusion	-
Dissociative disorders (trans and possession state)	Hypoperfusion	-	Hypoperfusion	Hypoperfusion	-
Dissociative fugue	Hypoperfusion	-	-	Hypoperfusion	-
Dissociative motor disorder	Hypoperfusion	Hypoperfusion	Hyperperfusion	Hypoperfusion	-
Mixed dissociative disorders	Hypoperfusion			Hypoperfusion	-

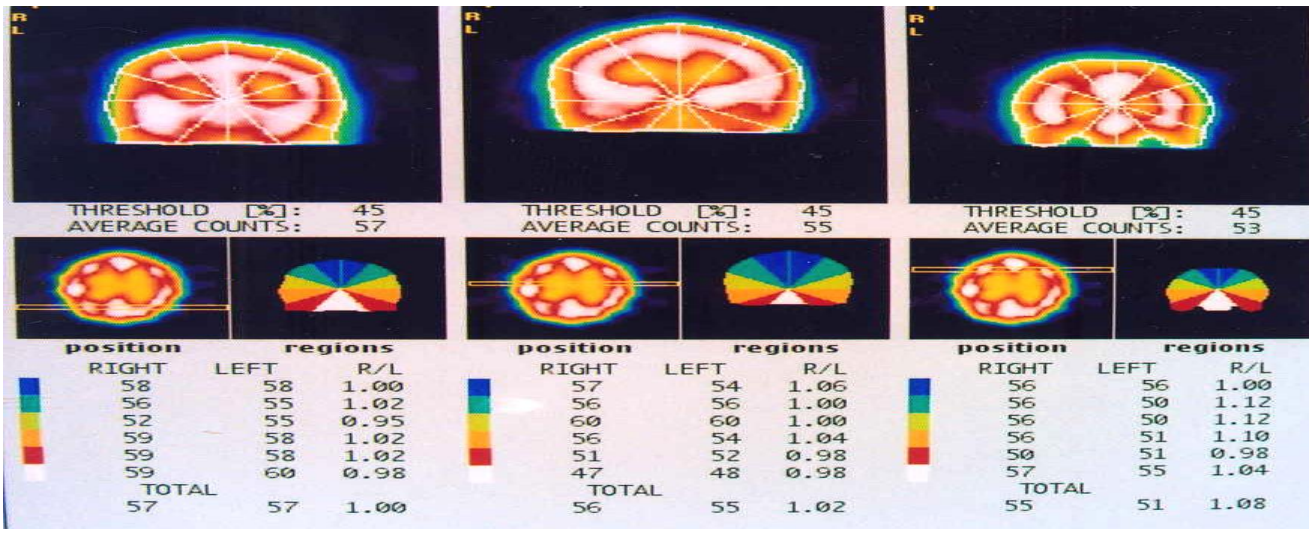

Figure 1: SPECT scan of patient of dissociative Amnesia

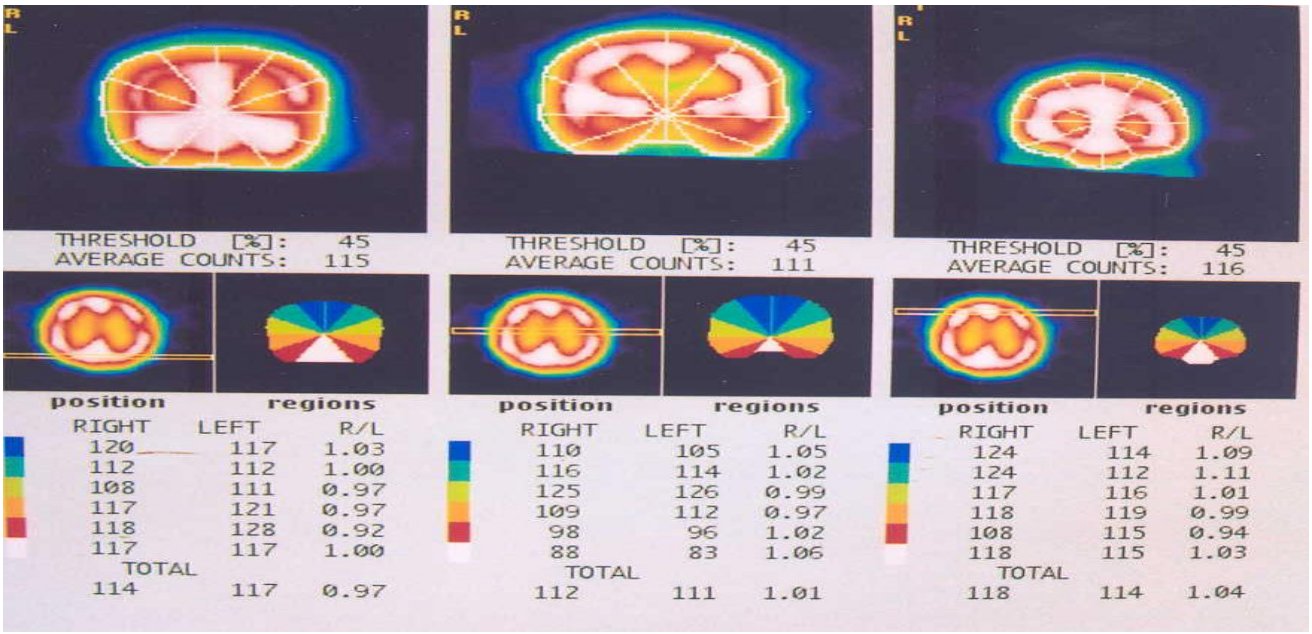

Figure 2: Patients of dissociative anesthesia and sensory loss

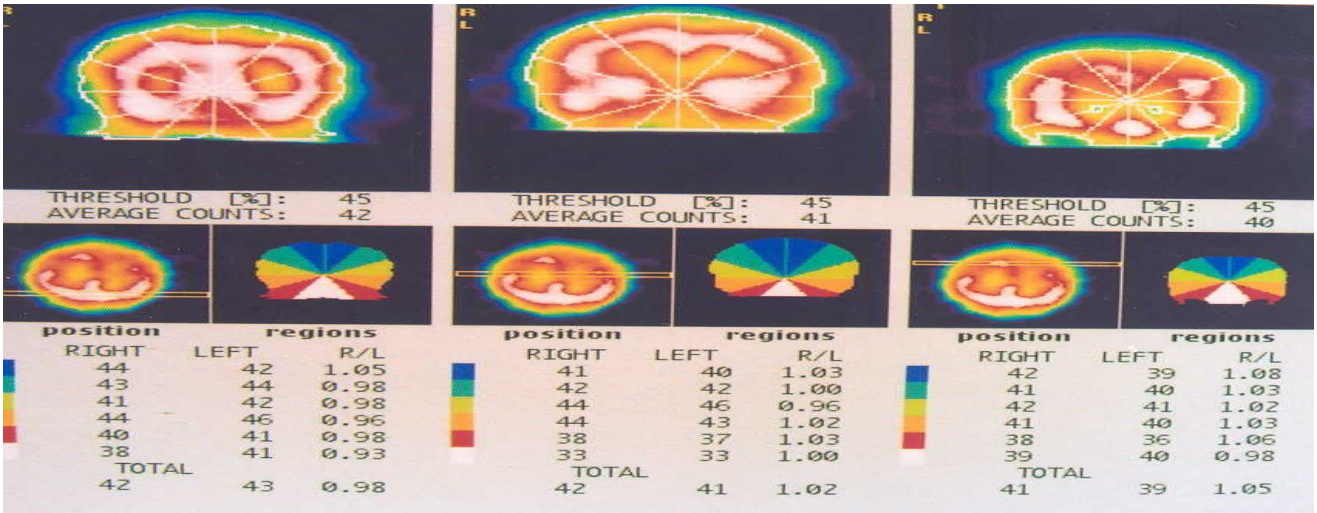

Figure 3: Patient of dissociative motor disorder.

cerebral anatomical aberration as such which

cerebral anatomical aberration as such which can be visualized on CT & MRI scans and EEG. So SPECT was opted that substantiates physiological brain aberrations rather than anatomical ones. The project is quite unique in the sense that almost no current work has surfaced which is based on the ICD-10 Criteria of diagnosis and no single study has encompassed so many subgroups of these disorders with such a large number of patients. Another important aspect is that all the important cortical regions rather than a single region could be implicated in dissociative disorders.

In dissociative amnesia marked hypoperfusion changes were found in both temporal lobes, mild hypoperfusion changes in frontal association areas and moderate hypoperfusion defects in both orbitofrontal regions. Temporal lobes contain the hippocampal formation which is responsible for the consolidation of short term memory into long term memory thus in a way it works as a data storage unit [13]. Hypoperfusion observed signifies the hypoactivity and hypofunctioning at the neuronal level. Decreased cerebral perfusion observed in frontal association areas and both of the orbitofrontal regions supports the fact that these areas not only receive input from the other cortical areas but also harbors the limbic system [14] which controls the emotional and intellectual patterns of the human being and in patients of dissociative amnesia who are emotionally disturbed there is forgetfulness for the recent past traumatic or stressful events thus reveal neuronal hypoactivity in these sensitive areas. In acute presentations no recent work is available on such patients diagnosed on basis of ICD-10 criteria.

Dissociative amnesia is associated with hypoperfusion in frontal, temporal and orbitofrontal areas. Dissociative aneasthesia and sensory loss is associated with no hypoperfusion but hyperperfusion in frontal, temporal and orbitofrontal region while perfusion in the frontomotor region was unaltered. Dissociative fugue is associated with hypoperfusion in left frontal and both temporal regions. Dissociative motor disorder was associated with bilateral hypoperfusion of frontal, frontomotor and temporal area as well as hyperperfusion in orbitofrontal area. Bilateral temporal and right frontal hypoperfusion is observed in mixed dissociative disorders.

The patients in the subgroup of Mixed Dissociative disorders showed marked hypoperfusion in left temporal lobe which was the dominant hemisphere. The overall cerebral perfusion pattern of this subgroup revealed significant hypoperfusion in right frontal association area, left frontal association area and bilateral temporal lobes more on the left side. Presumably these regions were predominantly hypoperfused due to accommodation of hippocampal formation by the temporal lobe which is a vital part of limbic system and is concerned with memory consolidation, and also its influence over the frontal association area which receives input from all the cortical areas and the limbic system [17]. A study conducted by Marcelo LB, Angel P and Carmen P, in Vietnam veterans with a long history of Dissociative amnesia and Dissociative flashbacks showed decreased cerebral perfusion in anterior temporal cortices, superior frontal cortex and inferior frontal cortex (parts of frontal association cortex) along with parietal cortex with cortex / cerebellum ratios ranging from 0.78 - 0.91, while our ratios ranged from 0.77-0.86 as compared to the controls lying 2SDs below their respective ratios. The team also reported increased cerebral perfusion in thalamic area with ratio of 1.14 [12].

In the two patients with dissociative anesthesia and sensory loss, both of them suffered from anesthesia of the skin of both arms. Results show marked hypoperfusion in both posterior parietal regions, significant hypoperfusion in right temporal lobe and in left temporal lobe. Like Dissociative motor disorders Dissociative anesthesia and sensory loss also develop over extended periods of time [15]. Posterior parietal region showed cortical hypoperfusion as this area is vital in assimilation and interpretation of

somatosensory input [16] and in these patients such sensations are disturbed. These patients also showed marked hyperperfusion in both frontal association areas and both orbitofrontal regions. The logical reason seems to be the same inhibitory influence of both of these cortical areas over the somatosensory cortex. It was found out those patients develop more hypoperfusion defects in the right temporal lobe, left temporal lobe and both of the frontal association areas as compared to the acute presentation of the disease.

Brain SPECT study utilizing Tc-99m HMPAO and other radio pharmaceuticals can prove to be a vital diagnostic modalities and their use should enable developing, further insight into diagnosis, monitoring of efficacy of the treatment and prognosis of this and possibly other psychiatric disorder.

Limitations of the study: Discussing the important possibilities of the Psychiatric limitations of the study there is difficulty in diagnosing of these cases especially the organic basis of the illness. Most of the time expensive investigations are required to reach the diagnosis. Also proper consent is required before proceeding to SPECT imaging techniques. Another important limitation is ethical issues of radiopharmaceutical and along with its expensiveness which makes this study more expensive than other studies. On the other hand there are some limitations of the SPECT techniques which includes utilization of a single head gamma camera which has a relative poorer spatial resolution in comparison to multihead gamma camera and also it was ideal to employ PET technique which is superior to SPECT modality in the identification of cerebral perfusion defects but it is not available in this region at the moment. The software generated geometrical ROIs utilized during processing of the images had the limitation of some degree of misalignment leading to overlapping of the anatomical regions. The regional cerebral blood flow in such regions could not be assessed with higher accuracy and it could have been possible with better and advanced quantification program like SPM or other advanced software.

CONCLUSIONS

Cerebral blood flow changes in the fronto parietal brain are associated with symptomotology in dissociative disorders.

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