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Research Article

**MOOD DISORDERS IN STROKE PATIENTS: IMPORTANCE
OF LOCALIZATION OF LESION**¹Dr Badria Munir,²Dr Hassaan Imtiaz,³Dr Taimoor Jaffar Ali,⁴Dr Abdullah Jamal,⁵Dr Faizan Rasool.¹MD, Clinical Research Fellow, Harvard Medical School and Hospital, Beth Israel Deaconess Medical Center, USA., ^{2,3,4,5}King Edward Medical University, Lahore, Pakistan.

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Abstract:

Background: Many studies have shown that post-stroke depression (PSD) results from left hemisphere depression. Two theories have stated on PSD. The first states that depression after brain injury or stroke is a psychological reaction to the consequences of stroke. The second suggests that depression is a consequence of specific brain lesion and presumably subsequent changes in neuro transmitter.

Methodology: Out of 184 patients, 48 met the inclusion criteria of this study. Out of those 48 patients only patients who were visualized on CT were included. 22 patients met the criteria and had positive CT with single left hemisphere lesion while 14 met the criteria and had single right hemisphere infarct. Patients were interviewed individually and the purpose of the study was explained prior to informed consent.

Results: The severity of lesion was significantly higher in patients with left anterior lesion as compared to any other. Whereas, the severity of depression correlated significantly with proximity of the lesion on CT scan to the frontal pole in the left anterior group. The right hemisphere showed the opposite trend; patients with right posterior lesion were more depressed than patients with right anterior lesion.

Conclusion: It shows that intra-hemispheric lesion location is somehow related to mood disorders in stroke patients.

Keywords: Cerebrovascular accident, ischemic stroke, depressive disorders disease, mental disorders, mood disorder, neuroanatomy, apathy, right cerebral hemisphere, right handed.

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INTRODUCTION:

During previous several years, investigations have been going on the occurrence of mood disorders following cerebral ischemia [1]. Literature has reported that the frequency and severity of mood disorders are remarkably higher during the initial period from six months to two years after stroke attack, and that too in majority of the cases which had left untreated from eight to nine months [2]. Studies have reported that the frequency and severity of depressive disorders depend on which hemisphere is involved. The severity of depression was significantly correlated with the proximity of the left hemisphere lesion to the frontal pole as measured on CT scan [3].

Investigators have reported that left hemisphere brain injury is directly linked with depressive mood whereas right hemisphere brain injury is associated with coolness, cheerfulness, and have an ability to reduce the difficulties [4]. It has also previously been reported that the intra-hemispheric location of the lesion is important in determining the psychopathological manifestations of brain injury. In general, left frontal injury has been associated with depressive symptoms while left parietal injury has been associated with unconcern and unawareness. In the right hemisphere, Ross and Rush (1981) have described a loss of ability to express emotion with more anterior lesions and a loss of emotional recognition with more posterior lesions, analogous to the language organization in the left hemisphere [5] [6]. However, the importance of the frontal lobe and the strong relationship between distance of the lesion from the frontal pole on CT scan and severity of depression has not been reported by other investigators. Our original observations in patients with left hemisphere injury were undertaken in a group of patients who were many months past the onset of their illness and in who there was marked variability in the duration of their illness [7]. In addition, we did not exclude any patients in whom there were premorbid risk factors for psychiatric disorder such as alcoholism, family or personal history of psychiatric disorder [8]. Therefore, in the current study, we examined a selected group of acute stroke patients within a few weeks of their injury that had identifiable lesions on CT scan and no risk factors for psychiatric disorder.

Methodology:**Study size:**

184 patients were included in this study conducted in tertiary care hospitals of Lahore.

Exclusion criteria:

Left handed, or had a previous personal history of psychiatric treatment, alcohol or drug abuse, family history of psychiatric disorder or if there was a clinical history or CT scan evidence of previous brain injury or the present stroke was not localized on CT scan to one hemisphere.

Psychiatric and Neurological Examination:

The neurological examination and diagnosis were made by the attending neurologist. After obtaining informed consent, patients were given a series of standardized quantifiable measures of mood, intellectual function and physical impairment which we have previously found to be reliable and valid in stroke patients. The Hamilton Depression Scale, a 17 item questionnaire measuring psychological and physiological symptoms of depression, was filled out by the interviewer. The Zung Depression Scale, a 20 question self-rated depression questionnaire was read to each patient, and their responses were scored using the four Zung categories. The modified Present State Examination (PSE), a semistructured psychiatric interview which elicited symptoms related primarily to mood and anxiety, was examiner-scored. The reliability and validity of this modified version of the PSE has been demonstrated in a previous publication. The Mini-Mental State Examination is an 11 item questionnaire which has been found to be reliable and valid in assessing cognitive function in stroke patients. Scores may range from 0 to 30, and a score of 23 or below is indicative of significant cognitive impairment. The Johns Hopkins Functioning Inventory is a 10 item questionnaire which evaluates the patient's degree of independence in activities of daily living such as walking, dressing and eating. Scores may range from 0 to 27.

Analysis of CT scan:

All CT scans were performed on the same scanner using identical slice thickness, angle to orbital-meatal line and size reduction. Analyses of CT scans were done on 9 consecutive dorsal slices 10 mm apart beginning with the first slice that included frontal lobe tissue. Overall brain size, excluding ventricles, and lesion size were determined in each CT slice by a computerized area calculation procedure. The area within the lesion was divided by the area within the brain, excluding the ventricles, giving the lesion size as a percentage of brain volume. Lesion borders on each slice were determined along the anterior-posterior (AP) axis, and a mean anterior and posterior border as a percentage of the maximum AP distance was calculated. The criterion used for establishing whether a lesion was anterior or posterior was as follows. The lesion was anterior if the anterior border of the lesion was rostral to 40 per cent of the AP

distance and the posterior border was anterior to 60 per cent of the AP distance. On the other hand, a lesion was posterior if its anterior border was posterior to 40 per cent of the AP distance and the posterior border was caudal to 60 per cent of the AP distance. Thus, we allowed a 20 per cent overlap of anterior and posterior lesions. Lesions that were anterior to 40 per cent of the AP distance and posterior to 60 per cent were not used in the data analysis and were called both anterior and posterior.

RESULTS:

Location of stroke lesion		
	Left hemisphere (n = 22)	Right hemisphere (n = 14)
Age (mean \pm SD)	57 \pm 12	61 \pm 10
Sex (male)	53%	73%
No. children (mean \pm SD)	1.6 \pm 1.3	2.5 \pm 2.1
No. siblings (mean \pm SD)	4.5 \pm 3.9	4.8 \pm 4.0
Time since stroke (mean days \pm SD)	12 \pm 11	10 \pm 7

Relationship of Anterior-Posterior and Right-Left Lesion Location to Psychopathology:

About half of patients with lesions were represented with depression and anxiety despite of right or left hemisphere. There were marked bundle of symptoms more frequently in one group than another. Depression and arising symptoms like early morning awakening, decreased cravings, and weight loss were found in 14 out of 22 patients with left hemisphere injury and only 2 out of 14 patients with right hemisphere injury. In intra hemispheric lesion 7 out of 10 patients with left posterior lesions, 0 of 6 with right anterior lesions and 1 of 6 with right posterior lesions had these symptoms ($P < 0.05$). On the other hand, patients with right hemisphere lesions were found to have inappropriate cheerfulness in 6 out of 14 cases (5 of 6 cases were in right anterior group) while this symptom was found in none of the 22 patients with left hemisphere injury ($P < 0.01$).

Analysis of score from depression scale varied according to the location of lesion and side of lesion. Patients suffering from left anterior hemispheric lesion had higher mean depression scores than patient

Results have shown that there is no statistically difference between the right and left hemisphere lesion groups. 10 patients were suffering from left anterior lesion, 8 with left posterior lesion, 6 with right anterior lesion and 6 with right posterior lesion. And there was no significant inter group differences in background demographic data for these four lesions. Patients were black males in their late fifties or early sixties from middle or lower socioeconomic class. Interview was taken within the first two weeks after stroke.

with left posterior lesions or right anterior lesions. Right posterior group differed from left anterior group.

Patients with right anterior lesions had significantly lower mean depression score overall depression score than right posterior infarcts comparatively to the findings of left hemisphere lesion. Using psychiatric Research Diagnostic Criteria, 6 of 10 patients with left anterior infarcts met the criteria for a diagnosis of major depressive disorder with the exception that in some patients, the duration of symptoms at the time of evaluation was less than two weeks and they; of course, all had brain injury (Table 4). Only 1 patient with a left posterior lesion met the symptom criteria for the diagnosis of major depression while 3 of 8 patients with posterior lesions and 1 of 10 with an anterior lesion, met the symptom criteria for a minor or dysthymic depression, although, again, the duration of symptoms criteria was not met. This distribution of diagnostic symptom cluster by left hemisphere lesion location was statistically different than a random distribution ($P < 0.05$).

	Left hemisphere		Right hemisphere	
	Anterior (10)	Posterior (8)	Anterior (6)	Posterior (6)
Major depression	6		1	1
Minor depression	1	1	3	1
Hypomania	0		0	1
None	3		4	3

Among the patients with right hemisphere strokes, 1 patient with a right posterior lesion had the symptoms of major depressive disorder and 1 patient had the symptoms of minor depressive disorder while no patients with right anterior lesions were depressed. Five of 6 patients with right anterior lesions were unduly cheerful (termed hypomania on the PSE), while only 1 patient with a right posterior lesion had this symptom ($P < 0.02$). These patients with inappropriate cheerfulness did not meet the diagnostic criteria for any specific psychiatric disorder.

Relationship between Aphasia and Psychopathology:

Although the neurological deficits found in the patients with right and left cerebral stroke were comparable, aphasia was found, as would be expected, only among patients with left cerebral injury. In order to evaluate whether aphasia was an important factor in the predominance of depression in left hemisphere stroke patients, we compared left hemisphere lesion patients with and without aphasia on the various psychopathology scales. There were no significant differences in the mean Zung, Hamilton or PSE scores between patients with aphasia and patients without aphasia.

In the present study, aphasia was found in 2 patients with left anterior lesions, 1 of whom had the symptoms of a major depression and 1 of whom had the symptoms of minor depression. Because there were only 2 patients with aphasia, it was not possible to determine whether the frequency of depression was higher among these patients as compared with patients with left anterior brain injury and no aphasia. However, of the 7 patients who had the symptoms of major depression, only 2 had aphasia (1 with Broca's and 1 with posterior lesion and global aphasia)

DISCUSSION:

We have demonstrated in a selected group of patients with single brain lesions and no predisposing factors for psychiatric disorder that there are important and statistically significant differences in the distribution, frequency and/or severity of depression between patients with anterior or posterior lesions within each

hemisphere. In addition, that severity of depression correlates with distance of lesion from the frontal pole across the entire right hemisphere and across the entire left hemisphere although the correlation is strongest within the left anterior group. This finding in the left hemisphere lesion group is a confirmation of previously reported findings in a group of chronic brain-injured patients and in patients with bilateral brain injury. [9] [10]. However, that the anterior and posterior groups had some overlap in their lesion locations and that the distribution of lesion locations did not cover the entire hemisphere. Another is that in the right hemisphere group results showed that there is a correlation between severity of depression and distance of the lesion from the frontal pole[12].

Since the patients with right hemisphere injury as a group had less severe depression than left hemisphere patients, the range of scores was lower and the correlation was heavily dependent on two patients with moderate to severe depression.

In addition, the interesting finding of inappropriate cheerfulness in patients with right anterior strokes could not be correlated with distance of lesion from the frontal pole. It is possible that severity of this symptom might correlate with proximity of the lesion to the frontal pole as depression did in the left hemisphere lesion group. The most obvious implication of this study is that the aetiology of the mood disorders found in these stroke patients is in some way related to the location of their brain injury with left anterior injury being particularly associated with depression and right anterior injury associated with inappropriate cheerfulness [13] [14] [15].

Thus, it seems highly likely that severity of impairment plays a role in at least some poststroke depression, the issue is only whether there is evidence for additional factors contributing to these mood disorders. There are several lines of evidence which suggest that neural factors may be involved.

First, this interesting relationship between the proximity of the lesion to the frontal pole and severity of depression is a phenomenon which we have repeatedly demonstrated in several studies.

Secondly, the strength of the correlation between distance from frontal pole and severity of depression explains 50 to 70 per cent of the variance while the relationship to physical or overall cognitive impairment explains 10 to 20 per cent of the variance [16].

Thirdly, the characteristic syndrome-like nature of the depression in many of the patients with left anterior lesions, including both mood and vegetative changes, suggests an 'endogenous' aetiology for the depression [17].

It's yet to find out the specific impairment which occurs in all or most of the severely depressed patients.

Broca's aphasia was found in only 1 of the 6 patients with left anterior lesions and major depressive symptoms. Another patient with an anterior lesion and global aphasia did not have major depressive symptoms and 5 of 7 patients with major depressive symptoms did not have aphasia. The most obvious explanation is that we have found a 'frontal syndrome' that is different in the two hemispheres (i.e. left lesions associated with a depressive syndrome, right lesions associated with inappropriate cheerfulness). Numerous investigators have described a 'frontal syndrome' and recognized the importance of the frontal lobes in affect. However, there is no known neuroanatomy or neurophysiology to account for the importance of the frontal lobe in affect [18].

Current findings have not only shown a frontal syndrome, but have also shown a graded effect of lesion location on mood from anterior to posterior. These two findings (i.e. the importance of the frontal lobe in mood disorders and the graded effect of lesion location on mood) suggest an intriguing neural hypothesis for these results. This study suggests that there may be a relationship between both inter and intra-hemispheric lesion location and mood disorder.

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