A Two-Year Longitudinal Study of Post-Stroke Mood Disorders: Findings During the Initial Evaluation

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SUMMARY A consecutive series of 103 stroke patients capable of undergoing a psychiatric interview were evaluated for mood disorders. Nearly 50% of patients studied in the acute stroke period had clinically significant depressions and one fourth had symptom clusters found in major depressive disorders. We confirmed our previous findings that lesion location is most important in determining frequency and severity of depression. In addition, we have identified other variables including functional physical impairment, intellectual impairment, quality of social support, and age which contribute to or modify depression. Post-stroke depressive disorders are multifactorial in their determination and expression and include both neurophysiological-neurochemical mechanisms and psychological factors in their etiology.

DURING THE PAST SEVERAL YEARS we have been investigating the occurrence of mood disorders in stroke patients1-5 and have reported that depression is found significantly more often and with greater severity in patients with left hemisphere as opposed to right hemisphere injury.6 Based on CT scan localization, we found that patients with left frontal brain injury have a greater prevalence and severity of depression than patients with lesions of other locations,7 and the severity of depression was significantly correlated with the proximity of the lesion to the frontal pole.8 We have studied depression and lesion location during both the chronic post-stroke period1-3 and the acute post-stroke period4,5 and found no differences between these two groups. In addition, we have recently reported in a follow-up study of 103 stroke outpatients, that the duration of untreated post-stroke depressions was at least 7 to 8 months in two-thirds of the patients and that, during the period from 6 months to 2 years post-stroke, there was a significant increase in the frequency and severity of depression as compared with other post-stroke time periods.3

To determine what other factors were important in post-stroke mood disorders, we have been conducting a two year prospective study of 103 stroke patients. This population of 103 stroke patients is an entirely different group than the 103 outpatients previously reported.2 By examining the present group of patients during the acute stroke period, we hoped to obtain reliable information about premorbid variables. We then hoped to use this data along with post-stroke clinical findings to look for associations between these variables and who developed depressions, who had the most prolonged depressions, and who recovered. This information could be used in subsequent studies to predict the development of mood disorders in stroke patients and if confirmed, would establish the prognostic variables in these mood disorders. We report here the findings from the initial evaluation of this particular study group.

Methods

A. Patient Selection

Between January, 1980 and August, 1981, in association with the Pilot Stroke Data Bank, a consecutive series of 164 patients admitted to the University of Maryland Hospital with a thromboembolic infarct (N = 128) or intracerebral hemorrhage (N = 36) were screened for inclusion in the study. Fifth-three of these patients were excluded because of decreased consciousness and/or aphasia with severe comprehension deficits, one patient refused to be interviewed and 7 patients were discharged before they could be studied. The remaining 103 patients are the subjects of this study.

B. Interviews

After obtaining informed consent, background data were collected from the patient and a relative. Patients were interviewed alone in a private room between 11 am and 2 pm, usually within two weeks following their stroke.

Three rating scales were used to quantify mood. The Zung Depression Scale5 is a 20 item, self-rated questionnaire that was read to each patient, and their responses were scored using the four Zung categories. The Hamilton Depression Scale7 is a 17 item scale that was rated by the interviewer following the examination. The Present State Examination (PSE)6 is a semi-structured quantitative psychiatric interview. This examination was modified to include only items related to anxiety and mood disorders.3 For all of the mood scales, a higher number indicates a greater severity of depression.

In addition to measurement of mood, social functioning was quantified using a semi-structured clinical interview designed for this study.5 We have previously described the reliability and validity of the Social Functioning Exam which contains 28 items measuring the quality and personal satisfaction derived from so-
cial roles. The Social Ties Checklist is a 10-item, yes-no questionnaire which assesses the number of established social connections.  

Intellectual impairment was measured using the Mini-Mental State Examination, an 11-item quantitative test of cognitive function. Scores may range from 0–30 with a score below 24 indicating significant cognitive impairment. Functional physical impairment was measured using the 10 item Johns Hopkins Functioning Inventory (JHFI), which assesses the patient’s independence in activities of daily living including walking, dressing, and eating. Scores range from 0–27 with higher scores indicating greater impairment.

Hollingshead social class is based on both occupational and educational criteria. It divides patients into 5 social classes with class I being the highest. Social class was determined for each patient.

C. Neurological Examination and Diagnosis

All patients were examined by the attending neurologist (TRP), using a neurological examination developed for the Pilot Stroke Data Bank and was administered and scored using standardized procedures and rating criteria. The diagnosis of thromboembolic infarct or intracerebral hemorrhage was also based on the Pilot Stroke Data Bank criteria.

D. Psychiatric Diagnosis

A psychiatric diagnosis was obtained using the symptoms elicited by the Present State Exam, and the DSM III criteria. Conversion from PSE symptoms to DSM III criteria required some clinical judgments because of the lack of exact comparability of symptoms (the method for conversion is available upon request).

E. Statistical Analysis

Means and standard deviations were calculated for the parametric data and intergroup comparisons were made using analysis of variance, student t-tests, and Pearson correlation coefficients. Non-parametric data such as frequencies of symptoms were compared using chi-squared tests.

Results

A. Study Population

One hundred and three patients were included in the present study. Background characteristics are shown in table 1. Patients were predominantly in their 50’s and 60’s, about 60% were male and almost two-thirds were black. Almost half the patients had less than a 9th grade education and were Hollingshead social class V. Only 1 in 10 patients had a family history of psychiatric disorder, but almost 1 in 4 had a prior history of stroke. The interviews were generally conducted within 2 weeks following the stroke.

B. Neurological Findings

Neurological findings in patients with right hemisphere, left hemisphere and brainstem strokes are shown on table 2. Eighteen patients had intracerebral hemorrhage and 85 had thromboembolic infarcts. All patients with intracerebral hemorrhage had lesions visualized on CT scan while 59 patients with thromboembolic infarcts had lesions demonstrable on CT scan. Based on CT scan localization 30 patients had cortical lesions, 22 had subcortical lesions, 16 patients had both cortical and subcortical lesions, 3 patients had brainstem-cerebellar lesions, 2 patients had lesions of both the subcortex and brainstem, 3 patients had ventricular hemorrhages, and 1 patient had lesions of both the cortex and brainstem.

C. Psychiatric Diagnosis

The numbers of patients meeting the DSM III symptom criteria for either major depression or dysthymic disorder are shown in table 3. Twenty-seven percent of the patients had demonstrated symptom clusters associated with major depression while 20% showed symptoms of dysthymic disorder (i.e. minor depression) and 53% had no psychiatric diagnosis. Nine patients with no psychiatric diagnosis (9% of total) had the symptom of inappropriate cheerfulness.

D. Relationship Between Mood Disorders and Neurological Symptoms

To determine whether depression was related to the severity of neurological impairment, we divided patients into groups depending upon the severity of their motor and sensory deficits. The neurological examination was done blind to the results of the psychiatric
between patients with either mild or severe weakness of either the right or left side of the body (table 4). Although the numbers of patients with severe touch-pain deficits did not allow us to make statistical comparisons between these two groups, the trends were in the same direction as the findings for motor weakness. Activities of daily living were more impaired in patients with greater touch-pain deficits, however, depression and Mini-Mental score were found not to be significantly worse in patients with mild to moderate as opposed to severe touch-pain deficits.

E. Relationship Between Mood Disorders and Lesion Location

In previous publication we have detailed the important relationships between the lesion location as identified on the CT scan and the severity of depression.1,4 In the present study, we examined an unselected series of patients some of whom had negative CT scans or CT scans with evidence of prior stroke or previous personal history of alcoholism or psychiatric disorder. In this general stroke population would the clinical or CT scan localization of the present lesion be sufficient to demonstrate either interhemispheric or intrahemispheric differences in severity of depression? As shown in table 5, overall right hemisphere, left hemisphere or brainstem localization did not differentiate groups as to severity of depression. However, when the lesion was localized to either frontal or parietal-occipital lobes, significant differences were found. Patients with left frontal lobe lesions had significantly greater mean depression scores on both the Zung and the Hamilton rating scales as compared to patients with lesions in any other location (table 5).

F. Relationship Between Mood Disorders and Social Functioning

As shown in table 6, there was a significant correlation between the Social Functioning Exam score and the three depression measures. Thus, in the acute stroke period, when social functioning scores probably reflect premorbid social adjustment, we found that the patients with the most severe depressions had the worst social functioning. This finding is supported by a significant correlation between the Social Ties score and the Hamilton Depression score (table 6). Social Ties is a count of the patient's social connections.

G. Relationship Between Intellectual or Functional Physical Impairment and Severity of Depression

As shown on table 6 both the functional physical impairment as measured by the JHFI and the global cognitive impairment as measured by the Mini-Mental State examination score correlated significantly with the severity of depression on all three depression scales. The correlation coefficients ranged between .38 and .22.

H. Relationship Between Depression and Demographic Variables

Patient's age significantly correlated with depression score on all three depression scales (table 6). This
Table 4  Neurological Deficits

<table>
<thead>
<tr>
<th>Weakness</th>
<th>Mild–mod.</th>
<th>Severe</th>
<th>(Significance)</th>
<th>Touch-pain deficit</th>
<th>Mild–mod.</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper extremity (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Right (n =)</td>
<td>24</td>
<td>13</td>
<td></td>
<td></td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>4.0±4.9</td>
<td>6.8±5.7</td>
<td>(ns)</td>
<td>5.7±4.9</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td>ADL</td>
<td>7.3±6.2</td>
<td>12.1±6.8*</td>
<td>(.02)</td>
<td>10.3±7.6</td>
<td>16.5</td>
<td></td>
</tr>
<tr>
<td>Mini-mental</td>
<td>21.1±6.0</td>
<td>17.5±8.4</td>
<td>(ns)</td>
<td>19.0±8.3</td>
<td>23.0</td>
<td></td>
</tr>
<tr>
<td>B. Left (n =)</td>
<td>20</td>
<td>10</td>
<td></td>
<td></td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Depression</td>
<td>4.3±4.5</td>
<td>3.4±4.8</td>
<td>(ns)</td>
<td>4.1±4.4</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>ADL</td>
<td>4.0±5.3</td>
<td>9.8±5.2*</td>
<td>(.005)</td>
<td>7.1±6.6</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td>Mini-mental</td>
<td>23.1±5.7</td>
<td>22.4±4.5</td>
<td>(ns)</td>
<td>23.7±4.9</td>
<td>26.3</td>
<td></td>
</tr>
<tr>
<td>Lower extremity (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Right (n =)</td>
<td>18</td>
<td>14</td>
<td></td>
<td></td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>3.9±4.9</td>
<td>6.6±5.4</td>
<td>(ns)</td>
<td>6.3±5.0</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td>ADL</td>
<td>5.7±5.0</td>
<td>12.5±6.1*</td>
<td>(.002)</td>
<td>10.5±7.9</td>
<td>16.5</td>
<td></td>
</tr>
<tr>
<td>Mini-mental</td>
<td>20.5±5.8</td>
<td>17.5±8.2</td>
<td>(ns)</td>
<td>19.0±8.7</td>
<td>23.0</td>
<td></td>
</tr>
<tr>
<td>B. Left (n =)</td>
<td>17</td>
<td>10</td>
<td></td>
<td></td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Depression</td>
<td>3.5±4.3</td>
<td>3.6±4.7</td>
<td>(ns)</td>
<td>3.8±4.3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>ADL</td>
<td>3.7±4.9</td>
<td>9.7±5.2*</td>
<td>(.005)</td>
<td>7.0±6.3</td>
<td>11.0</td>
<td></td>
</tr>
<tr>
<td>Mini-mental</td>
<td>22.4±5.9</td>
<td>22.0±4.3</td>
<td>(ns)</td>
<td>23.7±4.7</td>
<td>26.0</td>
<td></td>
</tr>
</tbody>
</table>

*p < .05. Right–left differences in depression scores were not significant, t = 1.52 p < .1 but tended to suggest greater depression in patients with left hemisphere strokes.

Depression — Based on a combination of depression scores from Zung, Hamilton and Present State Exam (1) — higher numbers indicate greater impairment.

ADL — Johns Hopkins Functioning Inventory score — higher numbers indicate greater impairment.

Mini-mental — Lower numbers indicate greater intellectual impairment.

Discussion

The present study demonstrates that approximately half of an unselected series of stroke patients have significant mood disorders. We also have shown several factors associated with the development and severity of these mood disorders. These include lesion location, functional physical impairment, intellectual impairment, social support, and the patient's age.

The evaluation of these patients was done using standardized, quantifiable questionnaires and rating scales. Although the depression rating scales used in this study were designed for patients with functional depressive disorders, we have found them to be both reliable and valid measures of depression in brain injured patients as determined by high correlation coefficients for interrater agreement, test-retest, and inter-scale correlation (1) (table 6). In addition, we have demonstrated the reliability and validity of the social functioning exam.

There are two major conclusions that can be drawn from this study. First, in a consecutive group of stroke patients, the only selection criterion being the capability of undertaking a verbal interview, we found that approximately 50% of acute stroke patients had a clinically significant mood disorder. Since the incidence of thromboembolic stroke each year in the United States is approximately 400,000 (12), this represents a large population of patients most of whom do not receive treatment for these depressive disorders. (3, 13)

The second major implication of this work is that the severity of post-stroke mood disorder appears to be dependent upon several factors. We confirmed our previous finding that lesion location is probably the most important single factor in the development of
post-stroke mood disorders and that patients with left frontal lesions are more frequently and severely depressed than patients with any other lesion location.\textsuperscript{1, 4} However, in addition to lesion location, there are other variables that are associated with the occurrence of depression and appear to contribute to the severity. These factors include the degree of intellectual or functional physical impairment, the quality of social supports available to the patient, and the patient's age.

The finding that younger age was associated with greater depression was unexpected. One possible explanation is that the younger patients experienced greater disruption to their lives following stroke as compared with older patients who were already retired and did not face as much social restructuring.

Our present findings should be compared with previously reported results.\textsuperscript{1-3} In prior studies with chronic stroke patients,\textsuperscript{1-3} we found no significant correlation between physical or cognitive impairment and severity of depression. In the present study, we did find significant correlations. We believe that there are two reasons for these differences. First, the previous studies were done with chronic stroke patients and the present study with acute stroke patients. It may be that the importance of physical or cognitive impairment for depression decreases as time goes on. Secondly, the strength of these relationships between impairment and depression are not strong even in the present study. The severity of impairments explains only about 10% of the variance in depression. Therefore, in a smaller population this level of correlation would not be significant or a slight change in the strength of the relationship over time could make them non-significant.

Another issue is the ability to generalize to the overall stroke population of these findings from the patient population that was used. Patients utilized in this study were inpatients at the University of Maryland Hospital and were predominantly lower socioeconomic class, black male patients more than half of whom were not married. In other populations of patients we might have found different results. However, in the present study we did not find any obvious subgroups of white and/or upper socioeconomic class patients in which there were significantly different findings.

Another issue is the stability of these findings. The present study was conducted in an acute stroke population, and, factors that correlate with depression in this immediate post-stroke period may differ from those found at a later post-stroke period, such as the severity of impairment. In previous investigations, however, we found that, in the chronic stroke period, the location of the lesion was also associated with the severity of depression.\textsuperscript{4} In addition, we have found in a group of stroke patients attending an outpatient clinic, that the depressive disorders lasted 7 to 8 months in most patients.\textsuperscript{3} Thus, although we would expect that at least some of the factors associated with post-stroke mood disorders will remain stable over time, we are following these patients in an effort to assess the stability of these findings.

In addition to the positive findings in this study, there were some negative findings that deserve discussion. First, there was no significant difference in mean depression score between patients with mild to moderate upper extremity or lower extremity weakness, as compared to patients with severe weakness. This finding, in combination with the finding of a moderate correlation between the activities of daily living and severity of depression suggest that the motor-sensory deficit per se may not be as important as the impairment of functional activity in determining depression.

Another significant negative finding of this study was the lack of difference in severity of depression among patients with right hemisphere, left hemisphere

### Table 6: Correlation Coefficients

<table>
<thead>
<tr>
<th></th>
<th>Hamilton</th>
<th>PSE</th>
<th>JHFI</th>
<th>Mini-mental</th>
<th>ST</th>
<th>SFE</th>
<th>Age</th>
<th>SES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zung</td>
<td>.80(\text{t})</td>
<td>.82(\text{t})</td>
<td>.36(\text{t})</td>
<td>-.28*</td>
<td>.13</td>
<td>.27*</td>
<td>-.24*</td>
<td>.21*</td>
</tr>
<tr>
<td>Hamilton</td>
<td>.85(\text{t})</td>
<td>.37(\text{t})</td>
<td>-.22*</td>
<td>.20*</td>
<td>.23*</td>
<td>-.27*</td>
<td>.17</td>
<td></td>
</tr>
<tr>
<td>PSE</td>
<td>.35(\text{t})</td>
<td>.63(\text{t})</td>
<td>-.38*</td>
<td>.14</td>
<td>.23*</td>
<td>-.32(\text{t})</td>
<td>.12</td>
<td></td>
</tr>
<tr>
<td>JHFI</td>
<td>.63(\text{t})</td>
<td>.14</td>
<td>.05</td>
<td>.16</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mini-mental</td>
<td>-.23*</td>
<td>-.19</td>
<td>-.06</td>
<td>-.27*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST</td>
<td>.45(\text{t})</td>
<td>.22*</td>
<td>.42*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SFE</td>
<td>-.16</td>
<td></td>
<td></td>
<td>.35(\text{t})</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.002</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(\text{t}p < .02.\)

\(\text{t}p < .001.\)

\(\text{ns} = \text{not significant; JHFI = Johns Hopkins Functioning Inventory (i.e. activities of daily living) — higher scores reflect greater impairment; Mini-mental = lower scores indicate greater intellectual impairment; ST = Social Ties checklist — higher scores indicate few social connections; SFE = Social Functioning Exam — greater scores indicate more impairment of functioning; SES = Socioeconomic Status — based on Hollingshead\textsuperscript{4} classification — higher numbers indicate lower social-economic class.}\)
or brainstem stroke. This finding is in contrast to our previous work in which we did find significant right-left differences when we selected right-handed patients with single acute stroke lesions and no prior history of psychiatric disorder or alcohol abuse.\(^3,4\) We believe that had we selected patients without previous history of brain injury, alcohol abuse or left-handedness, we would have reproduced our prior results (i.e. that depression is more frequent and severe in patients with left hemisphere brain lesions). We did, however, in the current study continue to confirm our previous finding that there are significant differences in severity of depression between patients with different lesion locations when we take the intrahemispheric site of injury into account.\(^4\) This finding suggests that the anterior-posterior differences in lesion location may be more important than overall right-left differences in determining the severity of depression. It is possible, however, that our exclusion of patients with severe aphasia during the acute stroke period may have eliminated many patients with left hemisphere lesions and severe depressions. These patients might have recovered sufficiently to be evaluated at follow-up and thus, were included in our previous studies.\(^1,3\) In addition, right-left differences in severity of depression might have been obscured by variables such as a previous stroke, personal psychiatric history, family psychiatric history, alcohol abuse, or left-handedness.

In conclusion, the present study demonstrates that in a relatively unselected series of patients with thromboembolic stroke or intracerebral hemorrhage, more than one-quarter of these patients have the symptoms of major depression. In addition, we have continued to confirm previous findings that the location of the lesion, particularly left anterior, is an important variable associated with the severity of depression. This finding, that a characteristic clinical syndrome is associated with injury to a specific brain region, suggests that post-stroke depression may be the behavioral manifestation of neurophysiological or neurochemical responses to the brain injury. In addition, however, we have identified other variables that appear to contribute to the development and severity of depression. These variables are functional physical impairment, intellectual impairment, quality of social functioning and age. These factors may either modify the neurophysiological process occurring in these patients or may themselves lead to the development of depression through a different etiological process.

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