Functional and Neuroanatomic Correlations in Poststroke Depression
The Sunnybrook Stroke Study

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Background and Purpose—The purpose of our study was to determine the functional and neuroanatomic correlates of poststroke depressive symptoms.

Methods—Patients with consecutive admissions to a regional stroke center for new-onset unilateral hemispheric stroke who met World Health Organization and National Institute of Neurological and Communicative Disorders and Stroke criteria were eligible for inclusion in a longitudinal study. Acutely, patients underwent CT scanning, and at 3 months and 1 year after stroke, depressive symptoms were assessed by using both the Montgomery-Asberg Depression Rating Scale and the Zung Self-Rating Depression Scale. The Functional Independence Measure (FIM) served as an indication of functional outcome and was obtained at 1 month, 3 months, and 1 year after stroke, along with other demographic information. The Talairach and Tournoux stereotactic atlas was used for the primary determination of CT lesion localization. Lesion proximity to the anterior frontal pole was also measured.

Results—Eighty-one patients participated in the longitudinal study. Stepwise linear regression analyses generated a highly significant model (F(3,76) = 9.8, R² = 28%, P < 0.0005), with lower 1-month total FIM scores, living at home, and damage to the inferior frontal region predicting higher depression scores at 3 months. Similarly, lower 3-month total FIM scores correlated with higher 3-month depression scores, and lower 1-year total FIM scores correlated with higher 1-year depression scores.

Conclusions—Functional measures correlated with poststroke depression across time and, together with neuroanatomic measures, predicted depressive symptoms longitudinally. Although inferior frontal lesion location, irrespective of side, appeared to play a role as a risk factor in this study, the degree of functional dependence after stroke imparted the greatest risk. (Stroke. 2000;31:637-644.)

Key Words: depression ■ stroke assessment ■ stroke outcome ■ tomography, x-ray computed

Excessive mortality and significant cognitive, physical, and psychosocial morbidity may occur after stroke. Mood disturbance can be an important sequel of stroke. Estimates of poststroke depression range from 18% to 78%, with the greatest risk occurring in the first 2 years, especially at 3 to 6 months after stroke.

Sparked by the early laboratory rat studies of Robinson and Coyle, attempts have been made by many researchers to determine the importance of lesion characteristics in depression after stroke in humans. Robinson, Starkstein, and colleagues have repeatedly demonstrated a specific relationship between left anterior or basal ganglia stroke lesion location and depression in the early stage of stroke, a finding that they attribute to asymmetry in the hemispheric distribution of catecholamines. Specifically, they speculated that disrupted cortical noradrenergic pathways originating in the locus ceruleus and projecting to the frontal cortex and then to the posterior cortical regions explain the association between anterior lesion location and the severity of depression. In a positron emission tomographic study, they suggested that failure to upregulate serotonin receptors after left hemisphere damage (LHD) contributed to the development of depression.

Although the role of lesion laterality and frontal proximity in poststroke depression has been widely accepted, attempts to replicate have yielded conflicting results, and numerous methodological issues remain unresolved. The original 1983 study (Robinson et al) had 48 patients consisting largely of middle-aged African American men from lower socioeconomic circumstances in a large urban center. Of the LHD patients, 30% had aphasia, and 25% had no visible CT
lesions. LHD patients had higher depression scores than did patients with right hemisphere damage (RHD) in the acute phase of stroke, and left anterior lesions were associated with greater frequency and severity of depression. Given the particular characteristics of this sample, generalizability may not hold. Some studies have replicated the findings of Robinson et al, but other studies have not, and comprehensive reviews attributed the divergent results to methodological differences, including cohort selection from different settings, previous history of psychiatric or neurological illness, definition and classification of stroke, phenomenology and nosology of depressive symptoms, and the validity of the rating methodology used. More recently, Shimoda and Robinson have suggested that time elapsed after onset may be the key factor, with the left frontal correlation applying primarily to depression in acute stroke. Very few studies have provided detailed lesion localization; most simply classify lesions as anterior or posterior or measure proximity to the frontal pole.

Cognizant of the methodological pitfalls inherent to this area of research, the authors designed the present study to follow prospectively a large relatively unselected sample of carefully diagnosed acute-stroke patients and to determine the frequency, severity, and persistence of depressive symptoms and their clinical and neuroanatomic correlates. A clearer understanding of the relationship between neurological damage and depression after stroke would provide insight into the neurobiology of mood disorders and assist clinicians in the early identification of patients at highest risk for mood disturbance and those most likely to benefit from treatment interventions. This, in turn, might lead to shortened hospital stays, contained healthcare costs, improved quality of life, and reduced mortality.

Subjects and Methods

Site and Patients

The Sunnybrook Stroke Study was conducted at a university-affiliated health science center serving as a regional stroke center to a predominantly middle-class residential northern suburb of Toronto, Ontario, Canada, with a catchment area population of 250,000 residents. Consecutive admissions from August 1990 and May 1993 were eligible for inclusion in the present study. Diagnosis of stroke was made clinically by an experienced stroke neurologist using World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) Project and National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) criteria. A multidisciplinary stroke care team including neurology, psychiatry, occupational therapy, physiotherapy, speech therapy, and social work was involved with each patient according to a standardized stroke care protocol, and rehabilitation was provided as appropriate, as part of the universal healthcare service. All patients underwent CT scanning, and those with subarachnoid hemorrhage and vertebrobasilar strokes were excluded as described previously. Patients with aphasia were not excluded and were always assessed unless they suffered from global aphasia or severe comprehension deficits as assessed by the Western Aphasia Battery. Written and informed consent was obtained from all patients or their substitute consent givers.

An important and unique feature of the present localization study was that a careful accounting of all exclusions was provided to give perspective on generalizability. By our predetermined exclusion criteria, the following 248 patients had to be excluded from the 449 originally entered into the study: 114 who died with bilateral hemisphere damage (BHD), 56 with LHD, and 55 with RHD, 10 who experienced a subsequent stroke while in the study, 8 with BHD, 72 with previous history of stroke (41 with LHD and 31 with RHD), and 44 with negative CT scans (18 with LHD and 26 with RHD). Of the 201 patients remaining, 112 (65 with LHD and 47 with RHD) were unable to complete the depression questionnaires for the following reasons: 27 were too ill medically or neurologically to cooperate with assessment (15 with LHD and 12 with RHD), 12 were too cognitively impaired (7 with LHD and 5 with RHD), 5 experienced a subsequent stroke before 3 months (4 with LHD and 1 with RHD), 4 were unable to speak English (1 with LHD and 3 with RHD), 24 had moved away or were unable to be located (13 with LHD and 11 with RHD), 23 refused to participate (10 with LHD and 13 with RHD), and 17 had comprehension deficits too severe to meaningfully understand the questions (15 with LHD and 2 with RHD). The number of patients excluded was counterbalanced between RHD and LHD, except for aphasia, yielding 89 patients for analysis. Finally, 8 patients (2 with LHD and 6 with RHD) were on antidepressants at 1 month and were analyzed separately because of the possible effect on depression scores of treated or partially treated states. This yielded a total of 81 patients (29 with LHD and 52 with RHD) in the localization study. This attrition underlines the challenge of conducting prospective studies in acute-stroke populations.

Measures

Shortly after admission, a standardized questionnaire was used to collect data on demographics, concurrent illness, past medical and psychiatric history, and medications for all acute-stroke patients. Those patients who consented to participate in the longitudinal study were followed up at 1, 3, and 12 months after stroke and were administered an assessment battery comprising demographics, depressive symptomatology, and functional assessment.

Demographics

Demographics included age at stroke onset, sex, comorbid illness, and history of depression. Living arrangement was recorded dichotomously as residing at home or not, and partner status was coded as married or not. These variables were selected as possible important covariates to be entered in all regression analyses. Antidepressant medication use was also recorded at each patient visit.

Depressive Symptomatology

Depressive symptomatology was evaluated at 3 and 12 months after stroke by a research nurse blind to lesion location and trained by a psychiatrist specializing in management of poststroke depression. Three months was chosen for initial depressive symptom assessment because it was close enough to the stroke to be temporally connected with the event but allowed sufficient time for early transient mood changes related to the acute insult to have settled. The objective observer-rated Montgomery-Asberg Depression Rating Scale (MADRS) is a 20-item scale measuring symptom severity, with a score ≥7 indicating depressive symptomatology. A subjective measure, the Zung Self-Rated Depression Scale (SDS) was obtained, with a score ≥50 indicating depressive symptomatology. Both scales measure severity and frequency dimensions and use complementary reporting techniques, ie, observer rating and self-report. A combined factor score was derived from the MADRS and SDS by using principal components factor analysis. Only 1 factor emerged from the factor analysis, which accounted for 78% of the variance and had an eigenvalue of 1.6. A cutoff score for the combined factor score was calculated by maximizing sensitivity and specificity to both the MADRS and SDS. A score above the cutoff was categorized as displaying depressive symptomatology. Sensitivity and specificity of the combined score to the MADRS were 73% and 86% and to the SDS were 90% and 88%, respectively. Last, any patient suspected by the stroke care team to be clinically depressed was assessed and treated as warranted by a consulting psychiatrist.
**Functional Assessment**

Functional assessment used the 18-item Functional Independence Measure (FIM), which scores levels of dependence from 18 (total assistance in all areas) to 126 (complete independence in all areas). In a previously published study, the FIM was shown to be highly correlated with both the standard Hemispheric Stroke Scale (PHSS) and the Oxford Handicap Scale. A total FIM score generated through summing subscale scores assessing self-care, sphincter control, mobility, locomotion, communication, and social cognition served as the overall measure of neurological status and functioning. FIM data were collected at 1 month, 3 months, and 1 year after stroke.

**CT Analysis**

CT scans were used for lesion localization and volume. CT scanning was generally carried out within 48 hours of hospital admission on a GE 9800 CT scanner (General Electric Medical Systems). Because CT scans may be negative if performed early after stroke, patients with an initially negative scan usually underwent repeat scanning within the first week after stroke. When lesions were evident on >1 CT scan, the film that maximally represented the lesion was used. According to a standardized stroke protocol, axial scans were performed parallel to the orbital-meatal plane, with a 1-cm slice thickness, and printed on x-ray film. The films were digitized with a Konica KFDR-S laser film scanner (Konica Corp) and saved as a bitmap file. The resulting image resolution was 8 bits per pixel with 175 μm of the CT image being represented by each pixel.

Neuroanatomical localization was determined with observers blind to the clinical data. For the primary determination of localization, lesions on CT scans were matched to the best fitting template from a set of 24 transverse slices selected from the Talairach and Tournoux atlas, a commonly used stereotactic anatomic reference system. To obtain an estimation of the degree of damage, a quantification method devised by Leibovitch et al. was used to index the vertical extent of a lesion according to the ratio of the number of slices in which a particular region was damaged over the total number of slices in which that same region appeared in the atlas. Quantification by this method was derived for the following 15 brain regions of interest: superior, middle and inferior frontal, medial frontal/anterior cingulate, sensorimotor strip, parietal, superior, and middle/inferior temporal, medial and lateral occipital, basal ganglia, thalamus, and anterior, central, and posterior white matter. Because there was a specific a priori interest in the relation of the frontal lobe and poststroke depression, 4 frontal subregions were examined. To improve skewness and kurtosis, square root transformation was applied to the CT data.

A further method sometimes used to analyze the effects of neurological damage on clinical outcome is the overlap of lesions of a small sample of patients grouped according to common criteria. Some stroke patients were diagnosed to be clinically depressed early in their course and were on antidepressants at 1 month of poststroke follow-up. Treatment of their depression frequently brought their depressive symptom scores into the normal range, precluding them from lesion analyses in the larger sample. Because their lesion localization was relevant to the lesion correlations, their lesions were traced onto 1 template series to evaluate the distribution of damage. The overlap method was then used to find areas of common damage.

To allow comparison with previous literature on the localization of damage in poststroke depression, a replication of the methodology reported by Robinson and colleagues was undertaken. Lesions traced on the digitized CT scans were used to generate numerical ratios (AP ratio), which were determined by measuring the distance of the most anterior border of the lesion from the frontal pole and dividing this by the overall anterior-posterior (AP) length of the cerebral hemisphere in the same slice (Figure 1). For those scans in which the lesion was visible on multiple slices, an average based on the AP ratio of each slice was calculated and used as the measure of proximity of the lesion to the frontal pole. AP ratio intrarater and interrater reliability was 0.98 and 0.85, respectively, with use of intraclass correlation. In keeping with previous studies, lesions were classified into 4 groups in relation to the AP diameter, namely, anterior, posterior, extended, and intermediate as demonstrated in Figure 1, panels A to D, respectively. AP measures were calculated online on a 17-in computer monitor with the use of Adobe Photoshop 4.0 (Adobe Systems Inc).

Lesion volume was measured on lesion tracings with the use of a digitizing tablet (Sigma Scan, version 3.0, Jandel Scientific). The lesion area was traced on each 1-cm-thick slice, and the areas were summed to derive the volume.

**Data Analysis**

Demographic and functional covariates followed by the CT data were entered into multiple linear regression analyses for the purposes of predicting and correlating with the combined depression scores at 3 months and 1 year. Similar regression equations were repeated with the AP ratio data. Five models were tested, 3 of which were predictive in nature and 2 of which were correlative. For the 3 predictive models, we used 1-month data to predict 3-month depression scores (model 1), 1-month data to predict 1-year depression scores (model 2), and 3-month data to predict 1-year depression scores (model 3). For the correlative models, we correlated 3-month data with 3-month depression scores (model 4) and 1-year data with 1-year depression scores (model 5). Thus, we used a Bonferroni correction of α=0.05/5 to correct for multiple models. To make some adjustment for allowing multiple variables the opportunity to enter the model, we also set the entry criterion with an acceptable level of error at 1%. We opted for the multiple linear rather than logistic regression modeling because dichotomization of the depression variables was arbitrary, and we believed that using the depression score as a continuous variable would be more sensitive.

**Results**

Patients participating in the longitudinal study have been described previously, and their characteristics are briefly summarized in Table 1. At 3 months, 36% of the sample (47% of RHD patients and 17% of LHD patients) were rated as having depressive symptoms on the basis of their combined depression scores. Comparisons between patients with and without marked depressive symptoms were conducted by use of univariate statistics (Table 1). There were no significant differences between the groups apart from those with depressive symptoms scoring more poorly on the FIM (86 versus 107, P<0.0005) and demonstrating greater frequency of damage (34% versus 8%, P<0.03) and vertical extent of damage (2.0 versus 0.4, P<0.02) to the inferior frontal region. Although 83% of those with depressive symptoms had RHD compared with 52% in the group without depressive symptoms (P<0.001), this right hemisphere predominance did not emerge in the multivariate analyses.

Stepwise least squares linear regression was conducted with the combined depression score as the dependent measure. Age, sex, living arrangements, marital status, history of depression, and total FIM score representing the demographic and functional covariates, followed by CT lesion variables (including CT lesion volume and side of stroke), were all entered as potential predictors of depression score (Table 2). A highly significant model was produced, with 1-month covariate data predicting depression scores at 3 months (F(1,56)=9.8, P<0.0005), accounting for 28% of the variance. The significant variables contributing to this model were lower total FIM score at 1 month, living at home, and damage to the inferior frontal region. Regression performed with only the 15 CT regions revealed that damage to the inferior frontal region still emerged as the only significant CT variable (P<0.001, standardized β=0.36) predicting depression.
scores, accounting for 13% of the model variance. Predictive models for 1-year depression scores were not significant.

Regression analyses were repeated with AP ratio data instead of the 15 CT lesion variables, and the results were similar to those reported in the preceding paragraph. Lower 1-month FIM score \((R^2=15\%, \text{ standardized } \beta=-0.62)\), living at home \((R^2=11\%, \text{ standardized } \beta=-0.45)\), and lower AP ratios \((R^2=9\%, \text{ standardized } \beta=-0.31)\), representing more frontal lesion location, significantly predicted higher 3-month depression scores \((P<0.05)\), accounting for 35% of the model variance. Regression performed with only the AP ratio also revealed a significant model predicting depression scores at 3 months \((P<0.001, \text{ standardized } \beta=-0.38)\), accounting for 15% of the model variance. When the qualitative AP lesion categories were analyzed by \(\chi^2\) test of independence, no significant differences emerged in relation to depressive symptom category (ie, depressed versus not depressed).

Correlative models (ie, correlating 3-month covariate data with 3-month depression scores and 1-year covariate data with 1-year depression scores) were also significant. FIM scores were strongly correlated with depression scores at 3 months \((r=0.38, P<0.0005)\) and at 1 year \((r=0.36, P<0.002)\). No CT variables entered the correlation analyses.

CT scan overlaps were carried out to compare those patients on antidepressant medication with those patients with or without depressive symptoms that were not on antidepressants (Figure 2). As illustrated, patients with depressive symptoms, including those on antidepressants, had the most significant overlap in the central region of the centrum semiovale.

**Discussion**

**Summary of Findings**

The major finding of the present study is that functional status in activities of daily living is the major correlate of depressive symptoms at each assessment and that this status at 1 month is the strongest predictor of 3-month depressive symptoms. Inferior frontal damage or proximity to the frontal pole as measured by the AP diameter (along with living arrangements) strengthens the prediction. The finding that functional status was an important predictor is consonant with previous studies.\(^5,16,29,47–49\) That patients living at home by 1 month were more likely to have depressive symptoms at 3 months may at first seem counterintuitive\(^47\) because their functional status was higher (mean FIM of 118±8 for patients living at home versus mean FIM of 91±21 for patients not living at

**Figure 1.** Examples of qualitative lesion categories. Four types of qualitatively different lesions are depicted in panels A through D. To determine the AP ratio, the distance from the anterior to the posterior pole is calculated in millimeters. Next, the distance from the most anterior part of the lesion to the anterior (frontal) pole is determined. Then, the AP ratio is calculated as the ratio of the distance from the most anterior part of the lesion (step 2) divided by the total AP distance (step 1). This was done for each slice on which the lesion appeared, and results were then averaged. Smaller AP ratios refer to more anterior lesions. Lesions are also qualitatively categorized depending on location. For lesions visible in multiple CT scan slices, the slice with the largest AP distance was used for this classification. A, Anterior. Lesion is located <40% and not >60% from the anterior pole. B, Posterior. Lesion is located >50% and not <40% from anterior pole. C, Extended. Lesion is located <40% and >60% from anterior pole. D, Intermediate. Lesion is located >40% and <60% from the anterior pole.
home). A plausible psychosocial explanation, however, might be that discharged patients were facing the impact of the stroke on their previous daily routine at this time, whereas those still in acute care or in rehabilitation had continuing multidisciplinary team support and were preoccupied with their physical recovery.

**Methodological Issues**

The present study distinguishes itself from previously published work in this area by the prospective follow-up of a large stroke sample coupled with detailed CT localization methodology. The authors chose to replicate frequently cited CT analysis methods to ensure the comparability of the present study with others but also carefully classified regional brain damage on the basis of a widely used standard reference system. Several relevant risk factors for poststroke depression, including age, sex, past history of depression, living arrangement, marital status, and degree of functional independence, were entered into each multivariate analysis along with the CT lesion parameters to elucidate the relative contribution of each potential risk factor. Few previous studies have had a sufficient sample size to allow detailed lesion information to be included in the multivariate analysis. Furthermore, few studies have accounted as meticulously for all exclusions. The 4:1 screening-to-entry ratio of the survivors is not atypical for a lesion localization study and demonstrates the difficulties inherent in sampling a consecutive stroke population, whose average age of 70 years was more representative of other stroke registries than the patients in the original seminal studies of Robinson and colleagues. Forty percent of the survivors were disqualified by lesion requirements (eg, a positive scan with a single lesion), and depression scores could not be obtained in a third of the remainder. Exclusions were counterbalanced between the risk factors, including the 7% who refused participation, except for more LHD participants with aphasia too severe for assessment. This resulted in a smaller number of LHD patients in the sample. Therefore, it is possible that depressive symptoms were underestimated, but these essentially nonverbal patients would not be assessable by the Diagnostic and Statistical Manual of Mental Disorders, edition 3 (DSM-III) criteria either. If they were assessed clinically to be depressed by the multidisciplinary team, they were seen by a geriatric psychiatrist who prescribed antidepressants on the basis of

<table>
<thead>
<tr>
<th>Variable</th>
<th>Absent (n=52)</th>
<th>Present (n=29)</th>
<th>Significance*</th>
<th>Overall Population (N=81)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset, y</td>
<td>71 ± 14 (25–91)</td>
<td>69 ± 13 (40–89)</td>
<td>NS†</td>
<td>70 ± 13 (25–91)</td>
</tr>
<tr>
<td>History of depression (presence)</td>
<td>5 (10%)</td>
<td>8 (28%)</td>
<td>NS‡</td>
<td>13 (16%)</td>
</tr>
<tr>
<td>FIM total score at 1 mo</td>
<td>107 ± 20 (55–126)</td>
<td>86 ± 34 (18–126)</td>
<td>&lt;0.0005†</td>
<td>100 ± 28 (18–126)</td>
</tr>
<tr>
<td>Living at home at 1 mo</td>
<td>31 (60%)</td>
<td>14 (48%)</td>
<td>NS‡</td>
<td>45 (56%)</td>
</tr>
<tr>
<td>Partner status (married)</td>
<td>29 (56%)</td>
<td>18 (62%)</td>
<td>NS‡</td>
<td>47 (58%)</td>
</tr>
<tr>
<td>Concomitant medical illness (presence)</td>
<td>12 (23%)</td>
<td>7 (24%)</td>
<td>NS‡</td>
<td>19 (23%)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>33 (63%)</td>
<td>17 (59%)</td>
<td>NS‡</td>
<td>50 (62%)</td>
</tr>
<tr>
<td>Right hemisphere stroke</td>
<td>27 (52%)</td>
<td>24 (83%)</td>
<td>&lt;0.01‡</td>
<td>51 (63%)</td>
</tr>
<tr>
<td>Left hemisphere stroke</td>
<td>25 (48%)</td>
<td>5 (17%)</td>
<td></td>
<td>30 (37%)</td>
</tr>
<tr>
<td>Lesion volume</td>
<td>31 ± 40 (0.5–173)</td>
<td>63 ± 84 (0.5–325)</td>
<td>NS†</td>
<td>43 ± 61 (0.5–325)</td>
</tr>
<tr>
<td>Inferior frontal (index of damage)</td>
<td>0.4 ± 1.4 (0–8)</td>
<td>2.0 ± 3.0 (0–8)</td>
<td>&lt;0.01†</td>
<td>0.9 ± 2.2 (0–8)</td>
</tr>
<tr>
<td>Inferior frontal (frequency of damage)</td>
<td>4 (8%)</td>
<td>10 (34%)</td>
<td>&lt;0.003‡</td>
<td>14 (17%)</td>
</tr>
<tr>
<td>AP ratio</td>
<td>0.4 ± 0.1 (0.1–0.7)</td>
<td>0.3 ± 0.2 (0.02–0.7)</td>
<td>&lt;0.05†</td>
<td>0.4 ± 0.2 (0.02–0.7)</td>
</tr>
</tbody>
</table>

Values are mean ± SD (with range in parentheses) or number of patients (with percentage in parentheses). NS indicates not significant. *α=0.05. †By t test. ‡By χ² test.

<table>
<thead>
<tr>
<th>Covariate Data</th>
<th>Depression Score</th>
<th>n</th>
<th>r</th>
<th>R²</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mo</td>
<td>3 mo</td>
<td>80</td>
<td>0.53</td>
<td>28%</td>
<td>10</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

Model significance was set at P = 0.01 (Bonferroni correction for 5 models with α = 0.05).

*Direction of correlation means that lower total FIM scores (ie, less independence), living at home, and increased damage to the inferior frontal region correlated with higher depression scores.
clinical judgment. For the purpose of the present study, such individuals would have been classified as depressed if they were on antidepressants.

Localization Within and Between Hemispheres

The landmark study by Robinson et al,9 which generated great interest in lesion patterns and poststroke depression, reported data on a unique sample of mostly younger black males of low socioeconomic status. Stroke registries and community studies of stroke patients50,51 reveal sample characteristics more closely aligned with the present study population. Despite this difference in sampling, our findings are consistent with those of Morris et al,15 who reported a specific relationship between lesion proximity to the frontal pole and severity of poststroke depression. Unlike these investigators, our research did not demonstrate hemispheric lateralization of depressive symptoms. There are several possible explanations for this discrepancy, including differences in sample selection already discussed as well as depression assessment and statistical analysis. One important reason may be the time of assessment, which was subacute in the present study, with follow-up at 1 year. The present study measured depressive symptomatology with 2 widely accepted, valid, and reliable depression scales. Other researchers18,20 demonstrating left-right differences in poststroke depression relied on modified diagnostic criteria and clinical interviews. The lack of structured diagnostic interviews for depression could be considered a potential limitation of the present study. In an earlier published report on this population, however, the easily administered MADRS and SDS both demonstrated acceptable external and concurrent validity, as well as internal consistency.20 Furthermore, these scales provide continuous data, which permit multiple regression analysis. Right stroke predominance has been reported in some other poststroke depression studies,2,15 and univariate statistical analysis of our data revealed a right hemisphere predominance in patients with depressive symptoms. However, multivariate analyses, which included other potential factors in poststroke depression, failed to maintain any effect of lesion laterality. Noteworthy is the relatively lower incidence of depressive symptoms in the LHD patients. In our sample, depressive symptoms emerged in almost half of the RHD patients compared with 17% of the LHD patients. Interestingly, a recent review of the growing literature on poststroke depression reveals that the majority of CT lesion localization studies to date do not demonstrate hemispheric specificity for depressive symptoms.24

The frontal lobe, however, has repeatedly emerged as playing an important role in mood regulation. Numerous structural and functional neuroimaging studies of affective disorders have been conducted on normal control subjects and those with primary and secondary depression, in addition to those studies in poststroke depression that have found an anterior lesion correlation.2,3,9,28,43,46,47,52,53 Positron emission tomographic imaging data suggest that inferior and orbitofrontal activation54 and anterior cingulate regions55 are related to behavioral and subjective changes in the affective experience of self-induced dysphoria. Working with patients experiencing primary depression, Sackeim et al56 revealed depressed patients to have a global decrease in cortical blood flow and a variety of regional cerebral blood flow changes, including decreased flow to inferior frontal regions. Greater left anterior cerebral blood flow was also noted in depressed patients at rest than in normal control subjects at rest by Uytendhooef et al.57 A careful study of depressed patients suffering from unipolar depression, bipolar depression, and obsessive-compulsive disorder with secondary depression by Baxter et al58 demonstrated a common reduction of left anterolateral prefrontal cortex glucose metabolism in all 3 depression types. Studies of depressed patients with brain injury other than stroke have also pointed to fronto orbital dysfunction. Mayberg et al59 demonstrated an inverse relationship between the magnitude of hypometabolism in the inferior and orbital regions of the frontal lobe and the severity of depression in patients with Parkinson’s disease. Likewise, in early Huntington’s disease, hypometabolism of the orbital
Emotional Valence

The neurological basis of emotion has intrigued clinicians and researchers alike. The occurrence of poststroke depression provides the opportunity for examination of potential neuroanatomic correlates of mood disturbance. In an early study of brain-damaged patients, Ross and Rush61 used clinicopathological conditions to put forward an initial model for the neurology of depression in which both hemispheres participate, each modulating certain signs and symptoms. Around the same time, Tucker62 reviewed the literature on limbic and prefrontal striatal pathways. Alexander et al63 proposed that limbic and prefrontal striatal pathways mediate human emotion. Hypotheses implicating the role of nonmotor basal ganglia–thalamocortical–frontocortical circuits in the modulation of certain affective states may help explain how lesions lying along tracts traversing the basal ganglia or frontal cortex would result in a dysfunction of the circuit and, consequently, mood dysregulation.

The present study attempts to uncover the functional and neuroanatomic correlations of poststroke depression. Although inferior frontal lesion location appears to play a role as a risk factor, the degree of functional dependence after stroke imparts the greatest risk in the present study. This finding highlights the need for clinicians to carefully screen for depressive symptoms in all stroke patients, regardless of lesion location.

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References


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