Improved Recovery in Activities of Daily Living Associated With Remission of Poststroke Depression

Eran Chemerinski, MD; Robert G. Robinson, MD; James T. Kosier, BS

Background and Purpose—Poststroke depression is associated with impaired recovery of activities of daily living (ADL) function compared with similar nondepressed patients. We examined the differences on recovery of ADL functions among poststroke depressed patients with remission of their depression compared with poststroke depressed patients without mood recovery over the first 3 to 6 months after stroke.

Methods—On the basis of a semistructured psychiatric examination and DSM-IV diagnostic criteria, a consecutive series of patients with poststroke major or minor depression (n=55) were selected. Their impairment in ADL function was assessed by means of the Johns Hopkins Functioning Examination during acute hospitalization and either 3 or 6 months later.

Results—Patients whose mood improved at follow-up (n=21) had significantly greater recovery in ADL functions at follow-up than patients whose mood did not improve (n=34). There were no differences in demographic variables, lesion characteristics, and neurological symptoms between the two groups. Furthermore, patients with either major or minor depression at the initial evaluation showed the same amount of recovery in ADL function if they improved at follow-up.

Conclusions—Our findings suggest that remission of poststroke depression over the first few months after stroke is associated with greater recovery in ADL function than continued depression. Early effective treatment of depression may have a positive effect on the rehabilitation outcome of stroke patients. (Stroke. 2001;32:113-117.)

Key Words: cerebrovascular disorders • depression • physical function

Stroke often leads to marked physical impairment. Studies have shown that early medical treatment and physical therapy after stroke may help in the recovery of activities of daily living (ADL) and lead to early hospital discharge.1

Depression is probably the most frequent emotional disorder that occurs after stroke. Numerous studies have reported frequencies for major depression ranging from 10% to 25%2–4 and for minor depression ranging from 10% to 40%.5,6

Several studies have shown that depression has a negative impact on recovery of ADL function in stroke patients. Kotilla et al,7 for example, reported poor outcome at 3 months and 1 year after stroke in patients with “inadequate emotional reactions.” However, there was no assessment of reliability or validity of these emotional reactions. Feibel and Springer8 reported that depressed patients at 6 months after stroke had greater difficulties in returning to their prior social activities compared with nondepressed patients. Also, Sinyor et al9 reported worse physical therapy outcome at 6 weeks after stroke in depressed patients compared with nondepressed patients. These studies, however, did not assess depression by means of standardized diagnostic criteria and did not examine the influence of lesion side, volume, or location on outcome.

In a study of patients with and without depression during the immediate period after stroke but with similar impairment in ADL scores, we found, 2 years later, that the depressed patients had significantly less recovery in their ADL functions than the nondepressed patients.10 The recovery curves for ADL function were not significantly different between patients with major depression versus those with minor depression,10 suggesting that both moderate and severe forms of depression lead to impaired recovery in ADL functions. Morris et al,11 who used an abbreviated version of the Barthel index, also reported that at 15 months after stroke, patients with major depression and those with minor depression had significantly greater physical disability than nondepressed patients.

Although it has been recognized that depression is associated with impaired recovery in ADL functions, it is unclear whether treatment of depression will improve recovery. Two studies have shown greater improvement in ADL scores in poststroke depressed patients who had a positive dexamethasone suppression test when they were treated in a double-blind study with the antidepressant trazodone over 6 weeks12 or in an open-label study with fluoxetine or nortriptyline.13 On the other hand, in 2 prior double-blind treatment trials, we

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failed to show any significant improvement in ADL among patients treated with nortriptyline compared with placebo.\textsuperscript{14,15}

In this study, we used standardized diagnostic criteria and a structured interview to diagnose patients with in-hospital poststroke depression. At 3- or 6-month follow-up, we divided these patients into those with and those without mood improvement and examined their functional recovery. We hypothesized that there would be greater recovery in ADL functions among depressed patients with remission of their depression compared with depressed patients without mood recovery over the follow-up period.

### Subjects and Methods

#### Patient Population

This study included 2 groups of patients. The first consisted of 75 patients admitted to the University of Maryland Hospital, Baltimore, with a diagnosis of acute intracerebral hemorrhage or cerebral infarction. These patients had a mean age of 58.9±13.4 years, 66% were black, 43% were men, and 74% were in Hollingshead social class IV or V. The second group consisted of 96 consecutive patients admitted to the Younkers Rehabilitation Unit of the Methodist Hospital in Des Moines, Iowa, who, after an acute intracerebral hemorrhage or cerebral infarction, agreed to participate in a longitudinal observation study. The mean age of these patients was 67.5±12.3 years, 96% were white, 63% were men, and 43% were in Hollingshead class IV or V. Patients were excluded if they had a decreased level of consciousness as determined by severe comprehension deficits as determined by their inability to complete part one of the Token Test.\textsuperscript{16} Taking these groups together, a total of 171 patients were evaluated. All subjects, with the agreement of at least 1 family member, signed an informed consent to participate in this study, approved by our institutional review board. Research staff ensured that only subjects capable of giving informed consent were allowed to participate in this study.

#### Psychiatric Examination

After obtaining informed consent, patients were evaluated by a psychiatrist who used a modified version of the semistructured interview, the Present State Examination (PSE).\textsuperscript{17} A diagnosis of “depression due to stroke with a major depressive–like episode” or minor depression (based on research criteria) according to DSM-IV\textsuperscript{18} criteria was made by means of symptoms elicited from the PSE, which had been modified to include all the appropriate DSM-IV symptoms. When patients were examined before the 2-week duration criteria were met, they were required to have the symptoms present since the onset of the stroke. The Hamilton Depression Scale (HDS, 17 items)\textsuperscript{19} was used to measure the severity of depressive symptoms. In this scale, scores range from 0 to 52, with higher scores indicating more severe depressive symptoms. Functional physical impairment was assessed by means of the Johns Hopkins Functioning Inventory (JHFI).\textsuperscript{20} The JHFI is a 10-item questionnaire that evaluates the patient’s degree of independence in ADL including dressing, eating, comprehension of spoken and written language, writing, performing routine tasks, finding one’s way around, expressing needs, and maintaining sphincter control. Scores may range from 0 to 27, with higher scores indicating more severe impairment. Patients’ cognitive functioning was assessed by means of the Mini-Mental State Examination (MMSE).\textsuperscript{21} in which scores range from 0 to 30, with lower scores indicating greater impairment. The reliability and validity of these instruments in a population of stroke patients have been demonstrated in prior publications.\textsuperscript{22}

#### Neuroimaging

A neurologist who was blind to the psychiatric findings evaluated the computed tomography scans obtained as part of the patient’s clinical care and transferred them onto standardized templates by using the method of Damasio.\textsuperscript{23} Lesion volume (expressed as a percentage of total brain volume) was calculated from the ratio of the largest cross-sectional area of the lesion on any CT scan slice to the cross-sectional area of whole brain on the slice passing through the body of the lateral ventricle. We have demonstrated the reliability of these measurements as well as their utility in stroke patients in a prior publication.\textsuperscript{24}

### Statistical Analyses

#### Characteristics of the Study Population

Our study population consisted of a group of 171 patients who had a mean age of 61.5±13.2 years, a median age of 64 years, and a range of 24 to 89 years. Of these patients, 57.3% were men, 51.4% were married, and 57.8% were white.

An initial analysis of our total group of patients showed a positive correlation between changes in HDS scores (ie, follow-up–initial HDS scores) and changes in JHFI scores (ie, follow-up–initial JHFI scores) \( \left[ F=10.4; \ df=1; 169, P=0.001, r=0.241 \right] \). Thus, greater improvement in mood was associated with more improvement in ADL function.

To examine our hypothesis that in poststroke depressed patients, remission of depression is associated with greater recovery in ADL function, we selected from our total population of patients only those \( (n=74) \) who had an in-hospital diagnosis of major or minor depression according to DSM-IV symptom criteria, by using the symptoms elicited from the PSE. We then divided them on the basis of whether or not their mood improved over the 3- or 6-month follow-up. Remission of depression was defined as a >50% reduction in HDS scores and no longer meeting criteria for either major or minor depression.

Nonremission of depression was defined as a ≤50% reduction in HDS scores at follow-up. Because poststroke depressed patients with mood improvement at the 3- or 6-month follow-up had lower (ie, less impaired) initial JHFI scores than the nonimproved patients, we matched patients having either major or minor depression whose depression had remitted at the 3- or 6-month follow-up \( (n=21) \) with patients whose depression had not remitted \( (n=34) \), based on comparable initial JHFI scores (ie, +0.3). In-hospital JHFI scores were 8.3±5.9 for the mood-improved patients and 8.0±5.0 for the nonimproved group, whereas at the 3- or 6-month follow-up, the JHFI scores were 3.3±2.9 and 5.8±4.0, respectively. ANOVA revealed a significant group-by-time interaction \( \left[ F=5.37; \ df=1; 53, P=0.015 \right] \). Depressed patients with remission at follow-up showed significantly greater recovery than the nonremitted group at the 3- or 6-month follow-up (Figure).

In our previous 2-year follow-up study of ADL recovery among patients with and without depression,\textsuperscript{10} a factor analysis of items in the JHFI revealed 3 distinct factors: factor 1 included 6 “motor” items such as ability to walk, dress, eat, write, find one’s way around a familiar setting, and perform routine tasks; factor 2 included 3 language items, including the comprehension of spoken and written language and the
ability to express one’s needs; and factor 3 included only sphincter control.

A repeated-measures ANOVA for each factor revealed a significant group (ie, remission versus nonremission)-by-time interaction for factor 1 \([F=4.93; \, df=1; \, 41, \, P=0.03]\) but not for factor 2 \([F=0.22; \, df=1; \, 42, \, P=0.6]\) or 3 \([F=0.48; \, df=1; \, 42, \, P=0.49]\).

Depressed patients with remission at the 3- or 6-month follow-up had an in-hospital HDS of 14.4±5.5, whereas patients without remission had an in-hospital HDS of 12.3±5.7. At the 3- or 6-month follow-up, the HDS scores were 3.8±2.9 and 13.0±6.3, respectively. ANOVA revealed a significant group-by-time interaction \([F=69.2; \, df=1; \, 53, \, P=0.0001]\). Obviously, the remitted group showed lower HDS than the nonremitted group over the 3- or 6-month follow-up.

There were no significant differences between the two groups in age, race, handedness, marital status, years of education, time since stroke, socioeconomic status, personal or family history of depression, history of alcohol abuse, or use of antidepressants. There was, however, a significant difference in sex. There was a significantly higher percentage of women in the nonremission group (68%) compared with the remission group (33%) \((\chi^2=6.2 \, df=1, \, P=0.01)\) (Table 1). When we reanalyzed the data by using only male patients, however, we continued to show a time-by-group interaction \([F=6.95; \, df=1; \, 23, \, P=0.014]\), indicating that the improved recovery in remitted patients was not due to male-female differences in ADL recovery.

Moreover, there were no significant differences in MMSE scores; side, volume, or location (ie, cortical or subcortical) of lesion; initial neurological deficits (motor, sensory, visual fields deficits, dysarthria, aphasia, apraxia, or neglect); or the percentage of patients assigned to a physical rehabilitation therapy program (Table 2).

![Figure 1. Poststroke patients with remission of depression showed significantly greater recovery in ADL than nonremitted patients at 3- or 6-month follow-up \([F=6.37; \, df=1; \, 53, \, P=0.015]\).](image)

**Comparison Between Patients With Major Depression and Those With Minor Depression**

To detect any differences in the association of remission of depression and ADL improvement between major or minor depression, patients whose depression remitted over the 3- or 6-months follow-up who could be matched for initial JHFI score \(\geq 0.10\) were divided into a major depressed/remission group \(n=9\) and a minor depressed/remission group \(n=9\).

In the hospital, JHFI scores were 7.4±3.5 for the remitted major depression patients and 7.5±5.2 for the remitted minor depression group, whereas, at the 3- or 6-month follow-up, the JHFI scores were 3.7±2.9 and 2.4±2.4, respectively. ANOVA did not reveal any significant group-by-time interaction between the two groups.

**TABLE 1. In-Hospital Demographic Characteristics of Mood-Improved and Mood-Nonimproved Groups**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mood Improved, n (%)</th>
<th>Mood Nonimproved, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD, y</td>
<td>60.2±3.0</td>
<td>59.1±2.3</td>
</tr>
<tr>
<td>Sex, female*</td>
<td>7 (33.3)</td>
<td>23 (67.6)</td>
</tr>
<tr>
<td>Race, white</td>
<td>14 (66.6)</td>
<td>14 (41.1)</td>
</tr>
<tr>
<td>Handedness, left</td>
<td>1 (4.7)</td>
<td>2 (5.8)</td>
</tr>
<tr>
<td>Marital status, married</td>
<td>12 (67.1)</td>
<td>11 (32.3)</td>
</tr>
<tr>
<td>Years of education, mean±SD</td>
<td>9.4±0.7</td>
<td>9.8±0.5</td>
</tr>
<tr>
<td>Days since stroke, mean±SD</td>
<td>12.1±3.0</td>
<td>11.8±1.9</td>
</tr>
<tr>
<td>SES,† class IV–V</td>
<td>16 (76.1)</td>
<td>27 (79.4)</td>
</tr>
<tr>
<td>Personal history of depression</td>
<td>4 (19)</td>
<td>5 (14.7)</td>
</tr>
<tr>
<td>Family history of depression</td>
<td>1 (4.7)</td>
<td>4 (11.7)</td>
</tr>
<tr>
<td>History of alcohol abuse</td>
<td>4 (19)</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>Antidepressant therapy</td>
<td>4 (19)</td>
<td>7 (20.5)</td>
</tr>
</tbody>
</table>

*P=0.01.
†From Reference 28.

**TABLE 2. In-Hospital Lesion and Neurological Characteristics of Mood-Improved and Mood-Nonimproved Groups**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mood Improved, n (%)</th>
<th>Mood Nonimproved, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE scores, mean±SD</td>
<td>22.9±4.9</td>
<td>22.7±6.3</td>
</tr>
<tr>
<td>Lesion side, left</td>
<td>9 (42.8)</td>
<td>6 (17.6)</td>
</tr>
<tr>
<td>Lesion volume, mean±SD</td>
<td>7.2±2.0</td>
<td>6.6±1.8</td>
</tr>
<tr>
<td>Lesion location, cortical</td>
<td>7 (33.3)</td>
<td>10 (29.4)</td>
</tr>
<tr>
<td>Motor deficits</td>
<td>10 (47.6)</td>
<td>22 (64.7)</td>
</tr>
<tr>
<td>Sensory deficits</td>
<td>5 (23.8)</td>
<td>8 (23.5)</td>
</tr>
<tr>
<td>Visual field deficits</td>
<td>6 (28.5)</td>
<td>6 (17.6)</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>4 (19.0)</td>
<td>8 (23.5)</td>
</tr>
<tr>
<td>Aphasia</td>
<td>3 (14.2)</td>
<td>8 (23.5)</td>
</tr>
<tr>
<td>Apraxia</td>
<td>7 (33.3)</td>
<td>6 (17.6)</td>
</tr>
<tr>
<td>Neglect</td>
<td>2 (9.5)</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>Physical therapy</td>
<td>14 (66.6)</td>
<td>16 (47)</td>
</tr>
</tbody>
</table>
Patients with remitted major depression had an in-hospital HDS of 16.6±4.5, whereas patients with remitted minor depression had an in-hospital HDS of 12±6.5. At the 3- or 6-month follow-up, the HDS scores were 5.5±2.8 and 2.1±2.4, respectively. ANOVA did not reveal any significant group-by-time interaction between the two groups.

There were no significant differences between the two groups in age, sex, race, handedness, marital status, years of education, time since stroke, socioeconomic status, personal or family history of depression, history of alcohol abuse, or use of antidepressants. Moreover, there were no significant differences in MMSE scores; side, volume, or location (ie, cortical or subcortical) of lesion; initial neurological deficits (motor, sensory, visual fields deficits, dysarthria, aphasia, apraxia, or neglect); or access to a physical rehabilitation therapy program between the two groups.

Discussion
This study found that patients who had a remission of their poststroke depression over the first few months after stroke also showed significantly greater improvement in their ADL function than patients whose depression did not remit. We consider this as an important finding, since Reding et al12 showed that early treatment of depression had a positive effect on the rehabilitation outcome of a small group of stroke patients who had positive dexamethasone tests.

Before further discussion of our results, it is important to acknowledge the methodological limitations of the study. First, the use of patients from 2 demographically distinct patient populations may have led to greater generalizability of findings or could have led to findings influenced by cohort effects. Second, our patients were predominantly of lower socioeconomic class. It is uncertain whether these findings pertain to other populations of stroke patients. Our measure of ADL function was the JHFI rather than a more commonly used instrument such as the Functional Independence Measure25 or the Barthel scale.26 These latter instruments use a wider range of scores and may be more sensitive to change. Thus, our finding that language function (ie, factor 2 of JHFI) did not change may have been related to the instrument we used.

Finally, although there were no significant differences in the frequency of antidepressant use among groups, some depressions were treated, but the vast majority spontaneously improved. There may be differences in ADL recovery between treated and spontaneously remitted depressions.

The major question raised by this study is why remission of either major or minor depression led to improved recovery in ADL over the first few months after stroke. One might speculate that the mechanisms of depression (eg, neurotransmitter depletion leading through some pathophysiology to the clinical manifestations of decreased concentration and energy) may have led to poor recovery. On the other hand, the fact that both major and minor depression showed an equal degree of recovery might lead to an alternate speculation that the effect of depression on physical impairment may be mediated by psychological rather than physiological mechanisms. For example, depressed patients may be hopeless about the future and thus may be less psychologically motivated to put any effort into rehabilitation or recovery. This could lead to slowed recovery in the depressed patients. This speculation that psychological rather than physiological mechanisms led to improved ADL recovery is also supported by our recent finding that recovery in cognitive function among patients who responded to treatment of poststroke depression occurred in patients with major but not minor depression.27 This finding related to cognitive recovery contrasts with our current findings but indicates that all poststroke recovery is not facilitated by any improvement in depression. Cognitive recovery appears to be aligned with the mechanism of major depression, whereas physical recovery appears to be aligned more broadly with an improvement in depression, thus suggesting perhaps a psychologically mediated mechanism. Whatever the explanation, the fact that remission of depression improves recovery from stroke impairments emphasizes the importance of recognizing and treating depression in patients with acute stroke.

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References

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