Early Depressed Mood After Stroke Predicts Long-Term Disability
The Northern Manhattan Stroke Study (NOMASS)

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Background and Purpose—Depression is highly prevalent after stroke and may influence recovery. We aimed to determine whether depressed mood acutely after stroke predicts subsequent disability and mortality.

Methods—As part of the Northern Manhattan Stroke Study, a population-based incident stroke case follow-up study performed in a multiethnic urban population, participants were asked about depressed mood within 7 to 10 days after stroke. Participants were followed every 6 months the first 2 years and yearly thereafter for 5 years for death and disability measured by the Barthel Index. We fitted polytomous logistic regression models using a canonical link to examine the association between depressed mood after stroke and disability comparing moderate (Barthel Index 60 to 95) and severe (Barthel Index <60) disability with no disability (Barthel Index ≥95). Cox proportional hazards models were created to examine the association between depressed mood and mortality.

Results—A question about depressed mood within 7 to 10 days after stroke was asked in 340 of 655 patients with ischemic stroke enrolled, and 139 reported that they felt depressed. In multivariate analyses controlling for sociodemographic factors, stroke severity, and medical conditions, depressed mood was associated with a greater odds of severe disability compared with no disability at 1 (OR 2.91, 95% CI 1.07 to 7.91) and 2 years (OR 3.72, 95% CI 1.29 to 10.71) after stroke. Depressed mood was not associated with all-cause mortality or vascular death.

Conclusion—Depressed mood after stroke is associated with disability but not mortality after stroke. Early screening and intervention for mood disorders after stroke may improve outcomes and requires further research. (Stroke. 2010;41:1896-1900.)

Key Words: depression • outcomes • stroke • recovery

Stroke is the leading cause of disability and the third leading cause of death in the United States. Recovery after stroke is affected by multiple factors, including initial disability, the volume of the infarct or hemorrhage, the anatomic location, prestroke functional status, marital status and a social support network, and access to rehabilitation services. Depression may be a risk factor for incident myocardial infarction and stroke. It is highly prevalent after stroke with a range from 16% to 72%. Major depression has also been found to have a strong effect on recovery from stroke as well as the likelihood of death on long-term follow-up. However, patients with stroke are not always fully evaluated for depression. The purpose of this study was to investigate the association of depressed mood with stroke outcome in a multiethnic, urban, population-based cohort and mortality after first stroke. Our hypotheses were that depressed mood after stroke would independently predict functional outcome at both 1 and 2 years after stroke and mortality within 5 years.

Methods

Recruitment of the Sample and Baseline Evaluation

The current sample was derived from Northern Manhattan Stroke Study (NOMASS) cases. Methods of recruitment, evaluation, and follow-up have been described previously. In brief, patients were eligible if they were diagnosed with their first ever ischemic stroke between July 1, 1993, and July 1, 1997, were aged >39 years, had been a resident of Northern Manhattan for >3 months at the time of stroke onset, and had access to a telephone. Cases of hemorrhage or transient ischemic attack were not eligible. Patients with stroke were examined by a study neurologist and a trained research physician. Participants who spoke Spanish at home were interviewed by native speakers. The interview and examination included a complete neurological examination and National Institutes of Health Stroke
Scale (NIHSS), demographic information, and medical history. Participants were asked the first question on the Hamilton Depression Rating Scale regarding their mood in the week after the onset of the stroke. We only included participants who had their initial assessment of depressed mood within 30 days of their stroke and who could answer the question themselves to minimize the possibility that recall bias depended on long-term stroke outcome. Social support was assessed by addressing marital status and social isolation. We defined social isolation as knowing <3 people well enough to visit within their homes (<3 friends). Standardized questions about vascular risk factors were adapted from the Centers for Disease Control and Prevention and the Behavioral Risk Factor Surveillance System. Hypertension, diabetes mellitus, cardiac disease, and hypercholesterolemia were defined as described previously. We did not collect data on the presence of a diagnosis, or treatment of, depression before or after stroke. Race–ethnicity was based on self-identification.

Follow-Up
Participants were examined at 6 months for the first 2 years of follow-up and then annually for 5 years to detect changes in health status, including death. Disability was measured using the Barthel Index (BI) of activities of daily living.

Statistical Analysis
Baseline characteristics were assessed in relation to depressed mood using a t test or χ² test as appropriate. We fitted polytomous logistic regression models using a canonical link to calculate ORs and 95% CIs for the association between an affirmative answer to the question and each of the 3 categories of BI of 0 to 60 (mild disability), 61 to 90 (moderate disability), and 91 to 100 (no disability). To test our hypothesis, we included 3 linear trend terms of BI and employed a polytomous logistic regression model.

Results
A question on depressed mood within 7 to 10 days after stroke was asked in 340 of 655 (51.9%) patients with ischemic stroke enrolled, and 139 of the 340 (40.9%) reported that they felt depressed. The participants who had a depressed mood ascertainned were more likely to be Hispanic and to have <3 friends and less likely to have completed high school and to have a severe stroke compared with those who did not. Reasons for not including depressed mood after stroke included aphasia or death within 30 days of stroke (n=113), impaired consciousness (n=12), interview >30 days after stroke (n=77), or loss to follow-up before ascertainment of depressed mood (n=37), and incomplete data (n=76). Baseline demographics of the sample used in the analysis are outlined in Table 1. Participants who reported a depressed mood were more likely to be physically inactive and have severe stroke than those who did not report

<table>
<thead>
<tr>
<th>Table 1. Baseline Characteristics of Participants With Stroke and Depressed Mood Assessed in the Northern Manhattan Stroke Study (n=340)</th>
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</thead>
<tbody>
<tr>
<td>**Mood Present, No. (Proportion) or Mean (SD; n=139)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>Race</strong></td>
</tr>
<tr>
<td>Non-Hispanic Ethnicity</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Less than a high school education</td>
</tr>
<tr>
<td>Greater than a high school education</td>
</tr>
<tr>
<td>Not married/widowed</td>
</tr>
<tr>
<td>Married</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>No diabetes mellitus</td>
</tr>
<tr>
<td>Physically inactive</td>
</tr>
<tr>
<td>Physically active</td>
</tr>
<tr>
<td>&lt;3 friends</td>
</tr>
<tr>
<td>≥3 friends</td>
</tr>
<tr>
<td>Medicaid or no insurance</td>
</tr>
<tr>
<td>Private insurance or Medicare</td>
</tr>
<tr>
<td>Cardiac disease*</td>
</tr>
<tr>
<td>No cardiac disease</td>
</tr>
<tr>
<td>Stroke severity</td>
</tr>
<tr>
<td>Mild†</td>
</tr>
<tr>
<td>Moderate</td>
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<tr>
<td>Severe</td>
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</table>

*History of coronary artery disease or prior myocardial infarction. †Mild: NIHSS <6; moderate: NIHSS 6–13; severe: NIHSS ≥14.
Depressed Mood at Years 1 and 2 of Follow-Up

When adjusted for sociodemographic factors (age, race–ethnicity, marital status, having Medicaid or no insurance, stroke severity physical activity, coronary artery disease, and diabetes), depressed mood was associated with functional disability (Model 1 in Table 3). In univariate analyses, depressed mood was not associated with moderate disability compared with no disability in any of the analyses.

We retained a polytomous model because the effect size of depressed mood on severe disability compared with no disability and that on moderate disability compared with no disability were different ($P=0.05$ for 1-year follow-up, and $P=0.01$ for 2 years follow-up comparing the estimates for moderate and severe disability). In a series of logistic models examining the association between having a depressed mood ascertained and functional outcomes, we found no associations indicating that having ascertainment of depressed mood did not depend on functional status.

Depressed mood was not associated with all-cause mortality (adjusted hazard ratio $1.15$, $95\%$ CI $0.76$ to $1.75$), vascular death (adjusted hazard ratio $1.52$, $95\%$ CI $0.81$ to $2.88$), or nonvascular death (adjusted hazard ratio $0.78$, $95\%$ CI $0.41$ to $1.50$).

**Discussion**

We found that patients with stroke who had a depressed mood within the week after their stroke were more likely to be severely disabled or died within 24 months after stroke. This disability started at the earliest time of follow-up of 6 months. Our findings were independent of stroke severity, sociodemographic factors, and medical comorbidities, but stroke severity was the strongest mediator, highlighting the importance of the initial deficit on ultimate outcome. We did not however find an effect on mortality or on moderate disability. The reasons for not finding an effect on moderate disability could be due to inadequate statistical power to detect subtle effects, a lack of a true effect, or still unmeasured confounders. The latter point is unlikely given that we observed an effect for severe disability in univariate and adjusted models and noted no trends in univariate analyses for moderate disability. Other studies have found that depressed mood is common after stroke and that it correlates with poor functional outcomes as measured by activities of daily living scales and cognitive performance. Depression has also been found to have a strong effect on recovery from stroke as well as the likelihood of death on long-term follow-up. We find it noteworthy that a single question about mood would have such predictive value with the understanding that patients with stroke have undergone a potentially life-changing event and any depressive symptoms could be reactive in nature.

Our findings regarding depressed mood and poststroke recovery, however, differ from other studies examining the link between poststroke depression and outcomes in ascertaining depressed mood in the acute setting after stroke. Controversy exists regarding the appropriateness of diagnosing depressed mood; non-Hispanic blacks were less likely to report a depressed mood. Over 5 years of follow-up, there were 105 deaths, of which 45 were vascular, 49 were nonvascular, and 11 with an unconfirmed cause of death.

The distribution of the participants’ disability by the presence of depressed mood is outlined in Table 2. At 1 year, there were 246 participants available for analysis with 207 available at Year 2 after excluding those with recurrent stroke, myocardial infarction, or death. Among those with depressed mood present at baseline, there was a greater proportion of participants in the severe disability category at 1 and 2 years. In univariate analyses, depressed mood was not associated with functional disability (Model 1 in Table 3). When adjusted for sociodemographic factors (age, race–ethnicity, marital status, having <3 friends, educational achievement, and insurance status), stroke severity, and medical and behavioral comorbidities (diabetes, physical inactivity, and coronary artery disease), depressed mood was associated with a greater odds of severe disability compared with no disability at 1 (OR $2.91$, $95\%$ CI $1.07$ to $7.91$) and 2 years (OR $3.72$, $95\%$ CI $1.29$ to $10.71$) after stroke. In secondary analyses, depressed mood was associated with severe disability in fully adjusted models starting at the first point of follow-up 6 months after stroke (adjusted OR $2.81$, $95\%$ CI $1.13$ to $6.99$), at 1.5 years after stroke (adjusted OR $5.64$, $95\%$ CI $1.93$ to $16.52$), and persisting until 3 years after stroke when it was no longer significantly associated (adjusted OR $3.57$, $95\%$ CI $0.89$ to $14.23$). Depressed mood was not associated with moderate disability compared with no disability in any of the analyses.

We retained a polytomous model because the effect size of depressed mood on severe disability compared with no disability and that on moderate disability compared with no disability were different ($P=0.05$ for 1-year follow-up, and $P=0.01$ for 2 years follow-up comparing the estimates for moderate and severe disability). In a series of logistic models examining the association between having a depressed mood ascertained and functional outcomes, we found no associations indicating that having ascertainment of depressed mood did not depend on functional status.

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Our findings regarding depressed mood and poststroke recovery, however, differ from other studies examining the link between poststroke depression and outcomes in ascertaining depressed mood in the acute setting after stroke. Controversy exists regarding the appropriateness of diagnos-
ing and therefore treating depression in the setting of an acute illness, particularly stroke. The clinician may be observing an acute “adjustment disorder,” physical symptoms (such as sleep disturbance and appetite disturbance) that could be due to stroke or depression, or the effects of brain injury itself. Although some of the psychosomatic symptoms of depression after stroke do not persist (sleep disturbances, loss of libido), depressed mood and other psychological symptoms that are ascertained in the acute setting (such as anhedonia and hopelessness) remain in patients ultimately diagnosed with depression. The distinction between “reactive” and endogenous depression may be arbitrary, because regardless of the cause, the presence of a depressed mood may lead to diminished motivation to perform rehabilitation or to participate in medical management for secondary stroke prevention. This is notable given that the prevalence of mood disorders increases significantly from 1 week to 3 months after stroke and may be 1 explanation for our observed results. Interestingly, 1 group demonstrated that poststroke depression influenced functional recovery after stroke, but not motor recovery as measured by the Fugl-Meyer scale, arguing for motivation being an important component.

The finding that depressed mood after ischemic stroke affects recovery may have important clinical and treatment implications. A recent study randomized nondepressed patients with stroke within 3 months to escitalopram versus placebo and found significant improvement in depression. Another group has established the superiority of a brief psychosocial–behavioral intervention with pharmacological treatment compared with pharmacological treatment alone. No clinical trials have been carried out to date in the more acute stroke setting (ie, <10 days).

The strengths of our study include evaluation of an older triethnic population for whom we know less regarding stroke recovery and a careful longitudinal design. We carried out systematic follow-up during multiple time points and were able to capture recurrent events that might influence our results. In the sample we used for this study, we ascertained the presence of depressed mood in the acute setting, which has been less frequently done. This study has several limitations. We did not collect information on prestroke diagnosis of major depression, which predicts poststroke depression in other studies. In other studies, however, the association between depression and poor functional outcomes remains when excluding those with premorbid depression. Depressed mood was assessed by a positive response to the first question on the Hamilton Depression Rating Scale, but a full depression assessment was not consistently done, and thus we cannot report the effect of poststroke major depression. However, the Hamilton Depression Rating Scale has been used previously to measure incident poststroke depression, and the prevalence of depression was 41% at 1 month, similar to the prevalence of depressed mood within 7 to 10 days of stroke in this study. In addition, depressed mood is 1 component of well-validated 2-question screening questionnaires, which have excellent sensitivity and specificity for depression. There remains wide variability in the scales that are used to assess poststroke depression, but most have yielded similar prevalence estimates. We included participants with mild aphasia, and many of these scales have not been well validated in that setting. Psychomotor retardation, inattention, aprosody, and other psychiatric symptoms are commonly seen in patients with right hemisphere ischemia and could masquerade as depressed mood, but in our analyses, the side of the lesion was not associated with any of the outcomes, and it was therefore not kept in the final model. We may have been underpowered given our sample size to detect more subtle effects on moderate disability compared with severe disability or mortality due to depressed mood. Poststroke depressed mood was not ascertained in all participants at the beginning of this study, and those who did not have the question ascertained were more likely to have a severe stroke; nonetheless, having the question asked was not associated with functional outcome, suggesting that this was not a factor in our results. Participants were excluded if enrolled after 30 days from their event to minimize bias caused by early recovery from the index stroke affecting the answer to the mood question. We acknowledge that our assessment was carried out soon after stroke, so we may be capturing an adjustment reaction rather than major depression, although others have demonstrated an association between early psychological symptoms of depression and eventual diagnosis of depression. We do not have information regarding poststroke physical activity and fitness, which others have found to be strongly predictive of recovery. Use of antidepressants after stroke was limited in our population and also not systematically collected in all participants on follow-up.

Further research into the effect of mood disorders on stroke recovery is needed. These data suggest that a single question about depressed mood can be an important predictor of poststroke disability. It is likely that early treatment, which may include a combination of psychosocial intervention, psychotherapy, and pharmacotherapy, is beneficial for stroke recovery, but a clinical trial is needed in the acute setting.

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Disclosures
None.

References


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