Poststroke Depression
An 18-Month Follow-Up
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Background and Purpose—This prospective study was designed to examine the course, associates, and predictors of depressive symptoms during the first 18 months after stroke.

Methods—A total of 100 patients were followed up for 18 months after stroke. Depressive symptoms were assessed at 2 weeks and 2, 6, 12, and 18 months after stroke with the Beck Depression Inventory and the Hamilton Rating Scale for Depression, and diagnoses were performed using criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition-Revised. Stroke severity was assessed with the Scandinavian Stroke Scale and cognitive functions with a comprehensive neuropsychological battery. Patients participated in a randomized clinical trial of antidepressive medication.

Results—In all, 54% of patients felt at least mildly depressive at some time during the follow-up; 46% of those who were depressive during the first 2 months were also depressive at 12 and/or 18 months. Only 12% of patients were depressive for the first time at 12 or 18 months. The male sex was associated with a more negative change in depressive symptoms during the follow-up. Older age was associated with depressive symptoms during the first 2 months, stroke severity from 6 to 12 months, and the male sex at 18 months. Depressive symptoms were unrelated to the lesion location.

Conclusions—Depressive symptoms are frequent and they often have a chronic course. Depression is associated with stroke severity and functional impairment, and with the male sex at 18 months. Attention should be focused on the long-term prognosis of mood disturbances and adaptation. (Stroke. 2003;34:138-143.)

Key Words: activities of daily living ■ cognition ■ depression ■ stroke

Depression is a usual consequence of stroke from the acute phase to at least 2 to 3 years after stroke.1–7 However, a consensus on the course and associated factors of depression has not been reached. Some studies have proposed that there is a higher risk of depression when the lesion is located in the left hemisphere,1,8 but other studies were not able to replicate these findings,3,9–14 nor could a systematic review by Carson et al15 support this hypothesis. The core of interest has moved from the question of location toward more psychological models.16 Stroke severity or physical disability and functional impairment are important factors associated with depression.3,6,14,17–19 Knowledge of the associations between cognitive deficits and depression is still lacking. Depressed patients have been more cognitively impaired in some studies,12,20–22 but not all studies have found this correlation.3 In all these studies, cognitive impairment was assessed with only a single score, most often the Mini-Mental State Examination (MMSE).23 Comprehensive neuropsychological examination was performed in only 1 follow-up study.2 In that study, depressive patients performed more poorly than nondepressive patients in almost all areas of cognitive functions, at both 3 and 12 months. We found an association between poorer verbal abilities and depression in the acute phase.14

Other possible risk factors include age, sex, living alone, lack of social support, and both personal and family psychiatric history. In some studies, elderly patients were found to have more depressive symptoms.2,19,21 Not all studies, however, have found differences in age between depressed and nondepressed patients.1,3,12,17 and Robinson et al24 found younger patients to have more depression in the acute phase. In some studies, women have been more depressive than men,12,17,21,22 but not all studies have been able to find this difference.1–3 Furthermore, Burvill et al4 found that when depressive, men had poorer prognosis in follow-up than women. Living alone and having few social contacts have been found to contribute to depression.1,12

Detecting and treating poststroke depression is important, because it has negative effects on functional recovery.25–27 Poststroke depression is also associated with poor psychosocial outcome and poor quality of life in longer periods of follow-up. This prospective study was designed to examine
which neuropsychological, clinical, or functional factors are associated with depression during the 18-month follow-up after stroke and to determine which factors predict the course of depression. Patients participated in a randomized placebo-controlled clinical trial of mianserin.

Subjects and Methods
The present study included 100 consecutive patients with their first significant ischemic stroke admitted to the Department of Neurology, University of Helsinki. Patients >70 years of age and those with a known history of alcohol abuse, dementia, psychosis, current antidepressant treatment, or severe concomitant disease were excluded. Confused patients unable to cooperate were also excluded. The patient or his/her next of kin gave informed consent. Patients were studied at 2 weeks and at 2, 6, 12, and 18 months after stroke. The present study is part of a larger project including a drug trial.28

Characteristics of the Patients
The characteristics of the patient group as a whole and of the treatment groups are presented in Table 1. Two patients died before the 6-month follow-up, 1 before the 12-month follow-up, and 1 before the 18-month follow-up. Two patients refused to participate at the 6-month follow-up and 4 at both

| TABLE 1. Characteristics of the Patient Group as a Whole and by Treatment Groups |
|-------------------------------|-------------------------------|-------------------------------|
|                      | Total n=100 | Mianserin n=51 | Placebo n=49 |
| Mean age (± SD)        | 55.2 (10.6) | 54.7 (10.1) | 55.7 (11.1) |
| Men/women             | 68/32       | 36/15       | 32/17       |
| Location of stroke    |             |             |             |
| Right hemisphere      | 38          | 19          | 19          |
| Left hemisphere       | 42          | 21          | 21          |
| Brain stem            | 20          | 11          | 9           |

Results

| TABLE 2. Numbers (and Percentages) of Patients With at Least Mild Depressive Symptoms* |
|-----------------------------------------------|-------------------------------|-------------------------------|
| All Patients                                | Mianserin                      | Placebo                      |
| Acute phase                                 | 24/89 (27)                    | 14/45 (31)                    | 10/44 (23)                    |
| 2 months                                    | 27/92 (29)                    | 11/46 (24)                    | 16/46 (35)                    |
| 6 months                                    | 21/90 (23)                    | 12/45 (27)                    | 9/45 (20)                     |
| 12 months                                   | 21/88 (24)                    | 11/43 (26)                    | 10/45 (22)                    |
| 18 months                                   | 22/85 (26)                    | 10/42 (24)                    | 12/43 (28)                    |

*Beck Depression Inventory score ≥10 points.
model accounted for 15% of the variance in change from the acute phase to 18 months [F(5,75)=3.74, P<0.01]. Male gender (P<0.01) and better initial ADL in the acute phase (P<0.05) were significant associates of poorer outcome. No significant model was found with the same independent variables above, when the change in HRSD was a dependent variable.

The lesion location significantly affected the change in HRSD score from the acute phase to 2 months [ANOVA F(2,88)=4.24, P<0.02]; only scores of brain stem patients declined (Figure 1). Significant effects of lesion location on HRSD changes were not found after 2 months; the effect on BDI changes was insignificant throughout the follow-up. When we studied separately those patients who were scored depressive at the acute phase, we could not find a significant association with depressive symptoms as measured with BDI or HRSD (1-way ANOVA) at any time. No significant interaction between age and sex, living condition and age, and living condition and sex was revealed in ANOVA. The interaction between lesion location and SSS was no longer found after the acute phase. If only patients in the placebo group are included, depressive symptoms associate significantly with BI (r=-0.46, P<0.01) at 6 months, SSS (r=-0.35, P<0.05) at 12 months, and sex (men 10.0 versus women 2.7, Mann-Whitney P<0.01) at 18 months.

Linear regression series were then performed to determine the strength of associations with those variables found to have significant correlations with BDI. We used the SPSS simultaneous entry method with age, sex and SSS, and right-hand tapping and logical memory at each time point as predictors, and BDI score each time as dependent variables. BI was not included because of strong correlation with SSS. The results presented in Table 3. At 18 months, men had for the first time higher depression scores than women in both BDI and HRSD (8.2 versus 4.0, Mann-Whitney P=0.001, and 4.9 versus 3.3, P<0.05, respectively). In all, 34% of men scored ≥10 in the BDI, versus only 8% of women (Pearson chi-square=6.5, P<0.05). Depressive patients performed slightly more poorly in all neuropsychological tests, which were done 3 times during the follow-up; however, the differences were mostly nonsignificant. For the further analyses we chose only 3 tests: logical memory, block design, and right-hand tapping. They were the most representative tests of the 3 factors (verbal abilities, visual abilities, and practical abilities) found in factor analysis in our previous study. Those who were aphasic (Western Aphasia Battery AQ score ≤93.7) showed no significantly higher BDI scores in any phase of the follow-up. The lesion location (left hemisphere, right hemisphere, brain stem) showed no significant association with depressive symptoms measured with BDI or HRSD (1-way ANOVA) at any time.

### TABLE 3. Results of Linear Regression Analyses

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<tr>
<td>Age</td>
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<td>-0.47†</td>
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<td>Logical memory</td>
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<td>-0.31†</td>
<td>-0.24*</td>
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<tr>
<td>Model</td>
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<td>F(5,86)=2.18</td>
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<td>F(5,82)=2.62</td>
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<td>F(5,81)=5.27</td>
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<td>F(5,79)=3.75</td>
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<td>P</td>
<td>&lt;0.05</td>
<td>NS</td>
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<td>Adjusted R²</td>
<td>0.11</td>
<td>0.06</td>
<td>0.09</td>
<td>0.20</td>
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Beck Depression Index as dependent variable. Univ indicates univariate associations; multiple; beta scores of the multiple regression models; NS, nonsignificant. *P<0.05, †P<0.01, ‡P<0.001.
are presented in Table 3. At 2 months, this model failed in significance, but from 6 to 18 months the models were significant and accounted for 9% to 20% of the variance. The independent significant variables were SSS at 6 and 12 months and male sex at 18 months. We controlled the importance of medication by also including it with the independent variables in linear regression analysis; it had no significant effect at any time.

**Acute Predictors of Later Depression**

Series of linear regression analyses were performed to determine the acute predictors of later depression. With the independent variables above, no significant model emerged to predict depression at 6 months. At 12 months [F(5,82)=3.06, P<0.05] and at 18 months [F(5,79)=3.19, P<0.05], 11% to 12% of the variance was accounted for, with the model with initial SSS and male sex being the only significant predictors, respectively. When we added acute BDI to the predictors, the model accounted for 35% of the variance at 12 months [F(6,76)=8.31, P<0.001], and BDI remained the only significant predictor. At 18 months, the model [F(6,74)=10.79, P<0.001] accounted for 42%, and acute BDI and sex were significant.

**Discussion**

We found mild depressive symptoms to be frequent and with little change in prevalence during the 18-month follow-up after stroke. Our rates of depressive symptoms (from 23% to 29%) are similar to or, more often, lower than those in many other studies.13,19,24,40 This may be due to the inclusion criteria of the patients and measures of depression used. Our patients were younger, with a mean age of only 55 years, had experienced their first significant stroke, and had no other severe concomitant diseases. Most similar rates are in a study17 using a self-rating scale, and the greatest differences are when comparing studies using DSM-III-R criteria with older patients.2,3

Depressive symptoms were often persistent after stroke. Almost half of the patients who were depressive in the acute phase and/or at 2 months were also depressive at 12 and/or 18 months. This is in line with several other studies.4,17,22 Robinson et al41 claim that the continuity of depressive symptoms may be particularly strong in patients who suffer milder depressive symptoms, as our patients did. Most cases that were rated depressive developed depressive symptoms in the first months following stroke, as was also found in 2 other studies.12,42 However, only 15% of the variance of change in depressive symptoms from the acute phase to 18 months could be accounted for, with male sex being the most significant associate of poorer outcome.

The association between stroke severity and functional outcome and depressive symptoms could be seen from 2 months onward. This result is consistent with most previous studies.3,6,17,18,22 Depressive patients also had slightly more cognitive impairment in neuropsychological tests, but the cognitive factors did not remain as independent predictors of depressive symptoms in linear regression analyses. Depressive patients also had significantly poorer cognitive test results than nondepressive patients in the study by Kauhanen et al,2 but the authors did not examine the possible underlying effects of age and overall stroke severity on cognitive impairment. These factors may have an important influence on results, especially with older patients. Neurologically unimpaired depressed patients generally had lowered cognitive profile, lengthened reaction time, and larger interindividual variations in a meta-analysis.43 According to this and our results, it may be of no use to search for any specific cognitive profile in neurologically impaired depressed patients.

Our study does not implicate the direction of causation when considering the association of these defects and depression. The association of stroke severity and depressive symptoms was significant after the acute phase when patients begin to be more aware of the complexity of the problems associated with stroke. Unawareness of cognitive deficits more typically follows right-hemispheric lesions: in our earlier study14 and in the study of Bolla-Wilson et al,44 both in the acute phase and in the early months following, there was an interaction of lesion location and cognitive impairment, but this disappeared after the acute phase. Poststroke depression itself may, however, result in intellectual impairment during longer follow-up.45 We found no significant differences in depression prevalence between right- and left-hemispheric lesions that are consistent with the recent review.15 In addition, the increasing prevalence of major depression during the follow-up, which was also found in other studies,2,38 may suggest that psychological rather than organic factors are more important.

Sex was not associated with depression in our study during the first year after stroke, nor in 2 other studies from Finland2,3 or a longitudinal study conducted in Sweden.1 Female sex has been found to be associated with poststroke depression in some studies6,22,46 and also in depression without stroke.47 Unexpectedly, men were more depressed 18 months after stroke than women in our sample. Our follow-up showed a much poorer prognosis for men than women: more than half of the men but fewer than one third of the women who were rated depressive in the acute phase and/or at 2 months were still rated as depressive at 12 and/or 18 months. Our rates are almost identical to those of Burvill et al,4 who also found that in men, the highest proportion of depression was in those <60 years of age, while in women the highest proportion of major depression was in the older age groups. The younger ages of our patients may have influenced the higher proportion of depressed men. Poststroke depression may be of a different nature in men and women. Physical disability may be of greater importance in men of working age, or men may have poorer coping abilities than women where health problems are concerned. Inability to work after stroke has been found to be associated with depression in young adults.6 The question of working ability may not be actual until after longer follow-up. Both cultural differences and questions raised by the growing field of gender-based biology should be considered. Increased age was associated with more depressive symptoms in the acute phase and at 2 months, which has also been found in 2 other studies from Finland.2,19
The present study stands out as a carefully examined prospective 18-month follow-up of 100 patients with detailed neuropsychological assessment. Our subjects were acute-phase inpatients; patients with extremely mild and/or no disabilities were not included, unlike the case in community samples. The randomized use of the antidepressant drug is a limitation in the study. The medication used may have reduced the symptoms of especially severe depression, and so the results may be more conservative. However, in some other studies, in which randomization was not used, 19% to 36% of depressed and 8% to 10% of nondepressed patients used antidepressive medication.2,17 In our study, we have been able to control the impact of medication somewhat better than in the above-mentioned studies. Scarcity of results can be due to inadequate statistical power.

We chose to measure the severity of depressive symptoms with well-known measures, both the self-rating BDI scale and the observer-rated HRSD. BDI is validated in stroke patients49 and has been used with stroke patients in previous studies.19 Self-rated or observer-rated scales have been used in several earlier studies.5,12,17,22 From a clinical standpoint, months are still needed to explore the real outcome of long-term prognosis of mood disturbances in patients once personal coping abilities, may become more important in later evaluation factors other than those directly stroke-related, such as often depressed than women 18 months after stroke. Adaptation to stroke: relationship to lesion location. Compr Psychiatry. 1983;24:555–566.

In conclusion, depressive symptoms are frequent and are likely to prevail at longer follow-up times. Depressive symptoms were associated with stroke severity and functional outcome from 2 months on. Unexpectedly, men were more often depressed than women 18 months after stroke. Adaptation factors other than those directly stroke-related, such as personal coping abilities, may become more important in later recovery. Clinicians should focus more attention on the long-term prognosis of mood disturbances in patients once experiencing depression, especially with more severe strokes and in male patients. Follow-up studies longer than 18 months are still needed to explore the real outcome of depressive stroke patients.

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References
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