A Two Year Longitudinal Study of Mood Disorders Following Stroke
Prevalence and Duration at Six Months Follow-up

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Summary: We are conducting a two year longitudinal study of mood disorders in a group of 103 stroke patients. During the first six month period following the stroke the prevalence of symptoms of major depression increased from 23 per cent to 34 per cent while the frequency of symptoms of dysthymic depression increased from 20 per cent to 26 per cent. In addition, 10 of 13 patients who had major depresssive symptoms during the initial evaluation continued to have these symptoms at six months follow-up and 4 of 9 patients who had minor depression in hospital developed major depression, while 5 of 9 continued to have minor depressive symptoms. Thus, the duration of depression following stroke is more than six months and the prevalence of major depressive symptoms increases steadily for the first half year after a cerebral hemorrhage or ischemic lesion.

During the past several years we have been investigating mood disorders in patients who have had strokes (Robinson and Szetela, 1981; Robinson and Benson, 1981; Robinson *et al*, 1983a-d). We found that psychopathological changes were related to the location of the hemispheric lesion; patients with left hemisphere lesions were more depressed than patients with right hemisphere lesions (Robinson *et al*, 1983a-b). In addition, we have reported on the importance of *intra*hemisphere lesion location, with left anterior infarcts producing the greatest severity of depression (Robinson *et al*, 1983a) even in the presence of bilateral brain injury (Lipsey *et al*, 1983) and right anterior infarcts producing an unduly cheerful but apathetic mental state (Robinson *et al*, 1983a and b). Although lesion location appeared to be the single most important factor in determining the severity of psychopathology, we found that the severity of impairment in activities of daily living and intellectual function as well as the quality of available social supports were also significantly correlated with the severity of post-stroke depression (Robinson *et al*, 1983c).

One of the most fundamental questions about depression following strokes, is whether they are simply transient fluctuations of mood or whether they represent a more stable long term mood disorder. That is, if post-stroke depression is to be an important variable in the long term prognosis and rehabilitation of the patient, they must be more than short-lived emotional states reflecting the clinical course of the acute illness. As a first effort to address this fundamental issue, we have previously reported the results of a follow-up study of out-patients attending a stroke clinic (Robinson and Price, 1982; Pearlson and Robinson, 1982). We reported that, of the 30 patients who were depressed at the initial interview, two-thirds of those interviewed between seven and eight months following the initial interview remained depressed. However, by 10 to 11 months after the initial evaluation less than 20 per cent of the patients remained depressed and by one year none of the patients remained depressed. These results suggest that post-stroke depressive disorders last for many months and may not be simply transient emotional states. However, this study, was carried out in an out-patient population at various periods of time after the stroke and because they were examined cross-sectionally, we did not know the time of onset of their depressive disorders. Thus, we wanted to study an unselected population of patients immediately following the stroke so that we could identify the onset of their depressive symptoms and follow them longitudinally.

In association with the NINCDS Pilot Stroke Data Bank (Kunitz *et al*, 1979), we have examined a group of 103 patients at the time of hospitalization for stroke and at follow-up intervals of three months, six months,

one year and two years. Our findings during the acute stroke period are reported elsewhere (Robinson *et al*, 1983c). In the present study we report on the prevalence and stability of depression in 61 patients evaluated in hospital and again during the first six month period.

Method

1. *Sample*

From January 1980 to July 1981 we examined in-patients at the University of Maryland Hospital who were included in the NINCDS Pilot Stroke Data Bank (Kunitz *et al*, 1979). The age of the patients ranged from 20 to 80 years. We studied the occurrence of mood disorders in all patients with a thromboembolic stroke or an intracerebral bleed; from this original group of 121 thromboembolic stroke patients and 33 patients with intracerebral bleed, we examined 103. Of the 51 patients who were not included, 43 had a decreased level of consciousness or severe aphasia with comprehension deficits and could not reliably respond to questions. Seven patients could not be examined prior to their discharge and one refused to be interviewed. With the exception of these patients who were excluded, there was no selection bias.

In our longitudinal studies, we have reinterviewed over 90 per cent of these patients who survived the first six months. For this short-term follow-up study, 61 patients were reinterviewed at least once. Forty patients were interviewed at three months, 50 were interviewed at six months and 29 patients were interviewed at both intervals. The patients interviewed at follow-up were predominantly those who were scheduled for continued medical care in the hospital's out-patient stroke clinic or neurology clinic. A greater number of patients were seen at six months than at three months follow-up because some patients at three months following stroke were in rehabilitation hospitals or other continuing care institutions and by six months follow-up they had returned home. During the first six months following the stroke, seven of the original 103 patients had died from the stroke or other illnesses. In addition, patients who were institutionalized elsewhere or whose medical care was routinely provided in other settings were not included in this follow-up sample. Comparability of the follow-up sample with the original 103 patients is shown in Table I.

2. *Interview*

Patients were interviewed in a private room in the late morning or early afternoon in an effort to minimize any possible effect of diurnal mood variation throughout the day. All of the original sample of 103 patients were interviewed in the hospital during the acute period following the stroke. Of the 61 patients

seen at follow-up, 56 were interviewed at the time of an out-patient visit, four were interviewed by telephone and one was interviewed during a further admission to hospital. No one refused participation in the follow-up.

3. *Neurological and psychiatric evaluation*

Both in-patient and follow-up neurological evaluations were done by the attending neurologist (T.R.P.) using the standardized examination and rating criteria established by the Pilot Stroke Data Bank. Similarly, the neurological diagnosis was made using Data Bank criteria which included both CT scan and other laboratory tests as well as clinical examination data.

The psychiatric examination included three standardized quantitative measures of mental state. The Zung Depression Scale was read to patients who were asked to rate themselves using the four Zung categories (Zung, 1965). The Hamilton Depression Scale is a 17 item interviewer rated scale (Hamilton, 1960). The Present State Exam (PSE) (Wing *et al*, 1974) was modified to rate symptoms of anxiety or mood change. This modified version of the PSE has been discussed in detail in a previous publication and all three instruments have been found to be both reliable and valid in the assessment of affective disorders following a stroke (Robinson and Benson, 1981; Robinson *et al*, 1983b).

Psychiatric diagnosis was made using the symptoms elicited from the PSE. Although all of these patients had a brain lesion, we wanted to compare their depressive symptoms to the major and minor depression categories described in the diagnostic criteria established by DSM III (American Psychiatric Association, 1980). We did this to distinguish the more severely depressed patients from those who were less severely depressed. Because there is not exact concordance between the PSE symptoms and DSM III symptoms, some clinical judgement was necessary. This use of the PSE for establishing DSM III symptom criteria has been discussed in previous publications (Robinson *et al*, 1983a and b), and the method used for conversion is available on request.

4. *Intellectual and Physical Impairment and Social Functioning*

In conjunction with the psychiatric evaluation, quantitative assessments were made of social functioning, intellectual and functional physical impairment. The Social Functioning Exam (SFE) and the Social Ties Checklist assess the number of, and personal satisfaction with, social supports available to the patient. These instruments have been described in detail in previous publications (Starr *et al*, 1983a-b). The Mini-Mental State Examination is a brief cognitive assessment (Folstein *et al*, 1975), and the Johns

Hopkins Functioning Inventory (JHFI) measures activities of daily living (Robinson and Szetela, 1981; Robinson and Benson, 1981). Results from the SFE will will presented in future publications.

5. Statistical Analysis

Means and standard deviations were calculated for all quantitative measurement scales. Intergroup comparisons were done using analysis of variance. Correlation coefficients were calculated using Pearson correlation statistics; non-parametric data was compared between groups using chi-squared statistics.

Results

1. Sample

The 61 patients seen at follow-up ranged in age from 24 to 78, mean 59.3 ± 13.0. Characteristics of the patients are shown in Table I. The group included predominantly lower socioeconomic class (Hollingshead and Redlich, 1958) black patients, the majority were males and more than half of the follow-up group were living alone. One-fourth of the patients had a prior stroke. All the patients were living at home and most of them could walk.

The demographic characteristics of the overall group of 103 patients was compared to the follow-up group (Table I). There were no statistically significant differences in the demographic characteristics of the overall group of 103 and the follow-up of 61. In addition, there were no significant differences in the demographic characteristics between the follow-up patients and the 42 patients whom we did not re-interview during the first six months. The follow-up patients also did not differ from the non-follow-up patients in their in-hospital depression scores, capacity for self-care (activities of daily living), cognitive functioning, or social functioning. However, since the follow-up group was able to live at home, they were probably less physically impaired than the overall group at six months following the stroke.

2. In-hospital scores

Diagnoses at the time of hospitalization for the 40 patients who were subsequently followed-up at three months and the 50 patients who were seen at six months are shown in Table II. We found that 13 of 50 patients (26 per cent) followed up at six months had the symptom clusters associated with major depression at the time of initial hospitalization. Patients demonstrated symptoms of depressed mood, hopelessness, irritability, feelings of worthlessness, loss of interest and concentration, weight loss, sleep disturbance, anergia or restlessness and inefficient thinking. In addition, 9 of 50 patients (18 per cent) seen at six months follow-up had symptoms of depressed mood or

TABLE I
Background characteristics fo study population

	Pateints seen during acute hospitalization (N = 103)	Patients seen during six months follow-up (N = 61)
Age (mean ± SD)	59 ± 13	59 ± 13
Race (% black)	65%	71%
Sex (% male)	61%	56%
Marital status		
(% married)	47%	44%
(% widowed)	23%	28%
Socioeconomic status		
Class I-III	23%	13%
Class IV & V	77%	87% *
Living alone	21%	15%
History of prior stroke(s)	24%	26%

loss of interest and at least three other symptoms of dysthymic or minor depressive disorder when they were in hospital. Consequently, almost 45 per cent of the patients had clinically significant depressive symptoms in hospital. In-hospital scores on the Zung, Hamilton and PSE as well as the intellectual and functional physical impairment as measured by the Mini-Mental State and Johns Hopkins Functioning Inventory were significantly different between groups of patients from various diagnostic categories (Table III).

As previously noted, the depression scores for patients seen at follow-up were not significantly different than scores of patients for whom we did not obtain a follow-up evaluation. In addition, when we looked at symptom clusters of the patients whom we did not reinterview for this study, 33 per cent had major depression and 19 per cent had minor depression. These distributions of diagnosis in follow-up versus non-follow-up patients were not significantly different ($\chi^2 = 1.41$).

3. Three month follow-up

Table IV shows the prevalence of clinically significant depression at three months follow-up as related to mood state in hospital. In this group 14 of 40 patients (35 per cent) were depressed in hospital and at follow-up 18 of 40 patients (45 per cent) were depressed; thus, there was an overall increase of 10 per cent in the prevalence of depression by the time of the first follow-up. In fact, over this first three month period half of the patients were significantly depressed at some time. Of the patients with major depression in hospital five were found to have major depressive symptoms at three months while only one patient had recovered (Table

TABLE II
Diagnoses of 61 patients in-hospital and at follow-up using DSM-III criteria (percentage figures in brackets)

	40 patients seen at three months		50 patients seen at six months	
	In hospital	3 months	In hospital	6 months
Major depression	6 (15%)	9 (22%)	13 (26%)	17 (34%)
Minor depression	8 (20%)	11 (27%)	9 (18%)	13 (26%)
No depression	26 (68%)	22 (55%)	28 (56%)	20 (40%)

TABLE III
Scores related to severity of affective disorder

	In hospital			Six month follow-up		
Diagnostic category	Major depression N = 13 (mean ± SD)	Minor depression N = 9 (mean ± SD)	No depression N = 28 (mean ± SD)	Major depression N = 17 (mean ± SD)	Minor depression N = 13 (mean ± SD)	No depression N = 20 (mean ± SD)
Zung*	55 ± 12	44 ± 8	33 ± 5	60 ± 13	44 ± 8	33 ± 6
Hamilton*	14 ± 7	8 ± 3	4 ± 3	13 ± 7	8 ± 5	3 ± 2
PSE*	20 ± 7	13 ± 5	3 ± 2	20 ± 9	11 ± 6	3 ± 2
Mini-Mental State	19 ± 8	22 ± 7	25 ± 4	19 ± 7	25 ± 5°	26 ± 5°
JHFI	11 ± 8	5 ± 5°	4 ± 4°	7 ± 5	1 ± 2**,°	2 ± 2**,°

*All values for each diagnostic category are significantly different from the others $P < .01$
**Significantly different than in-hospital value $P < .02$
°Significantly different than major depression $P < .05$

TABLE IV
Stability of depressive symptoms at three months follow-up

	Diagnostic status at three months follow-up		
Initial diagnosis during acute hospitalisation N = 40	Major depressive disorder	Dysthymic disorder	No depression
Major depressive disorder N = 6	5	0	1
Dysthymic disorder N = 8	2	5	1
No depression N = 26	0	6	20

Stability of depressive symptoms at six months follow-up

	Diagnostic status at six months follow-up		
Initial diagnosis during acute hospitalization N = 50	Major depressive disorder	Dysthymic disorder	No depression
Major depressive disorder N =13	10	2	1
Dysthymic disorder N = 9	4	5	0
No depression N = 28	3	6	19

IV). Of the eight patients with minor depression in hospital, seven continued to be depressed at three months; two patients had developed major depression while only one patient had recovered from the dysthymic symptoms. Thus, of those patients with depression in hospital, 86 per cent were still depressed at three months while 14 per cent were no longer depressed. Patients with no depression in hospital tended to have no depression when seen at three months although a significant number (6 of the 26) had developed dysthymic symptoms by three months follow-up. This distribution of hospital versus follow-up symptom clusters was statistically significant (χ^2 = 31.6, P <.01). Thus, the affective state as measured during the acute post-stroke period was likely to prevail at three months follow-up and, for those patients whose affective state changed, they were more likely to get worse.

4. Six month follow-up

At six months after the initial evaluation, 50 patients were interviewed. During this period there was a significant improvement in functional physical impairment for all diagnostic groups except the patients with major depression who remained more impaired than the minor depression or non-depressed groups (Table III). In addition, there was no significant improvement in the cognitive state of any of the groups and the patients with major depressive symptoms remained the most impaired.

Prevalence of depression increased during this six months following the stroke (Table II). While 22 of 50 patients were depressed in hospital, at six months follow-up 30 of 50 patients (60 per cent) were significantly depressed: thus, from hospital to follow-up there was a 16 per cent increase in the number of depressed patients and over this period 62 per cent had been significantly depressed at some time. In addition to this increasing prevalence of depression during the first six months after the stroke the patients who were originally depressed had not improved. Of the patients with major depressive symptoms in hospital, 10 of 13 continued to have major depressive symptoms at six months while only 1 patient had recovered (Table IV). Two patients with major depression in hospital were less depressed at follow-up but still had the symptoms of minor depression. Of the patients with minor depression in hospital, none had recovered and four had developed a major depression by the time of this follow-up. Thus, of the patients with clinically significant depression in-hospital, 95 per cent were still depressed at six months and only one patient had recovered. Of the patients with no depression in hospital, 9 (32 per cent) patients had developed a clinically significant depression at follow-up. This

distribution of hospital versus follow-up diagnosis was statistically significant (χ^2 = 28.04, P <.01). As with the three months follow-up group, the affective state as measured during the acute post-stroke period was likely to prevail at follow-up, and for those patients whose affective state changed, it was likely to worsen rather than improve.

Discussion

We have examined 61 stroke patients who were seen during the acute hospitalization and at least one time during the first six months after the stroke. We found that the prevalence and severity of depression following the stroke increased consistently from hospital to six months and that almost one third of the patients who were not depressed in hospital had a clinically significant depression at six months follow-up. Thus, over 60 per cent of the patients had been depressed at some time. Nearly two-thirds of the depressed patients (or about 40 per cent of the whole group) had symptom clusters associated with major depressive disorder and 10 of 13 patients (77 per cent) who had major depressive symptoms in the hospital continued to have these symptoms six months later. Although we are continuing to follow these patients, this first follow-up report demonstrates that post-stroke depressive disorders which are present during the acute period following infarction are likely to endure at least six months.

The interpretation of these results is limited by several factors. First, for this report we interviewed patients during a routine, scheduled follow-up appointment in the hospital's outpatient clinic. Patients from our original population who were not followed in this manner were not evaluated. The patients who were not followed up included some who required chronic institutional care and therefore may have been a more impaired group than those who were evaluated; the course of depression may have been worse in this group. However, we demonstrated that on demographic data and measures taken in hospital, including the JHFI (activities of daily living), the group interviewed was comparable to those not interviewed. In our on going longitudinal studies we have reinterviewed over 90 per cent of the survivors of the original group of 103 patients and in our long-term follow-up reports this issue of sample selection will be examined further. Secondly, the population used for this study was predominantly lower socioeconomic and black and the results from this group may not be valid for other populations. Thirdly, although we have previously demonstrated the importance of other factors such as lesion location and social supports in psychopathology, the numbers of patients in this study were too small to allow any meaningful division into lesion location or degree of social support. The course and development

of depressive disorders may vary depending upon which area of brain is injured, the severity of the impairment or the quality of social supports.

In previous studies we have suggested that some depressions associated with stroke may represent a major depressive disorder provoked by focal brain injury (Robinson et al, 1983a-b). This suggestion is supported by the work of other investigators who have demonstrated depressive symptom clusters in stroke patients (Gainotti, 1972; Folstein et al, 1977; Ross and Rush, 1981). Post (1962) noted the frequent association between stroke and endogenous depression and hypothesized that arteriosclerotic disease and depression might be aetiologically linked. Finkelstein et al (1982) have shown a failure to suppress serum cortisol following dexamethasone administration in stroke patients with mood and vegetative disturbances (Finkelstein et al, 1982). In the present study, our finding that at six months follow-up, major depressions were still present in 10 of 13 patients, is consistent with the natural history of untreated affective disorder (Rennie, 1942).

However, whether or not some of these depressions following strokes represent a form of affective disorder provoked by brain injury, we have shown that they are long term mood disorders and therefore, may have an important impact on functional recovery and rehabilitation. The lack of treatment of these depressions has been described as one of the major unmet needs of stroke patients (Feibel et al, 1979). In the present study we did not interfere with the usual course of hospital or out-patient treatment and consequently none of these patients were treated for depression. Given that the yearly incidence of stroke is about 400,000 in the U.S. (Wolf et al, 1977) and this lack of treatment efforts, these depressions represent a major clinical problem and require the development of effective treatment techniques as well as additional research.

Acknowledgements

References

AMERICAN PSYCHIATRIC ASSOCIATION (1980) Diagnostic and Statistical Manual of Mental Disorders. Washington D.C. 3rd edition.

FEIBEL J. H., BERK, S. & JOYNT, R. M. (1979) The unmet needs of stroke survivors. Neurology, 29, 592.

FINKELSTEIN, S., BERNOWITZ, L. I., BALDESSARINI, R. J., ARANA, G. W., LEVINE, D., WOOD, E., NEAR, D., MOYA, K. & STROLL, A. L. (1982) Mood vegetative disturbance and dexamethasone suppression test after stroke. Annals of Neurology, 12, 463-8.

FOLSTEIN, M. F., FOLSTEIN, S. E. & McHUGH, P. R. (1975) Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research, 12, 189-98.

—— MAIBERGER, R. & McHUGH, P. R. (1977) Mood disorder as specific complication of stroke. Journal of Neurology, Neurosurgery and Psychiatry, 40, 1018-20.

GAINOTTI, G. (1972) Emotional behavior and hemispheric side of the brain. Cortex, 8, 41-55.

HAMILTON, M. A. (1969) A rating scale for depression. Journal Neurology, Neurosurgery and Psychiatry, 23, 56-62.

HOLLINGSHEAD, A. B. & REDLICH, F. C. (1958) Social Class and Mental Illness. New York: Wiley.

KUNITZ, S. C., HAUEKOST, C. L. & GROSS, C. R. (1979) Pilot data bank networks for neurological disorders. Third Annual Proceedings: Symposium of Computers in Medical Care.

LIPSEY, J. R., ROBINSON, R. G., PEARLSON, G. D., RAO, K. & PRICE, T. R. (1983) Mood change following bilateral hemisphere brain injury. British Journal of Psychiatry, 143, 266-73.

PEARLSON, G. D. & ROBINSON, R. G. (1982) Lateralization of emotional or behavioral responses in intact and hemisphere damaged humans and rats. In The Expression of Knowledge (eds R. L. Isaacson and N. E. Spear). New York: Plenum.

POST, F. (1962) The significance of affective symptoms in old age. Maudsley Monograph, No. 10. London: Oxford University Press.

RENNIE, T. A. C. (1942) Prognosis in manic-depressive psychoses. American Journal of Psychiatry, 98, 801-14.

ROBINSON, R. G. & BENSON, D. F. (1981) Depression in aphasia patients: frequency, severity, and clinical pathology correlations. Brain and Language, 14, 282-91.

—— & SZETELA, A. (1981) Mood change following left hemisphere brain injury. Annals of Neurology, 9, 447-53.

ROBINSON R. G. & PRICE, T. R. (1982) Post-stroke depressive disorders: a follow-up study of 103 patients. Stroke, 13, 635-41.

—— KUBOS, K. L., STARR, L. B., RAO, K. & PRICE, T. R. (1983a) Mood disorders in stroke patients: Importance of lesion location. Brain, In press.

—— —— —— —— —— (1983b) Mood changes in stroke patients: Relationship to lesion location. Comprehensive Psychiatry, 24, 555-66.

—— —— —— & PRICE, T. R. (1983c) A two-year longitudinal study of post-stroke mood disorders: Findings during the initial evaluation. Stroke, 14, 736-41.

—— —— —— —— (1983d) Post-stroke affective disorders. In Cerebrovascular Diseases, Thirteenth Princeton Conference. (ed. M. Reivich and H. I. Hurtig). New York: Raven Press.

ROSS, E. D. & RUSH, A. J. (1981) Diagnosis and neuroanatomical correlates of depression in brain-damaged patients. Archives of General Psychiatry, 38, 1344-54.

STARR, L. B., ROBINSON, R. G. & PRICE, T. R. (1983a) The social functioning exam: An assessment for stroke patients. Social Work Research and Abstracts, 18, 28-33.

—————— (1983b) Reliability, validity and clinical utility of social functioning exam in the assessment of stroke patients. *Experimental Aging Research,* in press.

WING, J. K., COOPER, J. E. & SORTORIUS, N. (1974) *Measurement and Classification of Psychiatric Symptoms.* Cambridge: Cambridge University Press.

WOLF, P. A., DAWBER, T. R., THOMAS, H. E., COLTON, T. & KANNEL, W. B. (1977) Epidemiology of stroke. In: *Advances in Neurology, Stroke* (eds. R. A. Thompson and J. R. Green). New York: Raven Press, **16,** 5–19.

ZUNG, W. W. K. (1965) A self rating depression scale. *Achives of General Psychiatry,* **12,** 63–70.

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