## Mood Changes After Right-Hemisphere Lesions

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Ninety-three patients with acute stroke lesions restricted to the right hemisphere were examined for the presence of mood changes. While 46 patients showed no mood changes, 19 were unduly cheerful, 17 had developed major depression, and 11 had developed minor depression. Although there were no significant between-groups differences in other demographic variables, neurological deficits, activities of daily living, cognitive impairment, or quality of social support, patients with major depression had a significantly higher frequency of familial history of psychiatric disorder and lesions of the parietal cortex than patients with either no mood change or major depression following left-hemisphere lesions. On the other hand, undue cheerfulness was significantly associated with lesions of the right frontal operculum. These findings suggest that major depression following right-hemisphere lesions may have a different aetiology and mechanism than major depression following left frontal or basal ganglia lesions.

In previous studies of post-stroke mood disorders, we have consistently found significant associations between left anterior brain injury and major depression (Robinson et al, 1984; Starkstein et al, 1987a). Although this association between lefthemisphere lesions and either depression or a negativistic affective state has been reported by numerous studies (Gainotti, 1972; Gasparrini et al, 1978; Finklestein et al, 1982), some investigators have found a high frequency of depression associated with right- as well as left-hemisphere injury (Folstein et al, 1977; Sinyor et al, 1986). We have suggested (Robinson et al, 1987) that the failure to find a lateralised emotional response to injury may be due to methodological differences between studies in variables such as time since injury (lateralised differences are more evident during the acute poststroke period), intrahemispheric lesion location (lateralised differences are more evident with anterior than posterior brain injury), or prior brain injury (the most recent injury does not predict severity of depression) (Lipsey et al, 1983).

The formulation, however, that these methodological variables are important in determining the relative frequency of depression following righthemisphere injury, does not address the fundamental issue of whether the aetiology of depression associated with right- and left-hemisphere lesions may be different. Since we have described the phenomenology, natural course, and relationship to location of injury for depressive disorders associated with lefthemisphere lesions extensively in previous publications, the present study focuses on mood disorders associated with right-hemisphere injury.

We report here the results of an evaluation of 93 patients with right-hemisphere strokes for the

presence of mood changes (depression and undue cheerfulness) and their association with predisposing factors.

### Method

## Study population

Patients included in this study were selected from two hospital populations: (a) 254 consecutive admissions to the University of Maryland Hospital for treatment of acute thromboembolic infarction or intracerebral haemorrhage, and (b) a consecutive series of 68 patients admitted to the Montebello Rehabilitation Hospital for therapy following a cerebral infarct or haemorrhage. Patients with decreased consciousness (stupor or coma) or severe comprehension deficits (as determined by an independently administered standardised neurological examination and the finding that patients did not score within ten points on test-retest administration of the Zung Depression Scale) were excluded from the study.

For the present investigation, we included two groups of patients: (a) patients who had single right-hemisphere strokes based on CT findings and/or clinical diagnosis, and (b) a consecutive series of patients who developed major depression following left-hemisphere strokes. CT scans were performed in all patients included in the study. Patients with a previous history of stroke were excluded from the study.

## Neurological and psychiatric examination

The neurological examination and diagnosis for all University of Maryland patients (72 with right-hemisphere lesions and 24 with left-hemisphere lesions) was done using the criteria established by the Stroke Data Bank of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) (Kunitz *et al*, 1984). Patients at Montebello Hospital (21 with right-hemisphere lesions and 3 with left-hemisphere lesions) received a standard clinical neurological examination. All neurological examinations were performed blind to findings on psychopathological examination.

After giving informed consent, patients were administered a series of standardised quantitative measures of mood. cognitive function, and physical impairment. We have previously shown that these instruments give reliable and valid measurements in this stroke population (Robinson & Benson, 1981; Robinson & Szetela, 1981; Robinson et al, 1983). Examinations were administered in a private room between 11.00 a.m. and 2.00 p.m. to minimise any possible effect of diurnal mood variation. The Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960), a 17-item questionnaire measuring psychological and physiological symptoms of depression, was filled out by the interviewer. The Zung Self-Rating Depression Scale (Zung, 1965), a 20-item questionnaire, was read to each patient and his/her responses were scored using the four Zung categories. The modified Present State Examination (PSE; Wing et al, 1974), a semistructured psychiatric interview that elicits symptoms related to depression and anxiety, was scored by the examiner. The Mini-Mental State Exam (MMSE; Folstein et al, 1975) and the Johns Hopkins Functioning Inventory (JHFI; Robinson et al, 1983) were also administered to each patient. The MMSE is an 11-item examination that has been found to be reliable and valid in assessing a limited range of cognitive functions in stroke patients (Folstein et al, 1975; Robinson et al, 1986). Scores may range from 0 to 30 and a score of 23 or below indicates cognitive impairment. The JHFI contains ten items and evaluates degree of independence in activities of daily living such as walking, dressing, and eating (Robinson et al, 1983). Scores range from 0 to 27, and higher scores indicate greater degrees of impairment. Social functioning was quantified both by number of social connections using the Social Ties Checklist (STC) (maximum score of 10) and by personal satisfaction with social relations using the Social Functioning Exam (SFE) (scores range from 0 to 1000, with higher scores indicating poorer social functioning) (Starr et al, 1983).

Psychiatric diagnosis was established using DSM-III (American Psychiatric Association, 1980) symptom criteria for major depression or minor (dysthymic) depression. The symptoms used for these diagnostic criteria were elicited by the PSE. The method used to convert PSE symptoms to DSM-III major or minor depression diagnosis is available upon request. Undue cheerfulness was also determined from symptoms elicited by the PSE. The criteria for undue cheerfulness were as follows: a self-report of an elevated or expansive mood; or a clinical observation of inappropriate cheerfulness or elation, and a self-report of no feelings of sadness or depression.

Based on the hand used for writing, patients were considered right-handed, left-handed or mixed-handed.

While patients were interviewed generally within the second or third week after stroke, no interview was carried out after 60 days post-stroke.

## **CT** scan examination

CT scans were read by one of us (SES) who was blind to

the clinical findings. All CT scans had a consistent slice thickness and angle to the canthomeatal line. The damaged area was localised in specific brain regions following the procedure of Levine & Grek (1984). 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 the whole brain on the slice passing through the body of the lateral ventricles. We have previously demonstrated the reliability of this procedure and its high correlation with other methods of determining lesion volume (Robinson *et al*, 1986).

## Statistical analysis

Statistical analysis was carried out using means and standard deviations, analysis of variance (ANOVA) and Pearson correlation coefficients. Frequency distributions were analysed using  $\chi^2$  tests with Yates' modification for expected cell sizes below 5.

## Results

## **Background characteristics**

Demographic data are presented in Table I. The study population consisted mainly of males in their late 50s and early 60s. There was a slight preponderance of blacks, and the population was primarily from lower socioeconomic classes (i.e. Hollingshead class IV and V).

Although we did not obtain detailed family histories using multiple informants (Andreasen et al, 1977) we did obtain as much information about family history as we could from the patients and/or relatives who were available at the time of interview. The distribution of positive familial history of psychiatric disorder for first- and second-degree relatives (alcoholism (55%) and depression (45%)) was significantly different between the four groups ( $\chi^2 = 7.7$ , d.f. = 3, P < 0.05); and on individual comparisons, patients with major depression had a significantly higher frequency of positive family history of psychiatric disorder than patients with no mood disorders ( $\chi^2$  Yates = 4.08, d.f. = 1, P<0.05). Although there was also a trend for major and minor depressed patients to show higher frequencies of positive personal psychiatric history ( $\chi^2 = 6.3$ , d.f. = 3, P = 0.09), it did not reach statistical significance. Personal histories were positive for alcoholism and anxiety, while only one patient had a previous history of depression. No other significant differences were observed in the remaining demographic variables (Table I).

In order to establish if this higher frequency of family psychiatric history was specific for major depression following right-hemisphere lesions, we compared this group of patients with a consecutive series of 27 patients who developed major depression following left-hemisphere lesions (Table I). Patients with major depression following right-hemisphere lesions showed a significantly higher frequency of positive family history of psychiatric disorder than major depressed patients following left-hemisphere lesions (one patient had a family history of anxiety disorder in a first-degree relative) ( $\chi^2$  Yates = 4.44, d.f. = 1, P < 0.05).

## MOOD CHANGES AFTER RIGHT-HEMISPHERE LESIONS

## TABLE I Demographic data

|  |               | Right hemisphere      |                     |                     |                     |  |
|--|---------------|-----------------------|---------------------|---------------------|---------------------|--|
|  | No depression | Undue<br>cheerfulness | Major<br>depression | Minor<br>depression | Major<br>depression |  |
| Number of patients<br>Age: years                             | 46            | 19                    | 17                  | 11                  | 27                  |  |
| mean   | 64            | 60                    | 60                  | 62                  | 56                  |  |
| s.d.   | 10            | 14                    | 11                  | 8                   | 13                  |  |
| Sex: % females   | 35            | 42                    | 47                  | 36                  | 52                  |  |
| Race: % blacks   | 65            | 74                    | 41                  | 55                  | 59                  |  |
| Socio-economic status:<br>Hollingshead class                 |               |                       |                     |                     |                     |  |
| IV or V  | 87            | 74                    | 82                  | 82                  | 89                  |  |
| Marital status: % married Handedness:                        | 54            | 37                    | 42                  | 36                  | 44                  |  |
| % right-handed   | 87            | 90                    | 100                 | 100                 | 89                  |  |
| Education: years   |               |                       |                     |                     |                     |  |
| mean   | 6.5           | 8.2                   | 8.4                 | 8.8                 | 9.3                 |  |
| s.d.   | 3.7           | 4.3                   | 3.4                 | 3.5                 | 2.8                 |  |
| Familial history of<br>psychiatric disorders:                |               | _                     |                     | _                   |                     |  |
| % positive*<br>Personal history of<br>psychiatric disorders: | 6             | 5                     | 29                  | 9                   | 4                   |  |
|  | 16            | 5                     | 29                  | 36                  | 6                   |  |
| % positive   | 15            | 3                     | 27                  | 20                  | 6                   |  |
| Time since stroke: days<br>mean                              | 13.1          | 11.2                  | 16.0                | 20.9                | 14.5                |  |
| s.d.   | 12.7          | 6.5                   | 9.4                 | 18.6                | 14.5                |  |

\*P<0.05.

MMSE

SFE

STC

Social functioning

No depression Undue cheerfulness Major depression Minor depression Number of patients 46 19 17 11 **Depression** scores 15 (7.5) 12.2 (5.3) PSE<sup>2</sup> 4.0 (3.0) 8.3 (4.5) 23 (9.2) HRSD<sup>3</sup> 5.0 (4.1) 5.6 (3.1) 15.2 (5.3) Zung<sup>4</sup> 36 (6.7) 36 (5.4) 57 (9.3) 45 (9.0) Activities of daily living JHFI 5.6 (4.6) 5.2 (6.2) 7.7 (4.9) 5.8 (5.7) Cognitive impairment

23 (6.3)

291 (201)

4.3 (1.8)

23 (5.6)

332 (217)

4.3 (2.1)

24 (6.1)

358 (272)

3.8 (1.9)

24 (4.6)

251 (163)

3.5 (1.6)

| TABLE II              |                       |                     |  |  |  |  |
|-----------------------|-----------------------|---------------------|--|--|--|--|
| Scores of depression, | cognitive impairment, | activities of daily | living and social functioning <sup>1</sup> |  |  |  |

1. Standard deviations are in parentheses.

2. F = 51.2, d.f. = 3, 88, P < 0.001. 3. F = 26.5, d.f. = 3, 88, P < 0.001. 4. F = 34.4, d.f. = 3, 88, P < 0.001.

No significant differences were found in the remaining demographic variables (Table I).

## Neurological findings

There were no significant differences in the frequency of motor or sensory impairments among the four groups. Most patients had a hemiparesis (91%, 84%, 94% and 100% for non-depressed, unduly cheerful, major and minor depressed patients, respectively), and about half had sensory deficits (59%, 47%, 31% and 0%, respectively). A smaller proportion showed visual-field disturbances (26%, 5%, 19% and 0%, respectively), neglect (17%, 11%, 13% and 0%, respectively) and la%, respectively) and la%, respectively).

# Depression scores, physical impairment, cognitive impairment and social function

As expected, patients with major depression showed the highest depression scores, while patients with minor depression had scores between those of the major depressed and the non-depressed patients (Table II).

There were no significant between-group differences in scores of cognitive impairment (MMSE), activities of daily living (JHFI), social functioning (SFE) and social ties (STC) (Table II).

There were no significant correlations between PSE scores and scores of cognitive impairment (PSE v. MMSE, r = 0.15), activities of daily living (PSE v. JHFI, r = 0.23), social functioning (PSE v. SFE, r = 0.13) or social ties (PSE v. STC, r = 0.13).

## **CT** scan findings

Fifty-four patients had positive CT scans (Table III). The lesions were mainly ischaemic infarctions, and the distribution of infarcts and haemorrhages was not significantly different between the four groups (Table III). There were also no significant between-group differences in lesion volumes (F = 0.96, NS) (Table III). Patients with undue cheerfulness, however, showed a significantly higher frequency of lesions involving the frontal operculum compared with (major and minor) depressed and nondepressed patients ( $\chi^2 = 6.17$ , d.f. = 2, P < 0.05). On individual comparisons, patients with undue cheerfulness showed a significantly higher frequency of frontal opercular lesions than patients with (major and minor) depression ( $\chi^2$ Yates = 3.88, d.f. = 1, P < 0.05). On the other hand, patients with depression (both major and minor) showed a significantly higher frequency of lesions involving the parietal cortex than the other two groups  $(\chi^2 = 9.60,$ d.f. = 2, P = 0.022) (Table III). On individual comparisons, the depressed patients (major and minor) had a significantly higher frequency of parietal lesions than the unduly cheerful patients ( $\chi^2 = 9.21$ , d.f. = 1, P<0.01).

Although there were more depressions associated with posterior (parietal) than anterior lesions, there was no significant correlation between the distance of anterior lesion border from the frontal pole and severity of depression (PSE v. anterior border, r = 0.05) or between the distance of posterior lesion border from the frontal pole and severity of depression (PSE v. posterior border, r = 0.01). In addition, there was no significant correlation between lesion volume and severity of depression (PSE v. lesion volume, r = 0.10).

## Discussion

In the present study, we have examined the type and frequency of mood changes following righthemisphere strokes. During the acute post-stroke period, almost one-third of the patients developed depression (minor or major), while almost a quarter developed undue cheerfulness. Patients with major depression had a significantly higher frequency of

TABLE III Lesion location (number of patients)

|                             | No depression | Undue<br>cheerfulness | Major<br>depression | Minor<br>depression |
|-----------------------------|---------------|-----------------------|---------------------|---------------------|
| Number of patients with pos | sitive        |                       |                     |                     |
| CT scans                    | 25            | 12                    | 9                   | 8                   |
| Ischaemic strokes           | 22            | 11                    | 7                   | 7                   |
| Frontal dorsolateral        | 1             | 0                     | 2                   | 4                   |
| Frontal opercular           | 4             | 5                     | 0                   | 1                   |
| Temporal lobe               | 7             | 1                     | 2                   | 0                   |
| Parietal lobe               | 9             | 1                     | 6                   | 5                   |
| Occipital lobe              | 7             | 1                     | 3                   | 0                   |
| Basal ganglia               | 6             | 6                     | 2                   | 1                   |
| Thalamus                    | 4             | 1                     | 0                   | 0                   |
| Internal capsule            | 2             | 5                     | 0                   | 0                   |
| Corona radiata              | 1             | 1                     | 1                   | 2                   |
| Lesion volume               |               |                       |                     |                     |
| mean                        | 9.0           | 6.2                   | 10.0                | 7.4                 |
| s.d.                        | 6.3           | 4.0                   | 5.1                 | 6.5                 |

familial history of psychiatric disorder than patients with right-hemisphere lesions without major depression, or patients with major depression following left-hemisphere lesions. Depressed patients with right-hemisphere lesions also had a significantly higher frequency of lesions in posterior (mainly parietal) cortex than non-depressed or unduly cheerful patients. On the other hand, patients with undue cheerfulness showed a significantly higher frequency of lesions involving the frontal operculum.

Before further discussion, several limitations of this study should be pointed out. While family histories were obtained from patients and/or relatives, systematic interrogation using multiple informants was not carried out. Thus it is probable that the frequency of familial psychiatric history was underestimated, and it is also possible that the presence of depression may have biassed the report of a positive familial psychiatric history. The present findings therefore need to be replicated using multiple-informant family pedigrees (Andreasen et al, 1977). It should be emphasised, however, that these methodological limitations should have affected all groups equally and that they are not an explanation of why familial disorders were more frequent with right-hemisphere major depression than lefthemisphere major depression.

Another limitation is that the diagnosis of undue cheerfulness was not based on standard criteria, as unduly cheerful patients do not meet DSM-III criteria for hypomania. Notwithstanding, this phenomenon of euphoria or elation has for many years been reported in patients with right-hemisphere lesions (Gainotti, 1972; Cutting, 1978). Although no diagnostic criteria have been established for this phenomenon, we defined undue cheerfulness based on either the presence of a self-report of an expansive or elated mood (74% of the patients with undue cheerfulness had this symptom) or the clinical observation of inappropriate cheerfulness or excitement (26% of the patients). Although not a part of our criteria for undue cheerfulness, flight of ideas and increased energy were present in 37% of the unduly cheerful patients, while 11% had grandiose ideas.

Questions that now arise are, first, what is the pathogenesis of depression in patients with righthemisphere lesions, and second, is this pathogenesis different from that in patients with left-hemisphere lesions? There were no significant differences between depressed and non-depressed patients in terms of important demographic variables, such as age, sex, race, education and socio-economic status. Moreover, there were no significant between-group differences in scores of physical impairment, cognitive deficits, social functioning or social ties. The finding that patients with major depression following right-hemisphere lesions had a significantly higher frequency of family history of psychiatric disorder suggests that hereditary factors may play an important role in the production of major depression following right-hemisphere lesions, at least for a subgroup of patients.

Lesion location also seemed to play an important role in the production of depression, and the finding of a significantly higher frequency of depression following lesions in posterior cortical areas replicates our previous findings in a much smaller population (Robinson *et al*, 1984), and also agrees with findings of other investigators (Finset, 1988).

We have previously suggested that left anterior lesions may lead to depression by disrupting biogenic amine pathways, and that the correlation between severity of depression and proximity of the lesion to the frontal pole is a result of interrupting these pathways closer to their 'downstream' origin in the frontal pole. How parietal lesions in the right hemisphere may lead to depression is uncertain. However, the findings do suggest that the mechanism which produces major depression after right-hemisphere lesions may be different from those which lead to major depression after left anterior lesions.

Ross & Rush (1981) reported the case of a patient with a right temporo-parietal infarction who denied being depressed, but showed autonomic symptoms of depression and a depressive affect. A dexamethasone suppression test showed non-suppression and the depressive symptoms improved after treatment with tricyclic antidepressants. Based on these findings, Ross and colleagues have hypothesised that a patient's denial of depression may be secondary to the inability of mood information (generated in the right hemisphere by structures which were not involved by the lesion) to reach the verballyexpressive left hemisphere. They have suggested that expression and comprehension of emotions are organised in the right hemisphere in an analogous fashion to language in the left hemisphere. Although we did not examine our patients for disturbances in recognition or expression of emotion, we did find depression to be significantly associated with lesions in the parietal lobe. We require that a diagnosis of major depression includes the patient's admission that he or she is feeling depressed or sad. Thus, all patients we examined with major depression and parietal involvement clearly acknowledged internal feeling of depression. The extent to which aprosodic disturbances may interfere with the diagnosis of mood disorders in patients with right-hemisphere

injury, however, is uncertain. This issue will need to be examined systematically in another study.

The other mood change that was frequently identified among patients with right-hemisphere lesions was inappropriate cheerfulness, which was associated with lesions involving the right frontal operculum. Previous studies have found that lesions of the frontal cortex, mainly in the right hemisphere, are associated with elevated mood (Oppenheim, 1890; Kleist, 1931; Rylander, 1939; Starkstein *et al*, 1987b). We have suggested (Starkstein *et al*, 1987b) that these mood disorders may be related to disruptions in frontal cortical interaction with the limbic system, particularly the amygdala, septum, hypothalamus and mesencephalon (Nauta, 1971).

In conclusion, right-hemisphere strokes were associated with a high frequency of mood changes. Depression was associated with both genetic factors and lesions in posterior cortical areas, while undue cheerfulness was associated with lesions in the frontal operculum. Since demographic factors, neurological symptoms, severity of physical impairment, cognitive deficits and social support did not explain the presence of depression or undue cheerfulness, these findings suggest that mood changes following rightbrain lesions (as with left-hemisphere lesions) are not simply an understandable consequence of the impairment but may be the result of more complex biological processes. The neurophysiological mechanisms leading to major depression, however, may be different for left frontal/basal ganglia injury as compared with right parietal or brainstem injury (Starkstein et al, 1988).

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