Background Factors and Clinical Symptoms of Major Depression With Silent Cerebral Infarction

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Background and Purpose We previously reported that major depression developing during or after the presenile period is frequently combined with silent cerebral infarction and that these patients have a high risk of stroke. Therefore, we investigated whether the background factors and clinical symptoms of patients with major depression with silent cerebral infarction (SCI[+]) differed from those in patients with major depression without silent cerebral infarction (SCI[−]) before medical treatment.

Methods Patients with major depression with onset after 50 years of age who demonstrate no localized neurological symptoms -Z̅ (MRI) or other imaging modalities in a patient who shows evidence of stroke or focal neurological symptoms were excluded. The diagnostic criteria for major depression were those of the American Psychiatry Association (DSM-III-R). Patients aged older than 50 years were classified based on magnetic resonance imaging findings into the SCI(+) (n=37) or SCI(−) (n=20) group. The diagnostic criteria for major depression were those of the American Psychiatry Association (DSM-III-R). Patients were diagnosed with major depression according to the revised (DSM-III-R) criteria, and all were aged older than 50 years.

Results The SCI(+) group had a significantly lower frequency of family history of affective disorder but a significantly higher frequency of hypertension than did the SCI(−) group. The mean SDS score in the SCI(+) group was significantly higher than that in the SCI(−) group (P<0.01). The mean SDS score in the SCI(+) group was significantly higher than that of the perforating artery infarction group (P<0.05).

Conclusions Patients with major depression with silent cerebral infarction present more marked neurological factors and more severe depressive symptoms than do those without silent cerebral infarction. Because these features were more prominent in the patients with mixed artery infarction with broad obstructions, we consider that the area of brain damage caused by cerebral infarction is positively related to the severity of depressive symptoms. (Stroke. 1994;25:798-801.)

Key Words • cerebral infarction • depression • hypertension • magnetic resonance imaging

A symptomatic or silent cerebral infarction (SCI) is that detected by magnetic resonance imaging (MRI) or other imaging modalities in a patient who demonstrates no localized neurological symptoms or stroke. Patients with SCI, which is classified as a cerebrovascular disorder type III by the National Institute of Neurological Disorders and Stroke, may be at increased risk of subsequent overt stroke, and SCI may represent a prodromal stage before the development of overt stroke.

We previously studied the incidence of SCI detected by MRI in patients with presenile or senile major depression. Our findings suggested that organic depression related to SCI is present in approximately half of those with presenile-onset major depression and the majority of those with senile-onset major depression. Major depression with SCI may be a warning sign of cerebrovascular disease because it is associated with a high risk of subsequent symptomatic ischemic stroke. Therefore, we suspected that the background factors (heredity and risk factors for stroke) and clinical symptoms before medical treatment in patients with major depression with SCI differ from those in patients without SCI.

In this study we classified patients with major depression aged older than 50 years according to MRI findings as those with and without SCI. Differences between these groups in regard to family history of affective disorder, history of hypertension, diabetes mellitus, and hyperlipidemia; and depression scale score before medical treatment were investigated.

Subjects and Methods

The subjects were prospectively selected at their initial consultation for major depression at either the Department of Neurology and Psychiatry at Hiroshima Prefectural Hospital or the Department of Psychiatry and Neurosciences at Hiroshima University School of Medicine. All patients completed Zung's Self-rated Depression Scale (SDS) at the initial consultation. All patients were diagnosed with major depression according to Diagnostic and Statistical Manual of Mental Disorders, edition 3, revised (DSM-III-R) criteria, and all were aged older than 50 years.

Patients with alcoholism, cerebral degenerative disease, dementia, or systemic disease that could induce a depressive state were excluded, as were patients who had previously been treated with psychotropic drugs, including tricyclic antidepressants. All patients underwent MRI within 3 months after the first consultation. All patients received a neurological examination on the same day as the MRI study, and those with evidence of stroke or focal neurological symptoms were ex-
were calculated, and Student's t test was used to compare numerical data in the two groups.

The SCI were classified as not having SCI. Periventricular lesions on T2-weighted images less than 5 mm in diameter may also be small infarcts, whereas lesions greater than 20 mm were classified as large infarcts. Although detected lesions less than 5 mm may also be small infarcts, these were excluded from analysis because they are difficult to distinguish from "état crible." Regarding the number of small infarcts that can be interpreted as indicating SCI, Shimada et al. have reported that the mean number of small infarcts in hypertensive asymptomatic elderly subjects was 2.8±4.6, whereas that in normotensive elderly subjects was 1.1±1.5. Matsubayashi et al. have studied the relationship between small infarcts and cognitive function in normal elderly subjects and reported that four or more small infarcts are associated with the development of cognitive impairment. In the present study SCI were defined as the presence of four or more small infarcts in the same cerebral hemisphere or one or more large infarcts. Patients with fewer than four small infarcts and no large infarcts were classified as not having SCI. Periventricular hypointensity was not assessed.

For statistical analysis, mean±SD values of parametric data were calculated, and Student's t test was used to compare groups. The χ² test was used for comparison of nonparametric numerical data in the two groups.

### Results

The mean age of the 2 men and 18 women in the SCI(−) group (61.4±5.8 years) was significantly lower than that of the 15 men and 22 women in the SCI(+) group (67.5±7.8 years) (P<.01).

### Comparison of Background Factors in Both Groups

There was a family history of affective disorder in 7 (35.0%) of the 20 SCI(−) patients and in 3 (8.1%) of the 37 SCI(+) patients (P<.05) (Table 1).

Hypertension was present in 1 (5.0%) of the SCI(−) patients and in 15 (40.5%) of the SCI(+) patients (P<.01). In the latter group, hypertension was present in 7 (36.8%) of the 19 patients with perforating artery infarction, in 1 (16.6%) of the 6 patients with cortical artery infarction, and in 7 (58.3%) of the 12 patients with mixed artery infarction. There was no difference between groups in the incidence of diabetes mellitus, at 5.0% in the SCI(−) group and 2.7% in the SCI(+) group, or in the incidence of hyperlipidemia, at 15.0% and 13.5%, respectively.

### Comparison of Zung's Self-rated Depression Scale Score

The mean SDS score was 52.6±9.1 in the SCI(−) group and 58.8±7.0 in the SCI(+) group (P<.01) (Table 2). In SCI(+) patients the mean score was 56.4±6.3 in those with perforating artery infarction and 62.3±6.2 in those with mixed artery infarction (P<.05).

### Discussion

**Background Factors in Major Depression With Silent Cerebral Infarction**

The risk factors for symptomatic cerebral infarction include hypertension, diabetes mellitus, hyperlipidemia, and atrial fibrillation. Various studies have been conducted to determine whether the risk factors for SCI are the same as those for symptomatic cerebral infarction. A Dutch transient ischemic attack study revealed that patients with SCI have a high incidence of advanced age, hypertension, or smoking. Subsequently, in a study of brain screening subjects who had no history of cerebral disease and who were socially active and neurologically normal, Kobayashi et al. found that a history of hypotension was observed significantly more often in patients with SCI compared with those without SCI.
Hougaku et al.\(^\text{10}\) found that in patients with SCI the rate of complications was significantly higher in those with essential hypertension; they reported a strong causative relation of hypertension to perforating artery infarction. Lechner et al.\(^\text{11}\) found that the number of risk factors for cerebral infarction, such as hypertension or diabetes mellitus, was positively associated with the rate of complication after SCI. They also reported that abnormal MRI findings were recognized in all of their patients with three or more simultaneous risk factors.

In the present study of patients with major depression with onset after 50 years of age with and without SCI, hypertension was found to be more frequent in those with SCI, but no difference between the two groups was recognized in the incidence of diabetes mellitus or hyperlipidemia. Thus, we conclude that among patients with major depression, hypertension is more common in those with SCI.

The difference between the two groups in the rate of family history of affective disorder indicates that patients with major depression without SCI frequently have a family history of affective disorder but have fewer risk factors for cerebral infarction. Endogenous factors may be especially important in this group. In contrast, in patients with major depression with SCI, neurological factors may be more important. A sub-group of patients with depression of presenile or senile onset may manifest a sequence of events, ie, hypertension as a risk factor that causes either perforating artery infarction or mixed artery infarction and eventually leads to major depression. Post\(^\text{12}\) and Murphy\(^\text{13}\) described a group of patients with senile depression with poor long-term prognosis. Mendlewicz\(^\text{14}\) reported that as the age at the onset of depression increases, the incidence of hereditary involvement decreases. We therefore suspect that when SCI is present in patients with presenile or senile major depression, the role of neurological factors is increased while that of heredity is decreased, and that such patients have poor long-term prognosis because of cerebrovascular impairment.

### Clinical Symptoms of Major Depression With Silent Cerebral Infarction

Robinson et al.\(^\text{15-18}\) reported that the severity of poststroke depression was significantly increased in patients with left anterior lesions. In a comparative study of poststroke depression and endogenous depression using the Present State Examination (PSE), Lipsey et al.\(^\text{19}\) found that the symptomatic profiles of the two types of depression were similar, and there was no difference between the two groups in Hamilton depression scores. However, patients with poststroke depression showed significantly lower PSE scores. In the present study the SDS score of the patients with major depression with SCI was significantly higher than that of those without SCI. In a recent study of the relation between subjective symptoms and MRI findings in 124 normal adults, Kobayashi et al.\(^\text{20}\) found that the incidence of SCI and the SDS score in subjects who showed forgetfulness with decreased motivation and concentration were significantly higher than those in subjects who did not. Of our patients with major depression with SCI, those with mixed artery infarction showed significantly higher SDS scores than did those with perforating artery infarction. These results indicate that depression is more severe in patients with mixed artery infarction, and we consider this finding to be due to the larger area of brain damage caused by cerebral infarction.

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### References

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