Mesial Temporal Cortex Hypoperfusion Is Associated With Depression in Subcortical Stroke

M.G. Grasso, MD; P. Pantano, MD; M. Ricci, MD; D.F. Intiso, MD; A. Pace, MD; A. Padovani, MD; F. Orzì, MD; C. Pozzilli, MD; G.L. Lenzi, MD

Background and Purpose This study was conducted to evaluate local cerebral blood flow changes in patients with depression after a subcortical stroke.

Methods Clinical and neuropsychological assessments were performed in 15 patients with a single subcortical lesion. Depression was assessed by DSM-III-R. In addition, the Hamilton Rating Scale for depression, the Zung Self-Rating Depression Scale, and the Beck scale were administered to each patient. Single-photon emission-computed tomography studies were performed with 99mTc hexamethylpropyleneamine oxime.

Results In all patients cortical regions ipsilateral to subcortical lesions were significantly less perfused than the contralateral cortex. Cerebral blood flow values were significantly lower in depressed patients (n=8) than in nondepressed patients (n=7) only in the mesial temporal cortex of the affected hemisphere. Cerebral blood flow values in the mesial temporal cortex of the affected hemisphere significantly correlated with the severity of depression.

Conclusions Temporal lobe hypoperfusion may reflect a dysfunction of the limbic system, suggesting that this location may be critical for the occurrence of depressive symptoms in patients with subcortical stroke. (Stroke. 1994;25:980-985.)

Key Words • depression • subcortical infarction • tomography, emission-computed
with the orbitomeatal line perpendicular to the floor, using a laser reference system and ink dots on the skin. The head was then fixed to the head holder by tape. Patients were studied at rest (eyes closed, ears unplugged) in a dimly lit room with external stimuli reduced to a minimum. Scans started 5 minutes after tracer injection and lasted 25 minutes. Head radioactivity distribution was measured by a Tomomatic 564 (Medimatic) equipped with a high-resolution collimator. Six slices were obtained for each study with a spatial resolution of 9 mm and a slice thickness of 10 mm. After tomographic image reconstruction, 21 irregular regions of interest (ROIs) were located on the cortical ribbon and the deep gray matter of the unaffected hemisphere and then automatically mirrored onto the affected hemisphere by a vertical axis of symmetry (Fig 1).

For the location of the ROIs, we referred to a template set of transverse cuts parallel to the orbitomeatal line with anatomic landmarks.28 Counts in ROIs belonging to the same anatomicofunctional area were averaged, thereby obtaining a total of eight cortical regions (prefrontal, basal frontal, motor, mesial temporal, basal temporal, lateral temporal, parietal, and occipital areas) and three subcortical regions (thalamus, caudate nucleus, and lenticular nucleus) in each hemisphere. The size of the 11 regions varied from 2.2±0.4 cm² to 15.7±1.9 cm² in accordance with the more or less extensive representation of the different cerebral structures on the six SPECT tomograms analyzed. Frontal and temporal lobes were studied in more detail because they were found to be functionally affected in depressed patients in previous reports.29-31 Because absolute CBF values are not achieved using Tc HMPAO, we considered the ratio between mean counts in each region and the mean counts of all the ROIs as an index of CBF distribution.

Statistical Analysis
Statistical analysis was performed by $\chi^2$, ANOVA for non-repeated measures, Mann-Whitney U statistic, and regression analysis.

**Results**
Of the 15 patients, 8 were depressed and 7 nondepressed according to DSM-III-R. Demographic and clinical characteristics of both groups of patients are shown in Table 1.

No differences in age, sex, size, or the lesion, or Canadian Neurological Scale, Barthel Index, or MMSE scores were found between the two groups. In particular, no relation was found between depression and motor deficit. As expected, the Hamilton, Beck, and Zung scales showed significantly higher scores in depressed patients.

Of the 8 depressed patients, 5 presented with a pure white matter lesion and 3 with involvement of the basal ganglia; of the 7 nondepressed patients, 6 presented with a pure white matter lesion and 1 with involvement of the basal ganglia. A schematic representation of infarct location in both groups of patients is shown in Fig 2.

No significant difference was found in lesion volume (13.8±11.2 cm³ versus 8.3±10.3 cm³) between depressed and nondepressed patients, respectively. Normalized CBF values in the 11 regions of the two cerebral hemispheres in both groups of patients are shown in Table 2.

A three-way group x side x ROI ANOVA showed a significant effect of both side (df=1, F=25.77, $P=0.002$) and ROI (df=10, F=11.71, $P<0.003$) on CBF values. This global analysis indicated that in all patients the cerebral cortex ipsilateral to the subcortical infarct was hypoperfused to a different extent among the different ROIs. However, this global analysis is very conservative and might have overlooked possible regional differences between groups because of the limited number of subjects.

On the basis of previous reports on patients with depression showing functional abnormalities in the frontal and/or temporal lobe, we performed a univariate nonparametric analysis comparing CBF values in frontal and temporal structures between depressed and nondepressed patients. Normalized CBF values were significantly lower in depressed than in nondepressed patients in the mesial temporal cortex of the affected hemisphere ($P=0.03$, Mann-Whitney U statistic) (Fig 3). Mesial temporal cortex hypoperfusion significantly correlated with decreased CBF in ipsilateral basal temporal ($P<0.05$ after Bonferroni correction) but not in ipsilateral basal frontal cortex, thalamus, caudate, and lenticular nuclei. Normalized CBF values in the mesial

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**Table 1. Demographic and Clinical Characteristics In Depressed and Nondepressed Patients With Subcortical Stroke**

<table>
<thead>
<tr>
<th></th>
<th>Depressed (n=8)</th>
<th>Nondepressed (n=7)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>70.6 (8.1)</td>
<td>64.3 (11.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Sex ratio, M/F</td>
<td>3:5</td>
<td>4:3</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration, mo</td>
<td>2.6 (1.5)</td>
<td>2.3 (1.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Affected hemisphere</td>
<td>4L, 4R</td>
<td>4L, 3R</td>
<td>NS</td>
</tr>
<tr>
<td>CNS</td>
<td>6.8 (1.7)</td>
<td>6.3 (1.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Barthel Index</td>
<td>59.4 (23.8)</td>
<td>66.6 (22.3)</td>
<td>NS</td>
</tr>
<tr>
<td>MMSE</td>
<td>18.2 (9.9)</td>
<td>20 (10.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Hamilton scale</td>
<td>14.9 (3.4)</td>
<td>5.6 (2.4)</td>
<td>.0001</td>
</tr>
<tr>
<td>Beck scale</td>
<td>15.4 (2.6)</td>
<td>4.9 (3.3)</td>
<td>.0001</td>
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<tr>
<td>Zung scale</td>
<td>42.9 (6.9)</td>
<td>28.6 (4.7)</td>
<td>.0005</td>
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</table>

CNS indicates Canadian Neurological Scale; MMSE, Mini-Mental State Examination; L, left; and R, right. Values are expressed as mean (SD).
temporal cortex of the affected hemisphere were significantly correlated with the severity of depression as measured by the Beck scale ($r=.59, P=.02$) but not with either the volume of the subcortical lesion or the severity of the motor deficit (Canadian Neurological Scale score). Correlations between CBF values in the mesial temporal cortex and Hamilton and Zung scales did not reach statistical significance ($r=.41$ and $r=.35$, respectively).

**Discussion**

Depression was found to affect more than 50% of the patients in our series. The occurrence of depression is reported to be from 20% to 60%. However, our series is too small and may not be representative. The severity of depression did not correlate with the degree of neurological disability and with the extent or location of the lesion on CT or magnetic resonance imaging scans, in agreement with previous reports. In fact, poststroke depression studies performed with CT scan showed that location rather than extension of lesions is critical in depression. Although major depression after stroke has been described to be associated with either left anterior or right posterior lesions, this relation has not been confirmed. It is still uncertain whether there is a link between poststroke depression and location of brain damage. It has also been reported that subcortical lesions are associated with depression with the same frequency and severity as cortical lesions.

Our data, although obtained in a limited number of patients with subcortical stroke, show that neither location (white matter or basal ganglia) nor side (right or left) of lesions correlates with the occurrence of depression. That is, anatomic aspects of the lesion per se do not correlate with the occurrence of depression.

SPECT study of CBF offers the opportunity to evaluate functional changes occurring in the cerebral cortex after a subcortical lesion. Using $^{99m}$Tc HMPAO as a tracer, quantitative measurements of CBF are not feasible. Our results are expressed as the ratio between

<table>
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<th>Table 2. Normalized Cerebral Blood Flow Values of Cortical and Subcortical Regions In Depressed and Nondepressed Patients</th>
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<tbody>
<tr>
<td><strong>Depressed (n=8)</strong></td>
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<tr>
<td><strong>Region</strong></td>
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<tr>
<td>Temporal</td>
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<td>Lateral</td>
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<td>Basal</td>
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<td>Thalamus</td>
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<td>Lenticular nucleus</td>
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* $P=.03$, Mann-Whitney U statistic.
radioisotope activity in a given region and the mean 
global activity. The data, therefore, represent relative 
perfusion indexes.

This study shows that mesial temporal cortex ipsilat-
eral to subcortical ischemia is significantly less perfused 
in depressed than in nondepressed patients. This pat-
tern is observed in depressed patients with damage in 
either the left or the right hemisphere, indicating that 
the side of the subcortical lesion is not relevant in 
inducing local CBF abnormalities.

Reduction of CBF in the cerebral cortex of stroke 
patients may reflect oligemia/ischemia on a hemody-
namic basis and/or disconnection from subcortical nu-
cleri with widespread cortical projections (ie, diaschi-
sis).20-22 The reduction of CBF in the mesial temporal 
cortex found in our patients with a subcortical ischemic 
stroke in the middle cerebral artery territory, however, 
is more likely due to diaschisis because the mesial 
temporal cortex is supplied by posterior circulation. In 
addition, patients with severe stenosis of the neck 
vessels were excluded from our study.

Subcortical lesions could determine, through the in-
terruption of corticosubcortical connections, a func-
tional impairment of limbic cortex responsible for de-
pressive disorder. This hypothesis is partially supported 
by the observed significant correlation of CBF values 
between mesial temporal and basal temporal cortices in 
the affected hemisphere. In addition, mesial temporal 
hyoperfusion was significantly associated with the de-
gree of depression.

Our results are not in agreement with two previous 
studies that investigated CBF in poststroke depression. 
Yamaguchi et al25 studied CBF in 60 patients with one 
or more supratentorial cerebrovascular lesions using the 
$^{133}$Xe inhalation bidimensional method. The authors 
found that the severity of depression was inversely 
correlated with regional CBF values in the parieto-
occipital region of the right hemisphere and in the 
anterior temporal region of the left hemisphere. How-
ever, in this study bilateral lesions were present in 
approximately one third of the patients, and large 
lesions were also included. Schwartz et al26 studied 
regional CBF and depression in 14 stroke patients and 
found that depression scores correlated with the extent 
of hyoperfusion as measured by SPECT. However, 
SPECT hyoperfusion coincided with CT lesions that 
were heterogenous, widespread, and often involved 
both cerebral hemispheres. Therefore, no conclusive 
data resulted from these previous studies because the 
cerebral cortex was often directly and extensively in-
volved by the lesions. In our study only patients with a 
single subcortical lesion were selected to better evaluate 
a possible relation between depression after stroke and 
functional abnormalities in structurally healthy cortex.

A specific functional involvement of temporal areas in 
poststroke depression has not been previously described 
by SPECT CBF studies. However, frontal and temporal 
glucose hypometabolism has been observed in major 
depression and in depression associated with other 
neurological diseases, using positron emission tomogra-
phy.29,30 In primary depression some authors found 
melobic abnormalities involving both frontal and tem-
poral cortices,31 whereas others described glucose hy-
pometabolism in either temporal32 or frontal cortices.29 
In depression secondary to Parkinson’s disease and 
Huntington’s disease, Mayberg et al30-36-37 found meta-
bolic abnormalities in the orbital inferior frontal and 
temporal regions regardless of disease etiology. 

These previous observations, combined with the re-
sults of our study, suggest that interruption of pathways 
linking specific mesial temporal lobe regions may un-
derlie depressive phenomenology. Temporal lobe hy-
perfusion and/or hypometabolism likely reflects a dys-
function of the limbic system, suggesting that this 
location may be critical for the onset of mood symptoms.

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