Serotonin Transporter Gene Polymorphism in Chinese Patients With Poststroke Depression
A Case-Control Study

Jing Fang, MD, PhD; Weihong Yan, MD, PhD; Guo-Xin Jiang, MD, PhD; Wei Li, MD; Qi Cheng, MD, PhD

Background and Purpose—We sought to compare the distribution of the serotonin transporter gene SLC6A4 polymorphism between depressed and nondepressed poststroke patients.

Methods—Patients with cerebral stroke admitted to hospital during a 1-year period were enrolled in a 1:1 case-control study. All cases and controls were genotyped for polymorphism of the serotonin transporter-linked promoter region and the single-nucleotide polymorphism rs25531.

Results—Among 367 patients with cerebral stroke, 57 (15.5%) were diagnosed with poststroke depression at 1 month after stroke. In the patients with poststroke depression, 7 genotypes of the serotonin transporter gene SLC6A4 were detected, and the frequency of S/S homozygotes was significantly higher (P=0.049) than that in controls.

Conclusions—S/S homozygosity may be positively associated with the occurrence of poststroke depression in Chinese patients. (Stroke. 2011;42:00-00.)

Key Words: case-control study ■ poststroke depression ■ SLC6A4 gene polymorphism

Poststroke depression (PSD) is one of the common complications of stroke, which increases its fatality and morbidity rate.1 Approximately one third of all patients experience significant depressive symptoms after the onset of stroke, which may occur not only in the first few months of the disease.2

The serotonin transporter gene (SLC6A4, GenBank L05568) is considered a candidate gene containing the serotonin transporter-linked promoter region (5-HTTLPR) and the single-nucleotide polymorphism rs25531, which have been the targets of recent investigation. The association of the S/S genotype with PSD has been found in studies from several ethnic groups, although the distribution differs by race and ethnicity.3,4 Although a positive association between 5-HTTLPR and depression was found in a study from Sichuan, China,5 the association of the single-nucleotide polymorphism rs25531.

A diagnosis of PSD was made according to the Diagnostic and Statistical Manual-IV for depression. The Hamilton Rating Scale for Depression (17 items) was conducted at 1 month after stroke for patients who had clinical depressive symptoms lasting ≥2 weeks and whose self-rating depression scale score was ≥12. PSD was rated according to the Hamilton Rating Scale for Depression: any score ≥8 was considered indicative of depression, whereas any score ≤7 was considered indicative of nondepression.

For sample collection and genotyping, 5-mL blood samples were collected from all cases and controls, and oligonucleotide primers were designed as reported.6 Then polymerase chain reaction and restriction enzyme digestion were conducted. Statistical analysis was performed with SPSS 13.0, with the t test for comparing group means and the McNemar test for comparing differences between paired proportions, and the significance level was set at P<0.05.

Methods

Patients with acute ischemic or hemorrhagic stroke admitted to the Shanghai Ninth Hospital during the period July 2008 to June 2009 were recruited into the study; patients who were unable to complete the scale examination or who had been previously diagnosed with depression were excluded. Information was collected from patients including age, sex, stroke lesion location, and modified Rankin Scale score at 1 month after stroke.

Informed consent was obtained from each study participant.

Results

During the study period, 421 patients with acute cerebral stroke were admitted. After excluding 54 patients, 367
patients were enrolled in the study, and 57 patients (15.5%) were diagnosed with PSD. Variables matched for the PSD group and the control group are presented in Table 1.

With respect to genotype frequency, the distribution of the 5-HTTLPR and rs25531 polymorphisms in all 114 cases and controls was in Hardy-Weinberg equilibrium (5-HTTLPR $\chi^2=3.015, P=0.221$; rs25532 $\chi^2=2.639, P=0.267$). In all 114 cases and controls, 7 genotypes were detected in PSD patients and 8 in controls (the Figure and Table 2). After having compared different combinations of alleles between the 2 groups, we found that the frequency of the $S/S$ genotype was significantly higher ($P=0.049$) in the PSD group than in the control group, whereas there were no significant differences in frequencies of $S/L, L/L, A/A, G/G, A/G, S_A, S_G, L_A, L_G$ between the 2 groups ($P>0.05$).

### Discussion

A study from Hong Kong reported that 16.4% of patients were diagnosed with PSD at 3 months after stroke, a figure similar to ours (15.5%). In the current study, 7 genotypes appeared in the PSD group and 1 more appeared in the control group. Our results for genotype distributions are not consistent with those from other reports: not only are they different from those in white and black samples, but also they are different from a sample of Chinese Parkinson disease patients with depression. The differences might be explained by different characteristics of the samples or various criteria for the inclusion of cases.

It has been known that patients with 1 or 2 $S$ allele copies exhibit more depressive symptoms and have more diagnosable depression than do individuals homozygous for the $L$ allele.
allele.\textsuperscript{9,10} In our study, the frequency of S/S homozygotes was more predominant in the PSD group, which suggests a positive association between the S allele and PSD. A study with a small sample of white subjects reported a similar result: that the S allele was related to major depression after stroke.\textsuperscript{11} The possible mechanism proposed was that the S allele could decrease the expression of serotonin, leading to lower reuptake and storage of the neurotransmitter. An allele could decrease the expression of serotonin, leading to lower reuptake and storage of the neurotransmitter. An American study with multiracial patients showed that the 5-HTTLPR indicates the serotonin transporter-linked promoter region.

Table 2. Genotypes in the Poststroke Depression (PSD) and Control Groups

<table>
<thead>
<tr>
<th>rs25531</th>
<th>5-HTTLPR, PSD Group</th>
<th>5-HTTLPR, Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S/S No. (%)</td>
<td>S/L No. (%)</td>
</tr>
<tr>
<td>A/A</td>
<td>19 (33.3)</td>
<td>10 (17.5)</td>
</tr>
<tr>
<td>A/G</td>
<td>0 (0)</td>
<td>4 (7.0)</td>
</tr>
<tr>
<td>G/A</td>
<td>0 (0)</td>
<td>3 (5.3)</td>
</tr>
<tr>
<td>G/G</td>
<td>0 (0)</td>
<td>17 (29.8)</td>
</tr>
<tr>
<td>Total</td>
<td>29 (50.9)</td>
<td>17 (29.8)</td>
</tr>
</tbody>
</table>

5-HTTLPR indicates the serotonin transporter-linked promoter region.

References


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Disclosures

None.
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