Letters to the Editor

Apolipoprotein E4 Allele Frequency, Ischemic Cerebrovascular Disease, and Alzheimer’s Disease

The association of the apolipoprotein (apo) E4 allele and ischemic cerebrovascular disease has been addressed in two recent articles appearing in Stroke.1,2 We reexamined the data in terms of estimated frequency of the three common alleles. Comparison with other published control population studies is presented in the Table.

The apo E4 allele frequencies derived from both ischemic cerebrovascular disease studies are similar to those for all other published control groups, including the aged control series.2,4 However, the control population studied by Couderc et al1 has an unusually low apo E4 allele frequency (and an unusually high apo E3 frequency of 0.93) that probably reflects subject selection. This is the only group that differs significantly from the other published series of controls. We conclude from these data that the apo E4 allele frequency in ischemic cerebrovascular disease does not differ from that in control populations. We have recently reported a high apo E4 allele frequency in late-onset familial (0.42)3 and sporadic (0.40)4 Alzheimer’s disease. The data from the stroke series serve as additional controls, confirming the specificity of the increase of apo E4 allele frequency in late-onset Alzheimer’s disease.

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References

Response

The association of the apo E alleles with ischemic cerebrovascular disease has been effectively reported in two recent articles appearing in Stroke.1,2 However, Pedro-Botet et al2 and we1 have found a higher prevalence of E4 and E2, respectively, polymorphisms in patients than in aged control subjects. Surprisingly, we did not calculate the same apo E allele frequencies as Drs Saunders and Roses did from References 1 and 2 (see Table). We conclude from these data that the e3 allele frequency is decreased in patients with ischemic cerebrovascular disease compared with age-matched control subjects and that further studies are needed to determine how conditions e4 and e2 could be involved.

The difference between data from References 1 and 2 could be due to patient and control selection criteria. To constitute the control group, we selected hospitalized subjects free of cerebrovascular disease (assessed by computed tomography) who thus were not fully representative of the elderly population. Apo E allele frequencies in the general population were estimated in 497 healthy blood donors. Because e4 and e2 alleles are risk factors for atherothrombotic diseases, people bearing these alleles probably die younger on average. Thus, the e3 allele frequency in the population tends to increase with age, rendering comparisons less informative.4

Ten of the aged controls in our study suffered from senile dementia of the Alzheimer type and three had the apo E4/E3 phenotype. This observation is in good agreement with data from Strittmatter et al,3 who found that more than 50% of familial Alzheimer’s disease patients were E4.3 However, they used data from stroke series as controls. The point is that concomitant diseases in aged control series have to be precisely identified, and further studies are necessary to determine apo E allele frequencies by 10- or 5-year age groups.

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Table

<table>
<thead>
<tr>
<th>Population</th>
<th>Reference</th>
<th>No. chromosomes</th>
<th>Apo E4 frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>1</td>
<td>138</td>
<td>0.16</td>
</tr>
<tr>
<td>Aged controls</td>
<td>1</td>
<td>136</td>
<td>0.07</td>
</tr>
<tr>
<td>Patients</td>
<td>2</td>
<td>200</td>
<td>0.18</td>
</tr>
<tr>
<td>Aged controls</td>
<td>2</td>
<td>200</td>
<td>0.18</td>
</tr>
<tr>
<td>Aged controls</td>
<td>3</td>
<td>182</td>
<td>0.16</td>
</tr>
<tr>
<td>Normal controls</td>
<td>4</td>
<td>2000</td>
<td>0.14</td>
</tr>
</tbody>
</table>

ICV patients 1 0.065 0.848 0.087 69
Aged controls 1 0.007 0.926 0.066 68
Normal controls (HBD) 1 0.079 0.801 0.120 497
ICV patients 2 0.08 0.73 0.19 100
Aged controls 2 0.075 0.820 0.105 100
FAD patients 3 0.04 0.44 0.52 83
Aged controls 3 0.10 0.73 0.16 91

ICV indicates ischemic cerebrovascular disease; HBD, healthy blood donors; and FAD, familial Alzheimer’s disease.
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The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/24/9/1416.citation