Prevalence of Subcortical Vascular Lesions and Association With Executive Function in Mild Cognitive Impairment Subtypes

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Background and Purpose—Subcortical hyperintensities (SH) have not been systematically evaluated in mild cognitive impairment (MCI). We sought to describe their frequency and distribution, and to test their association with cognitive characteristics in MCI patients.

Methods—We performed standardized neuropsychological tests and an MRI scan in 170 consecutive MCI patients. Medial temporal lobe atrophy and SH, including periventricular, lobar white matter, basal ganglia and infratentorial hyperintensities, were assessed with visual semiquantitative scales.

Results—The median age was 68.1 years (range: 45.5 to 87.0), and the median Mini-Mental State Examination score 28.0 (range: 26.0 to 30.0). MCI subtypes were amnestic single domain (21.2%), amnestic multiple domain (52.3%), nonamnestic single domain (21.8%), and nonamnestic multiple domain (4.7%). SH were found in 157 patients (92.6%); periventricular hyperintensities (80.6%) and lobar white matter hyperintensities (83.5%) were the most prominent locations. There was no association between SH and MCI subtypes. Executive dysfunction was independently associated with SH (odds ratio \(2.53, 95\%\) CI: 1.20 to 5.32), periventricular hyperintensities (odds ratio \(2.51, 95\%\) CI: 1.13 to 5.55), and white matter hyperintensities (odds ratio \(2.08, 95\%\) CI: 1.01 to 4.25).

Conclusions—The prevalence of SH is high in MCI patients, irrespective of MCI subtypes. SH (especially periventricular hyperintensities, and lobar white matter hyperintensities) are associated with executive dysfunction. (Stroke. 2007;38: 2595-2597.)

Key Words: cognition ■ magnetic resonance imaging ■ mild cognitive impairment ■ subcortical vascular lesion

Mild cognitive impairment (MCI) is a transitional state between normal aging and dementia, defined as a cognitive complaint with impairment on at least 1 neuropsychological test, preservation of global cognitive functions, and no significant consequence on daily living activities.¹ Subcortical hyperintensities (SH) on T2-weighted MRI are common in nondemented elderly subjects.² MCI patients may have larger volumes of white matter lesions than controls.³ The distribution of SH has never been assessed in large series of MCI patients, and the clinical significance of these lesions remains poorly understood. In the present study we evaluated the prevalence and distribution of SH and their association with cognitive characteristics in MCI patients attending a memory clinic.

Patients and Methods

We included consecutive patients diagnosed with MCI¹ at the Lille Memory Clinic, between 1997 and 2004. MCI was divided into the following domains: amnestic single domain, amnestic multiple domain, nonamnestic single domain, and nonamnestic multiple domain.¹ We excluded patients with a history of stroke, transient ischemic attack or silent territorial cortical infarcts. Neuropsychological outcome measures included the Mini-Mental State Examination, the Dementia Rating Scale, and different measures for each cognitive domain⁴ (see supplemental material, available online at http://stroke.ahajournals.org). MCI was defined by the presence of at least one test scoring 1.5 standard deviations under the normal value, in 1 or more cognitive domains.¹

MRI scans were performed on a 1.5-T machine (T2-weighted, spin-echo and fluid attenuation inversion recovery sequences). Validated visual semiquantitative rating scales were used to assess the number and size of SH,⁵ including periventricular (PVH), lobar white matter (WMH), basal ganglia (BG) and infratentorial hyperintensities (ITF), and medial temporal lobe atrophy.⁶ Statistical analyses were performed with the SAS software. SH (and their subtypes) were studied as binary variables (cut-off: median of the distribution), and MCI subtypes as amnestic versus nonamnestic. Multivariable analyses were performed using a logistic regression adjusted for age, gender, vascular risk factors, educational...
level and medial temporal lobe atrophy. Dependent variables were SH, PVH, WMH, BG and ITF. All tests were 2-tailed.

Results
We included 170 patients. Clinical and neuropsychological characteristics are shown in the Table. SH were observed in 157 patients (92.4% [95% CI: 88.4 to 96.3]) and were more prominent in the white matter and frontal areas (Figure 1): 137 patients (80.6% [74.4% to 86.5%]) had PVH and 142 patients (83.5% [78.0% to 89.1%]) had WMH (Figure 2); BG were present in 35 patients (20.6% [14.5% to 26.7%]), among whom 13 had hyperintensities in the thalamus; 37 patients (23.0% [15.6% to 28.0%]) had ITF. Median scores were 6 for total SH, 1 for PVH, 4 for WMH, and 0 for BG and ITF.

SH and their subtypes were associated neither with global cognitive scores (Mini-Mental State Examination or Dementia Rating Scale) nor with amnestic versus nonamnestic MCI subtypes (data not shown). SH >6 (odds ratio [OR] = 2.53, 95% CI: 1.20 to 5.32), PVH >1 (OR = 2.51, 95% CI: 1.13 to 5.55), and WMH >4 (OR = 2.08, 95% CI: 1.01 to 4.25) were independently associated with executive dysfunction in a multivariable model, but with neither BG nor ITF. The other factors independently associated with PVH and WMH were age (OR = 1.13, 95% CI: 1.07 to 1.18) and MLTA (OR = 1.79, 95% CI: 1.02 to 3.14) for PVH, and age (OR = 1.08, 95% CI 1.04 to 1.13) for WMH.

Discussion
In 170 MCI patients attending a memory clinic, SH were very frequent (92%) and predominated in the periventricular and lobar white matter, especially in the frontal area. PVH and WMH were significantly associated with executive dysfunction, but not with memory or global cognitive functions.

In the absence of controls, our study does not indicate whether SH are more frequent in MCI patients than age-matched healthy individuals, and some associations may be missed. One originality of our study is to describe the distribution of SH. The prominence in the periventricular and lobar white matter is in line with a previous description in 30

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**Patient Characteristics**

<table>
<thead>
<tr>
<th>Age, years*</th>
<th>68.1 [45.5–87.0]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>98 (57.6%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>76 (44.7%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>22 (12.9%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>31 (18.2%)</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
</tr>
<tr>
<td>&lt;8 years</td>
<td>103 (60.4%)</td>
</tr>
<tr>
<td>9–12 years</td>
<td>34 (20.1%)</td>
</tr>
<tr>
<td>&gt;12 years</td>
<td>33 (19.5%)</td>
</tr>
<tr>
<td>MCI subtype</td>
<td></td>
</tr>
<tr>
<td>Amnestic single domain</td>
<td>36 (21.2%)</td>
</tr>
<tr>
<td>Amnestic multiple domain</td>
<td>89 (52.3%)</td>
</tr>
<tr>
<td>Nonamnestic single domain</td>
<td>37 (21.8%)</td>
</tr>
<tr>
<td>Nonamnestic multiple domain</td>
<td>8 (4.7%)</td>
</tr>
<tr>
<td>Mnesic dysfunction</td>
<td>125 (73.5%)</td>
</tr>
<tr>
<td>Executive dysfunction</td>
<td>72 (42.3%)</td>
</tr>
<tr>
<td>MMSE at baseline*</td>
<td>28.0 [26.0–30.0]</td>
</tr>
<tr>
<td>DRS at baseline*</td>
<td>137.0 [120.0–144.0]</td>
</tr>
</tbody>
</table>

*Median [range].

MMSE indicates Mini-Mental State Examination; DRS, Dementia Rating Scale.
cognitively impaired nondemented subjects, but had never been assessed in large MCI cohorts.

Similarly, the relationship between SH and cognitive characteristics has never been evaluated in MCI patients. The association between large amounts of SH (especially PVH and WMH) and executive dysfunction is consistent with recent data showing that patients with extensive WMH perform significantly worse in the executive domain. In contrast with previous data, the association we found between executive dysfunction and SH was independent of medial temporal lobe atrophy. SH may become clinically overt only above a certain threshold. Interestingly, neuropathological data suggest that extensive SH reflect increasing severity of ischemic damage, whereas punctuate SH may consist of perivascular demyelination.

SH scores did not differ between amnestic and nonamnestic subtypes, suggesting that memory impairment is not related with SH but may reflect an underlying degenerative process. The amnestic subtype of MCI is presumed to be degenerative in origin and may represent an early stage of Alzheimer disease. The fact that BG were not associated with cognitive parameters may be attributable to their low frequency.

In summary, SH were highly prevalent in a cohort of MCI patients attending a memory clinic, irrespective of subtypes, and predominated in the frontal and periventricular white matter. Patients with diffuse PVH or WMH had executive dysfunction more often. In a companion article, we investigated whether the amount of SH is also associated with the rate of cognitive decline in MCI.

Acknowledgments
The authors thank Nathalie Jourdan for the monitoring of the database.

Disclosures
None.

References
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Stroke. 2007;38:2595-2597; originally published online July 26, 2007; doi: 10.1161/STROKEAHA.107.486407
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

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/38/9/2595

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