Subcortical Hyperintensities Are Associated With Cognitive Decline in Patients With Mild Cognitive Impairment

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Background and Purpose—It has been suggested that subcortical lesions may influence cognitive performances at early stages of cognitive impairment but not in late stages of dementia. We aimed to test whether cognitive decline is associated with subcortical hyperintensities in patients with mild cognitive impairment (MCI).

Methods—We included 170 consecutive MCI patients (mean follow-up, 3.8 ± 1.6 years). We assessed subcortical hyperintensities on a baseline magnetic resonance imaging scan with a semiquantitative rating scale. The mean annual cognitive decline was calculated with the Mini-Mental State Examination and the Dementia Rating Scale at baseline and the end of follow-up.

Results—Compared with patients whose cognitive performances remained stable or improved during follow-up, patients whose cognitive performances declined often had a larger amount (greater than the median of the distribution) of periventricular (PVH) and white-matter hyperintensities. The rate of cognitive decline was higher with increasing PVH: mean change in the Mini-Mental State Examination score = 0.16 vs −0.66 points/year in patients with PVH in the first versus third tertile (P = 0.0002). The rate of decline in executive functioning was also higher with increasing PVH: mean change in the Dementia Rating Scale initiation subscore = −0.05 vs −1.42 points/year in patients with PVH in the first versus third tertile (P = 0.04). These associations were independent of vascular risk factors, temporal lobe atrophy, and MCI subtype and were stronger in patients with baseline executive dysfunction.

Conclusion—White-matter hyperintensities and especially PVH were significantly associated with cognitive decline in MCI patients. This result was independent of the MCI subtype but stronger in cases of executive dysfunction at baseline.

Key Words: mild cognitive impairment ■ subcortical vascular lesions ■ white matter ■ cognitive decline ■ magnetic resonance imaging

The impact of subcortical lesions on the outcome of patients with mild cognitive impairment (MCI) is unclear. In several nondemented population–based studies, white-matter lesions predicted a higher rate of cognitive decline1–4 and conversion to dementia,5–7 especially when located in the periventricular white matter.1,7 At autopsy, subjects with lacunar infarcts needed fewer lesions indicative of Alzheimer disease (AD) to be demented.8,9 AD patients with ischemic lesions had worse cognitive performances than did AD patients without.8,9 Other studies did not find any association between subcortical lesions and the rate of cognitive decline in AD patients.10–12 It has thus been suggested that white-matter lesions and cerebral infarcts may influence cognitive performance and cognitive decline at very early stages of cognitive impairment but not at later stages of degenerative dementia.13,15 If this is true, then subcortical lesions should be associated with a higher rate of cognitive decline in patients with mild cognitive impairment (MCI). To our knowledge, this hypothesis has not been evaluated yet. Two studies have investigated the association of subcortical lesions with the rate of conversion to overt dementia,16,17 and they provided conflicting results. The first study found that white-matter changes on computed tomography scans were associated with a higher rate of conversion to AD in 27 MCI patients.16 The other study failed to demonstrate any association between vascular lesions on cerebral magnetic resonance imaging (MRI) scans in 52 MCI patients and conversion to dementia.17 In addition to using different imaging techniques, these studies also differed by the criteria used to define progression to dementia.16,17

Compared with the conversion rate to dementia, the rate of cognitive decline is more sensitive and can be analyzed after a shorter follow-up. The present study was performed in a large cohort of MCI patients who were followed up in a...
memory clinic and aimed to assess the relation between the progression of cognitive decline and subcortical hyperintensities (SH) measured semiquantitatively on MRI.

**Methods**

This observational study was conducted in consecutive patients diagnosed with MCI during their first evaluation at the Lille Memory Clinic between 1997 and 2004. MCI was divided into amnestic single domain, amnestic multiple domain, nonamnestic single domain, and nonamnestic multiple domain categories. We excluded patients with a history of stroke or transient ischemic attack or silent territorial cortical infarcts.

The neuropsychological battery performed in each patient included the Mini-Mental State Examination (MMSE), the Mattis Dementia Rating Scale (DRS), memory tests (the forward and backward digit span, visuospatial spans, an adapted version of the free and cued selective reminding test, and the supraspan tests), attentional and executive tests (the Trail Making test, the Stroop test, and verbal fluency tests), praxis tests from the Consortium to Establish a Registry for Alzheimer’s Disease neuropsychological tests, and language assessment (confrontation naming of 36 items, comprehension, and written language assessment). MCI was defined by global test scores in the normal range and the presence of at least 1 cognitive test score below the commonly accepted cutoff of 1.5 standard deviations less than the normal value.

To assess cognitive decline, we compared performances on both the MMSE and the DRS at baseline and at the last visit at our institution. In addition, we compared the memory subscore (DRS-memory) and the initiation subscore (DRS-initiation) of the DRS at baseline and at the last visit to evaluate the decline in memory and executive function. The mean annual decline for each of the 4 cognitive variables (Δ score) was defined as the difference between the mean score at the last visit and the mean score at baseline, divided by the duration of follow-up in years. We also used all MMSE scores recorded at any follow-up visit to describe the cognitive decline with a random-effects model for repeated measures, as detailed later.

MRE scans were performed at baseline on a 1.5-T machine (T2-weighted, spin-echo, and fluid attenuation inversion recovery sequences; echo time, 20 and 60 ms; repetition time, 2500 ms; section thickness, 5.0 mm). SH were assessed by an investigator blinded to the cognitive status of the patients, who used a semi-quantitative rating scale. Hyperintensities in the basal ganglia and infratentorial region were not associated with a decline in MMSE or DRS scores. Patients whose MMSE scores declined during the follow-up period more often had a large amount (higher than the median of the distribution) of SH, PVH, and WMH in the subgroups of patients whose MMSE scores declined, remained stable, or improved during follow-up. The rate of cognitive decline was not significantly associated with a decline in MMSE or DRS scores. Patients whose MMSE scores declined during the follow-up period more often had a large amount (higher than the median of the distribution) of SH, especially PVH and WMH, compared with patients whose MMSE scores did not decline (Table 2). A decline in DRS scores was associated with larger amounts of PVH only (Table 2). Figure 1 illustrates the decreasing median value of SH, PVH, and WMH in the subgroups of patients whose MMSE scores declined, remained stable, or improved during follow-up.

The rate of cognitive decline was not significantly associated with WMH but was more important with increasing PVH tertiities in a multivariable model adjusted for age, sex, educational level, vascular risk factors, medial temporal lobe atrophy, MCI subtype, and baseline cognitive performances.

**Results**

We included 170 patients with a mean follow-up of 3.8±1.6 years. The mean number of visits was 4.3±1.6. Baseline characteristics of our population are shown in Table 1. The distribution of SH has been described in a companion article. The mean decline in cognitive functions during follow-up was −0.27±1.04 points/year for the MMSE score, −0.85±3.37 points/year for the DRS score, −0.66±3.15 points/year for the DRS-initiation subscore, and −0.75±4.44 points/year for the DRS-memory subscore.

Hyperintensities in the basal ganglia and infratentorial region were not associated with a decline in MMSE or DRS scores. Patients whose MMSE scores declined during the follow-up period more often had a large amount (higher than the median of the distribution) of SH, especially PVH and WMH, compared with patients whose MMSE scores did not decline (Table 2). A decline in DRS scores was associated with larger amounts of PVH only (Table 2). Figure 1 illustrates the decreasing median value of SH, PVH, and WMH in the subgroups of patients whose MMSE scores declined, remained stable, or improved during follow-up.

![Table 1. Baseline Characteristics of the Population](image)

<table>
<thead>
<tr>
<th>N</th>
<th>170</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y*</td>
<td>68.1 (45.5–87.0)</td>
</tr>
<tr>
<td>Women</td>
<td>98 (57.6%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>76 (44.7%)</td>
</tr>
<tr>
<td>Diabetes mellitus</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 y</td>
<td>103 (60.5%)</td>
</tr>
<tr>
<td>9–12 y</td>
<td>34 (20.1%)</td>
</tr>
<tr>
<td>&gt;12 y</td>
<td>33 (19.4%)</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>Executive dysfunction at baseline</td>
<td>72 (42.4%)</td>
</tr>
<tr>
<td>MMSE score at baseline</td>
<td>28.0 (26.0–30.0)</td>
</tr>
<tr>
<td>DRS score at baseline</td>
<td>137.0 (120.0–144.0)</td>
</tr>
<tr>
<td>DRS-initiation score at baseline</td>
<td>35.0 (24.0–37.0)</td>
</tr>
<tr>
<td>DRS-memory score at baseline</td>
<td>24.0 (14.0–25.0)</td>
</tr>
</tbody>
</table>

The MMSE maximum score is 30. The DRS maximum score is 144. *Median and [range].
The results remained unchanged after additional adjustment for baseline cognitive performances (data not shown). The association of cognitive decline with PVH was substantially unchanged after stratification according to MCI subtype (Table 4), and there was no interaction between MCI subtype and PVH tertiles for all cognitive measures. The difference in mean annual cognitive decline between patients with PVH in the first tertile and patients with PVH in the third tertile was more important in patients with executive dysfunction at baseline (Table 4). There was a significant interaction between executive dysfunction at baseline and PVH for the association with DRS-initiation (multivariable $P$ for interaction=0.02). The association of cognitive decline with PVH was unchanged after stratification by history of hypertension, degree of medial temporal lobe atrophy, and age—higher versus lower than the median (data not shown).

To further illustrate the association of MMSE decline with PVH, we compared MMSE scores at all follow-up visits between subjects with PVH $>1$ (median of the distribution) and those with PVH $\leq 1$ in a random-effects model for repeated measures. This model showed that the decline in MMSE scores over time was significantly more important in subjects with a large number of PVH (Figure 2).

### Discussion

Our study has shown that among 170 consecutive MCI patients followed up in a memory clinic during 3.8 years, those who declined had larger numbers of PVH and WMH at baseline. The annual rate of global cognitive decline was higher with increasing amounts of PVH. Large amounts of PVH at baseline also tended to be predictive of a more rapid decline in executive functions (as assessed by the DRS-initiation subscore) but were not associated with memory decline in the present cohort. The association between the rate of cognitive decline and PVH was present irrespective of MCI subtype but was especially striking in patients with executive dysfunction at baseline. It was not dependent on vascular risk factors and medial temporal lobe atrophy. To our knowledge, the present study is the first to show such findings.

Whether the positive association between SH (especially PVH) and cognitive decline is causal or not cannot be established from this study. However, the same association was found with different statistical models and different cognitive measures, suggesting that the association is not spurious. Furthermore, the association remained significant in a multivariable model that included age, sex, educational level, vascular risk factors, medial temporal lobe atrophy, MCI subtype, and baseline cognitive scores. Noteworthy, the association was similar when adjusting only for the main potential confounders, and age, sex, and educational level (data not shown). The fact that the association was also similar after stratification by MCI subtype, hypertension, degree of temporal lobe atrophy, and age also supports the concept that the association is genuine. Furthermore, the presence of a dose effect of PVH is suggestive of a causal relation.

The mechanism by which white matter lesions may affect cognitive decline in MCI patients is unclear. Histopathologic studies of white matter lesions reveal diffuse pallor of the white matter, with rarefaction of myelin sheaths and reactive gliosis. White matter lesions may thus affect cognition by

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**Table 2. Severity of SH According to the Presence or Absence of a Decline in MMSE and DRS Scores**

<table>
<thead>
<tr>
<th></th>
<th>MMSE Score Declined</th>
<th>MMSE Score Stable/Improved</th>
<th>$P$</th>
<th>DRS Score Declined</th>
<th>DRS Score Stable/Improved</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>79</td>
<td>91</td>
<td></td>
<td>108</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>SH $&gt;6$, %*</td>
<td>60.8</td>
<td>41.8</td>
<td>0.01</td>
<td>52.8</td>
<td>46.8</td>
<td>0.45</td>
</tr>
<tr>
<td>WMH $&gt;4$, %</td>
<td>57.0</td>
<td>39.6</td>
<td>0.02</td>
<td>50.0</td>
<td>43.6</td>
<td>0.42</td>
</tr>
<tr>
<td>PVH $&gt;1$, %</td>
<td>68.4</td>
<td>41.8</td>
<td>0.0005</td>
<td>60.2</td>
<td>43.6</td>
<td>0.04</td>
</tr>
<tr>
<td>BG $&gt;0$, %</td>
<td>16.5</td>
<td>24.2</td>
<td>0.21</td>
<td>21.3</td>
<td>19.4</td>
<td>0.76</td>
</tr>
<tr>
<td>ITF $&gt;0$, %</td>
<td>19.5</td>
<td>24.7</td>
<td>0.42</td>
<td>20.8</td>
<td>25.0</td>
<td>0.53</td>
</tr>
</tbody>
</table>

BG indicates basal ganglia hyperintensities; ITF, infratentorial foci of hyperintensities.

*The median of the distribution was used as a cutoff value for SH as well as for all subtypes of SH.
disconnecting the cortex from subcortical nuclei or distant cortical territories. However, this would explain an association between white matter lesions and baseline cognitive function but not with cognitive decline. One possible explanation of our results may be that patients with larger amounts of white matter lesions have more rapidly evolving small-vessel disease and thus, an increasing load of white matter damage over time. In patients with fewer white matter lesions at baseline, these may just be a coincidental finding or reflect less aggressive small-vessel disease. Supporting this hypothesis, the long-term follow-up of the Austrian Stroke Prevention study showed that lesion severity at baseline was the only significant predictor of white matter lesion progression after 6 years of follow-up. Punctate white matter lesions did not progress over time and were therefore, considered benign.

A recent prospective study in elderly individuals also found that the main predictor of white matter lesion progression was the baseline level of these lesions. Alternatively, white matter lesions may trigger or enhance neurodegenerative processes when the lesion load reaches a certain threshold. It has indeed been hypothesized in recent years that neurovascular lesions could play a major role in the pathogenesis of AD via mechanisms such as altered clearance of amyloid β-peptide or enhanced neuronal vulnerability due to a chronic hypoperfusion state. Analyses of conversion to dementia are currently under way in our cohort, and it will be crucial to compare the rate of conversion to AD according to the amount of SH. Finally, one cannot exclude a reverse causal relationship, whereby neurodegenerative lesions responsible for a rapid cognitive decline would enhance the formation of white matter lesions via mechanisms such as altered clearance of amyloid β-peptide or enhanced neuronal vulnerability due to a chronic hypoperfusion state.

Table 3. Decline in Cognitive Performances According to PVH Tertiles

<table>
<thead>
<tr>
<th></th>
<th>Tertile 1*</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
<th>P†</th>
<th>P‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>78</td>
<td>48</td>
<td>44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ΔMMSE, points/y</td>
<td>+0.16</td>
<td>−0.30</td>
<td>−0.66</td>
<td>0.02</td>
<td>0.0002</td>
</tr>
<tr>
<td>Mean ΔDRS, points/y</td>
<td>−0.24</td>
<td>−0.98</td>
<td>−1.60</td>
<td>0.28</td>
<td>0.06</td>
</tr>
<tr>
<td>Mean ΔDRS-initiation, points/y</td>
<td>−0.05</td>
<td>−0.96</td>
<td>−1.42</td>
<td>0.15</td>
<td>0.04</td>
</tr>
<tr>
<td>Mean ΔDRS-memory, points/y</td>
<td>−0.65</td>
<td>−0.79</td>
<td>−0.57</td>
<td>0.74</td>
<td>0.87</td>
</tr>
</tbody>
</table>

ΔScore is the difference between the mean score at the last visit and the mean score at baseline, divided by the duration of follow-up in years. Negative values correspond to declining performances.

*Lowest tertile.
†P for trend adjusted for age, sex, vascular risk factors, educational level, temporal lobe atrophy, and MCI subtype.
‡Multivariable P value for the difference between the first and third tertiles of PVH.

Table 4. Decline in MMSE and DRS-Initiation Scores According to PVH Tertiles in Different Population Subgroups

<table>
<thead>
<tr>
<th>Patients with executive dysfunction at baseline</th>
<th>Tertile 1*</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
<th>P†</th>
<th>P‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>27</td>
<td>23</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ΔMMSE, points/y</td>
<td>+0.18</td>
<td>−0.53</td>
<td>−1.07</td>
<td>0.05</td>
<td>0.002</td>
</tr>
<tr>
<td>Mean ΔDRS-initiation, points/y</td>
<td>+1.05</td>
<td>−0.70</td>
<td>−3.03</td>
<td>0.13</td>
<td>0.001</td>
</tr>
<tr>
<td>Patients without executive dysfunction at baseline</td>
<td>n</td>
<td>24</td>
<td>52</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Mean ΔMMSE, points/y</td>
<td>+0.17</td>
<td>−0.02</td>
<td>−0.35</td>
<td>0.42</td>
<td>0.09</td>
</tr>
<tr>
<td>Mean ΔDRS-initiation, points/y</td>
<td>−1.04</td>
<td>−0.64</td>
<td>+0.20</td>
<td>0.57</td>
<td>0.17</td>
</tr>
<tr>
<td>Patients with memory dysfunction at baseline (amnestic MCI subtype)</td>
<td>n</td>
<td>55</td>
<td>35</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Mean ΔMMSE, points/y</td>
<td>+0.15</td>
<td>−0.43</td>
<td>−0.86</td>
<td>0.02</td>
<td>0.0002</td>
</tr>
<tr>
<td>Mean ΔDRS-initiation, points/y</td>
<td>−0.18</td>
<td>−1.09</td>
<td>−1.56</td>
<td>0.20</td>
<td>0.07</td>
</tr>
<tr>
<td>Patients without memory dysfunction at baseline (nonamnestic MCI subtype)</td>
<td>n</td>
<td>12</td>
<td>24</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Mean ΔMMSE, points/y</td>
<td>−0.10</td>
<td>−0.01</td>
<td>−0.31</td>
<td>0.78</td>
<td>0.41</td>
</tr>
<tr>
<td>Mean ΔDRS-initiation, points/y</td>
<td>−0.59</td>
<td>−0.21</td>
<td>−1.41</td>
<td>0.80</td>
<td>0.64</td>
</tr>
</tbody>
</table>

ΔScore is the difference between the mean score at the last visit and the mean score at baseline, divided by the duration of follow-up in years. Negative values correspond to declining performances. Negative values correspond to declining performances.

*Lowest tertile (tertiles were recalculated in each subpopulation).
†P for trend adjusted for age, sex, vascular risk factors, educational level, temporal lobe atrophy, and MCI subtype.
‡Multivariable P value for the difference between the first and third tertiles of PVH.
matter lesions, as suggested by experimental studies showing β-amyloid–mediated vascular changes.40,41 Future prospective studies in MCI cohorts, including repeated MRI scans to assess the progression of SH and their association with cognitive decline, are needed to improve our understanding of the mechanisms underlying our observation.

We found that the rate of global cognitive decline and the rate of decline in executive functions were associated with increasing PVH but not WMH. Even though the distinction between PVH and WMH may in some instances seem artificial, because WMH that appear isolated on axial views can in fact be contiguous to PVH when visualized on 3-dimensional MRI,42 it is clinically significant. Indeed, PVH and subcortical or deep white matter lesions (ie, WMH) have been associated with different clinical conditions.1,43,44 Vascular risk factors were shown to be correlated more strongly with PVH than with WMH,45 but this is unlikely to be the only explanation for our results, as they remained unchanged after adjustment for vascular risk factors. It has been suggested that lesions affecting the periventricular area may impair cognitive functioning more easily than lesions affecting the subcortical area. Indeed, the periventricular area has a high density of long associating fibers, which connect the cortex with subcortical nuclei and other distant brain territories, whereas the subcortical area contains more short associating fibers or U fibers that link adjacent gyri.1 Our results are in line with the population-based Rotterdam Study, in which white matter lesions predicted a higher rate of cognitive decline and conversion to dementia, especially when they were located in the periventricular white matter.1,4,7 As in our study, those authors found that periventricular white matter lesions were particularly associated with a decline in information processing speed and executive functions.4 Similarly, recent data from the PROSPER MRI substudy also suggested that the baseline volume of PVH and not WMH is longitudinally associated with reduced mental speed processing but not with a decline in memory functions.43 The disruption of long associating fibers by PVH maybe particularly deleterious for executive domain functions.46

In the present study, increasing amounts of PVH were associated with a more rapid decline in global cognitive functions and in executive but not memory functions. Our results suggest that SH and especially PVH could contribute to cognitive decline by affecting mainly executive but not memory functions. Memory decline is particularly related to medial temporal lobe atrophy47 and maybe less affected by white matter lesions.48 In the general population, it has been suggested that the lack of association of PVH with memory decline may be due to the fact that executive functions, especially cognitive speed, decline first, before other cognitive domains such as memory.43 This hypothesis cannot be verified in our study, because all patients were already cognitively impaired at their first visit to our memory clinic. The mean decline in executive functions was, however, not more important than the decline in memory functions, as assessed by the DRS subscores.

We demonstrated a more prominent association of PVH with cognitive decline (especially a decline in executive functions) in subjects with executive dysfunction at the initial evaluation. In a companion article,34 we have shown that patients with executive dysfunction at the initial evaluation had a larger amount of SH. It may thus be hypothesized that patients with executive dysfunction at baseline have more diffuse and therefore more rapidly evolving white matter lesions.7,38 Future prospective studies on MCI cohorts with repeated MRI scans are needed to confirm this hypothesis.

Whereas MCI subtypes are useful predictors of the type of further dementia,19 they did not influence the association of SH with cognitive decline in our cohort. Indeed, stratifying on and adjusting for MCI subtype did not modify the association between SH and cognitive decline. Even though we cannot exclude insufficient statistical power to detect an interaction with MCI subtype, our results suggest that PVH contribute to cognitive decline by affecting mainly executive functions, irrespective of the MCI subtype.

The main limitations of our study are the retrospective design and the sample size. However, although imaging was assessed retrospectively, neuropsychological evaluations were standardized, and clinical data, such as vascular risk factors, are routinely collected on a standardized questionnaire at each follow-up visit in our memory clinic.49 Even though our study included the largest sample of MCI patients compared with previous reports, it is still underpowered to answer several questions. In particular, the statistical power may have been insufficient to detect an association between cognitive decline and basal ganglia or infratentorial hyperintensities, which were less prevalent than PVH and WMH. Our sample size was also inadequate to study the association of cognitive decline with the different locations of PVH and WMH (frontal, parietal, temporal, or occipital), which may have some importance. Indeed, recent neuroimaging studies, including diffusion tensor imaging and functional MRI, suggest that temporoparietal connections are more affected than frontal connections in early AD50 and that executive functions are associated not only with prefrontal but also with posterior, mainly parietal, regions.51 It could therefore be important to assess the specific role of white matter lesions according to their frontal, parietal, or temporal location. Finally, owing to repeated measures of MMSE and DRS, we cannot exclude some degree of practice effect, but it is unlikely to have been a major problem. A practice effect
would mainly reduce the power of the study by minimizing cognitive changes (in particular, when the follow-up period is very short, which was not the case here). One could object that the patients may not benefit equally from this potential practice effect, but this is rather unlikely, because our results were unchanged after adjustment for baseline cognitive performances. Concerning the semiquantitative rating of subcortical lesions used in our study, it may be argued that is not accurate enough, but it has been shown to correlate well with quantitative volumetric measurements.32,52

In summary, the present study found that WMI and especially PVH were significantly associated with cognitive decline in MCI patients, in particular with a decline in executive functions, independent of MCI subtype, medial temporal lobe atrophy, and vascular risk factors. It suggests that in patients with MCI, diffuse SH and in particular PVH should prompt the clinician to follow up these patients more closely, because they seem to be at risk to decline faster. To our knowledge, ours is the first study to assess the relation between SH and cognitive decline in a large cohort of MCI patients. Further studies are needed to confirm these results and to improve our understanding of the underlying mechanisms.

Acknowledgment
The authors thank Nathalie Jourdan for monitoring the database.

Disclosures
None.

References
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Stroke. 2007;38:2924-2930; originally published online September 20, 2007;
doi: 10.1161/STROKEAHA.107.488403
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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