Extent and Distribution of White Matter Hyperintensities in Normal Aging, Mild Cognitive Impairment and Alzheimer’s Disease

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How different in Extent and Distribution

- Normal Aging (NA)
- Mild Cognitive Impairment (MCI)
- Alzheimer’s Disease (AD)

White Matter Hyperintensities (WMH)
## Subject Demographics

<table>
<thead>
<tr>
<th></th>
<th>AD</th>
<th>MCI</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (F/M)</td>
<td>26 (16/10)</td>
<td>29 (12/17)</td>
<td>33 (23/10)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>79.6 ± 6.8*</td>
<td>74.6 ± 8.1</td>
<td>73.4 ± 8.1</td>
</tr>
<tr>
<td>range</td>
<td>63-93</td>
<td>60-88</td>
<td>61-91</td>
</tr>
<tr>
<td>Education (y)</td>
<td>11.7 ± 5.2</td>
<td>12.6 ± 5.4</td>
<td>10.9 ± 5.8</td>
</tr>
<tr>
<td>range</td>
<td>0-18</td>
<td>0-21</td>
<td>0-20</td>
</tr>
<tr>
<td>MMSE</td>
<td>19.5 ± 6.8a</td>
<td>26.6 ± 2.3</td>
<td>27.9 ± 2.7</td>
</tr>
<tr>
<td>range</td>
<td>0-27</td>
<td>20-30</td>
<td>19-30</td>
</tr>
<tr>
<td>Vascular risk score</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>range</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain volume (%)</td>
<td>77.3 ± 4.2b</td>
<td>80.7 ± 4.2</td>
<td>83.3 ± 4.3</td>
</tr>
<tr>
<td>WMH volume (%)</td>
<td>1.33 ± 1.30c</td>
<td>0.92 ± 0.93</td>
<td>0.56 ± 0.67</td>
</tr>
</tbody>
</table>

Data represented as mean ± standard deviation.

* $p < 0.01$ between AD and NA,

a $p < 0.001$ between AD and others.

b $p < 0.01$ between AD and others,

c $p < 0.001$ between AD and NA.
Methods

Image Analysis

Schema for WMH segmentation and nonlinear transformation for mapping


Composite image
We computed the number of voxel of WMH in each ROI, and calculated percentage of voxel which have WMH in each ROI of each subject.
1. Groups were compared using analysis of variance (ANOVA) or Kruskal-Wallis test as appropriate according to the distribution of the data, with post hoc analysis.

2. Correlations were evaluated by Spearman’s ranks correlation test.

3. Results are expressed as mean values ± standard deviation.

4. A $p$ value less than 0.05 was considered significant.

5. Data were analyzed using the Statistical Package for Social Sciences (SPSS for Windows, version 12.0; SPSS Inc, Chicago, IL).
WMH frequency maps in all subjects

(A-1) X = 21 (A-2) X = 2
(B-1) Z = 28 (B-2) Z = 22
(C-1) Y = -4 (C-2) Y = -26

(D) P
Three-dimensional reconstruction of the WMH (orange) and ventricular (grey) maps. Orange color indicates the frequency of voxels containing the WMH more than 10%.

(A): group of NA
(B): group of MCI
(C): group of AD
Group difference of WMH severity in each ROI

(A) Periventricular region

(B) Corpus callosum region

* $p < 0.05$, ** $p < 0.01$.

Error bars indicate standard deviation of the mean.
<table>
<thead>
<tr>
<th></th>
<th>Pa</th>
<th>Pb</th>
<th>Pp</th>
<th>Po</th>
<th>Cg</th>
<th>Cs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AD</td>
<td>0.060</td>
<td>0.068</td>
<td>0.202</td>
<td>0.350</td>
<td>0.120</td>
<td>0.276</td>
</tr>
<tr>
<td>MCI</td>
<td>0.237</td>
<td>0.355</td>
<td>0.477*</td>
<td>0.553**</td>
<td>0.319</td>
<td>0.055</td>
</tr>
<tr>
<td>NA</td>
<td>0.220</td>
<td>0.298</td>
<td>0.411*</td>
<td>0.394*</td>
<td>0.159</td>
<td>0.164</td>
</tr>
<tr>
<td><strong>MMSE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AD</td>
<td>0.355</td>
<td>0.149</td>
<td>0.078</td>
<td>-0.042</td>
<td>0.085</td>
<td>0.032</td>
</tr>
<tr>
<td>MCI</td>
<td>-0.054</td>
<td>0.018</td>
<td>-0.116</td>
<td>-0.160</td>
<td>0.252</td>
<td>-0.003</td>
</tr>
<tr>
<td>NA</td>
<td>0.084</td>
<td>-0.085</td>
<td>-0.051</td>
<td>0.316</td>
<td>0.198</td>
<td>0.192</td>
</tr>
</tbody>
</table>

* * p < 0.05, ** p < 0.01 corrected.

Abbreviations:
- Pa: anterior periventricular region
- Pb: body of periventricular region
- Pp: posterior periventricular region
- Po: occipital periventricular region
- Cg: genu of corpus callosum
- Cs: splenium of corpus callosum
Conclusion

We believe the methods developed here conclusively show the difference of WMH distribution of each cognitive stage.

These observations also support the notion of both a common ischemic etiology and Wallerian degeneration as a mechanism of WMH in each cognitive stage.

Our study shows that measurements of the extent and distribution of WMH in both corpus callosum and periventricular area are suitable for assessment for NA, MCI and AD.
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