Thalamic Lesions in Vascular Dementia
Low Sensitivity of Fluid-Attenuated Inversion Recovery (FLAIR) Imaging

António J. Bastos Leite, MD; Elisabeth C.W. van Straaten, MD; Philip Scheltens, MD, PhD; Geert Lycklama, MD, PhD; Frederik Barkhof, MD, PhD

Background and Purpose—The criteria of the National Institute of Neurological Disorders and Stroke (NINDS)–Association Internationale pour la Recherche et l’Enseignement en Neurosciences (AIREN) include thalamic lesions for the diagnosis of vascular dementia (VaD). Although studies concerning VaD and brain aging advocate the use of fluid-attenuated inversion recovery (FLAIR) or T2-weighted images (T2-WI) to detect ischemic lesions, none compared the sensitivity of these sequences to depict thalamic lesions.

Methods—We performed a blinded review of T2-WI and FLAIR images in 73 patients fulfilling the radiological part of the NINDS-AIREN criteria (mean age, 71 years; range, 49 to 83 years). This sample was drawn from a large multicenter trial on VaD and was expected to have a high prevalence of thalamic lesions. In a side-by-side review, including T1-weighted images as well, lesions were classified according to presumed underlying pathology.

Results—The total number of thalamic lesions was 214. Two hundred eight (97%) were detected on T2-WI, but only 117 (55%) were detected on FLAIR (χ² = 5.1; P < 0.05). Although the mean size of lesions detected on T2-WI and not on FLAIR (4.4 mm) was significantly lower than the mean size of lesions detected on both sequences (6.7 mm) (P < 0.001), 5 of the 29 lesions >10 mm on T2-WI were not visible on FLAIR. FLAIR detected only 81 (51%) of the 158 probable ischemic lesions and 30 (60%) of the 50 probable microbleeds.

Conclusions—FLAIR should not be used as the only T2-weighted sequence to detect thalamic lesions in patients suspected of having VaD. (Stroke. 2004;35:415-419.)

Key Words: dementia, vascular ■ magnetic resonance imaging ■ thalamus

In 1937, Papez described an anatomic circuit beginning and ending in the hippocampal formation possibly related to emotional experience. The projections of the Papez circuit involve the fornix, mammillary bodies, mammillothalamic tracts, anterior thalamus, cingulate cortex, and cingulate bundles. The early notion that the Papez circuit subserves emotion has been abandoned and replaced by the proposal it is primarily involved in mnemonic functions. Lesions of the major components of this circuit have been shown to disrupt memory in humans, particularly those localized in the anterior group of thalamic nuclei. However, lesions affecting other thalamic components or connections not considered in the circuit, such as the mediodorsal (dorsomedial), intralaminal, and pulvinar nuclei or the thalamofrontal networks, may also cause cognitive deficits and marked behavioral changes.

MRI and CT are crucial for the diagnosis of cerebrovascular diseases. The first studies using CT for the evaluation of brain lesions in patients with ischemic stroke confirmed the importance of thalamic infarctions as a cause of dementia. Therefore, the criteria of the National Institute of Neurological Disorders and Stroke (NINDS)–Association Internationale pour la Recherche et l’Enseignement en Neurosciences (AIREN) include radiological evidence of thalamic lesions for the diagnosis of probable vascular dementia (VaD). Moreover, a single thalamic infarction may induce VaD.

MRI studies concerning VaD and brain aging advocate the use of fluid-attenuated inversion recovery (FLAIR) or T2-weighted images (T2-WI) to detect and characterize brain abnormalities. However, to our knowledge no comparative study was performed to assess which MRI sequence yields the highest sensitivity for thalamic lesions. In this study we sought to compare the sensitivity of each of these sequences to depict thalamic lesions in patients with VaD.

Subjects and Methods

Patients

The subjects were derived from cases belonging to the VantagE study, a multicenter, phase III, prospective, randomized, double-blind clinical trial on the effects of rivastigmine in patients with
TABLE 1. Lesions on T2-WI and FLAIR

<table>
<thead>
<tr>
<th>Signal on FLAIR</th>
<th>Not Detected</th>
<th>Hyperintense</th>
<th>Hypointense</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not detected</td>
<td>0</td>
<td>77</td>
<td>20</td>
<td>97</td>
</tr>
<tr>
<td>Hyperintense</td>
<td>3</td>
<td>49</td>
<td>0</td>
<td>52</td>
</tr>
<tr>
<td>Hypointense</td>
<td>3</td>
<td>14</td>
<td>30</td>
<td>47</td>
</tr>
<tr>
<td>Predominantly hypointense</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Hypointense with hyperintense rim</td>
<td>0</td>
<td>13</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>158</td>
<td>50</td>
<td>214</td>
</tr>
</tbody>
</table>

TABLE 2. Detection on FLAIR and Distribution by Size of Focal Lesions on T2-WI

<table>
<thead>
<tr>
<th>Size on T2-WI</th>
<th>Not Detected</th>
<th>Detected</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–5 mm</td>
<td>66</td>
<td>53</td>
<td>119</td>
</tr>
<tr>
<td>5–10 mm</td>
<td>26</td>
<td>34</td>
<td>60</td>
</tr>
<tr>
<td>&gt;10 mm</td>
<td>5</td>
<td>24</td>
<td>29</td>
</tr>
</tbody>
</table>

Discussion

Our study shows that FLAIR imaging is not very sensitive in detecting focal thalamic lesions and is therefore not well suited as a stand-alone sequence in the evaluation of patients suspected of VaD.
FLAIR sequences employ a long inversion time that suppresses the signal from CSF and a long TE that provides heavy T2 weighting. Therefore, the major interest of FLAIR is to detect and characterize brain lesions around CSF spaces.

Most studies advocate superiority of FLAIR over conventional spin-echo imaging in a wide range of pathologies. FLAIR images also have the advantage of easily identifying CSF-like lesions. Some studies showed that FLAIR was more often associated with image artifacts or could not corroborate the aforementioned superiority of FLAIR. Disadvantages of FLAIR include a reduced sensitivity to detect infratentorial or spinal cord lesions. The reason for this is unknown but most likely reflects different relaxation characteristics in those regions, both in normal-appearing tissue and in lesions. For example, T1 and T2 relaxation times of infratentorial lesions in patients with multiple sclerosis are closer to the relaxation times of local normal-appearing white matter than those of supratentorial lesions, resulting in reduced contrast between posterior fossa lesions and the background. Age-related increases in T1 relaxation times of human brain also have been shown, particularly in the thalami, and may serve to explain the lack of sensitivity of FLAIR for thalamic lesions in elderly patients with VaD.

Alternatively, the occurrence of cystic changes in lacunar infarctions will lead to a prolongation of T1 relaxation time, and the signal from these lesions may be suppressed, as in CSF spaces. The same may occur with multiple sclerosis lesions severely hypointense on T1-WI. MRI-pathological correlation studies performed to determine the background of age-related subcortical gray and white matter hyperintensities on T2-WI found different types of pathology: infarctions, gliosis, myelin and axonal loss, breakdown of the ependymal lining, and enlarged perivascular spaces. Areas of myelin pallor can be hypointense on T2-WI but isointense on T1-WI, and it seems possible that differences in type of pathology can also influence detection on FLAIR.

Although the proposed neuropathological classification of lacunae includes both ischemic (type I) and hemorrhagic (type II) vascular abnormalities and enlarged perivascular spaces (type III), in VaD it is important to differentiate the vascular lesions. MRI-pathological correlation studies found that the great majority of enlarged perivascular (Virchow-Robin) spaces normally surround perforating arteries that enter the striatum in the anterior perforated substance, just above the internal carotid artery bifurcation and lateral to the anterior commissure. They are responsible for the so-called état criblé of the basal ganglia and are much less frequently located in the thalami. Therefore, it is unlikely that those lesions classified as cystic infarctions on the basis of MRI are in fact Virchow-Robin spaces or could account for the greater number of lesions detected on T2-WI. Actually, FLAIR performed more poorly for all types of presumed pathology.

A limitation of our study is that we used images acquired on a wide range of scanners and sequences, not all of which

<table>
<thead>
<tr>
<th>TABLE 3. Detection on FLAIR and Signal on T2 and T1-WI</th>
</tr>
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<tbody>
<tr>
<td>Detected on FLAIR</td>
</tr>
<tr>
<td>Hyperintense on T2-WI</td>
</tr>
<tr>
<td>Isointense on T1-WI</td>
</tr>
<tr>
<td>Hypointense on T1-WI</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
may be optimally tuned. On the other hand, this reflects the normal variability of vendor-supported sequences, and given the more complex contrast mechanisms in FLAIR, these may be less stable than for T2-WI. For the detection of type II hemorrhagic lacunae, both spin-echo and FLAIR are insensitive compared to T2*-WI gradient-echo sequences. But these were not available in the context of this trial. Nevertheless, we detected a fair amount of probable microbleeds.

In conclusion, the accuracy of T2-WI for the detection of thalamic lesions in patients with probable VaD is far superior to FLAIR. Given the great clinical importance of these lesions, FLAIR should not be used as the only T2-weighted sequence in patients suspected of having VaD.

In addition to the posterior fossa and spinal cord, the diencephalon seems to represent another region not suitable for evaluation by FLAIR MRI.

### References


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