Grading white matter lesions on CT and MRI: a simple scale

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Abstract
We developed and tested a simple three-point scale for grading white matter lesions in anterior and posterior regions of the brain. Twenty four CT scans and 24 MRI scans were separately judged by 11 and five observers, respectively, on the presence and severity of white matter lesions. The observers were radiologists and neurologists. For CT scans, these periventricular changes were graded according to their extent as absent, or partly involving the white matter, or extending up to the subcortical region. The MRI lesions were graded as no lesion or only a single one, multiple focal lesions, and multiple confluent lesions. The pairwise agreements of all possible combinations of observers for each scan were corrected for chance (kappa statistics; maximal agreement 1-0). The weighted kappa value, for anterior and posterior regions combined, was 0.63 for CT scans, and 0.78 for MRI scans. This three-point scale for two separate regions seems suitable as a basis for cross-sectional or longitudinal studies of large series of patients.

Periventricular leukoencephalopathy is a more or less symmetrically diminished density of the white matter on CT scans of elderly individuals.1-5 The frontal and the parieto-occipital white matter are most often affected, although not always to equal degrees,6 frequently in association with ventricular enlargement. Magnetic resonance imaging (MRI) has proved more sensitive in detecting white matter lesions than CT.7-9 The hypodense lesions on CT correspond with areas of increased signal intensity in T2 weighted MRI. They are most often found in patients with stroke, hypertension or dementia.10-16 Neuropathological studies have shown that these lesions on CT or MRI correspond with demyelination, astrocytic gliosis, arteriolar sclerosis, or dilated perivascular spaces, and are often associated with lacunar infarcts.17 18

Further studies of the incidence, causes and prognosis of periventricular white matter lesions are impeded by the lack of reliable criteria for the presence and severity of these lesions. The presence of white matter lucencies on CT has in some cases been quantified in Hounsfield units,11 12 but in most previous studies a subjective assessment was made of the extent or degree of attenuation of these lesions at one site, compared with the surrounding brain.10 12 17 19 20 Other CT studies have distinguished different types according to the anatomical distribution of white matter lesions, but did not take account of the severity.13

In MRI studies, a variety of scales has been used for measuring the severity of white matter lesions. In most cases two categories of lesions were distinguished that often occur together, that is, periventricular lesions and focal lesions.14-16 21-26 Sometimes these lesions have been separately graded22 24 and elsewhere they were taken together.21 22 27 The extent of the periventricular lesions in the white matter may range from narrow rims around the frontal horns to thick bands extending deep in the white matter, and focal lesions may be single, multiple or confluent.

Whether these white matter lesions imply functional impairment is not entirely clear. Studies about cognitive functions in patients with white matter lesions on CT or MRI have given conflicting results.18 20 24-26 Although this may have been caused by differences in patient selection, another and perhaps neglected factor may be the severity of the lesions in the frontal or parieto-occipital white matter. In future studies in which periventricular leukoencephalopathy is related to function or to future events, white matter lesions on CT or MRI should be graded according to both the anatomical pattern and the severity.

An ideal rating scale for white matter lesions on CT or MRI should meet the following requirements. First, it should include the anatomical distribution as well as the severity of white matter lesions, with clear definitions for the different categories. Secondly, the scale should be simple. Finally, the reliability of the scale should be assessed in an inter-observer study. One such study has been reported, but without mention of the type of scale or the actual measure of agreement.29 In this study, we have developed a scale for CT and another for MRI, consisting of similar categories for anterior and posterior regions, but with different definitions for the kind of lesions on CT or MRI. We determined the extent of agreement among different observers by means of kappa statistics, which accounts for chance agreement.

Methods
A method for systematic evaluation of the
white matter lesions on CT and MRI was gradually developed in small and repeated interobserver studies; the results with a more sensitive scale (four grades for different regions) have not been included in this report, because of considerable disagreement. We finally distinguished two regions that are most frequently affected: one region around the anterior horns of the lateral ventricles, and another consisting of the white matter around the posterior part of the cella media and the posterior part of the centrum semiovale. White matter lesions in these two regions of interest were separately evaluated on three subsequent CT or MRI slices: one through the choroid plexus of the posterior horns, one through the cella media, and one through the centrum semiovale (fig 1). These three levels can be considered representative of the total white matter, since they include the largest cross-sectional areas.

**MRI assessment**

Twenty four MRIs, obtained from a study of elderly hypertensive patients, were selected to represent an even distribution according to the severity of white matter lesions, judged by increased signal-intensity on T2-weighted images. All MRI were performed with a 1.5 T Philips gyrosan. Multiple slice spin-echo (SE) sequences were performed with a repetition time (TR) of 2000 ms and an echo time (TE) of 50 and 100 ms, producing a T2-weighted image. A heavily T1-weighted image was produced with a TR of 1500 ms, an inversion time (TI) of 575 ms, and a TE of 30 ms. Five observers were asked to grade the severity of the white matter lesions in the same slices as for CT assessment, again separately for the anterior and posterior region, in one of three categories. Focal lesions were judged present when the diameter was 1 mm or more on the hard copy images (true dimensions approximately 2 mm). The severity of the lesions was graded according to their number and configuration: grade 0, no lesion or only a single one; grade 1, multiple focal lesions; grade 2, multiple confluent lesions scattered throughout the white matter. Since periventricular lesions nearly always accompanied focal or confluent lesions, we did not grade these separately. The grades for the two regions were considered separately as well as added together.

**Statistical analysis**

The degree of agreement among many observers was expressed by means of kappa statistics. Kappa values were calculated for each CT or MRI, and for all possible combinations of the 11 and five observers, respectively. For the grades with both regions added
together, kappa values were corrected by taking the
degree of disagreement into account
(weighted kappa). In doing so, we attributed
twice as much weight to a difference of two
grades as to a difference of one grade, and three
times as much weight to a difference of three
grades (linear disagreement weights). Kappa
values range between 0 (only chance
agreement) and 1 (perfect agreement).

Results
CT assessment
With 11 observers, each set of scans of one
patient gives rise to 55 pairwise comparisons,
and with 24 scans the total number of
comparisons is 1320. The kappa value for the
anterior region alone was 0.51, and for the
posterior region 0.57. When the grades of both
regions were added together, the overall kappa
value was 0.42, with a weighted kappa of 0.63
(table). One region was considered more affected
than the other in 104 of 264 assessments.

On separate analysis of CT images made
with the third generation scanners, the weighted
kappa values were similar to those of the
total series. In a further study with the same 24
CT scans, five of 11 observers were explicitly
instructed to give separate grades for the
anatomical extent of hypodensity and for the
degree of radiolucency of the white matter;
subsequently, they were asked to combine both features by attributing one grade. The interobserver agreement for the degree of radiolucency
was equal to that of the anatomical extent, and
the combination of these separate features did
not lead to better agreement than in the first
round.

MRI assessment
With five observers and 24 scans, the number
of comparisons was 240. Perfect agreement for
white matter lesions existed in 190 of these for
the anterior region, and in 183 for the posterior
region. The kappa value for the anterior region
was 0.68, and for the posterior region 0.65.
When the two grades were added together, the
overall kappa value was 0.60, and the weighted
kappa 0.78. One region was graded as more
severely affected than the other in 34 of 120
assessments.

Discussion
The reliability in measuring the severity of
white matter lesions on CT and MRI has received little attention so far. An unequivocal grading scale is necessary for quantifying this
abnormality, particularly in clinical and
radiological studies involving large numbers of
subjects, with cross-sectional or longitudinal
design. The kappa values for assessments of the
two regions with MRI (0.68 and 0.65) were
higher than those for CT assessments of the
same regions (0.51 and 0.57). The weighted
agreements with the CT and MRI scale were
0.63 and 0.78, respectively, and these values
can be considered good. That inter-observer agreement is lower for CT than for MRI may be mainly caused by the
ill-defined margins of hypodensity on CT scan,
which often makes the differences with normal
white matter small. Another complicating fac-
tor with CT are partial volume effects with
cerebrospinal fluid or grey matter. Finally,
lacunar infarcts often occurred in our series, as
in other reports, and these are sometimes
difficult to distinguish from diffuse leuko-
encephalopathy, if the lacunes are only faintly
seen on CT.
The severity of white matter lesions on MRI showed considerable variation. The greater image contrast of these lesions with the surrounding normal brain allows more reliable assessment. Moreover, exact measurement of the size of these lesions is possible. In two recent small series of patients, the diameter of these lesions has been measured and added together. The three standardised axial levels for assessment in this study also offer the opportunity of measuring the cross-sectional areas of MRI lesions, and of detecting changes in longitudinal studies.

We found that the lesions in anterior or posterior white matter were not equally severe in about a third of the CTS and MRSI in our series. Also, the involvement of certain deep subregions, such as the internal or external capsule, is a conspicuous feature in some cases. In two CT studies, the extent of abnormal lucencies were assessed in several regions, resulting in a very sensitive summed score. In one MRI study, the size of the lesions has been measured in four regions and added together. However, this method results in greater interobserver disagreement, and it makes the scale impractical for use in large series of patients. It is unknown whether the distribution of lesions between anterior and posterior regions is only a matter of chance or whether it has pathogenetic significance. In view of the conflicting results about the existence of neuropsychological impairment in patients with white matter lesions, the distinction in anterior and posterior regions may be helpful.

In conclusion, the use of the three-point scale for white matter lesions on CT and MRI is suitable for analysing large series of patients. The three-point rating scale for MRI lesions in two regions has already been fruitfully applied in a recently completed study of elderly hyperensive patients.

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