

# Characterization of Cerebral Microangiopathy Using 3 Tesla MRI: Correlation With Neurological Impairment and Vascular Risk Factors

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**Purpose:** To investigate whether clinical and neuropsychological impairment in cerebral small-vessel disease (CSVD) can be evaluated by means of morphological magnetic resonance imaging (MRI).

**Materials and Methods:** MRI at 3 Tesla in T2- and T1-weighted sequences was evaluated in 44 patients with cerebral microangiopathy, and 30 patients with combined cerebral micro- and macroangiopathy. The MR characteristics were correlated to clinical data, attentional impairment, and the patients' individual vascular risk factor profiles. Fifteen healthy age-matched control subjects participated in the study to assess MR signal changes in nonhypertensive elderly subjects.

**Results:** Patients and normal controls differed significantly in the extent of MR signal changes. A close relation between age, obesity, hypertension, and MR signal abnormalities was evident in all patients. Patients with pure CSVD additionally showed an association between their MR-defined severity of disease and their degree of neurological impairment, and their vascular risk score. In contrast, attentional impairment did not relate to the MR-defined severity of CSVD.

**Conclusion:** MR signal changes in CSVD show a close relationship to some risk factors of individual patients.

**Key Words:** MR rating score; high-resolution MRI; vascular risk profile; attentional impairment; cerebral microangiopathy; minor stroke syndrome

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HIGH-RESOLUTION MAGNETIC RESONANCE IMAGING (MRI) has tremendously improved the detection of morphological brain abnormalities in general, and of qualitative changes of the brain parenchyma in particular. These predominantly concern alterations of the white matter, and promise an improvement in the clinical characterization of neurological diseases associ-

ated with morphological abnormalities in this compartment. Cerebral small-vessel disease (CSVD) is the common pathological feature of a series of subtypes of cerebral microangiopathy (1-3). The structural damage of the deep white matter is due to a perfusion deficit caused by an undefined mechanism and resulting in a variety of clinical symptoms, neuropsychological abnormalities, and MRI characteristics.

In clinical terms, the co-occurrence of minor stroke symptoms, such as pure motor or sensory stroke, and a history of hypertension are suggestive of CSVD. Still, subclinical neurological and neuropsychological signs may considerably vary in CSVD. Occasionally they are mild, and therefore are easily overlooked in everyday clinical practice, thus obscuring the clinical diagnosis. The association between the degree of clinical and neuropsychological impairment and imaging characteristics in CSVD has been investigated in several previous studies (4-7). Unfortunately, a comparison of their results is hampered by differences in terminology and in the scales used for grading the severity of MRI signal changes. For these reasons, MRI has not yet contributed to a better understanding of the underlying etiology and pathology of CSVD, but rather has added to the diagnostic complexity of this disease. More importantly, the true grade of tissue alteration remains unclear, in spite of its precise visualization. To complicate matters further, MRI has revealed a wide spectrum of age-associated brain abnormalities (8), mainly consisting of hyperintense foci in the deep and subcortical white matter, and of signal hyperintensities around the lateral ventricles. Although it has been suggested that these MRI abnormalities may contribute to the development of cognitive impairment, their correlation with neuropsychological dysfunction is limited. A threshold beyond which such a relation may exist has not yet been defined. Thus, differentiation between age-related white matter changes and those related to CSVD is currently not possible.

This study aimed to set the basis for a more selective approach towards the clinical significance of white matter signal changes. For this purpose, we reevaluated high-resolution MRI on a cohort of 74 patients with pure CSVD or combined cerebral micro- and macroangiopathy, and sought to relate the observed morphological abnormalities to individual clinical and neuropsych-

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chological data. It has been argued earlier (9) that the nature and extent of white matter changes is associated with the stroke subtype and outcome. Additionally, the vascular risk profiles of individual patients were compared to the MR abnormalities, to evaluate the hypothesis that the vascular risk profile determines the morphological abnormality (10).

## MATERIALS AND METHODS

### Selection of Patients and Controls

A total of 74 patients (19 females and 55 males; mean age:  $59.4 \pm 8$  years) with typical neurological symptomatology of CSVD (such as motor stroke, sensory stroke, atactic hemiparesis, and dysarthria (clumsy hand syndrome)) and a history of hypertension were included in this MR study. The patients were under examination by the Daycare Clinic of Cognitive Neurology, University of Leipzig, and received morphological MRI as well as an extensive clinical investigation. Depending on accompanying cerebral macroangiopathy, the patients were divided into two subgroups for further evaluation: group A, pure cerebral microangiopathy ( $N = 44$ ); and group B, combined cerebral micro- and macroangiopathy ( $N = 30$ ).

Cerebral microangiopathy was declared when both the typical neurological symptomatology and white matter MR signal changes were assessed. Cerebral macroangiopathy was declared when, according to recently published criteria, territorial or watershed cerebral infarctions were diagnosed on MRI. Patients of group B were included in the chronic stage of macroangiopathy, i.e., the onset of symptoms was  $>8$  months prior to participation in our study. Additionally, patients of group B had all been diagnosed with CSVD due to minor stroke events and had a known history of hypertension for at least 1 year. The selection of the two patient groups was chosen to address different issues: 1) the correlation of clinical deficits and MR abnormalities (group A), and 2) the influence of cerebral macroangiopathy on MR abnormalities in CSVD (group B).

A comprehensive clinical examination, including medical history, physical, and detailed neurological examinations was performed. The Scandinavian Stroke Scale (SSS) (11) was applied to assess the degree of neurological impairment. The scores generally range from 2 to 58. The lower the score, the more severe are the neurological deficits; 58 points indicate no neurological impairment. A vascular risk factor profile was assessed in each individual patient, including the following categories: smoking status (packs/day), diabetes, arterosclerosis, fat metabolism, obesity (body mass index (BMI)  $> 30$ ), hypertension, and elevated serum level of homocystein. According to the amount of risk factors present in each individual patient, a risk factor score was calculated ranging from 1 to 7.

At the time of this investigation, CSVD patients exhibited only residual symptoms of their previous neurological complaints. Morphological T2- and T1-weighted MRI was performed in all patients. Moreover, 15 age-matched control subjects (six females and nine males; mean age:  $59.7 \pm 17$  years) underwent MRI to evaluate T2 and T1 MR signal changes in nonhypertensive elderly subjects.

### Neuropsychological Assessment

Neuropsychological testing concentrated on evaluating cognitive deficits in the domain of attention. Attentional processes were assessed using the subtests Alertness, Divided Attention, and Go/No-Go from the "test of attentional processes" (TAP) (12). The Alertness test measures simple reaction times to a briefly presented stimulus (tonic alertness), and thus approximates the subject's cognitive information-processing speed. In a second phase, a warning is presented immediately before the critical stimulus. Thus, the difference between reaction times with and without warning can be calculated (phasic alertness). The Divided Attention test measures the ability of the subject to react simultaneously to visual and auditory stimulus configurations. The Go/No-Go test serves as a measure of selected attentional processes. According to abnormal test values in the three domains—tonic, phasic, and divided attention—the overall impairment was rated from 0 to 3 degrees of severity, with 0 indicating normal test values and 3 indicating pathological results in the three attentional subtests.

### MRI Protocols

All investigations were performed using a Bruker 3 T/100 Medspec, whole-body system. Signal transmission and reception were performed using a 28-cm i.d. quadrature birdcage resonator. Either a whole-body gradient set (30 mT/m switchable within 500  $\mu$ s) or a head gradient insert (Magnex: 40 cm i.d., 35 mT/m, 150  $\mu$ s switching time) were employed. Each patient underwent morphological MRI, using T2- and T1-weighted sequences in the axial plane.

T1 was performed using a multislice MDEFT sequence (13). The special feature of the particular sequence used (14) is that a single non-slice-selective inversion pulse is used to obtain data from a number of slices, with each resulting image having an identical contrast and reduced inflow effects. The use of a single inversion pulse drastically reduces the amount of RF power required, an important consideration at 3T. The sequence used here obtained one line of k-space data from each slice per inversion pulse, using a 10-msec inversion pulse and 4-msec  $90^\circ$  sinc excitation. Other parameters were: FOV = 250 mm, slice = 5 mm, gap = 2 mm, TR = 2, TI = 650 msec, acquisition matrix =  $256 \times 252$  reconstructed to  $256 \times 256$ , TE = 9.2 msec, and acquisition bandwidth = 20 kHz.

T2 was performed using the rapid acquisition with relaxation enhancement (RARE) imaging sequence with the following parameters: geometry as above, matrix =  $512 \times 512$ , acquisition bandwidth = 50 kHz, TE = 19 msec, effective TE = 133 msec, RARE factor = 16, refocusing pulse angle =  $120^\circ$  (to reduce the specific absorption rate (SAR)), and TR = 8.5 seconds.

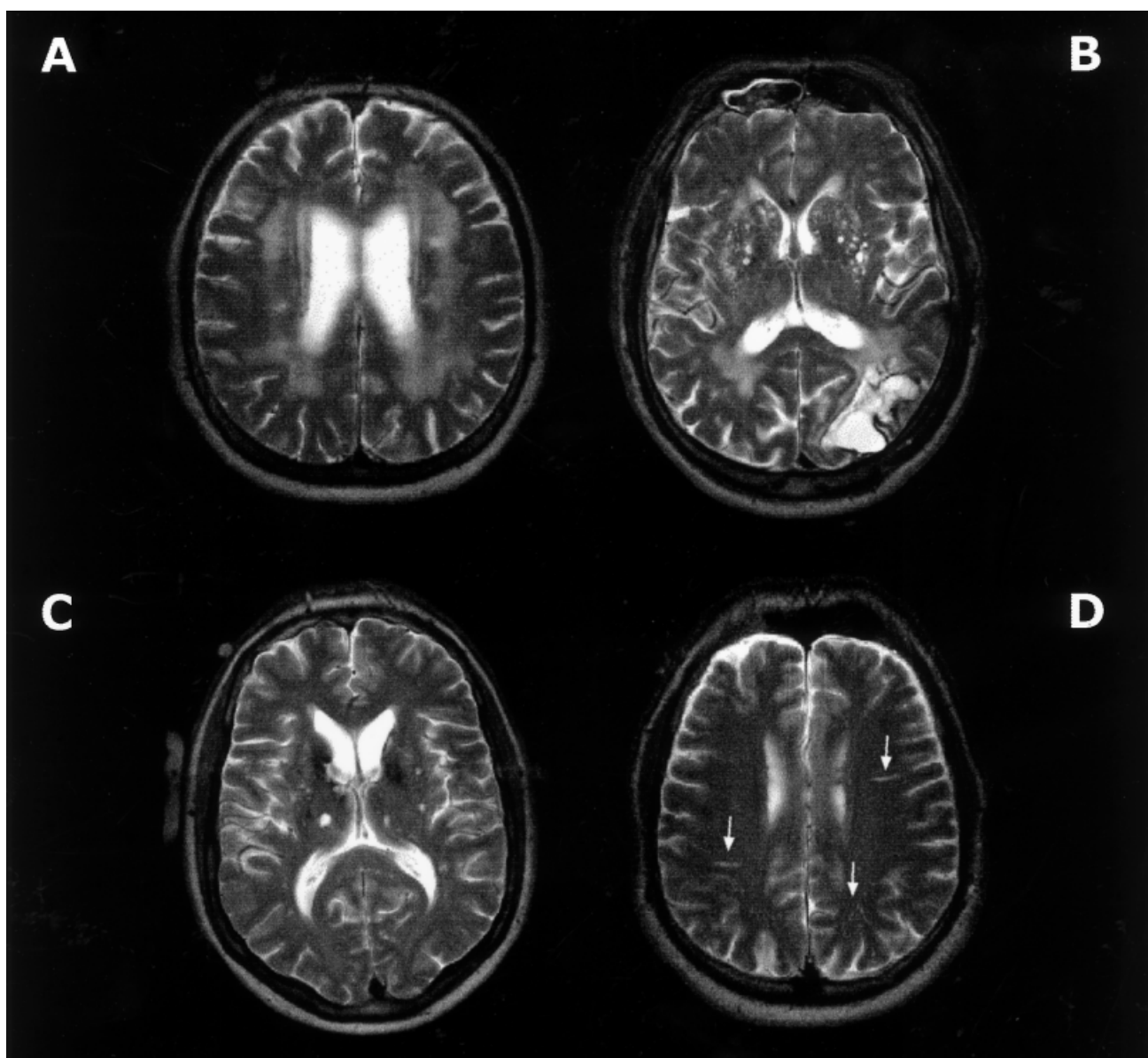
### MR Rating Procedure

Because of the lack of a generally accepted score for quantifying the severity of MR signal changes associated with CSVD (15), a special score was developed based on 2D factors. An extended version of the simple three-point scale for grading white matter lesions in

anterior and posterior regions of the brain, developed and tested by van Swieten, et al (16), was employed. The presence and severity of white matter lesions was graded according to their extent and uni- or bilateral distribution on the T2-weighted scan. Vascular lesions, such as lacunes, were graded by their appearance as a focal single lesion or as multiple focal lesions, and multiple confluent lesions. In an extension of the van Swieten scale, the occurrence of periventricular caps and rims were graded with one to three points each, depending on the extent of MR signal changes. Furthermore, the degree of "état criblé" of the basal ganglia was assessed and graded, depending on unilateral focal, global, or bilateral involvement. Additionally, brain stem involvement was graded with one to three points.

As a marker of early CSVD, the appearance of small hyperintense vessel lines in the periventricular white matter was evaluated. In addition to its presence on the T2-weighted scan, the T1 sequence was scanned for the vessel sign. The visibility of changes on both T2 and T1 indicate a higher degree of morphological impairment. These are caused by susceptibility gradients around the vessels and become visible at 3T imaging. The hyperintense small vessel sign can be masked fully in standard clinical MR scanners, especially when lower-resolution matrices are chosen. Figure 1 visualizes the typical MR signal changes in CSVD, which were rated in this study.

MR scoring was performed by two blinded, neurologically expert investigators. Scores theoretically



**Figure 1.** Abnormal MR signal changes on the T2-weighted image are the basis of the performed MR staging. (A) Periventricular caps and rims, and the degree of diffuse white-matter hyperintensities were rated, as well as (B) the severity of basal ganglia involvement and (C) the presence of lacunar infarcts. The enlargement of perivascular spaces, referred to as (D) the hyperintense vessel sign, was also evaluated. The hyperintense vessels are marked by white arrows. The applied MR score is based on an extended three-point scale developed by van Swieten, et al (16). Scores range from 0 to 21; the higher the score, the more MR abnormalities were assessed.

range from 0 to 21. The severity of CSVD was assessed based on the MR score: <6 points = low-degree CSVD, 6–12 points = moderate severity, and >12 points = severe CSVD. The interobserver agreement (Cohen's kappa) was also assessed (17).

### Statistical Analysis

Analyses were conducted using computerized statistical software (version 5.01, SPSS Inc., Chicago, IL). Independent *t*-tests were used to test differences between the two patient groups and the normal controls. Normally distributed data were expressed as mean  $\pm$  standard deviation. A *P*-value of <0.05 was considered statistically significant. To assess the relationship between clinical data and the spatial distribution and extent of MR signal changes, bivariate correlation analysis using Pearson's coefficient was performed. Age, sex, smoking status, and other vascular risk factors, as well as baseline diseases such as hypertension and diabetes, were introduced as possible dependent variables and related to the MR signal changes. Moreover, multiple analyses of variance (ANOVAs) were executed to determine which parameter or combination of parameters was directly associated with the MR signal changes. The following factors were introduced into the ANOVA: 1) the risk factor profile, 2) the neurological score, and 3) the neuropsychological score. The resulting *F* values are a measure of the explained variance to these factors. Calculation of significance levels yielded the contributors that had a significant influence on the observed changes.

## RESULTS

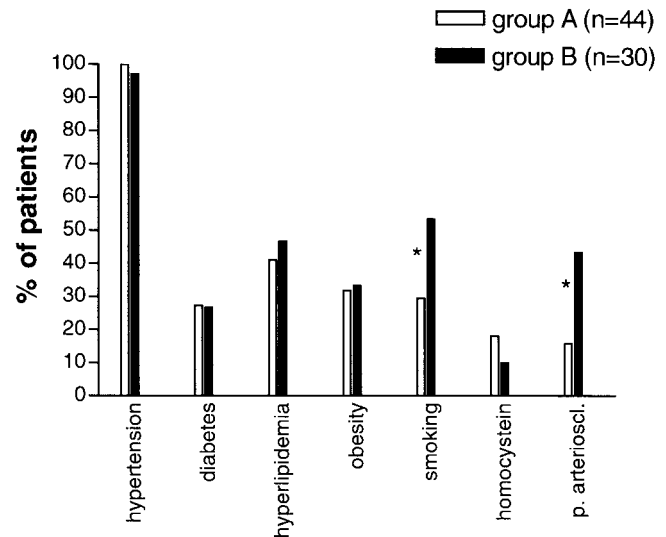
### Clinical and Neuropsychological Characterization of Patients

#### Neurological Impairment

At admission, residual neurological deficits, such as slight motor paresis of the upper or lower limb, supranuclear facial paresis and residual oculomotor disturbances, dysarthria, and residual paraesthesia, were present in 32 out of 44 patients in group A. Two patients suffered from limb-kinetic ataxia. SSS scores, assessed prior to the MR session, ranged from 40 to 58, indicating no or mild-to-moderate neurological deficits. The mean score was  $49 \pm 9$ . In contrast, all patients of group B experienced more severe residual symptoms (even in the chronic stage of macroangiopathy), such as sensory motor paresis, hemianopia, and aphasia. Stroke scores were below 45 points in all patients, with a mean of  $39 \pm 6$ , which was significantly different from the mean score assessed in group A ( $P < 0.05$ ).

#### Attentional Impairment

Difficulties in learning and retention of newly acquired information were reported in 54 patients. A further complaint was the inability to adapt to normal everyday and family life after discharge from the hospital. Attentional impairment concerned 71.9% of group A patients, 28.1% had normal test values, 18.8% showed abnormal scores in one attentional domain, 15.6% were impaired in two attentional subtests, and 37.5% had severe problems throughout attentional testing. In



**Figure 2.** Comparative distribution of risk factors in patients with pure CSVD (group A) and concomitant macroangiopathy (group B).

group B, 9.1% of patients had normal attentional test scores, 31.8% were impaired in one subtest, 22.7% showed abnormal values in two subtests, and 36.4% had severe problems throughout attentional testing. The overall attentional score did not differ significantly between groups A and B. A significant difference between groups was found for the subtest Divided Attention (group A:  $12.84\% \pm 9\%$ ; group B:  $3.58\% \pm 4\%$ ,  $P = 0.008$ ).

#### Vascular Risk Profile

With respect to vascular risk factors, all patients of group A exhibited chronic hypertension, 27.3% suffered from diabetes mellitus, 40.9% showed a disturbed fat metabolism (hyperlipidemia), 31.8% suffered from obesity (BMI > 30), 18.2% had elevated homocystein serum levels, and 29.5% smoked more than one pack per day. Moreover, 15.9% suffered from peripheral arteriosclerosis, and 63.2% of the patients had more than one risk factor.

In group B the distribution of risk factors was as follows: chronic hypertension 97%, diabetes 26.7%, adipositas 33.3%, hyperhomocysteinemia 10%, hyperlipidemia 46.7%, smoking 53.3%, and peripheral atherosclerosis 43.3%. Two or more risk factors were exhibited by 86.7% of the patients. The mean risk factor profiles of the two patient groups differed significantly (group A:  $3.1 \pm 1.3$ ; group B:  $4.0 \pm 1.6$ ,  $P = 0.02$ ). The distribution of risk profiles within the two patient groups is displayed in Figure 2.

#### Morphological MRI

MRI at 3T, particularly the T2-weighted sequence, allowed the characterization of detailed white-matter abnormalities in the group of patients and normal controls. The overall interobserver agreement was high: 92% ( $N = 67$ ) of patients received identical scores from the independent raters. A kappa coefficient (according to Cohen) of 0.81 was assessed. No disagreement occurred in the classification of mild microangiopathy. All

patients who had received different scores were found in the groups showing moderate and severe MR abnormalities. Moreover, assessment of T1 and T2 agreement of the hypertense vessel sign did not coincide in 10 patients. In the cases that were not rated equally, MRI scans were reevaluated by both observers for a final verdict.

In the group of age-matched controls, only a few white-matter abnormalities were detected, such as small hyperintense vessel lines in the periventricular white matter in five subjects and small periventricular caps in another three subjects. MRI scores ranged between 0 and 3.

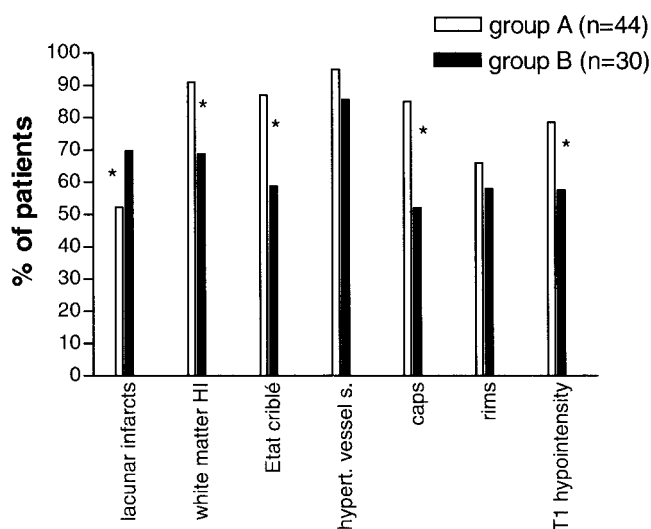
In the patient group, overall MRI scores ranged from 4 (indicating a minor degree of microangiopathic MR changes) to 18 (indicating severe MR abnormalities). The occurrence and distribution of MR abnormalities is summarized in Figure 3. According to the MR rating in group A, 36.4% had slight CSVD, 52.2% had moderate CSVD, and 11.4% had severe CSVD. In group B, 26.7% of patients had slight, 46.7% had moderate, and 26.7% had severe CSVD according to MR criteria. With respect to the overall MR score, no significant difference was found between the two patient groups ( $P > 0.05$ ). However, controls and patients differed significantly ( $P < 0.001$ ).

In group A, 52.3% of patients had lacunar infarcts, and white-matter hyperintensities were seen in 90.9% of patients. Basal ganglia involvement was present in 87% of patients, while brainstem involvement occurred in 22% of all patients. Basal ganglia involvement and confluent white-matter hyperintensities were extensively present in patients with high scores of MR changes, whereas the hyperintense small vessel sign was seen in 95% of patients and even appeared with a high three-point score, when only a few other MR abnormalities were present on the T2-weighted scan. In 78.5% of cases, the vessel sign was found on the T1-weighted MR scan (Fig. 3). Caps and rims were detected, to varying extents, in 88% of all patients.

In group B, lacunar infarctions were diagnosed in 66.7% of patients, and white-matter hyperintensities were found in 68.7% of patients. Basal ganglia involvement was assessed in 58.7% of patients, and brainstem involvement was found in 13.5% of patients in group B. The hyperintense vessel sign received lower rankings in the group of combined micro- and macroangiopathy as compared to group A, and was present in 85.6% of patients on the T2-weighted sequence. In contrast, appearance of the hypertense vessel sign on T1 was assessed in 57.5% of patients. A significant difference between patient groups was found with respect to white-matter hyperintensities: group A had a mean score of 1.3, while group B showed a mean score of 0.8 ( $P < 0.05$ , *t*-test for unpaired samples).

### Correlations of MR Signal Changes and Clinical Data

To address the question of whether the degree of MRI signal changes can serve as a diagnostic tool for judging the severity of clinical and neuropsychological deficits



**Figure 3.** Comparative distribution of MR characteristics in patients with CSVD (group A) and concomitant macroangiopathy (group B), which are the basis of the applied MR rating scale.

in CSVD, the association between MR scores and various other clinical data was examined. The results are shown in Table 1.

The MR score did show the strongest association with the severity of CSVD as defined by the neurological score ( $r = 0.87$ ,  $P < 0.001$ ). Only patients of group A were included in this analysis ( $N = 44$ ). Statistically significant close correlations for the entire patient group ( $N = 74$ ) were found for MR score and age ( $r = 0.27$ ;  $P = 0.04$ ), MR score and obesity ( $r = 0.34$ ,  $P = 0.08$ ), and MR score and hypertension ( $r = 0.29$ ,  $P = 0.02$ ). In contrast, no significant relations were found between MR abnormalities and the presence of diabetes, elevated homocystein, hyperlipidemia, smoking status, and peripheral atherosclerosis. No significant relation was found between morphological impairment and attentional deficits in the patients ( $r = -0.38$  and  $P = 0.32$ , and  $r = 0.14$  and  $P = 0.67$ , respectively). The results of the correlation analysis performed separately for the two groups yielded further interesting relations with respect to group A: the MR-defined severity of CSVD was associated with the duration of hypertension and with the vascular risk factor profile. In particular, enlargement of the perivascular space had a close and significant relation with the clinical parameter hypertension and duration of hypertension ( $r = -0.35$ ,  $P < 0.04$ ). Moreover, visibility of MR signal changes on the T1 image related to higher severity of disease as defined by T2-defined criteria in group A ( $r = 0.38$ ,  $P = 0.03$ ).

ANOVA revealed those factors that showed a significant relation to the assessed MR signal changes. The following F values were found in group A: neurological score ( $F = 3.13$ ,  $P = 0.034$ ), risk factors score ( $F = 2.37$ ,  $P = 0.095$ ), and neuropsychological score ( $F = 0.4$ ,  $P = 0.42$ ). Thus, calculation of significance levels identified only the stroke score as having a significant influence on the observed MR signal changes. In group B no significant influence was detected by ANOVA.

**Table 1**  
Correlations Between MR Defined Severity of CSVD and Clinical Data

Correlations of MR abnormalities and clinical data	All patients <sup>a</sup> (n = 74)	Group A <sup>a</sup> (n = 44)	Group B <sup>a</sup> (n = 30)
Age	0,40	0,45*	0,37*
Scandinavian stroke score	—	−0,87**	—
Attentional impairment	0,03	0,03	−0,01
Vascular risk score	0,25	0,40*	0,14
Hypertension	0,28*	0,46*	0,01
Duration of hypertension	0,25	0,45*	0,07
Diabetes	0,14	0,29	−0,05
Homocystein >15 μmol/liter	−0,05	−0,23	−0,23
Hyperlipidemia	−0,11	0,12	−0,17
Obesity	0,34*	0,39**	0,18
Smoking status	0,09	−0,22	0,05
Peripheral arteriosclerosis	0,14	0,02	0,20

<sup>a</sup>Significant correlations: \* $P \leq 0.05$ ; \*\* $P < 0.001$ .

## DISCUSSION

This study focused on MR signal changes related to CSVD with and without concomitant macroangiopathic vascular lesions. The MR abnormalities detected in the patient groups were compared to those in an age-matched control group. Our first major finding was that our MR scores clearly allow a differentiation between patients and normal controls. In the literature, there is no agreement regarding the clinical relevance of diffuse white-matter hyperintensities when they occur in elderly healthy people (18,19,20). Hyperintense periventricular capping of the frontal and parietal horns, and a smooth halo of periventricular hyperintensity—as assessed in some of our normal controls—have been linked to disruption of the ependymal lining, subependymal gliosis, and concomitant loss of myelin. However, larger patchy and confluent hyperintensities that have been described as indicating more extensive ischemic damage consistent with advanced CSVD were absent in our controls. Nonvisibility of the slight abnormalities in the control group on the individual T1 image supports the absence of relevant ischemic damage. As indicated by low MR ratings scores, the white-matter changes in our controls were only minor, a finding that was reported previously for larger cohorts of normal individuals (4).

We also addressed the question of whether CSVD with (group A) and without (group B) concomitant macroangiopathy can be differentiated based on the presence and distribution of MR patterns. Several significant differences were found. Group A patients showed significantly more white-matter hyperintensities and basal ganglia involvement, as compared to those in group B. Furthermore, rankings of the hypertense small vessel sign as a measure of the perivascular space enlargement were significantly higher in group A than in group B. The issue of microangiopathic changes in concomitant macroangiopathy has been addressed previously (21,22). These authors found significantly higher scores for periventricular hyperintensity, white-matter hyperintensity, basal ganglia hyperintensity,

and total subcortical hyperintensity scores in their group of pure CSVD compared with the group that exhibited macroangiopathy as well. The enlargement of the perivascular space was also significantly greater in their CSVD group than in their macroangiopathic group. Our results are in accordance with these findings, and seem to reflect differences in the pathogenesis of infarction between the two groups. Silent subcortical hyperintensity lesions and enlargement of perivascular space are useful for distinguishing between white-matter signal changes resulting from large-vessel disease and pure CSVD. This may have significant implications for the management of patients with lacunar infarctions. It suggests that the pathogenesis of lacunar infarction is variable and may necessitate additional screening for accompanying cerebral macroangiopathy.

A further goal of this study was to investigate the relationship between imaging data and neurological and attentional impairment, as well as the individual vascular risk profile. Age, severity of hypertension, and obesity were significantly related to the MR-defined pathology in all patients. While no other relationship was found in group B, further significant correlations were observed in group A. MRI-based CSVD severity significantly correlated with the degree of neurological impairment, as assessed by the SSS, and chronic hypertension and its duration. Thus, we conclude that the hypertense vessel sign on the T2 image is an appropriate measure of the influence of hypertension even in an early stage of the disease. A close association between elevated blood pressure and confluent white-matter hyperintensities and their progression was also described in an earlier follow-up study in patients (23), while a similar relation between age, blood pressure, and MR-defined lacunar infarctions was observed in a large cohort of elderly normal controls by Shintani and coworkers (5).

We used the presence of T1 hypointensity of white-matter changes as a further valid measure to differentiate between pathological and age-related morphological changes. This phenomenon occurs regardless of the field strength of the scanner. Hypointense lesions on conventional T1-weighted MRI within areas of white-matter damage clearly indicate more extensive tissue destruction, i.e., lacunar or even larger infarcts. Such changes have been shown to be almost invariably associated with pronounced CSVD consisting of lipohyalinosis and fibrohyalinosis (24).

Attentional impairment assessed by alertness testing did not correlate with the degree of MR abnormalities. As attention, and in particular alertness, is a measure of cognitive processing time, a clear correlation between attentional parameters and the degree of white-matter hyperintensities representing loss of fibers and reactive gliosis would be assumed. However, according to previous reports (25), no linear worsening of cognitive functions accompanies the increase of white-matter changes of CSVD as assessed by T2-weighted MRI. On the contrary, it was assumed that cognitive impairment is closely related to the degree of cortical atrophy (6). However, rating the degree of cortical atrophy was excluded from our MR rating score. We believe that reliable evaluation of cortical atrophy based on MR images necessitates the additional introduction of cortical seg-

mentation procedures, and can not be sufficiently performed based on the observers' visual judgment alone.

In conclusion, MR signal changes in CSVD show a close relationship with some risk factors of individual patients. This association is masked when concomitant macroangiopathy, caused by other etiological cofactors, is present. The overall proportion of MR signal abnormalities, as assessed by T2-image hyperintensity, correlates with the clinical severity of the CSVD and allows differentiation between CSVD and age-related signal changes. T1-image hypointensity, on the other hand, is an appropriate indicator of tissue destruction.

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