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Short report

Magnetic resonance imaging studies in multiple sclerosis twins

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SUMMARY Magnetic resonance (MR) imaging examinations were performed on a series of seven sets of twins (four monozygotic and three dizygotic) and one set of triplets who were clinically discordant for multiple sclerosis (MS). MR abnormalities were detected in some of the unaffected monozygotic pairs of twins.

A major issue in the search for the cause of multiple sclerosis (MS) is whether its development can mainly be attributed to hereditary or environmental factors. The results of several studies in MS twins have been ambiguous which can largely be explained by bias in the selection of patients.[1–6] Some recent population-based studies, probably minimising unacceptable bias, showed concordance rates to be significantly higher in monozygotic twin pairs than in dizygotic pairs.[5,6] These studies suggest a major genetic component in the susceptibility to MS.

Since several studies support the possibility of subclinical MS in general and especially in relatives of MS patients, the analysis of studies on twins on clinical grounds only, might be misleading.[7–9] Therefore, magnetic resonance (MR) imaging was performed in our twin pairs all clinically discordant for the disease.

Methods

Twins

Twelve sets of twins and one set of triplets were identified by public appeal; seven twin pairs and the set of triplets volunteered for the MR studies.

A careful history was taken from all participants. The study population included only twin pairs in which the patient had been given a diagnosis of clinically definite MS or laboratory supported definite MS according to the Poser-criteria.[10] All twin pairs proved to be clinically discordant for MS: the non-diseased member of the twin pair did not have any complaints which indicated neurological disease in the past or present.

The zygosity diagnosis in all pairs was established by extended blood and serum group determinations. The triplet pair and four twin pairs were monozygotic; the remaining three twin pairs were dizygotic. The monozygotic twins were all women; the three dizygotic twin pairs consisted of four men and two women (two men and one woman had the disease). The mean age of the monozygotic twins was 39 years and the dizygotic twins 42 years. The mean age of onset of the disease in the monozygotic twins was 31 years, whereas it was 32 years in the dizygotic twins. Many environmental variables (childhood infections, trauma, dietary factors) were evaluated and compared in the twin pairs. No consistent pattern was detected in these data which could be explained mainly by the fact that all the twins involved had shared the same environment in their early years.

MR Imaging

The MR studies were performed with a 0·6 tesla superconductive magnet. Proton density, T2W and T1W spin-echo (SE) and inversion-recovery (IR) series were obtained in all candidates.

Sagittal SE 350 / 35 / 2/ 192 × 256.
Transverse SE 2500 / 30/ 60 / 90 / 120 / 128 × 256.
Transverse IR 1400 / 400 / 30 / 2 / 128 × 256.

Results

As shown in the table MR was abnormal in seven of the eight patients considered to have definite MS. In

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Table *Results of MR imaging in MS twins*

Pair	*Zygosity, Age*	*Clinical MS*	*White matter MR-abnormalities*
1a	MZ, 37	+	+
1b		−	+
2a	MZ, 32	+	+
2b		−	+
3a	MZ, 47	+	+
3b		−	−
4a	MZ, 40	+	+
4b		−	+
5a	DZ, 32	+	+
5b		−	−
6a	DZ, 65	+	+
6b		−	−
7a	DZ, 30	+	+
7b		−	−
8a	MZ, 40	+	−
8b		−	−
8c		−	−

MZ: monozygotic
DZ: dizygotic

these patients areas of increased T1 and T2 were detected in the white matter of the brain. The most common site for the lesions was the periventricular region but lesions in the brain stem and cerebellum were also detected. Moderate to severe central and cortical atrophy was seen in four of the eight patients.

Abnormalities of identical nature were detected in three of the four unaffected monozygotic twins. The number and the intensity of the lesions tended to be less in unaffected individuals than in patients and no central or cortical atrophy was found in the clinically unaffected members of the twin pairs. An example of a monozygotic twin pair where both the affected individuals and the unaffected had white matter abnormalities on MR Imaging is given in the figure (a: affected, b unaffected).

In the unaffected dizygotic twin pairs no abnormalities consistent with MS were found; in one of these (7b in the table) two small lesions with increased T1 and T2 were seen but they were not localised in the white matter. All MR examinations in the monozygotic triplet were reported to be normal (table).

Discussion

Our results clearly demonstrate the presence of white matter abnormalities in asymptomatic twins of patients with MS. These findings agree with those of Ebers *et al*[5] and McFarland *et al*[11] who also found abnormalities on MR in some unaffected members of MS twin pairs. On the other hand Kinnunen *et al*[12] did not find any MR abnormalities in 11 unaffected twins, both monozygotic and dizygotic. The failure to detect abnormalities in this last study might be due to a very low magnetic field (0·02 tesla) being used. In our study lesions with increased T1 and T2 on MR were seen in three out of four unaffected monozygotic twins and in

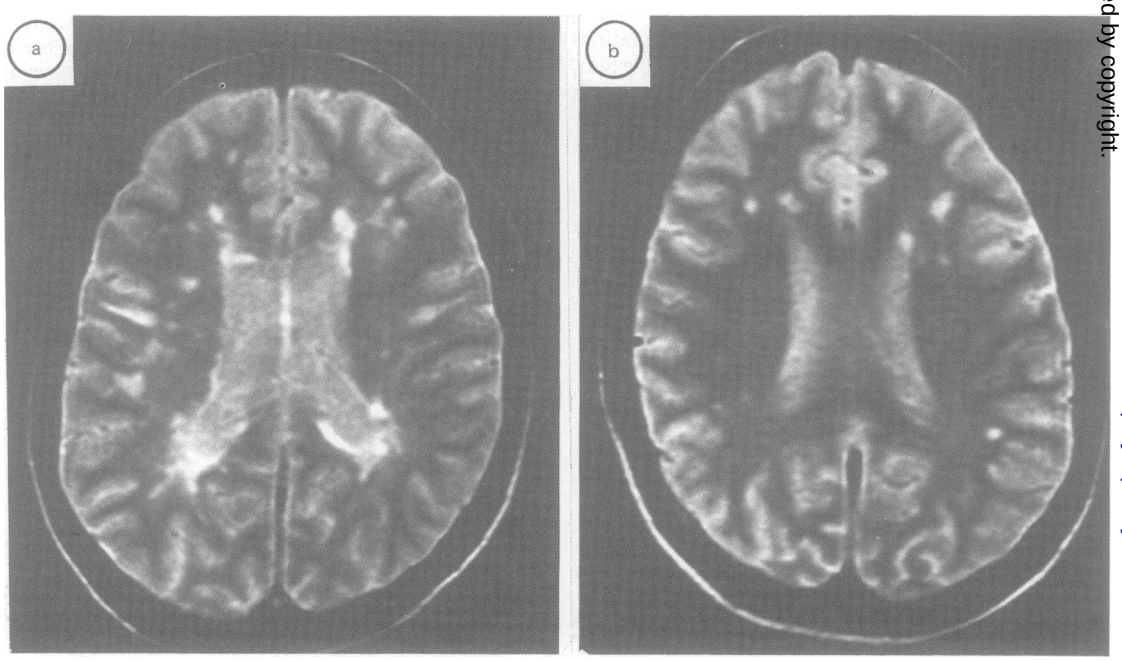

Fig *MR images demonstrating white matter abnormalities in both members of a monozygotic twin pair (a: patient, b: non-patient).*

none of the three unaffected dizygotic twins. The difference in concordance rates between monozygotic and dizygotic twin pairs cannot be accounted for by differences in age, or age at onset of the disease, since these parameters, and therefore the mean remaining time at risk for the development of MS, were essentially the same in both groups.

Although our twin pairs were identified by public appeal, we do not believe that our results have been influenced by this selection. The excess of monozygotic twins in our series suggests some selection bias, but this is unlikely due to the complete absence of clinically concordant (both MS) twin pairs.

Other paraclinical abnormalities like oligoclonal bands in cerebrospinal fluid (CSF) or electrophysiological abnormalities have been identified previously in asymptomatic twins and in normal relatives of MS patients.[8 9] The significance of these findings remains obscure. Although longitudinal follow up suggests the possibility of subclinical disease in at least some of the asymptomatic twins, the CSF abnormalities observed might also be related to an immune response similar to that seen in the affected twins but not associated with clinical disease.[8] Because Nuwer *et al*[9] found a very high percentage of electrophysiological abnormalities in relatives of MS patients and because the percentage that eventually will develop clinical MS probably does not exceed 2%, these authors do not suggest their findings to be due to subclinical demyelination.

The presence of MR lesions in periventricular white matter in apparently healthy individuals, especially when over the age of 60 years, was demonstrated by Ormerod *et al*.[13] Although the origin of these changes is uncertain, we suggest they could be a consequence of cerebral involvement in vascular disease. All our patients, however, were below this age and did not have any clinical signs of cerebrovascular disease or systemic vascular disease.

In our view we cannot assume that asymptomatic twins with MR abnormalities have subclinical MS or will develop clinical MS. If these patients develop clinical signs of MS in the future, then our findings, which show the percentage of MR concordance rates being much greater in monozygotic twins than in dizygotic twins, would agree with previous studies. This probably indicates a major genetic component playing a role in the susceptibility to MS.

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