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ORIGINAL RESEARCH

# Magnetic Resonance Imaging and Clinical Features of the Demyelinating Degeneration of White Matter in Young Patients

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**Objective:** Magnetic resonance imaging (MRI) of brain white matter demyelination often focuses on demyelinating disease, cerebral small vascular disease diagnosis, and follow-up of cognitive dysfunction for observation. This study explored MRI findings and clinical manifestations of demyelinating degeneration of white matter in young patients.

**Methods:** A total of ninety-four patients with white matter degeneration diagnosed with MRI were enrolled in this study from January 2014 to July 2018. These patients were divided into two groups: the demyelinating disease group (n = 43) and the non-demyelinating disease group (n = 51). The imaging findings and clinical manifestations of the two groups were analyzed.

**Results:** Compared with the non-demyelinating group, there were more female than male patients in the demyelinating group ($P < 0.05$). In addition, of the 45 patients with an imaging result of "demyelinating degeneration of white matter and multiple sclerosis," 39 patients met the diagnosis of multiple sclerosis (86.7%). In comparison, of the 49 patients with an imaging result of "demyelinating degeneration of white matter," only four patients met the diagnosis for demyelinating disease (8.2%).

**Conclusion:** In patients complaining of headaches, dizziness, vertigo, and other symptoms and in the case of an imaging result showing the demyelinating degeneration of white matter alone, the possibility of a clinical diagnosis of a demyelinating disease is minimal.

**Keywords:** young patients, MRI, demyelinating degeneration of white matter, headache, dizziness

## Introduction

With an improved image resolution of magnetic resonance imaging (MRI) in neurological outpatient clinics, head MRI examinations often reveal single or multiple punctate or patchy long T1 or long T1 signals, long T2 signals, and fluid-attenuated inversion recovery (FLAIR) hyper-intensive signals. In this case, the imaging report is the "demyelinating degeneration of white matter".[1–3]

MRIs of brain white matter demyelination often focus on demyelinating disease, cerebral small vascular disease diagnosis, and follow-up of cognitive dysfunction for observation. It is an important way that a patient and the non-neurological specialist obtained cerebral white matter pulp degeneration-related primary information associated with the clinical manifestations of blindness, paralysis, dementia, and other symptoms.

Due to the lack of understanding about demyelination, the patients match their symptoms to the imaging results. Some patients have psychological reactions, such

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as tension, anxiety, depression, fear, and even pessimism. These symptoms have also affected some patients' daily learning abilities, work abilities, and quality of life.

This study retrospectively analyzed the clinical manifestations and imaging features of young people with white matter demyelinating degeneration revealed by cranial MRI. The purpose of this investigation is to enable clinicians to make a comprehensive judgment on the clinical manifestations and examination results of patients, identify patients with demyelinating disease, and try to avoid and relieve non-demyelinating patients' unnecessary psychological burdens as soon as possible.

# Materials and Methods

## Clinical Data

The present study was a cross-sectional study. From January 2014 to July 2018, 94 patients 18–44 years old visited our outpatient clinic. They were diagnosed with mild demyelinating degeneration of white matter, demyelinating degeneration of white matter, or demyelinating degeneration of white matter with multiple sclerosis (MS) by MRI. The images of these patients were reviewed by two experienced radiologists, who were blind to the clinical information. According to the clinical diagnosis, the patients were divided into two groups: the demyelinating disease group (n = 43) and the non-demyelinating disease group (n = 51). Then, the imaging findings and clinical manifestations of the two groups were analyzed.

The diagnosis of MS and clinically isolated syndrome (CIS) was based on McDonald's 2017 multiple sclerosis diagnostic criteria.[4] Diagnosis of neuromyelitis optica spectrum disease (NMOSD) was based on the international consensus on diagnostic criteria for neuromyelitis optica spectrum disorders in 2015.[5] This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Peking University Third Hospital (NO.: IRB00006761-M2019096). All patients provided signed informed consent.

## Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) the age of the patients ranged from 18 to 44 years old, and (2) the cranial MRI diagnosis showed brain white matter degeneration. Exclusion criteria were as follows: (1) patients with incomplete data for cranial MRI examination, (2) patients that had other serious, complicated diseases, such as malignant tumors, liver and kidney dysfunction, and (3) pregnant or lactating patients.

## Head MRI

The FLAIR image with hyper-intense signals was observed. According to the Fazekas scale, the white matter in the paraventricular space and deep brain was scored, and the two scores were added together. 1–2 points were defined as mild, and 3–4 points were defined as moderate.[6,7] Paraventricular: no lesion, 0 points; cap-like or pencil-like lesions, 1 point; lesions with a smooth halo, 2 points; and paraventricular irregular hyperintense signals extended to the deep white matter, 3 points. Deep white matter: no lesion, 0 points; punctate lesions, 1 point; lesions are beginning to fuse, 2 points; and the lesions were fused in a large area, 3 points.

## Adjuvant Examination Results

In the demyelinating disease group: 27 patients had spinal cord inflammatory lesions diagnosed by MRI. In the 43 cases of CSF examination, three cases had increased white blood cells (10–23) $\times$ $10^6$/L, seven cases had increased protein (0.62–0.89 g/L), 24 cases had positive oligoclonal bands, 16 cases had an increased 24-hour IgG synthesis rate, and 18 cases had an increased IgG index. One patient tested positive for the AQP4 antibody, while 42 patients tested negative for it. Forty-three patients had no abnormalities in the blood rheumatism immune examination. In the non-demyelinating disease group, cerebrospinal fluid tests were normal in two cases. Carotid artery ultrasonography revealed carotid plaque in four patients and subclavian artery plaque in one patient; the size was 0.15–0.23 cm, and no lumen stenosis was found. In one patient, the vertebral artery thinned evenly on one side. Head MRI revealed mild stenosis of the middle cerebral artery in one patient and uniform thinning of the vertebral artery in one patient.

Cervical MRI revealed cervical disc herniation and dural sac compression in two patients. Brainstem electric response audiometry revealed a high-frequency hearing loss in two patients, low-frequency hearing loss, and slightly decreased vestibular function in two patients. In one patient, the fibrillation potential of limb, paravertebral muscle, and lower limb muscle was observed in the resting state on the electromyograph. The blood vitamin B12 level was $1.27\times10^{-7}$ g/L in one patient, and 19 patients had no abnormalities in the blood rheumatism immune examination. Sixteen patients scored 10–21 points on the Hamilton

Anxiety Rating Scale (HAM-A) testing in certain hospitals and scored 8–15 points on the Hamilton Depression Rating Scale (HAM-D). Seven patients scored 9–11 points on the Fatigue Severity Scale-14 (FSS). Seven patients were tested on the Montreal Cognitive Assessment Scale (MoCA), and six patients scored 30 points, and one patient scored 28 points (2 points were subtracted for delayed recall).

## Statistical Methods

Data were analyzed using the statistical software SPSS 20.0. Measurement data were expressed as mean ± standard deviation (x ± SD), and count data were expressed as a percentage (%). The normality of variables was tested using a W-test. The homogeneity of variance was tested using an F-test. A multi-group comparison was conducted using univariate analysis of variance, and backtesting was conducted using Fisher's least significant difference (LSD) test. Non-normally distributed mean or normally distributed mean with the heterogeneity of multiple samples were evaluated using a non-parametric test. $P < 0.05$ was considered statistically significant.

# Results

## General Data

From January 2014 to July 2018, 96 patients were screened. Ninety-four patients who met the inclusion criteria and were not excluded were enrolled in this study. Two patients were excluded because they did not have complete cranial MRI examination data. For the demyelinating disease group, 14 patients were males, and 29 were females. The average age of the patients was 30.8 ± 8.1 years old. For the non-demyelinating group, 27 patients were males, and 24 were females, and the average age of the patients was 32.3 ± 6.9 years old. Compared with the non-demyelinating disease group, there were more female patients than male patients in the demyelinating disease group. The difference was statistically significant ($X^2 = 3.941$, $P = 0.047$), and the difference in age between the two demyelinating groups was not statistically significant ($t = 1.055$, $P = 0.294$, Table 1).

The first symptoms in the demyelinating disease group were 15 cases of numbness in one lower extremity, 10 cases of weakness in one lower extremity, eight cases of vision loss on one side, three cases of numbness in both lower extremities, two cases of vertigo, one case of numbness and weakness of both lower extremities, back pain, walking instability, and dizziness. In the non-demyelination group, there were 21 cases with headaches, 14 cases of vertigo, seven cases of paroxysmal loss of consciousness, two cases of paroxysmal loss of consciousness with limb twitching, dizziness, paroxysmal speech disorder with limb weakness, paroxysmal limb weakness, hearing loss, tinnitus, weakness of one upper limb, and 1 case of weakness of both lower limbs.

## Clinical Manifestations

The demyelinating disease group had 32 patients with limb weakness, 29 patients had sensory loss, 25 patients had paraesthesia, 24 patients had impaired visual acuity, nine patients had sphincter dysfunction, five patients had ataxia, diplopia and nausea occurred in four patients, vertigo and dysarthria occurred in three patients, vomiting occurred in two patients, and blepharoptosis, dizziness, neck pain, and back pain occurred in one patient. The non-demyelinating disease group had headaches occurring in 32 patients, dizziness occurring in 15 patients, vertigo occurring in 14 patients, nausea occurring in eight patients, seven patients had a paroxysmal loss of consciousness, vomiting occurred in five patients, four patients had impaired hearing, three patients had tinnitus, paroxysmal loss of consciousness with tetany and paroxysmal unstable walking occurred in two patients, and paroxysmal slurring of speech with limb weakness in one limb, paroxysmal limb weakness in one limb, bilateral upper limb weakness with muscle atrophy, bilateral lower limb weakness with sensory ataxia, and memory loss occurred in one patient.

## Medical History

The demyelinating disease group had one patient with hypertension, three patients with hyperlipidemia, one patient was a smoker, one patient had a history of premature delivery, and thirty-one patients had a history of one to three attacks of neurological deficits in the past 13 months to 12 years. The non-demyelinating disease group had four patients with hypertension, two patients had diabetes mellitus, six patients had hyperlipidemia, three patients had hyperhomocysteinemia, fourteen patients had a history of headaches, two patients had epilepsy, five patients were smokers, five patients had a premature delivery history, two patients had a history of dystocia, and four patients had a history of carbon monoxide poisoning. Among them, one patient had

**Table 1** Comparison of Clinical Data Between the Demyelinating Disease Group and the Non-Demyelinating Disease Group

| Index | Demyelinating Disease Group | Non-Demyelinating Disease Group |
|---|---|---|
| N | 43 | 51 |
| Gender (Male/Female) | 14/29 | 27/24 |
| Age (Year) | 30.8±8.1 | 32.3±6.9 |
| Fazekas score of 1 point | 43 | 46 |
| Fazekas score of 2 points | 0 | 5 |
| Recurrence or aggravation of Symptoms | 4 | 1 |
| Multiple sclerosis | 41 | 0 |
| Optic neuromyelitis spectrum disease | 1 | 0 |
| Clinical isolation syndrome | 1 | 0 |
| Migraine | 0 | 7 |
| Vasovagal syncope | 0 | 5 |
| Transient ischemic attack | 0 | 4 |
| Micturition syncope | 0 | 2 |
| Meniere disease | 0 | 2 |
| Epilepsy | 0 | 2 |
| Anxious depressive state | 0 | 16 |
| Fatigue induced symptoms | 0 | 7 |
| Other | 0 | 6 |
| Limb weakness | 32 | 2 |
| Paresthesia | 25 | 1 |
| Anesthesia | 29 | 0 |
| Vision loss | 24 | 0 |
| Sphincter dysfunction | 9 | 0 |
| Ataxia | 5 | 0 |
| Double vision | 4 | 0 |
| Dysarthria | 3 | 0 |
| Vertigo | 3 | 14 |
| Headache | 0 | 32 |
| Dizziness | 1 | 15 |
| Nausea | 4 | 8 |
| Vomiting | 2 | 5 |
| Ptosis | 1 | 0 |
| Neck pain | 1 | 0 |
| Back pain | 1 | 0 |
| Paroxysmal limb weakness | 0 | 7 |
| Hearing loss | 0 | 4 |
| Tinnitus | 0 | 3 |
| Parastic loss of consciousness, limb twitching | 0 | 2 |
| Unsteady walking during seizures | 0 | 2 |
| Paroxysmal limb weakness | 0 | 1 |
| Paroxysmal speech adverse side limb weakness | 0 | 1 |
| Paroxysmal loss of consciousness | 0 | 7 |
| Memory loss | 0 | 1 |
| Muscle atrophy | 0 | 1 |
| Imaging report demyelination + multiple sclerosis | 39 | 6 |
| Imaging report demyelination | 4 | 45 |

memory loss. None of the patients had a history of alcoholism, brain injury, stroke, or central nervous system infection.

## Changes in the MRI

The demyelinating disease group had one patient with a single round lesion near the cortex, 32 patients had oval

and patchy lesions in the deep white matter of the brain lobes and the centrum semiovale, 38 patients had lesions perpendicular to and around the lateral ventricle (at least three lesions), eight patients had patchy lesions on the brain stem, three patients had patchy lesions on the cerebellum, one patient had two punctate lesions on the frontal lobe, and one patient had three punctate lesions on the frontal and parietal lobes. The non-demyelinating disease group had two patients with punctate lesions on the frontal lobe, eight patients had two punctate lesions on the frontal, parietal, temporal, and occipital lobes, 11 patients had three punctate lesions, 14 patients had four to seven punctate lesions, and nine patients had more than seven punctate and patchy lesions. The patchy lesions were less than 0.9 cm in diameter. Furthermore, 37 patients had lesions on the frontal lobe, 22 patients had lesions on the parietal lobe, 19 patients had lesions on the temporal lobe, six patients had lesions on the occipital lobe, and two patients had lesions on the thin layer of the frontal horn, with a Fazekas scale score of 1 point. One patient had lesions on the thin-layer of the frontal and occipital horns combined with punctate lesions (three) on the frontal and temporal lobes, four patients had multiple punctate and patchy lesions with fusion on the frontal, parietal, and temporal lobes, centrum semiovale, and paraventricular space, with a Fazekas scale score of 2 points.

MRI showed 40 lobar lesions, and all the imaging reports were "white matter demyelinating degeneration." Four cases were clinically diagnosed with demyelinating disease, two cases with MS, one case with NMOSD, and one case with CIS. Ninety percent of the patients were clinically diagnosed with non-demyelinating disease. Three cases with thin-layer lesions on the ventricle, frontal, and occipital horn were all diagnosed as "demyelinating degeneration of white matter." The clinical diagnosis was a non-demyelinating disease. Ten cases with infratentorial lesions (all with supratentorial lesions) were diagnosed as "white matter demyelinating degeneration, multiple sclerosis." There were 45 cases of lobular plaques and/or oval lesions, 37 cases of "white matter demyelinating degeneration, multiple sclerosis," and eight cases of "white matter demyelinating degeneration." The accuracy, sensitivity, and specificity of imaging diagnosis of multiple sclerosis were 68.9%, 96.9%, and 53.8%, respectively. Forty-two cases of paraventricular plaques and/or oval lesions were reported as "white matter demyelinating degeneration, multiple sclerosis." The accuracy rate and sensitivity of multiple sclerosis were 88.1% and 97.4%, respectively (Table 2).

## Re-Examination results of the MRI

The demyelinating disease group had a clinical recurrence in four patients with MS 5–16 months later. In these patients, the partial reduction or disappearance of the original lesions or new lesions was observed using head MRI in three patients. In the remaining one patient, a head MRI revealed a partial reduction of the new lesion and original lesions. A decrease in visual acuity was found in one patient with NMOSD nine months later, but no change was observed in the head MRI images (two punctate lesions on the frontal lobe). Head MRI observed new lesions in the centrum semiovale or periventricular and partial reduction or disappearance of the original lesions in six patients who had no recurrence in one year of follow-up. No new lesions and partial reduction or disappearance of the original lesions were observed by head MRI in 23 patients who had no recurrence in one year of follow-up. No change was found in eight patients who had no recurrence in one year of follow-up. No change (three punctate lesions in the frontal and parietal lobes) was found in one patient with CIS who

**Table 2** Characteristics of MRI Sites and Clinical and Imaging Results

| | Demyelinating Disease | | Non-Demyelinating Disease | |
|---|---|---|---|---|
| | **Imaging Showed "Demyelination of White Matter +MS"** | **Imaging Showed "Demyelination of White Matter"** | **Imaging Showed "Demyelination of White Matter +MS"** | **Imaging Showed "Demyelination of White Matter"** |
| Punctate lesion of the brain lobes | 0 | 4 | 0 | 36 |
| Lobular and/or ovoid lesions | 31 | 1 | 6 | 7 |
| Paraventricular plaques and/or ovoid lesions | 37 | 1 | 4 | 0 |
| Thin layer lesions of ventricle frontal and occipital horn | 0 | 0 | 0 | 3 |
| Supratentorial patchy lesions with supratentorial lesions | 10 | 0 | 0 | 0 |

had no recurrence after one year of follow-up. In the non-demyelinating disease group, no significant change was found in head MRI, and no abnormalities were found in SWI or T2* weighted images in 51 patients 11–13 months later. Lower limb weakness occurred in one patient with amyotrophic lateral sclerosis. No new symptoms were found in the remaining 50 patients.

## Results of the Diagnosis

In the demyelinating disease group, 41 patients had MS. Among these patients, 39 patients had an imaging result of "demyelinating degeneration of white matter and MS," two patients had an imaging result of "demyelinating degeneration of white matter," one patient had NMOSD, one patient had CIS, and the imaging result was "mild demyelinating degeneration of white matter." In the non-demyelinating disease group, seven patients had migraines, five patients had vasovagal syncope, four patients had a transient ischemic attack, two patients had epilepsy, two patients had micturition syncope, two patients had Meniere's disease, one patient had cluster headaches, one patient had trigeminal neuralgia, one patient had a subacute combined degeneration of the spinal cord, one patient had amyotrophic lateral sclerosis, one patient had sudden deafness, one patient had nervous tinnitus, and 16 patients had anxiety and depression. The symptoms in seven patients were related to fatigue. The imaging results of 45 patients were "mild demyelinating degeneration of white matter" or "demyelinating degeneration of white matter," and the imaging results of six patients were "demyelinating degeneration of white matter and MS." Of the 45 patients with the imaging result of "demyelinating degeneration of white matter and MS," 39 patients met the diagnosis of MS (86.7%). Of the 49 patients with the imaging result of "mild demyelinating degeneration of white matter" or "demyelinating degeneration of white matter," four patients met the diagnosis of demyelinating disease (8.2%) ($X^2 = 58.247$, $P < 0.001$, Figures 1–3).

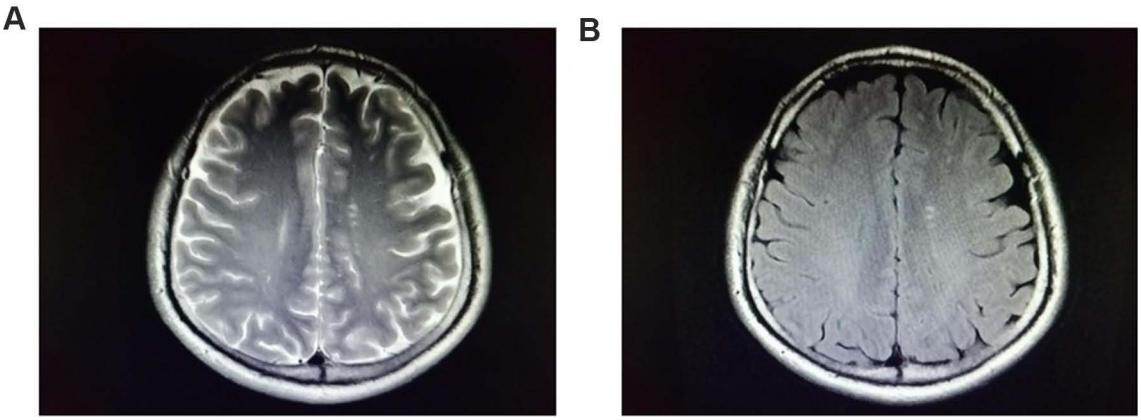


**Figure 1** A 30-year-old female with a long point-like T2 signal (**A**) in the left parietal lobe and fluid-attenuated inversion recovery hyper signal (**B**), magnetic resonance imaging reported "white matter demyelinating degeneration" and a clinical diagnosis of "anxiety and depression.".

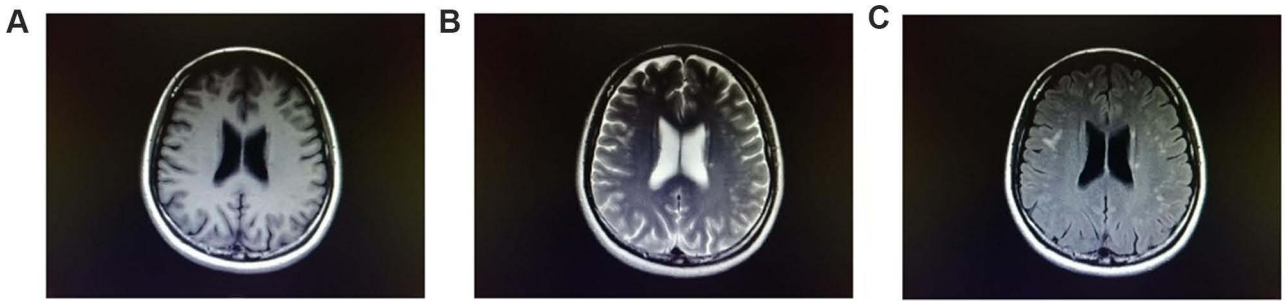


**Figure 2** A 39-year-old female, with multiple dots and patches of long T1 (**A**) and long T2 signals (**B**) in the cerebral lobes near bilateral ventricles, and high fluid-attenuated inversion recovery signals (**C**), reported "white matter demyelinating degeneration, multiple sclerosis" by magnetic resonance imaging, clinically diagnosed as "anxiety and depression," and a history of carbon monoxide poisoning.

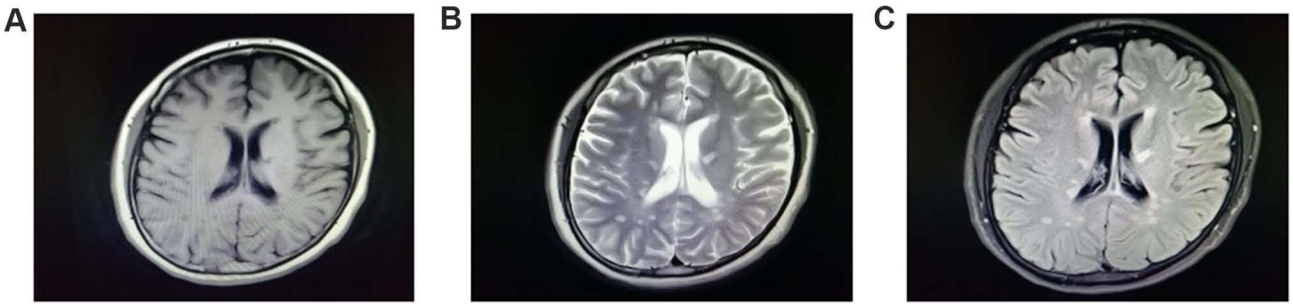


**Figure 3** A 28-year-old female with multiple dots and patches of long T1 (**A**) and long T2 signals (**B**) in the lobes near bilateral ventricles and fluid-attenuated inversion recovery hyperintensity (**C**). Magnetic resonance imaging reported "white matter demyelinating degeneration, multiple sclerosis," clinically diagnosed as "multiple sclerosis.".

## Discussion

This study revealed that, compared with the non-demyelinating disease group, there were more female patients than male patients in the demyelinating group and the difference in age between the two groups was not statistically significant. Of the 45 patients with the imaging result of "demyelinating degeneration of white matter and MS," 39 patients met the diagnosis of MS (86.7%). Of the 49 patients with the imaging result of "demyelinating degeneration of white matter," only four patients (8.2%) met the diagnosis of demyelinating disease.

A demyelinating disease is a group of brain and spinal cord diseases mainly characterized by destruction of the myelin sheath or myelinoclasis lesions,[8,9] which are classified into two types: hereditary and acquired types. Acquired demyelinating diseases can be classified as demyelinating diseases secondary to other diseases (such as ischemia, hypoxia, poisoning, and nutritional deficiency) and primary immune-mediated inflammatory demyelinating disease. Demyelinating disease in neurology refers to the latter. It mainly includes MS,[10] NMOSD, acute disseminated encephalomyelitis (ADEM), and CIS.[11–13] Its diagnosis is clinically made, based on a combination of clinical manifestations and auxiliary examinations but not based on imaging findings alone. However, from the patient's perspective, it is easy to consider that the results of the head MRI reports suggest illness. Clinicians must comprehensively analyze results based on the patients' clinical manifestations and secondary examinations.

In the present study, in the non-demyelinating group, most of the first symptoms were complaints of head discomfort, headache (41.2%), and vertigo (27.5%). The typical clinical manifestations were headaches (62.7%), dizziness (29.4%), and vertigo (27.5%), and three patients (5.9%) had neurological deficits lasting more than 24 hours. In the demyelinating disease group, most of the first symptoms were complaints of lower limb discomfort and visual impairment, numbness of the lower limbs (44.2%), weakness of the lower limbs (25.6%), and decreased vision (18.6%). The typical clinical manifestations were limb weakness (74.4%), sensory loss (67.4%), abnormal sensations (58.1%), decreased vision (55.8%), and sphincter dysfunction (20.9%) and 42 patients (97.7%) had neurological deficits lasting for more than 24 hours. In the non-demyelinating disease group, head MRI revealed that the paraventricular lesions included lesions of the thin layer of the margin of the frontal and occipital horns. The lesions of the cerebral lobes were primarily punctate, and a few were patchy lesions. Moreover, the number was few and commonly found in the frontal lobe, and the sizes were mostly small. A few lesions were fused, and the number was large. No subtentorial lesions were found. In the demyelinating disease group, head MRI revealed that the lesions were mostly oval and patchy, primarily found in the lobes of the centrum semiovale and the lateral ventricle. The lesions near the lateral ventricle were mainly perpendicular to the lateral ventricle, which included subtentorial and subcortical lesions. There were few patients with simple punctate lesions.

In the demyelinating disease group, 41 patients (95.3%) had MS. Among these patients, the clinical manifestations and imaging changes of 40 patients met the diagnostic criteria of MS. One patient complained of dizziness and had ten punctate and patchy demyelinating lesions in the centrum semiovale and paraventricle revealed by head MRI. Among these, three lesions were slightly vertically distributed in the ventricles with enhancement (–). One year later, the patient had dizziness and a sense of instability while walking. Still, no positive

signs were found by the nervous system examination. Head MRI revealed that new lesions with enhancement (+) occurred in the centrum semiovale, the dynamic change of image met the diagnostic criteria of MS. Thirty-three patients (76.7%) had changes in the lesions on head MRI, including new lesions (23.3%), diminished lesions, or disappearance of lesions. Five patients (11.6%) had a clinical recurrence. Among these patients, one NMOSD patient with recurrence had no new pathological changes shown in the images. One CIS patient had no change in the dynamic observation of the lesions on head MRI, which was not in accordance with the characteristics of demyelinating autoimmune disease. In the non-demyelinating disease group, no changes in the dynamic observation were found on head MRI. Patients with the imaging result of "demyelinating degeneration of white matter" and the imaging result of MS mostly met the diagnostic criteria of demyelinating disease. A few patients with an imaging result of "simple demyelinating degeneration of white matter" met the diagnostic criteria of demyelinating disease, and the difference was statistically significant. There were more female patients than male patients in the demyelinating group, and the difference between the non-demyelinating group and the demyelinating group was statistically significant.

MRI showed the highest accuracy (100%) in diagnosing demyelinating disease with subpatentorial lesions combined with supratentorial lesions, followed by paraventricular and lobular plaques and/or oval lesions. Paraventricular (41/42) and lobar (37/45) plaques and/or oval lesions were more likely to be reported as multiple sclerosis with higher accuracy and sensitivity. Six demyelinating diseases on the clinical diagnostic imaging report for "brain white matter demyelination degeneration, multiple sclerosis patients, four cases exist near the ventricle, and cerebral lobe lesions, one case of video report" brain white matter demyelination degeneration "next to the clinical diagnosis of MS patients exist ventricle and cerebral lobe lesions, only by imaging characteristics to identify such patients have difficulty, it needs to be combined with clinical manifestations and other auxiliary examinations. The imaging reports of thin-layer lesions on the ventricle frontal and occipital horn and lobular lesions were all "demyelinating degeneration of white matter." Ninety percent of the patients were clinically diagnosed with a non-demyelinating disease, and patients with such imaging characteristics were less likely to be clinically diagnosed with demyelinating disease.

The clinical manifestations of the demyelinating disease are complex and changeable, the lesions are multiple, and atypical cases or early diseases are likely to be misdiagnosed.[14,15] Poisoning can also induce demyelinating lesions, illness, or intrauterine distress during the gestation period, and dystocia and premature delivery can affect the fetal brain.[16,17] In severe cases, these can cause ischemic-hypoxic encephalopathy. In mild cases, they can induce a demyelination change without obvious clinical symptoms. With an increase in age, demyelinating changes can be caused in the chronic ischemia of the brain tissue with arteriolosclerosis, especially in patients with stroke risk factors, but mild changes in the white matter do not cause cognitive impairment.[18,19] There are both congenital and acquired factors in the demyelinating changes in images. Still, except for patients with demyelinating autoimmune disease and those with definite risk factors for stroke, it is difficult to confirm the cause of a small amount of punctate demyelinating lesions in young patients when using MRI. In contrast, a small number of punctate demyelinating changes are not associated with the patient's symptoms.

In the non-demyelinating disease group, the patients' symptoms were mostly related to anxiety, depression, and fatigue (45.1%), followed by syncope and migraines (13.7%). In young stroke patients, patients with transient ischemic attacks accounted for 7.8%. All of these patients were males over 40 years old, and three of them had lesions on the thin layer of the frontal and occipital horns, and these patients met the characteristics of chronic ischemia. Six patients with symptoms similar to MS (headache, dizziness, and vertigo) on head MRI were correlated to anxiety, depression, and fatigue, four patients had a history of carbon monoxide poisoning, two patients had a history of dystocia, and the changes in the image results may be related. Only one patient with a history of carbon monoxide poisoning self-described as a reduction in memory, and the Montreal Cognitive Assessment Scale (MoCA) score was normal (28 points). MoCA was 30 points in the remaining six patients with more imaging lesions. Still, an image re-examination revealed that no new lesions were found, and no lacunar cerebral infarction and micro-bleeding were found, which could not be diagnosed as cerebral small vessel disease.[8]

The study claims that "demyelinating degeneration of white matter" suggested by MRI scans need not necessarily (with a small probability, 4/49 for this sample) imply a diseased brain state. Hence, this MRI result should not

be considered alarming, like getting diagnosed with "demyelinating degeneration of white matter and MS." The take-home (ie, degeneration seen on MRI scans may not necessarily imply a diseased state) sounds reasonable looking at the included data.

Demyelination of multiple sclerosis lesions tends to occur in watershed areas. Hypoperfusion and tissue hypoxia have an important relationship between multiple sclerosis pathology and cerebral artery perfusion.[20–22] In animal models, rapid inflammatory response induces acute tissue hypoxia in experimental autoimmune encephalitis (EAE), resulting in the enlarged vascular lumen and increased number of vessels, which is associated with neurological impairment.[22] By reducing the level of oxidative molecules during inflammation, oxidative damage to mitochondria and subsequent focal axon degeneration can be alleviated.[23] Among neurodegenerative diseases, cerebrovascular diseases have cycles that promote chronic hypoperfusion and insufficiency of pericytes and astrocytes. Changes in BBB permeability, oxidative stress, inflammation, and mitochondrial damage, and other factors may cause nerve damage. The "vasoneuroinflammation" model of neurodegenerative diseases centered on the dysfunction of NVU (the neurovascular unit) can be applied to MS.[24,25] Amyloid-β precursor protein (AβPP) is a one-way transmembrane protein expressed at high levels in the brain. AβPP is upregulated in both acute and chronic MS lesions and is considered a sensitive marker of axonal injury.[26] The toxic effect of AβPP, ischemia, excitatory toxicity, oxidative stress, and iron excess can all cause damaged oligodendrocytes. Injured oligodendrocytes, on the one hand, lead to the loss and degeneration of the myelin sheath. On the other hand, it releases iron, promotes the aggregation of AβPP in the cortex, and further aggravates neuronal injury.[27]

At present, a lot of research on brain white matter demyelination etiology, pathology as the advanced factors, but clinical patients part single white matter damage, such as congenital factors, such as poisoning, no further impact on patients, not left obvious sequela damage, but on the image exist for a long time, this group of clinical demyelinating disease there is only a handful of nutrient deficiency and stroke risk factors, both the intervention. After a one-year follow-up, there was no progress in white matter lesions.

"Demyelinating degeneration of white matter" seen on MRI scans may not necessarily imply a diseased state. Some patients have no clinical signifiers to undergo a head MRI again. However, even after receiving an explanation, the patient does not conform to demyelinating disease or cerebral small vessel disease. There are still some patients concerned about the possibility of blindness and paralysis caused by demyelinating disease and then visit a doctor after re-examining the images and asking the doctor to determine whether changes in the images are present.

This study still has some limitations. First, this study was a cross-sectional study but not a randomized controlled trial; therefore, there is still a certain risk of bias. Second, this study is a single-center clinical trial; the included sample size is small, and multi-center clinical trials with larger sample sizes are still needed. Finally, the correlation between the demyelinating degeneration of white matter revealed by MRI and the clinical manifestations still needs further study. The considered groups are imbalanced in gender, and the sample size is extremely small, hence involving more chance than larger samples. Thus, this observation should be validated on an independent dataset in the future.

## Conclusion

The diagnosis of demyelinating disease requires a combination of clinical manifestations and auxiliary examinations. There are many reasons for demyelinating changes shown on head MRI images in patients complaining about headaches, dizziness, vertigo, and other symptoms. In the case of the imaging result of demyelinating degeneration of white matter alone, the possibility of clinical diagnosis of the demyelinating disease is very low.

## Disclosure

The authors declare that there is no conflict of interest.

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