MRI phase changes in multiple sclerosis vs neuromyelitis optica lesions at 7T

ABSTRACT

Objective: To characterize paramagnetic MRI phase signal abnormalities in neuromyelitis optica spectrum disorder (NMOSD) vs multiple sclerosis (MS) lesions in a cross-sectional study.

Methods: Ten patients with NMOSD and 10 patients with relapsing-remitting MS underwent 7-tesla brain MRI including supratentorial T2* -weighted imaging and supratentorial susceptibility weighted imaging. Next, we analyzed intra- and perilesional paramagnetic phase changes on susceptibility weighted imaging filtered magnetic resonance phase images.

Results: We frequently observed paramagnetic rim-like (75 of 232 lesions, 32%) or nodular (32 of 232 lesions, 14%) phase changes in MS lesions, but only rarely in NMOSD lesions (rim-like phase changes: 2 of 112 lesions, 2%, p < 0.001; nodular phase changes: 2 of 112 lesions, 2%, p < 0.001).

Conclusions: Rim-like or nodular paramagnetic MRI phase changes are characteristic for MS lesions and not frequently detectable in NMOSD. Future prospective studies should ask whether these imaging findings can be used as a biomarker to distinguish between NMOSD- and MS-related brain lesions.
METHODS  

Study participants. Ten patients with NMOSD underwent ultra-high field MRI at 7T. Inclusion criteria were diagnosis of NMOSD as defined by the current international consensus diagnostic criteria for NMOSD,2 age of at least 18 years, and no contraindications to 7T MRI. Four of these patients have been previously reported in a 7T MRI study on T2*w lesion morphology3 and were rescanned. Nine patients with NMOSD were seropositive for aquaporin-4 immunoglobulin G. Ten patients with relapsing-remitting MS were recruited as controls. More details are presented in table 1.

The study was approved by the local ethics committee (EA 1/054/09). Written consent was obtained from all participants before examination.

MRI acquisition. Ultra-high field MRIs were acquired using a 7T Siemens whole body scanner (Magnetom; Siemens, Erlangen, Germany) by applying a 24-channel receive head coil (Nova Medical, Wilmington, MA) equipped with a birdcage volume coil used for transmission. The imaging protocol included supratentorial 2-dimensional T2*w fast low angle shot (echo time = 25.0 milliseconds (ms), repetition time = 1,820 ms, spatial resolution = 0.5 × 0.5 × 2 mm³, supratentorial coverage, number of slices = 35) and supratentorial 3-dimensional gradient echo flow-compensated susceptibility weighted imaging (SWI) (echo time = 14 ms, repetition time = 25 ms, flip angle = 12°, spatial resolution = 0.5 × 0.5 × 1.0 mm³) yielding magnitude, SWI-filtered phase and reconstructed SWI images.

RESULTS  

In total, we detected 112 brain lesions in patients with NMOSD, and 232 brain lesions were visualized in patients with MS on supratentorial T2*w images.

Next, rim-like or nodular paramagnetic (positive) intraslesional phase changes were analyzed (figure). In MS, 32 of 232 lesions (14%) in 7 of 10 patients were characterized by a nodular paramagnetic (positive) phase shift and thus appeared “hyperintense” on magnetic resonance (MR) phase images corresponding to a hypointense signal on T2*w and/or SWIs (lesion category I; figure, A).

Furthermore, a distinct rim-like paramagnetic (positive) phase shift was visible in 75 of 232 MS lesions (32%) in all but one patient with MS (lesion category II; figure, B).

Contrarily, the vast majority of NMOSD lesions were neither characterized by nodular (2 of 112 lesions, 2%, p < 0.001) nor rim-like intraslesional phase changes (2 of 112 lesions, 2%, p < 0.001; table 2).
A significant proportion of lesions in patients with NMOSD (107 of 112 lesions, 96%) or MS (116 of 232 lesions, 50%) did not show any MRI phase changes (lesion category III; figure, C), and a total number of 9 MS and 1 NMOSD lesions presented with rather unspecific MRI phase changes (lesion category IV; figure, D).

In addition, the existence of an intralesional central vein was analyzed on T2*w images. As reported previously,3,4 a central vein was typically visible in the inner third of MS lesions (193 of 232 lesions, 83%) but only rarely existent in NMOSD lesions (28 of 112 lesions, 25%, \( p < 0.001 \)). The morphology of NMOSD and MS lesions is detailed in table 2.

**Interrater reliability.** Interrater reliability was assessed in a subgroup of 10 randomly selected patients. ICC was >0.8 for lesion count (ICC = 0.90), the number of lesions with a central vein (ICC = 0.95), and the number of lesions with rim-like (ICC = 0.96) or nodular (ICC = 0.84) phase changes indicating good interrater reliability of these parameters.

**DISCUSSION** In this study, we compared the morphology of NMOSD vs MS lesions on high spatial resolution SWI-filtered phase images and observed distinct lesion characteristics that were nearly exclusively found in MS but not in NMOSD lesions. Thus, this work adds to the ongoing discussion5 on the diagnostic value of phase white matter signal abnormalities in differentiating MS from other diseases.

In MS, the source of the phase contrast in or around lesions remains speculative, but iron-rich
In conclusion, paramagnetic intraleSIONal phase changes were virtually absent in NMOSD but frequently detectable in MS. Future work should address the question of whether these imaging findings in or around lesions can indeed be used as a biomarker to better distinguish MS from NMOSD.

**AUTHOR CONTRIBUTIONS**

T.S., P.D., L.H., K.R., T.N., I.K., F. Paul, Y.G., and J.W.: study concept and design. T.S., F. Pache, P.D., P.N., and J.W.: acquisition of data. T.S., S.S., and K.M.: analysis. T.S., S.S., K.M., F. Pache, P.D., L.H., K.R., P.N., S.C., T.N., I.K., F. Paul, Y.G., and J.W.: interpretation. T.S., S.S., K.M., F. Pache, P.D., L.H., K.R., P.N., S.C., T.N., I.K., F. Paul, Y.G., and J.W.: critical revision of the manuscript for important intellectual content. T.S., L.H., K.R., T.N., I.K., F. Paul, Y.G., and J.W.: study supervision.

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### Table 2 Lesion morphology on gradient echo images

|                | Lesion count | Lesions with nodular positive phase changes | Lesions with rim-like positive phase changes | Lesions without phase alterations | Lesions with unspecific phase alterations | Perivascularb | p     |
|----------------|--------------|--------------------------------------------|--------------------------------------------|-----------------------------------|------------------------------------------|---------------|-------|
| **NMOSD**      |              |                                            |                                            |                                   |                                          |               |       |
| No.            | 112          | 2                                          | 2                                          | 107                               | 1                                        | 28            | 0.063 |
| Mean ± SD      | 11 ± 13      | 0.2 ± 0.4                                  | 0.2 ± 0.4                                  | 11 ± 13                           | 0.1 ± 0.3                                | 3 ± 4         | 0.001 |
| Range          | 1–35         | 0–1                                        | 0–1                                        | 1–35                              | 0–1                                      | 0–11          |       |
| **RRMS**       |              |                                            |                                            |                                   |                                          |               |       |
| No.            | 232          | 32                                         | 75                                         | 116                               | 9                                        | 193           | 0.015 |
| Mean ± SD      | 23 ± 15      | 3 ± 3                                      | 8 ± 10                                     | 12 ± 12                           | 1 ± 2                                    | 19 ± 13       | 0.247 |
| Range          | 2–50         | 0–8                                        | 0–33                                       | 0–40                             | 0–6                                      | 2–41          |       |
| p              | 0.063        | 0.015                                      | <0.001                                     | 0.481                             | 0.247                                    | <0.001        |       |

Abbreviations: NMOSD = neuromyelitis optica spectrum disorder; RRMS = relapsing remitting multiple sclerosis.

a Lesion count = total number of lesions detectable on T2*-weighted images.
b Perivascular = visibility of a small central vein within the lesion center.
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