

## Supplementary Material

**Supplemental Table 1 | Associations of cervical cord volumes and SC WM percentage with the 9HPT and T25FW**

| Cervical cord volume   |                           |                           |
|------------------------|---------------------------|---------------------------|
|                        | AQP4-IgG+NMOSD            | MOGAD                     |
| 9HPT dominant hand     | $\beta=0.27$ , $p=0.162$  | $\beta=-0.19$ , $p=0.514$ |
| 9HPT non-dominant hand | $\beta=0.13$ , $p=0.571$  | $\beta=0.04$ , $p=0.874$  |
| T25FW                  | $\beta=-0.21$ , $p=0.443$ | $\beta=-0.41$ , $p=0.096$ |
| SC WM percentage       |                           |                           |
|                        | AQP4-IgG+NMOSD            | MOGAD                     |
| 9HPT dominant hand     | $\beta=0.14$ , $p=0.487$  | $\beta=0.12$ , $p=0.678$  |
| 9HPT non-dominant hand | $\beta=0$ , $p=0.999$     | $\beta=0.45$ , $p=0.083$  |
| T25FW                  | $\beta=-0.15$ , $p=0.579$ | $\beta=0.31$ , $p=0.225$  |

AQP4-IgG+NMOSD, aquaporin-4 antibody seropositive neuromyelitis optica spectrum disorders; MOGAD, myelin oligodendrocyte antibody associated disease; T25FW, timed 25-foot walk test mean time; 9HPT. 9-hole peg test mean time.

**Supplemental Table 2 | Descriptive longitudinal clinical and SC phenotypic case series of patients with additional attacks between MRI visits**

| Patient   | Clinical History  | SC MRI findings  |
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| <p>Subject 1, F, 51y</p> <p>Diagnosis: AQP4-IgG+NMOSD</p> <p>Age at onset: 22 y</p> <p>Attacks before Baseline</p> <ul style="list-style-type: none"> <li>- Over 29 years after disease onset multiple episodes of ON (1/year)</li> <li>- 25 years after disease onset single episode of Myelitis and ON</li> </ul> <p>Prior immunotherapy</p> <ul style="list-style-type: none"> <li>- Single administration of mitoxantrone, discontinuation due to sepsis</li> <li>- Octagam: 43 months</li> <li>- Single administration of Rituximab (persistent B-cell depletion)</li> </ul> | <p><b>Baseline visit 09/2017:</b></p> <p>Disease duration: 29 y</p> <p>EDSS: 3.5</p> <p>Pain location: feet</p> <p>Average Pain Intensity 24h: 0/10</p> <p>Average Pain Intensity 4w: 1/10</p> <p>Neuropathic Pain Score: 7/35</p> <p>No immunotherapy</p> <p><b>Clinical visit 10/2018:</b></p> <p>Attack 04/2018: ON RE</p> <p>Symptoms: Visual impairment restricted walking distance and impaired balance</p> <p>Therapy: IVMP</p> <p>Attack 09/2018: ON RE</p> | <p><b>09/2017: Scanner 1</b></p> <p>GM (mL): 0.079 (20.73%)</p> <p>WM (mL): 0.302 (79.27%)</p> <p>Cervical Cord (mL): 0.38</p> <p><b>10/2018: Scanner 1</b></p> <p>GM (mL): 0.091 (22.81%)*</p> <p>WM (mL): 0.308 (77.19%)**</p> <p>Cervical Cord (mL): 0.40</p> |

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| <p>No relevant comorbidities</p>  | <p>Symptoms: Visual impairment</p> <p>Therapy: 6x IA</p> <p>EDSS: 4.0</p> <p>Pain location: Head/neck, legs</p> <p>Average Pain Intensity 24h: 1/10</p> <p>Neuropathic Pain Score: 6/35</p> <p>No immunotherapy</p>   | <p>*It can be seen that 1 month after an ON attack, the GM percent in the SC increased by 2% from baseline and the cervical cord volume also increased.</p> <p>**WM% does not increase, and as it is complementary to the GM % in the cord, it decreased over time.</p> |
| <p>Subject 2, F</p> <p>Diagnosis: AQP4-IgG+NMOSD</p> <p>Age at onset: 60y</p> <p>Attacks before baseline</p> <ul style="list-style-type: none"> <li>- One myelitis</li> </ul> <p>No prior immunotherapy</p> | <p><b>Baseline Visit 11/2017:</b></p> <p>Disease duration: 11 months</p> <p>EDSS: 6.5</p> <p>Pain location: trunk</p> <p>Average Pain Intensity 24h: N.A.</p> <p>Average Pain Intensity 4w: 10/10</p> <p>Neuropathic Pain Score: 8/35</p> <p>No Immunotherapy</p> <p><b>Clinical Visit 11/2018:</b></p> <p>Attack 06/2018: Myelitis</p> | <p><b>11/2017: Scanner 1</b></p> <p>GM (mL): 0.07 (16.75%)*</p> <p>WM (mL): 0.347 (83.01%)**</p> <p>Cervical Cord (mL): 0.42</p> <p><b>11/2018: Scanner 1</b></p> <p>GM (mL): 0.079 (19.95%)*</p>   |

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| <p>Comorbidities:</p> <ul style="list-style-type: none"> <li>- Spinal canal stenosis C4-6 with intervertebral disc graft C4/5 without myelopathy</li> </ul> <p>Recurrent myoclonus attacks of the arms without loss of consciousness (differential diagnosis: spinal myoclonus)</p> | <p>Symptoms: sensorimotor spinal cord syndrome below Th10, bladder and bowel disturbance</p> <p>Therapy: N.A., no IVMP</p> <p>EDSS: 6.0</p> <p>Pain location: trunk</p> <p>Average Pain Intensity 24h: 8/10</p> <p>Average Pain Intensity 4w: N.A.</p> <p>Neuropathic Pain Score: 15/35</p> <p>Immunotherapy: Rituximab since 12/2017</p> | <p>WM (mL): 0.317 (80.05%)**</p> <p>Cervical Cord (mL): 0.40</p> <p>*It can be seen that with an additional myelitis within 5 months of the second MRI visit, the GM% increased by 3%, even though the cervical cord volume decreased.</p> <p>**WM% also decreases (~3% between visits), and as it is complementary to the GM % in the cord.</p> |
| <p>Subject 3, F, 51 y</p> <p>Diagnosis: MOGAD</p> <p>Age at onset: 47y</p> <p>Attacks before baseline</p> <ul style="list-style-type: none"> <li>- Four myelitis attacks</li> <li>- Three brainstem attacks</li> </ul>  | <p><b>Baseline Visit 09/2018:</b></p> <p>Disease duration: 30 months</p> <p>EDSS: 3.5</p> <p>Pain location: Head/neck, trunk, hip, legs, feet</p> <p>Average Pain Intensity 24h: 5.5/10</p>   | <p><b>09/2018: Scanner 1</b></p> <p>GM (mL): 0.082 (17.71%)*</p> <p>WM (mL): 0.381 (82.29%)**</p> <p>Cervical Cord (mL): 0.46</p>  |

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| <p>Prior immunotherapy</p> <ul style="list-style-type: none"> <li>- Three cycles of Rituximab</li> <li>- Mycophenolate mofetil + Prednisolon since 02/2017</li> </ul>            | <p>Average Pain Intensity 4w: 5/10</p> <p>Neuropathic Pain Score: 17/35</p> <p>Immunotherapy: Mycophenolate mofetil since 02/2017.</p>  |   |
| <p>Comorbidities</p> <ul style="list-style-type: none"> <li>- Cervical spine syndrome</li> <li>- Vitamin D deficiency</li> <li>- Migraine</li> <li>- Anxiety disorder</li> </ul> | <p><b>Clinical Visit 09/2020:</b></p> <p>Attack 01/2019: Myelitis</p> <p>Symptoms: Paresthesia, Hyperalgesia</p> <p>Therapy: IVMP, PLEX</p> <p>Pain location: Head/neck, trunk, hip, legs, feet</p> <p>Average Pain Intensity 24h: 4.75/10</p> <p>Average Pain Intensity 4w: 5/10</p> <p>Neuropathic Pain Score: 22/35</p> <p>Immunotherapy: Tocilizumab + IVIG since 04/2020</p> | <p><b>09/2020: Scanner 2</b></p> <p>GM (mL): 0.067 (16.30%)*</p> <p>WM (mL): 0.344 (83.70%)**</p> <p>Cervical Cord (mL): 0.41</p> |

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|  | <b>Clinical Visit 08/2021:</b><br><br>Attack 12/2020: Myelitis<br><br>Symptoms: Numbness in the area of the anus - aggravation of previous symptoms (burning whole body pain, backpain)<br><br>Therapy: oral prednisone, PLEX<br><br><br><br><br>Pain location: Head/neck, trunk, hip, legs, feet<br><br>Average Pain Intensity 24h: 2/10<br><br>Average Pain Intensity 4w: 3/10<br><br>Neuropathic Pain Score: 22/35<br><br><br>Immunotherapy: Tocilizumab + IVIG since 04/2020 | <b>08/2021: Scanner 2</b><br><br>GM (mL): 0.061<br>(15.17%)*<br><br>WM (mL): 0.341<br>(84.83%)**<br><br>Cervical Cord (mL): 0.40<br><br><br><br><br>*It can be seen that the GM% consistently decreases by ~1% between visits and the cervical cord volume also decreases with additional myelitis attacks between visits.<br><br>**WM% also increases (~1% per visit), and as it is complementary to the GM % in the cord. |
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| <p>Subject 4, F</p> <p>Diagnosis: MOGAD</p> <p>Age at onset: 53 y</p> <p>Attacks before baseline</p> <ul style="list-style-type: none"> <li>- Two confirmed brainstem attacks, one including the cervical myelon</li> </ul>                     | <p><b>Baseline Visit 09/2018:</b></p> <p>Disease duration: 29 months</p> <p>EDSS: 2.0</p> <p>Average Pain Intensity 24h: 5/10</p> <p>Average Pain Intensity 4w: 7/10</p> <p>Neuropathic Pain Score: 8/35</p> <p>No Immunotherapy</p>   | <p><b>09/2018: Scanner 1</b></p> <p>GM (mL): 0.073 (18.43%)*</p> <p>WM (mL): 0.323 (81.57%)**</p> <p>Cervical Cord (mL): 0.40</p>   |
| <p>Prior immunotherapy</p> <ul style="list-style-type: none"> <li>- Azathioprine: 3 months (discontinuation due to elevation of liver transaminases)</li> <li>- Low-dose prednisone p.o.: 24 months</li> </ul> <p>No relevant comorbidities</p> | <p><b>Clinical Visit 10/2019:</b></p> <p>Attack 04/2019: Myelitis</p> <p>Symptoms: Sensory spinal cord syndrome with dysesthesia below Th12</p> <p>Therapy: IVMP</p> <p>EDSS 3.0</p> <p>Pain location: Head/neck, arms, hands, legs, feet</p> <p>Average Pain Intensity 24h: 6/10</p> <p>Average Pain Intensity 4w: 0/10</p> <p>Neuropathic Pain Score: 6/35</p> | <p><b>10/2019: Scanner 1</b></p> <p>GM (mL): 0.061 (16.27%)*</p> <p>WM (mL): 0.314 (83.73%)**</p> <p>Cervical Cord (mL): 0.38</p> <p>*It can be seen that with an additional myelitis attack between visits, the GM% was decreased by ~2% in a year and the cervical cord volume decreased as well.</p> |

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|  | Immunotherapy: Rituximab since 03/2019 | **WM% increases, and as it is complementary to the GM % in the cord. |
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AQP4-IgG+NMOSD, Aquaporin-4-IgG positive neuromyelitis optica spectrum disorder; EDSS, Expanded disability status scale; F, female; GM, grey matter; h, hours; IA, immunoadsorption; IVMP, intravenous methylprednisolone; m, male; mL, milliliters; MOGAD, myelin oligodendrocyte glycoprotein associated disease; PLEX, plasma exchange; p.o., per os; RE, right eye; SC, spinal cord; w, weeks; WM, white matter; y, years. Asterisks denote observational notes made in each patient visit pertaining to their SC MRI.