

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
<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"> - Over 29 years after disease onset multiple episodes of ON (1/year) - 25 years after disease onset single episode of Myelitis and ON <p>Prior immunotherapy</p> <ul style="list-style-type: none"> - Single administration of mitoxantrone, discontinuation due to sepsis - Octagam: 43 months - Single administration of Rituximab (persistent B-cell depletion) 	<p>Baseline visit 09/2017:</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>Clinical visit 10/2018:</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>09/2017: Scanner 1</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>10/2018: Scanner 1</p> <p>GM (mL): 0.091 (22.81%)*</p> <p>WM (mL): 0.308 (77.19%)**</p> <p>Cervical Cord (mL): 0.40</p>

<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"> - One myelitis <p>No prior immunotherapy</p>	<p>Baseline Visit 11/2017:</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>Clinical Visit 11/2018:</p> <p>Attack 06/2018: Myelitis</p>	<p>11/2017: Scanner 1</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>11/2018: Scanner 1</p> <p>GM (mL): 0.079 (19.95%)*</p>

<p>Comorbidities:</p> <ul style="list-style-type: none"> - Spinal canal stenosis C4-6 with intervertebral disc graft C4/5 without myelopathy <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"> - Four myelitis attacks - Three brainstem attacks 	<p>Baseline Visit 09/2018:</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>09/2018: Scanner 1</p> <p>GM (mL): 0.082 (17.71%)*</p> <p>WM (mL): 0.381 (82.29%)**</p> <p>Cervical Cord (mL): 0.46</p>

<p>Prior immunotherapy</p> <ul style="list-style-type: none"> - Three cycles of Rituximab - Mycophenolate mofetil + Prednisolon since 02/2017 	<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"> - Cervical spine syndrome - Vitamin D deficiency - Migraine - Anxiety disorder 	<p>Clinical Visit 09/2020:</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>09/2020: Scanner 2</p> <p>GM (mL): 0.067 (16.30%)*</p> <p>WM (mL): 0.344 (83.70%)**</p> <p>Cervical Cord (mL): 0.41</p>

	<p>Clinical Visit 08/2021:</p> <p>Attack 12/2020: Myelitis</p> <p>Symptoms: Numbness in the area of the anus - aggravation of previous symptoms (burning whole body pain, backpain)</p> <p>Therapy: oral prednisone, PLEX</p> <p>Pain location: Head/neck, trunk, hip, legs, feet</p> <p>Average Pain Intensity 24h: 2/10</p> <p>Average Pain Intensity 4w: 3/10</p> <p>Neuropathic Pain Score: 22/35</p> <p>Immunotherapy: Tocilizumab + IVIG since 04/2020</p>	<p>08/2021: Scanner 2</p> <p>GM (mL): 0.061 (15.17%)*</p> <p>WM (mL): 0.341 (84.83%)**</p> <p>Cervical Cord (mL): 0.40</p> <p>*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.</p> <p>**WM% also increases (~1% per visit), and as it is complementary to the GM % in the cord.</p>
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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"> - Two confirmed brainstem attacks, one including the cervical myelon 	<p>Baseline Visit 09/2018:</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>09/2018: Scanner 1</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"> - Azathioprine: 3 months (discontinuation due to elevation of liver transaminases) - Low-dose prednisone p.o.: 24 months <p>No relevant comorbidities</p>	<p>Clinical Visit 10/2019:</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>10/2019: Scanner 1</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>

	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.