

# PATTERN OF MECHANICAL PAIN SENSITIVITY ASSESSED BY QUANTITATIVE SENSORY TESTS IN DANISH PATIENTS WITH NEUROMYELITIS OPTICA SPECTRUM DISORDER

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## Introduction

- Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare recurrent autoimmune disease (1,2).
- Pain has only recently been acknowledged in NMOSD (3).
- Quantitative sensory testing of these patients has revealed inconsistent results including dynamic mechanical allodynia, and paradoxical heat sensations (4).
- Pattern of altered sensitivity to mechanical or thermal stimuli within craniofacial regions is still lacking (5).

## Aim

To identify if any abnormalities exists in sensitivity to mechanical stimuli within craniofacial regions of NMOSD.

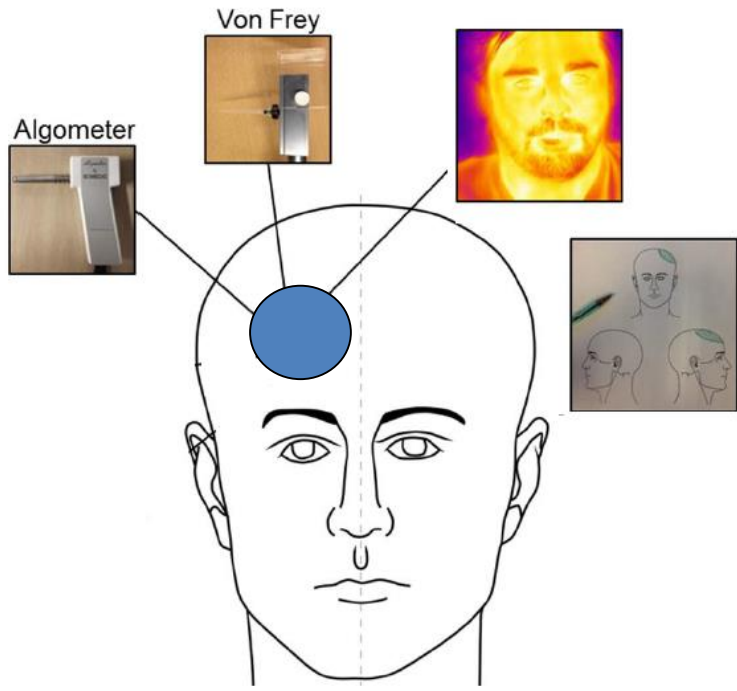
## Methods

- Patients (N=8) diagnosed with NMOSD were invited and 4 patients (3 F, 1 M, 35 ± 6.38 years) were enrolled.
- Mechanical pain thresholds were assessed by brush test, electronic von Frey test, and pressure algometry at frontalis, temporalis, and masseter muscles.
- Facial pain and headache were determined through questionnaires and interviews. Pattern of facial temperature was captured by a thermographic camera.
- All analysis of collected data was done by utilizing the software SPSS statistics ver. 25. with a significant p-value of ≤ 0.05.

**Table 1.** Summary of demographic information and other relevant details of the four enrolled patients

Patient Demographics				
	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	41	36	37	26
Gender	Female	Female	Male	Female
Height (cm)	162	173	196	180
Weight (kg)	70	65	93	74
BMI (kg/m2)	26.67	21.72	24.21	22.84
Medication	N/A	Yes	Yes	N/A
Allergies	Yes	Yes	No	Yes
Recent medicine intake	No	No	Yes	No
NMO-IgG/AQP4 *	Positive	Negative	Negative	Postive

\* Neuromyelitis Optica - Immunoglobulin G / Aquaporin 4

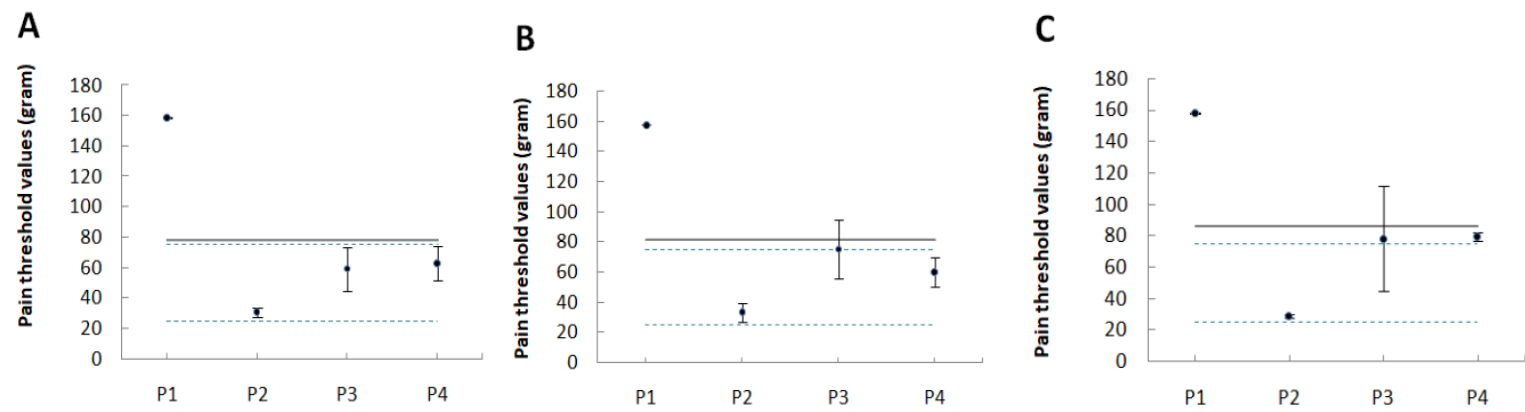


**Figure 1.** Assessments included tactile thresholds, and mechanical pain thresholds. Area mapped on face charts was recorded and a thermo-image was taken. Only temporalis muscle site is shown here.

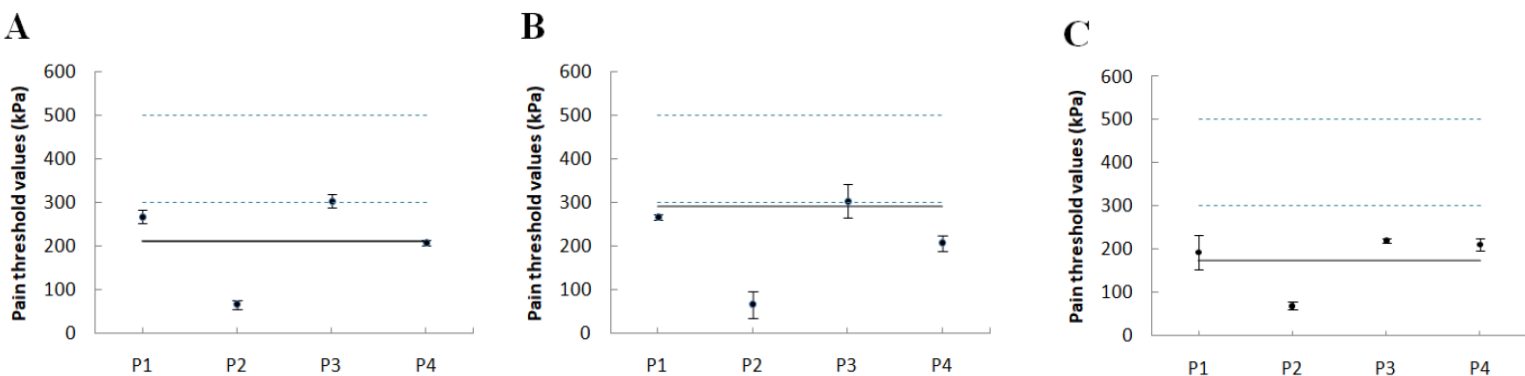
## Results

- Lowered pressure pain threshold (PPT) values were found in all patients.
- None of the patients exhibited a dynamic mechanical allodynia. Von Frey responses were within the normal range.
- Frequent mild to moderate craniofacial pain was reported and described as "cramping" and "tender", predominantly around the eyes, and occiput.
- Influence of pain on general activity and mood were reported.
- No abnormalities or asymmetry in facial skin temperature were detected.

## Results



**Figure 2.** Patients' pooled (left and right sides) mean EvF pain threshold values (± SD) for frontal (A), temporal (B) and masseter (C) muscles. The grey lines represent the group mean pain threshold values for frontal (group mean = 77.79), temporal (group mean = 81.48) and masseter (group mean = 85.97) muscles; the dotted blue lines represent the normal reference value range for EvF pain threshold (25 - 75 grams). Total number of patients = 4 (P1 - P4).



**Figure 3.** Patients' pooled (left and right sides) mean algometry pressure pain threshold values (± SD) for frontal (A), temporal (B) and masseter (C) muscles. The grey lines represent the group mean pain threshold values for frontal (group mean = 210.24), temporal (group mean = 291.69) and masseter (group mean = 173.34) muscles; the dotted blue lines represent the normal reference value range for algometry pain threshold (300 - 500 kPa). Total number of patients = 4 (P1 - P4). kPa: Kilopascal.

**Table 2.** Verbal Rating Scale (VRS) of patients' pain severity (no, mild, moderate, and severe pain) and occurrence (currently, past week, month and three months) in the craniofacial region within the past three months before experimental examination. Total number of patients = 4. N: number, % is indicated in brackets.

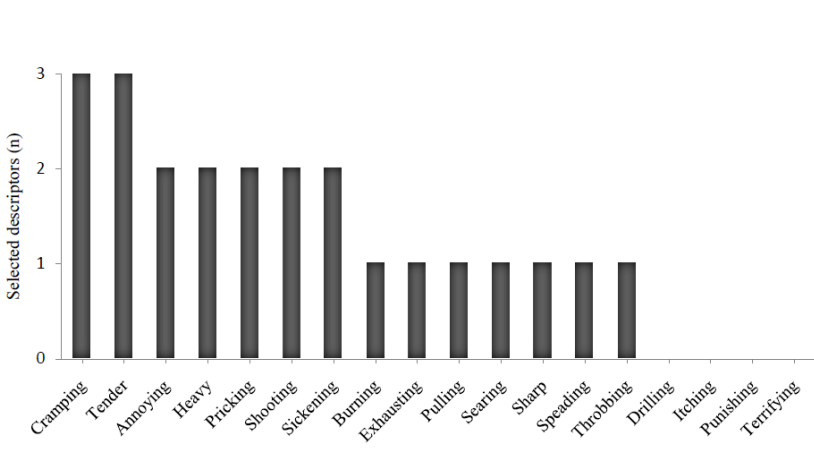
	Verbal Rating Scale			
	Today (n)	Past week (n)	Past month (n)	Past 3 months (n)
No pain	3 (75%)	1 (25%)	1 (25%)	0 (0%)
Mild pain	1 (25%)	3 (75%)	2 (50%)	1 (25%)
Moderate pain	0 (0%)	0 (0%)	1 (25%)	3 (75%)
Severe pain	0 (0%)	0 (0%)	0 (0%)	0 (0%)

**Table 3.** Numerical rating scores (NRS) of pain severity (Mean + SD) within the last 24 hours divided into worst, mildest, average and current pain. Measurements were rated with an 11-point score (0 = no pain, 10 = most imaginable pain) and scores were categorized in 4groups (0 = no pain, 1 - 3 = mild pain, 4 - 6 = moderate pain and 7 - 10 = severe pain).

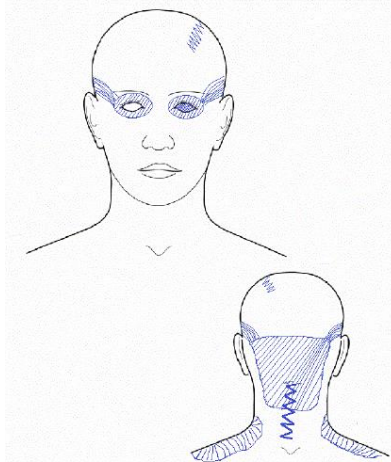
	Pain severity last 24 hours			
	Worst	Mildest	Average	Current
Mean ± SD	2.75 ± 2.75	0.75 ± 0.5	1.875 ± 1.93	1 ± 1.41
Patien (n)	4	4	4	4

**Table 4.** Pain influence on daily life aspects (Mean ± SD). Pain influence were rated with a scale ranging from 0 to 10 (0 = no influence, 10 = complete influence).

	Pain influence on daily life					
	General activity	Mood	Work	Relations with other people	Sleep quality	Joy of life
Mean ± SD	3.75 ± 3.1	3.13 ± 2.78	2.5 ± 1.73	0.875 ± 0.25	2.125 ± 2.59	1 ± 1.35
Patients (n)	4	4	4	4	4	4



**Figure 4.** Bar-chart of pain descriptors from the SF-MPQ. Total number of patients = 4. N: number of selection for each descriptor



**Figure 5.** Body chart of pain location in NMOSD patients (superimposed)

**Table 5.** Patients' overall mental health based on group mean scores obtained from 3 questionnaires (Mood and Stress Questionnaire, PHQ - 9 and BIPQ (daily mental fatigue)). The Mood and Stress Questionnaire evaluated depression, anxiety and stress with a likert scale ranging from 0 - 3 (0 = "never or not at all", 3 = "Always or severely"). PHQ - 9 evaluated only depression also with a likert scale ranging from 0 - 3 (0 = "Never", 3 = "Almost every day"). BIPQ evaluated daily mental fatigue with a 11 point scale (0 = "No fatigue", 10 = "always"). PHQ - 9: Patient Health Questionnaire 9, BIPQ: Brief Illness Perception Questionnaire.

	Patient mental health scores				
	Mood and Stress Questionnaire			PHQ - 9	Daily mental fatigue
	Depression	Anxiety	Stress		
Mean ± SD	2.5 ± 1.91	2.25 ± 2.63	3.25 ± 2.5	7.5 ± 6.24	5.5 ± 3.67
Patient (n)	4	4	4	4	4

Analysis of the thermographic images from the enrolled patients' facial region, demonstrated no noticeable thermal distribution variations from the symmetrical pattern of a normal facial skin temperature. Average and standard deviation of right and left side were 33.05±0.58°C, and 33.05±0.42°C, respectively.

## Conclusions

- Quantitative sensory tests within craniofacial region demonstrated a tendency towards lower PPT values.
- Pain was a common finding.
- Results call for a larger study for further investigations that will potentially lead to an optimal pain management.

## References

- Trebst C, Jarius S, Berthele A, et al. Update on the diagnosis and treatment of neuromyelitis optica: recommendations of the Neuromyelitis Optica Study Group (NEMOS). J Neurol. 2014;261:1–16.
- Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015;85:177–89.
- Bradi M, Kanamori Y, Nakashima I, et al. Pain in neuromyelitis optica--prevalence, pathogenesis and therapy. Nat Rev Neurol. 2014;10:529–36.
- Pellkofer HL, Havla J, Hauer D, Schelling G, Azad SC, Kuempfel T, Magerl W, Hugel V. The major brain endocannabinoid 2-AG controls neuropathic pain and mechanical hyperalgesia in patients with neuromyelitis optica. PLoS One. 2013 Aug 9;8(8):e71500.
- Nielsen GAR, Nielsen HH, Illés ZL, Gazerani P. Prevalence and Pattern of Craniofacial Pain and Headache in Danish Patients with Neuromyelitis Optica Spectrum Disorder. European Neurological Review. 2018;13(1):44–52