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Neuroinflammation in the nerve roots and dorsal root ganglion decreases following 6 weeks of neural tissue management: PET/CT imaging findings in a patient with painful cervical radiculopathy

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ABSTRACT

Background: There is increasing interest in uncovering working mechanisms of physiotherapy interventions. Advanced medical imaging enables *in-vivo* visualisation and quantification of neuroinflammation. This case report reveals for the first time how neuroinflammation in the nervous system may change following neural tissue management.

Case description: A 56-year-old man presented with a 9-month history of left C7 painful radiculopathy. He reported arm and neck pain, and numbness in the C7 dermatome. Elbow extension strength was reduced. The neurodynamic test (median nerve) was positive. MRI confirmed nerve root compression due to disc herniation C6/C7. Dynamic [^{11}C]DPA713 PET/CT imaging revealed neuroinflammation at the neuroforamen and spinal cord. While being on the surgical waitlist, he received six weeks of neural tissue management, which included 12 sessions of nerve and joint mobilisation, and a home program of neurodynamic exercises.

Outcome: At 6-weeks follow-up, arm and neck pain intensity had markedly reduced, which was maintained at 6 months. These improvements coincided with a substantial decrease in neuroinflammation at the affected neuroforamen (PET/CT: V_T: from 12.96 to 6.21). No meaningful decrease was observed in the spinal cord (V_T: from 6.43 to 5.38).

Discussion: Following six weeks of neural tissue management, *in vivo* measures of neuroinflammation reduced substantially at the affected nerve roots and dorsal root ganglion, which coincided with decreased neck and arm pain.

Conclusion: Changes in neuroinflammation exceeding the smallest detectable difference can be measured following neural tissue management in a patient with painful cervical radiculopathy. A randomised trial to validate these findings is warranted.

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1. Background

Preclinical (i.e., animal) research revealed neuroimmune activation following peripheral nerve injury at the dorsal root ganglion (DRG), spinal cord, and brain (Austin and Moalem-Taylor, 2010; Grace et al., 2014). These neuroimmune reactions include macrophage activation in the DRG and aberrant microglia and/or astrocyte (glial) activation within the spinal cord (Schmid et al., 2013) and brain (Austin and Moalem-Taylor, 2010; Grace et al., 2014). Activated microglia and astrocytes release inflammatory mediators such as reactive oxygen species (ROS) and inflammatory cytokines that activate or sensitise the nociceptive circuitry (Chen et al., 2018; Cserép et al., 2020).

Systematic reviews of animal research have revealed that several conservative interventions are capable of attenuating these neuroimmune reactions, such as joint and nerve mobilisation (Lutke Schipholt et al., 2021) and aerobic exercises (Koop et al., 2023; Matesanz-García et al., 2023; Sleijser-Koehorst et al., 2023). These interventions may present promising therapeutic strategies that target the pathophysiological processes, resulting in pain relief. Randomised clinical trials (e.g. (Nee et al., 2012b),) and systematic reviews (e.g. (Basson et al., 2017; Lascurain-Aguirrebeña et al., 2024),), showed that neurodynamics or neural tissue management (NTM) improves pain, disability and function in patients with nerve-related neck/arm pain and may be more effective than alternative interventions (e.g., physical exercise) or no treatment.

The therapeutic aim of NTM is to use movement to improve pain and function by restoring the altered homeostasis in and around the nervous system (Coppieters et al., 2024). During activities of daily living, the nervous system requires the ability to absorb tension and compression, and slide and stretch, which is important to maintain or restore nerve health (Ellis et al., 2022). However, this ability is often compromised in a compression neuropathy due to increased mechanosensitivity. NTM techniques for radiculopathy are intended to move the nervous system within the intervertebral foramina and spinal canal, relative to surrounding structures (Coppieters and Alshami, 2007; Lohman et al., 2015). Although preclinical studies show that nerve mobilisation can alter neuroimmune responses in experimental models, evidence in humans remains limited to indirect observations (Lutke Schipholt et al., 2021). For example, a reduction in oedema (i.e., one of the cardinal signs of inflammation) in the median nerve at the wrist has been observed following neurodynamic exercises for carpal tunnel syndrome (Schmid et al., 2012). Unfortunately, using standard blood sampling and measuring inflammatory markers systemically seems too rudimentary to be able to detect these very localised changes in inflammation (Lutke Schipholt et al., 2025a). While preclinical (e.g., animal) studies allow dissection of neuronal tissue and detailed immunohistochemical analysis, these invasive methods are not ethically permissible in human participants. As a result, *in vivo* assessment of neuroinflammation, particularly at specific anatomical sites, remains challenging. Therefore, more advanced techniques are needed that are able to specifically measure tissue changes locally. One promising avenue is the use of imaging modalities such as positron emission tomography combined with computed tomography (PET/CT), which allows for *in-vivo* visualisation of neuroinflammatory processes at the site of pathology.

Neuroinflammation can be measured in humans using PET/CT (Loggia et al., 2015). During neuroinflammation, the expression of a protein called TSPO (i.e., 18 kDa translocator protein) increases significantly in activated glial cells (i.e., the immune cells of the nervous system) (Banati, 2002; Venneti et al., 2013). Radiotracers (also called radioligands) are specifically developed molecules labelled with a small amount of radioactive material that are injected in the bloodstream to enable the visualisation and quantification of various biological processes (such as neuroinflammation) using advanced medical imaging. [^{11}C]DPA713 is a radiotracer specifically developed to bind to TSPO ([^{11}C] refers to a radioactive isotope of carbon (i.e., carbon-11) and DPA713 is a ligand that binds to TSPO). Because of the increased expression of TSPO in activated glial cells in neuroinflammation, the [^{11}C]DPA713 radiotracer will accumulate at the area of neuroinflammation, and its radioactive emissions can be detected with PET imaging. Recently, we showed localised neuroinflammation in people with painful cervical radiculopathy (Lutke Schipholt et al., 2025a). Neuroinflammation was detected in the spinal nerve compared to pain-free control participants and compared to unaffected (reference) tissues (Lutke Schipholt et al., 2025b). Furthermore, neuroinflammation was associated with an increased likelihood of neuropathic pain (Lutke Schipholt et al., 2025a).

The primary aim of this case report was to examine whether clinical improvements following NTM are associated with localised improvements in neuroinflammation at the level of the spinal nerve and spinal cord using advanced *in vivo* PET/CT imaging using [^{11}C]DPA713 in a patient with painful cervical radiculopathy. To our knowledge, this is the first instance where localised changes in neuroinflammation in the nervous system are investigated following any conservative intervention for any form of musculoskeletal condition.

2. Case description

Reporting occurred in line with the CARE guidelines for case reports (Gagnier et al., 2013) and TIDIER guidelines for intervention description (Hoffmann et al., 2014; Riley et al., 2017). The study was approved by the Medical Ethics Committee of Amsterdam University Medical Centre, location VUmc (Approval number: 2020.179). After signing informed consent, the participant provided their relevant medical history, completed several questionnaires documenting the impact of painful cervical radiculopathy on activities of daily living, psychological well-being, clinical symptoms, underwent a standardised neurological clinical assessment and blood withdrawal to measure systemic inflammation. Details about the questionnaires and blood withdrawal are summarised in Appendix A.

2.1. Patient details

The patient was a 56-year-old male with a military profession and father of two children (14 and 19 years). He was diagnosed with a left C7 painful cervical radiculopathy. The diagnosis was made by a neurologist and was based on both patient interview and clinical examination items, and relevant MRI findings (Sleijser-Koehorst et al., 2021, 2025). He experienced radicular arm pain (VAS: 42/100) and neck pain (VAS: 42/100), and numbness in the distal left C7 dermatome. Magnetic resonance imaging (MRI) showed nerve root compression due to a C6/C7 disc herniation (Fig. 1).

The symptoms had started nine months earlier, for no apparent reason. Over time, there was a progressive increase in arm pain intensity, but no subjective worsening of neurological deficits. The patient was on the waiting list for anterior cervical discectomy with fusion surgery. His body mass index (BMI) was 31.6 (height 178 cm, weight 100 kg), and although classified as being obese, he had a muscular body phenotype.

Bedside neurological examination revealed loss of light touch sensation over the volar and dorsal aspects of the left thumb and index finger, which reflects the C6 or C7 dermatome (Apok et al., 2011). Pinprick testing was normal. Strength testing revealed weaker elbow extension on the affected side (Medical Research Council (MRC) scale: 4/5), reflective of the C7 myotome. Strength test of other muscles was normal. Some reflexes were abnormal, but comparable on both sides: brachioradialis reflex (C5-C6) and triceps reflex (C7-C8) were absent on both sides. Biceps reflex (C5-C6) was normal on both sides.

Physical examination showed reduced cervical range of motion (30° left and 57° right rotation). Upper limb neurodynamic testing for the median nerve (ULNT1) was positive, indicative of increased mechanosensitivity of the nervous system (Nee et al., 2012a). The patient's arm pain could be reproduced with the ULNT1 and his arm pain could be influenced with structural differentiation (i.e., wrist extension and

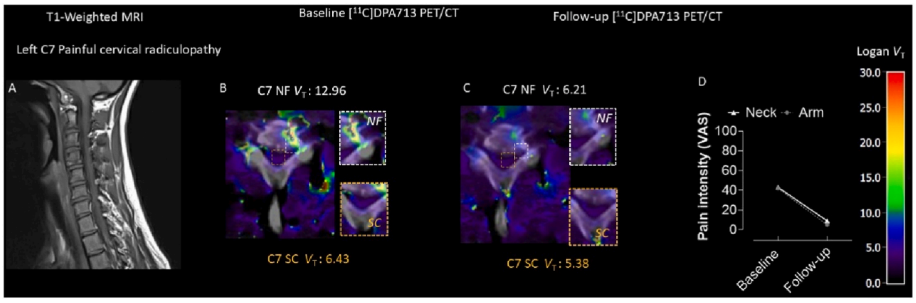

Fig. 1. Neuroinflammation at baseline and after six weeks of neural tissue management (follow-up) in a patient with painful cervical radiculopathy. A: T1-weighted MRI. B: Baseline parametric cross-sectional image of [^{11}C]DPA713 binding merged with CT, with a zoomed view at the neuroforamina (NF) and spinal cord (SC). Higher volume of distribution (V_T) indicates more tracer binding, suggesting higher levels of neuroinflammation. C: Follow-up parametric cross-sectional image of [^{11}C]DPA713 binding merged with CT, with a zoomed view at the neuroforamina (NF) and spinal cord (SC). D: Baseline and follow-up pain intensity measured using pain visual analogue scale (VAS) for 24-h mean neck pain and arm pain.

cervical contralateral lateral flexion increased arm pain).

The questionnaires indicated severe disability (Neck Disability Index (NDI): 28/50), no clinically meaningful fear of movement (Tampa Scale for Kinesiophobia (TSK): 28/44), mild central sensitisation (Central Sensitisation Inventory (CSI): 38/100), poor sleep quality (Pittsburg Sleep Quality Index (PSQI): 9/21), possible neuropathic pain (painDETECT (PD-Q): 15/38), and no depressive symptoms (Depression, Anxiety, Stress Scale 21 (DASS21 – Depression): 2/21), mild anxiety (DASS21 – Anxiety: 5/21) and no stress (DASS21 – Stress: 4/21) symptoms.

When his symptoms started, he occasionally used acetaminophen (paracetamol; 500 mg/dose) and non-steroid inflammatory drugs (naproxen; 220 mg/dose), which provided short-term pain relief. In the four weeks preceding taking part in this research project, he did not take medication or seek treatment for his neck-arm pain and did not undergo physiotherapy. Following consultation with the neurosurgeon, he was placed on the waiting list for anterior cervical discectomy with fusion surgery six-weeks before participating in this research project. He indicated he was keen to attempt conservative management while being on the surgical waitlist.

2.2. Intervention

The NTM protocol was based on successful randomised clinical trials examining the effects of a 4-week program of NTM for people with nerve-related neck and arm pain (Nee et al., 2012b) and nerve-related back and leg pain (Ferreira et al., 2016; Hall et al., 2017). The NTM intervention was modified to a 6-week program, with a detailed overview available in the original paper (Nee et al., 2011). In short, NTM included several key components, including a brief educational element, nerve and joint mobilisation, and a home program of neurodynamic exercises. The patient attended twelve treatment sessions over 6 weeks. A musculoskeletal physiotherapist with ~14 years of relevant clinical experience delivered the treatments.

Two messages were emphasised in the education component: (1) that the symptoms were, at least in part, related to a nerve that had become overly sensitive to movement, and (2) that it was safe to move, in order to alleviate unnecessary concerns regarding movement. The educational component was intentionally brief, as we wanted to assess the role of NTM, rather than a combined effect of pain science education and NTM (i.e., a multimodal intervention).

Nerve and joint mobilisation techniques were aimed at gently moving the nervous system relative to its surrounding structures without exacerbating symptoms. At most, the participant was allowed to feel a gentle stretching sensation, which should subside quickly after the exercises. Joint and nerve mobilisation included a cervical contralateral lateral glide (Coppieters et al., 2003; Rodríguez-Sanz et al., 2017) (Supplementary Fig. S1) and sliding and/or tensioning techniques (Nee et al., 2011) (Supplementary Fig. S2). Furthermore, the patient received a cervico-thoracic traction manipulation (also referred to as Nelson manipulation), which is safe and effective in patients with cervical radiculopathy (Young et al., 2019).

The home program of neurodynamic exercises involved a sliding technique for the median nerve and cervical nerve roots (Supplementary Fig. S3). In this technique, movements that lengthen the nerve bed were counterbalanced by movements that shorten it (Coppieters and Butler, 2008). These sliding techniques result in significant nerve movement with minimal increase in nerve strain (Coppieters and Alshami, 2007). The patient was instructed to perform 10 to 15 repetitions of these sliding techniques, three times per day on days they did not have an in-person treatment session. On treatment days, the patient performed a single set of the sliding technique. The clinician assessed and guided the patient to ensure correct execution of the neurodynamic exercises, adjusting as needed. Patient compliance with the neurodynamic exercises was monitored through an activity diary. No adverse events following NTM were reported. The interval between the last in-person NTM session and the follow-up PET/CT scan was 4 days. The patient performed home exercises one day before the follow-up PET/CT scan.

2.3. Neuroinflammation imaging

A detailed technical description of the PET/CT scanning protocol and analyses to quantify neuroinflammation are beyond the scope of this case report. Here, we provide a brief overview of the methods, and more details can be found elsewhere (Lutke Schipholt et al., 2025a, 2025b). Scans were performed using a Philips Ingenuity PET/CT (Philips Medical Systems, Best, The Netherlands) targeting affected and unaffected cervical spinal nerve roots, DRGs, spinal cord segments from C4 to C8 and the ascending aorta. The patient received an injection of the tracer [^{11}C]DPA713 of 359 MBq at baseline and 378 MBq at the six-week follow-up scan. Each scan lasted 60 min. To support image interpretation, blood samples were collected during the scan. Images were analysed using ACCURATE software to identify regions of interest and assess tracer binding (Boellaard, 2018; Burggraaff et al., 2020). The primary outcome was the volume of distribution (V_T), which reflects the amount of tracer binding in tissue as a proxy for neuroinflammation. Based on previous test–retest data, changes in V_T greater than 5.60 in the nerve roots and DRGs, or 11.90 in the spinal cord, were considered meaningful and can be considered larger than measurement error and therefore reflecting a true change (Lutke Schipholt et al., 2025b).

3. Outcome

3.1. Clinical outcomes

Following 6 weeks of NTM, there was a reduction in arm pain

intensity (baseline VAS: 42/100; follow-up VAS: 6/100) and neck pain intensity (baseline VAS: 42/100; follow-up VAS: 8/100). At six months follow-up (telephone consult only), the patient reported that improvements in his arm pain and neck pain were maintained (See Table 1). At 6-week follow-up, elbow extension strength was normal (MRC scale: 5/5). Light touch sensation over the volar and dorsal aspects of the left thumb and index finger had normalised. There was no change in reflexes. The ULNT1 was negative as recognisable symptoms could no longer be produced. Cervical ROM had increased (left rotation: from 30° to 60°; right rotation: from 57° to 70°). Disability had decreased from severe to mild disability (NDI: 13), central sensitisation had decreased from mild to subclinical (CSI: 29), the pain type had changes from possible neuropathic to nociceptive (PDQ: 10) and sleep quality had improved from mild sleep difficulty to good sleep quality (PSQI: 4). Systemic inflammation decreased (baseline hsCRP: 2.45 mg/L; follow-up hsCRP: 0.82 mg/L).

Table 1
Patient characteristics, and clinical outcome measures at baseline and follow-up.

Patient characteristics			
Diagnosis	Left C7 cervical radiculopathy due to disc herniation		
Sex	Male		
Age	56 years		
Symptom duration	9 months		
Body Mass Index	32		
TSPO polymorphism	High-affinity binder		
Clinical outcome measures	Baseline	Follow-up (6 weeks)	Follow-up (6 months)
Arm pain (mean previous 24 h), (0–100)	42 (VAS)	6 (VAS)	0 (NPRS)
Neck pain (mean previous 24 h) (0–100)	42 (VAS)	8 (VAS)	5 (NPRS)
Elbow extension (C7) strength: MRC (0–5)	4	5	–
Sensation: Light touch C7 dermatome	Sensation loss	Normal	–
Sensation: Pinprick C7 dermatome	Normal	Normal	–
Brachioradialis reflex	Bilateral absent	Bilateral absent	–
Biceps reflex	Normal	Normal	–
Triceps reflex	Bilateral absent	Bilateral absent	–
Neurodynamic test (ULNT1) affected side	Positive	Negative	–
Neurodynamic test (ULNT1) unaffected side	Negative	Negative	–
Cervical range of left rotation (degrees)	30	60	–
Cervical range of right rotation (degrees)	57	70	–
Disability, NDI (0–50)	28	13	–
Likelihood fear of movement, TSK-11 (0–44)	28	29	–
Likelihood central sensitisation, CSI (0–100)	38	29	–
Likelihood neuropathic pain, painDETECT (0–38)	15	10	–
Likelihood insomnia, PSQI (0–21)	9	4	–
Depressive symptoms, DASS21 (0–21)	2	5	–
Anxiety symptoms, DASS21 (0–21)	5	5	–
Stress symptoms, DASS21 (0–21)	4	0	–
hsCRP (mg/L)	2.45	0.82	–

Abbreviations: VAS: Visual Analogue Scale; ULNT1: Upper Limb Neurodynamic Test for the median nerve; NDI: Neck Disability Index; TSK: Tampa Scale of Kinesiophobia; CSI: Central Sensitisation Inventory; PSQI: Pittsburg Sleep Quality Index; DASS21: Depression, Anxiety, Stress Scale; hsCRP: high-sensitivity C-reactive protein. The follow-up at 6 months was conducted over the phone using the verbal numeric pain rating scale (0–100), and was limited to arm and neck pain intensity.

3.2. Imaging outcomes

At baseline, there was more neuro-inflammation at the left neuroforamen C7 (V_T: 12.96) compared to the other neuroforamina on the ipsilateral side (V_T range C4 – C8 (excluding C6/C7): 5.12 to 9.82) and on the contralateral side (V_T range C4 – C8: 5.75 to 9.90) (Figs. 1 and 2; Table 2). For the spinal cord at baseline, there was no clear pattern of elevated neuroinflammation at the affected level(s), compared to the adjacent spinal cord levels (Table 2).

Following 6 weeks of NTM, neuroinflammation at the affected neuroforamen had decreased (baseline V_T: 12.96; follow-up V_T: 6.21) (Figs. 1 and 2; Table 2). This difference (6.75) was larger than the smallest detectable difference (5.60). The detected reduction in neuroinflammation at the affected spinal cord level was small (baseline V_T: 6.43; follow-up V_T: 5.38) and the difference (1.05) was substantially smaller than the smallest detectable difference (11.9). None of the unaffected cervical levels (neuroforamina and spinal cord) showed neuroinflammation differences greater than the smallest detectable difference (Table 2).

4. Discussion

This study used [^{11}C]DPA713 PET/CT imaging to assess neuroinflammation in the nerve root, dorsal root ganglion (DRG) and spinal cord of a patient with painful cervical radiculopathy undergoing NTM over a six-week period. The advanced imaging showed (1) a clearly heightened neuroinflammation at the affected neuroforamen, and (2) a substantial and localised reduction in neuroinflammation at the affected neuroforamen. Despite increasing evidence linking neuroinflammation to musculoskeletal pain, such as inflammation of spinal nerves and roots in cervical radiculopathy (Lutke Schipholt et al., 2025a) and lumbar radiculopathy (Albrecht et al., 2018), and brain neuroinflammation in chronic low back pain (Torrado-Carvajal et al., 2021), this is the first study to visualise and quantify *in vivo* changes in neuroinflammation following an intervention in a human subject.

The reduction in neuroinflammation coincided with clinically meaningful improvements in arm and neck pain intensity, sleep quality, neuropathic pain, and systemic inflammation. While the changes cannot be ascribed to the NTM intervention, the observed clinical improvements are in line with findings from RCTs ([REF: Nee 2012]) and systematic reviews (Basson et al., 2017; Lascurain-Aguirrebeña et al., 2024). Furthermore, the improvements occurred relatively fast (i.e., 6 weeks), whereas the condition was long-standing (i.e., 9 months) with persistent, severe and previously non-improving symptoms. This, together with the strong reduction in both neuroinflammation and clinical outcomes during the intervention period, makes it plausible that both the clinical and neuroimmune improvements were related to the NTM intervention. This assumption is further supported by RCTs of animal studies where NTM (i.e., joint and nerve mobilisation) is associated with strong reductions in neuroinflammation in the spinal nerve, DRG and spinal cord (da Silva et al., 2015; Giardini et al., 2017; Salniccia et al., 2023).

Preclinical studies suggest that the movement of neurons and peripheral nerves, as well as the mobilisation of structures encompassing sensitised neural tissues, contribute to the restoration of the perturbed homeostasis at the entrapment site and throughout the nervous system, including a reduction in neuroinflammation (Coppieters et al., 2024; Lutke Schipholt et al., 2021). A potential mechanism by which NTM might reduce neuroinflammation is that tissue stretching itself may have anti-inflammatory properties. Neuropathic pain following peripheral nerve injury is associated with activation of pro-inflammatory genes, primarily via toll-like receptor 4 (TLR-4) signalling in the DRG (Acioglu et al., 2022; Bettoni et al., 2008; Bruno et al., 2018). TLR-4 activation leads to nuclear translocation of NF-κB, driving pro-inflammatory gene

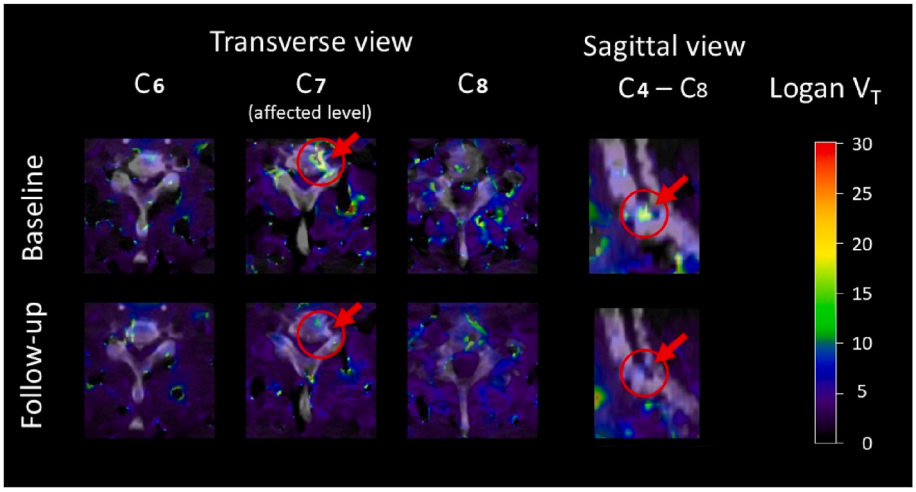

Fig. 2. Neuroinflammation at baseline and after six weeks of neural tissue management (follow-up) in a patient with painful C7 cervical radiculopathy. To quantify [^{11}C]DPA713 binding at the neuroforamina and spinal cord, we utilised an image-derived input single tissue compartmental (1T2k) model. For visualisation purposes, we generated volume of distribution (V_T) images using Logan plot analysis, with a time threshold of t* = 30 min. Transverse C6 to C8 and sagittal C4 to C8 represent the cervical level. The red arrows indicate the left C7 neuroforamina.

Table 2
Radioligand binding at the spinal nerve and spinal cord at baseline and follow-up.

		Neuroinflammation metric 1T2k V_T		
	Level	Baseline	Follow-up	Percentage change
DRG & spinal nerves left	C4	5.12	6.16	+20.3 %
	C5	6.91	7.72	+11.7 %
	C6	5.97	6.43	+7.7 %
	C7 (affected level)	12.96	6.21	−52.1 %
	C8	9.82	9.49	−3.4 %
DRG & spinal nerves right	C4	6.06	6.28	+3.6 %
	C5	5.88	6.75	+14.8 %
	C6	9.56	8.09	−15.4 %
	C7	9.90	9.02	−8.9 %
	C8	5.75	7.32	+27.3 %
Spinal cord	C4	6.49	7.11	+9.6 %
	C5	5.88	6.08	+3.4 %
	C6	5.61	6.06	+8.0 %
	C7	6.43	5.38	−16.3 %
	C8	7.21	7.67	+6.4 %

Abbreviations: 1T2k: single-tissue compartmental model; V_T: volume of distribution; DRG: dorsal root ganglion.

expression (Bruno et al., 2018). Normally, this is inhibited by IκB, but tissue stretching may stabilise IκB, possibly via mechanotransduction effects, thereby preventing NF-κB activation and reducing cytokine production (Dossumbekova et al., 2007; Król et al., 2022). Further research is needed to clarify if and how NTM may modulate these inflammatory pathways.

Although a major advancement, we have to acknowledge several limitations of [^{11}C]DPA713 PET/CT imaging in clinical research. First, the method involves exposure to ionizing radiation, which, although relatively low, still carries a cumulative risk, particularly in studies requiring repeated scans. Second, quantitative PET/CT is resource-intensive, with high associated costs and significant time demands for both scanning and image analysis. Furthermore, not all patients are suitable candidates for this imaging modality due to individual genetic variability (TSPO polymorphisms), which can influence radioligand binding and must be considered during participant selection and data interpretation. While the translocator protein (TSPO) is widely regarded as a marker of neuroinflammation, it is not exclusive to activated microglia. Its expression may also reflect activity in astrocytes, endothelial cells, and vascular smooth muscle cells, depending on disease pathology, progression stage, and anatomical context (Nutma et al., 2021a, 2021b). Additionally, [^{11}C]DPA713 binding does not distinguish between pro-inflammatory and anti-inflammatory phenotypes, underscoring the potential value of developing radioligands capable of differentiating between distinct immune responses (Van Weehaeghe et al., 2019).

5. Conclusion

This case report demonstrates that *in-vivo* changes in inflammation of the nerve root and DRG, exceeding the smallest detectable difference, can be measured in a patient with a painful cervical radiculopathy following NTM. Having established the feasibility of this approach in a single case, RCTs are warranted and imperative.

CRediT authorship contribution statement

Ivo J. Lutke Schipholt: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Michel W. Coppieters:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Meghan A. Koop:** Writing – review & editing, Project administration, Investigation, Formal analysis. **Ronald Boellaard:** Writing – review & editing, Visualization, Supervision, Software, Conceptualization. **Elsmarieke van de Giessen:** Writing – review & editing, Resources. **Carmen Vleggeert-Lankamp:** Writing – review & editing, Project administration. **Paul R. Depauw:** Writing – review & editing, Investigation. **Bart N.M. van Berckel:** Writing – review & editing, Conceptualization. **Adriaan A. Lammerstma:** Writing – review & editing, Methodology. **Maqsood Yaqub:** Writing – review & editing, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Gwendolyne G.M. Scholten-Peeters:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition,

Formal analysis, Data curation, Conceptualization.

Ethics approval and consent for publication

This study was approved by the Medical Ethics Committee of Amsterdam University Medical Centre, location VUmc (Approval number: 2020.179).

Consent for publication

The participant has provided written consent for participation in the study and for publication of the findings.

Availability of data and materials

Investigators whose proposed use of the data had been approved by an independent review committee identified for this purpose can access the data for individual participant data meta-analysis. Data will be available beginning 9 months and ending 36 months following article publication. Proposals may be submitted up to 36 months following article publication. After 36 months, the data will be available in our University's data warehouse, but without investigator support other than deposited metadata. Information regarding submitting proposals and accessing data may be found at https://research.vu.nl.

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Competing interests

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.msksp.2026.103502.

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