

COMMENTARY TO HABILITATION THESIS¹

Brief characteristic of the investigated matter

Despite substantial progress in the diagnosis and management of neurological disorders, key components of their clinical spectrum remain underrecognized, particularly non-motor symptoms and systemic comorbidities, which are often not adequately captured by standard diagnostic and therapeutic frameworks.

The present body of work focuses on two clinically significant yet often overlooked domains—neuropathic pain and fertility disorders. Both domains share a common feature: they are frequently underrecognized in clinical practice and show a weak association with conventional measures of disease activity, despite their substantial impact on quality of life. Accordingly, this habilitation thesis underscores the need to systematically integrate these domains into comprehensive clinical assessment and supports a shift toward a more individualized and multidisciplinary model of care.

Neuropathic pain is defined as pain arising as a direct consequence of a lesion or disease affecting the somatosensory nervous system at the peripheral or central level. It represents a complex clinical syndrome with heterogeneous pathophysiological mechanisms, variable clinical presentation, and often a limited response to conventional therapies. Its diagnosis requires integration of clinical assessment, neurophysiological testing, and modern approaches to pain phenotyping. The collection of commented works addressing this topic includes several validation studies of Czech-language versions of selected instruments used in the diagnosis of neuropathic pain [2–4], as well as a set of original studies focusing on sensory profiling in patients with diabetic sensorimotor polyneuropathy (DSPN) [5,6] and chronic neuropathic extremity pain in multiple sclerosis (MS) [10]. Furthermore, we investigated risk factors for the development of neuropathic pain in these clinical entities [5,10], as well as in low back pain [11–12], and factors associated with the occurrence of anxiety and depression in patients with DSPN [13].

Fertility disorders in neurological diseases constitute a distinct, multidimensional clinical entity, involving central dysregulation of the hypothalamic–pituitary–gonadal

¹ The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant's contribution in terms of both quality and content.

axis as well as peripheral nervous system involvement, autonomic dysfunction, and iatrogenic influences, including pharmacotherapy. These disturbances may substantially impair quality of life in patients of reproductive age. The works addressing this topic included in the presented collection comprise several review articles [15–18, 20], case reports [21–23], and an original study focusing on fertility disorders in selected muscular dystrophies [19].

Objectives of the work

The aim of the neuropathic pain-focused component of this work was to introduce into clinical practice in the Czech Republic selected tools commonly used within the diagnostic algorithm of neuropathic pain, including, where appropriate, validation of their Czech-language versions. These included primarily the Neuropathic Pain Symptom Inventory (NPSI) [2], as well as quantitative sensory testing (QST), including the DFNS protocol—a comprehensive, standardized tool for assessing a broad spectrum of sensory modalities developed by the Deutscher Forschungsverbund Neuropathischer Schmerz (German Research Network on Neuropathic Pain) [3]—and dynamic QST methods [4].

These app

roaches were subsequently applied in a series of original studies aimed at identifying characteristic sensory profiles in patients with both painful and non-painful diabetic sensorimotor polyneuropathy (DSPN) [5,6] and chronic neuropathic extremity pain in multiple sclerosis (MS) [10]. We further sought to identify risk factors for neuropathic pain in these conditions [5,6,10], as well as in chronic low back pain syndromes [11–12]. In DSPN, an additional objective was to refine estimates of the prevalence of anxiety and depressive symptoms in patients with painful disease and to identify associated risk factors [5,13].

Several studies also evaluated the diagnostic contribution of additional modalities, including sympathetic skin response (SSR) [14], contact heat-evoked potentials (CHEPs) [9], intraepidermal nerve fiber density (IENFD) from skin biopsy [8], and selected parameters of peripheral nerve conduction studies, specifically A-waves [7], across specific clinical contexts, including those related to neuropathic pain.

In the original study addressing fertility disorders in muscular dystrophies, ovarian reserve was assessed across different disease forms using serum anti-Müllerian hormone (AMH) levels [19].

The review articles aimed to summarize current knowledge on the menstrual cycle [17], fertility disorders [15,18], assisted reproduction [18], quality of life [20], and autonomic dysfunction [16] in patients with MS. Case reports illustrated potential complications of assisted reproduction in this population [23] and highlighted diagnostic challenges associated with specific MS variants, particularly the tumefactive form [21–22].

Methods

Validated diagnostic instruments were translated using a forward–backward translation process and subsequently validated according to standard procedures in representative patient cohorts [2,3]. The original studies involved detailed patient phenotyping, including comprehensive assessment of sensory function using the DFNS-QST protocol and/or dynamic QST methods, as well as standardized questionnaires assessing neuropathic pain (e.g., NPSI), anxiety, depression, and pain catastrophizing [5,6,10–13]. The resulting data were subjected to statistical analysis, including cluster analysis [6]. These analyses were conducted in relatively large cohorts of patients with diabetic neuropathy [5,6,13], multiple sclerosis (MS) [10], and chronic low back pain [11–12]. In particular, the diabetic neuropathy cohorts, derived from a large multicenter collaborative project, were highly representative. The largest published study included nearly 800 participants (patients with painful and non-painful diabetic neuropathy, diabetes without polyneuropathy, and healthy controls) [13], while other studies included 499 [6] and 232 participants [5], respectively.

Additional studies incorporated complementary diagnostic modalities, including sympathetic skin response (SSR) [14], contact heat-evoked potentials (CHEPs) [9], intraepidermal nerve fiber density (IENFD) from skin biopsy [8], and A-waves assessed within peripheral nerve conduction studies [7].

In the original study focusing on fertility disorders, serum anti-Müllerian hormone (AMH) levels were evaluated as a marker of ovarian reserve across different types of muscular dystrophies [19]. The remaining works within this thematic area comprised review articles [15–18, 20] and case reports [21–23].

Results

The validation studies enabled the introduction of Czech-language versions of the Neuropathic Pain Symptom Inventory (NPSI) [2] and the comprehensive DFNS QST protocol [3], and facilitated the implementation of QST, including its dynamic modalities, into clinical practice in the Czech Republic [1,3,4].

Subsequent original studies consistently demonstrated that neuropathic pain is most commonly associated with a deafferentation (“sensory loss”) profile across all evaluated clinical entities, including DSPN, radicular syndromes, and chronic neuropathic extremity pain in multiple sclerosis (MS) [5,6,10,11]. In contrast, gain-of-function abnormalities (hyperalgesia, allodynia) were relatively uncommon in both MS and in painful and non-painful DSPN [5,6,10]. Disease severity emerged as the principal risk factor for neuropathic pain in DSPN, with additional contributions from diabetic nephropathy and female sex [5].

Marked neuropsychological alterations were also observed in patients with DSPN, including increased anxiety, more frequent depressive symptoms, and elevated pain catastrophizing [5,13]. These features were significantly more pronounced in the painful compared with the non-painful form of the disease [13].

In chronic low back pain, the neuropathic component was most prevalent in radicular syndromes [11]. Common screening tools, such as PainDetect, tended to underestimate this component, supporting the use of complementary diagnostic approaches [11].

Although degenerative spinal changes were common, none of the evaluated MRI parameters independently predicted the presence of a neuropathic pain component [12]. In contrast, female sex and higher overall pain intensity were significant predictors [12].

CHEPs demonstrated the ability to detect spinothalamic tract dysfunction in patients with degenerative cervical spine disease, potentially identifying emerging spinal cord involvement prior to clinically manifest myelopathy [9].

Longitudinal assessment of IENFD showed a modest age-related decline in healthy individuals (approximately 2% annually), whereas patients with diabetic polyneuropathy exhibited a markedly accelerated loss (approximately 12% per year) [8].

The presence of A-waves as an isolated electrophysiological abnormality in nerve conduction studies was associated with a significantly increased risk of subsequent peripheral neurogenic abnormalities, indicating an early stage of peripheral nerve dysfunction [7].

At the group level, SSR parameters were significantly altered in patients with small fiber neuropathy and mixed polyneuropathy; however, its diagnostic utility at the individual level remained limited [14].

In the fertility-focused section, women with myotonic dystrophy type 1 exhibited significantly reduced AMH levels compared with age-matched controls, supporting the presence of diminished ovarian reserve and a potentially shortened reproductive window. In contrast, AMH levels were preserved in myotonic dystrophy type 2, facioscapulohumeral muscular dystrophy, and carriers of Duchenne muscular dystrophy, suggesting that reduced ovarian reserve is not a universal feature across muscular dystrophies [19].

The review articles synthesize current evidence on the relationship between the menstrual cycle and MS [17], as well as fertility disorders [15,18], assisted reproduction [18], quality of life [20], and autonomic dysfunction [16] in this population. Case reports further illustrate complications of assisted reproduction in women with MS [23] and highlight diagnostic challenges associated with specific MS variants, particularly the tumefactive form [21–22].

Applicant's contribution in terms of both quality and content

In the body of work focused on neuropathic pain, the author was primarily responsible for patient recruitment across nearly all included studies, as well as for data processing and manuscript preparation [1–14]. In selected projects, particularly those addressing multiple sclerosis [10], she also contributed to study design and coordinated the research team.

In the section focused on fertility disorders, her contribution was centered predominantly on study and manuscript conception, and she served as the lead author in most publications [15–23].

[1]

VLCKOVA, E. and **SROTOVA, I.** Sensory Examination. *Ceska A Slovenska Neurologie A Neurochirurgie*. 2014, **77**(4), 402–418. ISSN 1802-4041.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
10	20	50	40

[2]

SROTOVA, I., E. VLCKOVA, J. STRAKOVA, S. KINCOVA, L. RYBA, L. DUSEK, B. ADAMOVA and J. BEDNARIK. Validation of the Czech Version of the Neuropathic Pain Symptom Inventory (NPSIcz). *Ceska A Slovenska Neurologie A Neurochirurgie* [online]. 2015, **78**(1), 45–56. ISSN 1802-4041. Available at: doi:10.14735/amcsnn201545

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	10	50	30

[3]

SROTOVA, I., E. VLCKOVA, J. STRAKOVA, S. KINCLOVA, B. ADAMOVA, L. DUSEK, J. JARKOVSKY and J. BEDNARIK. Validation of the Czech Version of the Quantitative Sensory Testing Protocol. *Ceska A Slovenska Neurologie A Neurochirurgie*. 2015, **78**(4), 442–452. ISSN 1802-4041.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	10	40	30

[4]

KINCOVA, S., E. VLCKOVA, **I. SROTOVA**, J. RAPUTOVA and J. BEDNARIK. Dynamic Methods of Quantitative Sensory Testing. *Ceska A Slovenska Neurologie A Neurochirurgie*. 2016, **79**(1), 68–76. ISSN 1802-4041.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40	10	30	20

[5]

RAPUTOVA, Jana, **Iva SROTOVA**, Eva VLCKOVA, Claudia SOMMER, Nurcan UECEYLER, Frank BIRKLEIN, Heike L. RITTNER, Cora REBHORN, Blanka ADAMOVA, Ivana KOVALOVA, Eva Kralickova NEKVAPILOVA, Lucas FORER, Jana BELOBRADKOVA, Jindrich OLISOVSKY, Pavel WEBER, Ladislav DUSEK, Jiri JARKOVSKY and Josef BEDNARIK. Sensory phenotype and risk factors for painful diabetic neuropathy: a cross-sectional observational study. *Pain* [online]. 2017, **158**(12), 2340–2353. ISSN 1872-6623. Available at: doi:10.1097/j.pain.0000000000001034

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40	0	30	0

[6]

RAPUTOVA, Jana, Aneta RAJDOVA, Jan VOLLERT, **Iva SROTOVA**, Cora REBHORN, Nurcan UECEYLER, Frank BIRKLEIN, Claudia SOMMER, Eva VLCKOVA and Josef BEDNARIK. Continuum of sensory profiles in diabetes mellitus patients with and without neuropathy and pain. *European Journal Of Pain* [online]. 2022, **26**(10), 2198–2212. ISSN 1532-2149. Available at: doi:10.1002/ejp.2034

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30	0	20	20

[7]

SROTOVA, Iva, Eva VLCKOVA, Ladislav DUSEK and Josef BEDNARIK. A-waves increase the risk of developing neuropathy. *Brain And Behavior* [online]. 2017, **7**(8, Article e00760). ISSN 2162-3279. Available at: doi:10.1002/brb3.760

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	0	50	0

[8]

DIVISOVA, S., E. VLCKOVA, **I. SROTOVA**, S. KINCOVA, M. SKORNA, L. DUSEK, P. DUBOVY and J. BEDNARIK. Intraepidermal nerve-fibre density as a biomarker of the course of neuropathy in patients with Type2 diabetes mellitus. *Diabetic Medicine* [online]. 2016, **33**(5), 650–654. ISSN 1464-5491. Available at: doi:10.1111/dme.12890

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	0	20	0

[9]

JOPPEKOVA, Lubica, Adam BETIK, Lucia BAKOSOVA, **Iva SROTOVA**, Tomas ROHAN, Milos KERKOVSKY, Marek DOSTAL, Jan STULIK, Martin NEMEC, Jan VALOSEK, Eva VLCKOVA and Josef BEDNARIK. Dermatomeal Contact Heat Evoked Potentials for the Detection of Subclinical Cervical Spinal Cord Injury in Asymptomatic Degenerative Cervical Cord Compression. *European Journal Of Neurology* [online]. 2025, **32**(12, Article e70454). ISSN 1468-1331. Available at: doi:10.1111/ene.70454

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	0	20	30

[10]

SROTOVA, Iva, Jan KOCICA, Jan VOLLERT, Jan KOLCAVA, Monika HULOVA, Jiri JARKOVSKY, Ladislav DUSEK, Josef BEDNARIK and Eva VLCKOVA *(corresponding author)*. Sensory and pain modulation profiles of ongoing central neuropathic extremity pain in multiple sclerosis. *European Journal Of Pain* [online]. 2021, **25**(3), 573–594. ISSN 1532-2149. Available at: doi:10.1002/ejp.169

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	0	30	40

[11]

ANDRASINOVA, Tereza, Eva KALIKOVA, Roman KOPACIK, **Iva SROTOVA**, Eva VLCKOVA, Ladislav DUSEK, Josef BEDNARIK and Blanka ADAMOVA. Evaluation of the Neuropathic Component of Chronic Low Back Pain. *Clinical Journal Of Pain* [online]. 2019, **35**(1), 7–17. ISSN 1536-5409. Available at: doi:10.1097/Ajp.0000000000000653

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	0	20	0

[12]

VAGASKA, Eva, Alexandra LITAVCOVA, **Iva SROTOVA**, Eva VLCKOVA, Milos KERKOVSKY, Jiri JARKOVSKY, Josef BEDNARIK and Blanka ADAMOVA. Do lumbar magnetic resonance imaging changes predict neuropathic pain in patients with chronic non-specific low back pain? *Medicine* [online]. 2019, **98**(17, Article e15377). ISSN 1536-5964. Available at: doi:10.1097/Md.00000000000015377

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	0	10	0

[13]

KEC, David, Aneta RAJDOVA, Jana RAPUTOVA, Blanka ADAMOVA, **Iva SROTOVA**, Eva Kralickova NEKVAPILOVA, Radka Neuzilova MICHALCAKOVA, Magda HORAKOVA, Jana BELOBRADKOVA, Jindrich OLSOVSKY, Pavel WEBER, Gabriel HAJAS, Michaela KAISEROVA, Radim MAZANEC, Veronika POTOCKOVA, Edvard EHLER, Martin FORGAC, Frank BIRKLEIN, Nurcan UCEYLER, Claudia SOMMER, Josef BEDNARIK and Eva VLCKOVA. Risk factors for depression and anxiety in painful and painless diabetic polyneuropathy: A multicentre observational cross-sectional study. *European Journal Of Pain* [online]. 2022, **26**(2), 370–389. ISSN 1532-2149. Available at: doi:10.1002/ejp.1865

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30	0	10	20

[14]

VLCKOVA, E., **I. SROTOVA** and J. BEDNARIK. Sympathetic Skin Response in the Diagnosis of Small Fibre Neuropathy. *Ceska A Slovenska Neurologie A Neurochirurgie*. 2016, **79**(1), 52–60. ISSN 1802-4041.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	0	40	0

[15]

OKACOVA, I. *(corresponding author)*, Y. BENESOVA, P. STOURAC, H. PIKULOVA, P. PRAKSOVA, A. MITASOVA, S. SKUTILOVA, M. KERKOVSKY and J. BEDNARIK. Neurological Complications Associated with Assisted Reproductive Technology - a Case Report. *Ceska A Slovenska Neurologie A Neurochirurgie*. 2012, **75**(5), 637–640. ISSN 1802-4041.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	50	70	70

[16]

OKACOVA, I. *(corresponding author)*, Y. BENESOVA, E. VLCKOVA, M. KERKOVSKY, P. PRAKSOVA, M. HLADIKOVA, J. KOSIK, D. ULDRIJANOVA, P. STOURAC and J. BEDNARIK. Tumefactive Variant of Multiple Sclerosis - Two Case Reports. *Ceska A Slovenska Neurologie A Neurochirurgie*. 2013, **76**(5), 641–647. ISSN 1802-4041.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	50	70	30

[17]

PETRASOVA, Martina, **Iva SROTOVA *(corresponding author)***, Jan KOLCAVA, Pavel STOURAC, Ludmila HYNKOVA, Milos KERKOVSKY, Hana PIKULOVA, Eduard NEUMAN, Leos KREN and Eva VLCKOVA. Case report: Diagnostic challenge: a new multiple sclerosis “relapse” leading to the diagnosis of anaplastic astrocytoma. *Frontiers In Neurology* [online]. 2024, **14**(1324269, Article 1324269). ISSN 1664-2295. Available at: doi:10.3389/fneur.2023.1324269

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30	50	60	60

[18]

SROTOVA, I. *(corresponding author)*, I. CRHA, E. VLCKOVA, M. SVOBODOVA, E. NEKVAPILOVA, R. STOURAC and J. BEDNARIK. Multiple Sclerosis, Infertility and its Treatment. *Ceska A Slovenska Neurologie A Neurochirurgie*. 2015, **78**(6), 655–660. ISSN 1802-4041.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	20	50	70

[19]

SROTOVA, I., E. VLCKOVA and J. BEDNARIK. Autonomic Dysfunction and its Diagnostic Tools in Multiple Sclerosis. *Ceska A Slovenska Neurologie A Neurochirurgie*. 2016, **79**(2), 188–198. ISSN 1802-4041.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30	0	50	50

[20]

FLASAROVA, S., **I. SROTOVA *(corresponding author)***, M. HLADIKOVA and M. PETRASOVA. Multiple sclerosis and the menstrual cycle. *Ceska A Slovenska Neurologie A Neurochirurgie* [online]. 2024, **87**(5), 317–321. ISSN 1802-4041. Available at: doi:10.48095/cccsnn2024317

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	50	50	50

[21]

MEKINOVA, Lenka, **Iva SROTOVA**, Petra HANAKOVA, Pavlina DANHOFER, Robert HUDECEK and Michal JESETA. Assisted Reproduction Therapy in Patients with Multiple Sclerosis: Narrative Review and Practical Recommendations. *Healthcare* [online]. 2025, 13(23, Article 3155). ISSN 2227-9032. Available at: doi:10.3390/healthcare13233155

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	30	50	40

[22]

PARMOVA, Olesja, Eva VLCKOVA, Monika HULOVA, Livie MENSOVA, Igor CRHA, Petra STRADALOVA, Eva KRALICKOVA, Lenka JURIKOVA, Martina POBORSKA, Radim MAZANEC, Ladislav DUSEK, Jiri JARKOVSKY, Josef BEDNARIK, Stanislav VOHANKA and **Iva SROTOVA *(corresponding author)***. Anti-Mullerian hormone as an ovarian reserve marker in women with the most frequent muscular dystrophies. *Medicine* [online]. 2020, **99**(23, Article e20523). ISSN 1536-5964. Available at: doi:10.1097/Md.00000000000020523

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	50	50	50

[23]

SROTOVA, I.*(corresponding author)*, V. BENETINOVA, M. HLADIKOVA and M. PETRASOVA. Aspects affecting quality of life in patients with multiple sclerosis. *Ceska A Slovenska Neurologie A Neurochirurgie* [online]. 2025, 88(4), 243–248. ISSN 1802-4041. Available at: doi:10.48095/cccsnn2025243

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	70	70	60