M U N I

COMMENTARY TO HABILITATION THESIS[1]

Brain Connectivity and Plasticity in Neurodegenerative Diseases: From Neuroimaging to Neuromodulation

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Brief characteristic of the investigated matter

The habilitation thesis focuses on structural and functional brain alterations in neurodegenerative diseases, particularly Alzheimer's disease, Parkinson's disease and Lewy body diseases. It examines how neurodegeneration affects brain structure, white matter microstructure, functional connectivity and cognitive functions, and how these changes may be modified through neuromodulation and behavioural interventions. The selected publications form a coherent research programme progressing from the identification of neuroimaging biomarkers to the investigation of brain network dysfunction and neuroplasticity. The work combines advanced MRI techniques, functional connectivity analyses, non-invasive brain stimulation, behavioural interventions and digital biomarkers.

Objectives of the work

The overall aim of this work is to advance the understanding of brain connectivity and neuroplasticity in neurodegenerative diseases by integrating multimodal neuroimaging, neuromodulation, and behavioral intervention approaches to identify biomarkers of cognitive dysfunction and explore mechanisms that may support the preservation of cognitive function. More specifically, this work sought to characterize structural and functional brain network alterations associated with cognitive impairment and evaluate their potential as imaging biomarkers and therapeutic targets for interventions promoting adaptive neuroplasticity.

Objectives of this habilitation thesis were as follows:

1. To characterize alterations in structural and functional brain connectivity associated with cognitive impairment across neurodegenerative diseases using multimodal neuroimaging techniques.
2. To identify neuroimaging biomarkers of neurodegeneration and cognitive decline, and to determine their relationship with cognitive domains including attention, executive functions, memory, visuospatial processing, and language.
3. To investigate the capacity for neuroplasticity in the aging and diseased brain by evaluating the effects of NIBS and behavioral interventions on brain connectivity and cognitive function.

Metodologies

The work used a multidisciplinary approach combining clinical and neuropsychological assessment with structural, diffusion and functional MRI. Structural MRI was used to investigate patterns of grey matter atrophy, while diffusion MRI techniques, including diffusion tensor imaging, and diffusion kurtosis imaging, were applied to assess brain

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microstructure. Resting-state and task-based fMRI were used to study functional connectivity, dynamic brain network organization and neural mechanisms of cognitive processing. Non-invasive brain stimulation, including repetitive transcranial magnetic stimulation and transcranial direct current stimulation, was applied to investigate the modulation of cognitive performance and functional brain networks. Intervention studies examined the effects of dance and physical activity on brain plasticity were also applied. The most recent work also investigated digital speech measures as potential biomarkers of cognitive decline.

Results

The results demonstrate that Alzheimer's disease, Parkinson's disease and Lewy body diseases are associated with distinct but partially overlapping patterns of structural and functional brain alterations. These changes are closely related to cognitive performance. Advanced diffusion MRI techniques provided complementary information about neurodegenerative changes, while analyses of Parkinson's disease subtypes demonstrated heterogeneity in microstructural abnormalities. Early alterations of the locus coeruleus were identified in prodromal Lewy body disease, supporting its potential role as an early biomarker. Functional MRI studies demonstrated altered striato-cortical connectivity, disruption of large-scale brain networks and abnormalities of dynamic functional connectivity. Language impairment was associated with altered activation and connectivity within distributed language networks. The neuromodulation studies showed that non-invasive brain stimulation can influence cognitive performance and functional brain organization. Theta-burst stimulation affected attention-related and default mode networks, providing evidence for the modulation of distributed neural systems. Intervention studies using dance and physical training were associated with improvements in physical fitness and measurable changes in brain microstructure and functional organization, supporting the persistence of neuroplastic potential in older adults. Digital speech analyses further demonstrated the potential of accessible biomarkers for monitoring cognitive decline.

Applicant's contribution

The applicant has made a substantial contribution to the conception, design and development of the presented research publications. The contribution includes the development of research questions and protocols, data acquisition and analysis, interpretation of results and preparation of scientific publications. A particular contribution lies in connecting structural neuroimaging, functional connectivity and neuroplasticity within a single research framework. The applicant has contributed expertise in brain network analysis and non-invasive brain stimulation.

Significance

The main significance of the habilitation work lies in its integrative approach to neurodegenerative diseases. The results demonstrate that cognitive impairment reflects not only structural neuronal loss but also disruption of communication within distributed brain networks. The work contributes to the identification of structural, functional and digital biomarkers of neurodegeneration and provides evidence that advanced neuroimaging methods offer complementary information about disease mechanisms. Importantly, the findings support the potential for modulation of brain networks through non-invasive brain stimulation and behavioural interventions. This creates a basis for future individualized approaches combining neuroimaging biomarkers with targeted therapeutic interventions. Overall, the habilitation thesis

represents a coherent contribution to the fields of neurodegeneration, brain connectivity and neuroplasticity and provides a strong foundation for further translational research aimed at improving the diagnosis, monitoring and treatment of neurodegenerative disorders.

Bibliographic records for the selected publications in order of appearance in habilitation thesis, along with the author's contribution to each study, are provided below.

[1] ANDERKOVA, Lubomira, Ilona ELIASOVA, Radek MARECEK, Eva JANOUSOVA and Irena REKTOROVA. Distinct Pattern of Gray Matter Atrophy in Mild Alzheimer's Disease Impacts on Cognitive Outcomes of Noninvasive Brain Stimulation. Journal Of Alzheimers Disease [online]. 2015, 48(1), 251–260. ISSN 1875-8908. Available at: doi:10.3233/Jad-150067
Document Type: Article; IF = 3,920; median IF NEUROSCIENCES – 2,706; according to IF NEUROSCIENCES Q2; according to AIS NEUROSCIENCES Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	20	80	50

[2] KUNST, Jonas, Radek MARECEK, Patricia KLOBUSIAKOVA, Zuzana BALAZOVA, **Lubomira ANDERKOVA**, Nela NEMCOVA-ELFMARKOVA and Irena REKTOROVA. Patterns of Grey Matter Atrophy at Different Stages of Parkinson's and Alzheimer's Diseases and Relation to Cognition. Brain Topography [online]. 2019, 32(1), 142–160. ISSN 1573- 6792. Available at: doi:10.1007/s10548-018-0675-2
Document Type: Article; IF = 2,759; median IF CLINICAL NEUROLOGY – 2,611; according to IF CLINICAL NEUROLOGY Q2; according to AIS CLINICAL NEUROLOGY Q2

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

[3] HOPE, Tuva R., Per SELNES, Irena REKTOROVA, **Lubomira ANDERKOVA**, Nela NEMCOVA-ELFMARKOVA, Zuzana BALAZOVA, Anders DALE, Atle BJORNERUD and Tormod FLADBY. Diffusion tensor and restriction spectrum imaging reflect different aspects of neurodegeneration in Parkinson's disease. Plos One [online]. 2019, 14(5, Article e0217922). ISSN 1932-6203. Available at: doi:10.1371/journal.pone.0217922
Document Type: Article; IF = 2,740; median IF MULTIDISCIPLINARY SCIENCES – 1,866; according to IF MULTIDISCIPLINARY SCIENCES Q2; according to AIS MULTIDISCIPLINARY SCIENCES Q2

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

[4] MINSTEROVA, Alzbeta Sejnoha, Patricia KLOBUSIAKOVA, Adrian PIES, Zoltan

GALAZ, Jiri MEKYSKA, **Lubomira NOVAKOVA**, Nela Nemcova ELFMARKOVA and Irena REKTOROVA. Patterns of diffusion kurtosis changes in Parkinson's disease subtypes. Parkinsonism & Related Disorders [online]. 2020, 81, 96–102. ISSN 1873-5126. Available at: doi:10.1016/j.parkreldis.2020.10.032
Document Type: Article; IF = 4,891; median IF CLINICAL NEUROLOGY – 3,290; according to IF CLINICAL NEUROLOGY Q1; according to AIS CLINICAL NEUROLOGY Q1

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

[5] ZELEZNIKOVA, Zaneta, **Ľubomira NOVAKOVA**, Lubomir VOJTISEK, Lubos BRABENEC, Kristina MITTEROVA, Ivona MORAVKOVA and Irena REKTOROVA. Early Changes in the Locus Coeruleus in Mild Cognitive Impairment with Lewy Bodies. Movement Disorders [online]. 2025, 40(2), 276–284. ISSN 1531-8257. Available at: doi:10.1002/mds.30058
Document Type: Article; IF = 7,700; median IF CLINICAL NEUROLOGY – 2,800; according to IF CLINICAL NEUROLOGY Q1; according to AIS CLINICAL NEUROLOGY Q1

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	80	40	60

[6] ANDERKOVA, Lubomira, Marek BARTON and Irena REKTOROVA. Striato-cortical Connections in Parkinson's and Alzheimer's Diseases: Relation to Cognition. Movement Disorders [online]. 2017, 32(6), 917–921. ISSN 1531-8257. Available at: doi:10.1002/mds.26956
Document Type: Article; IF = 8,324; median IF CLINICAL NEUROLOGY – 2,645; according to IF CLINICAL NEUROLOGY Q1; according to AIS CLINICAL NEUROLOGY Q1

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	80	80	80

[7] NOVAKOVA, Lubomira, Martin GAJDOS, Marek BARTON, Lubos BRABENEC, Zaneta ZELEZNIKOVA, Ivona MORAVKOVA and Irena REKTOROVA. Striato-cortical functional connectivity changes in mild cognitive impairment with Lewy bodies. Parkinsonism & Related Disorders [online]. 2024, 121(106031, Article 106031). ISSN 1873-5126. Available at: doi:10.1016/j.parkreldis.2024.106031
Document Type: Article; IF = 3,400; median IF CLINICAL NEUROLOGY – 2,500; according to IF CLINICAL NEUROLOGY Q2; according to AIS CLINICAL NEUROLOGY Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	80	80	80

[8] GAJDOS, Martin, Marie SCHEJBALOVA, Martin LAMOS, Pavel RIHA, **Lubomira NOVAKOVA**, Marketa NECASOVA, Nela Nemcova ELFMARKOVA, Eva VYTVAROVA, Michal MIKL and Irena REKTOROVA. Dynamic functional connectivity is related to cognitive performance of prodromal Lewy body dementia. Journal Of Neural Transmission [online]. 2026. ISSN 1435-1463. Available at: doi:10.1007/s00702-026-03148-6

Document Type: Article; IF = 4,400; median IF CLINICAL NEUROLOGY – 2,800; according to IF CLINICAL NEUROLOGY Q1; according to AIS CLINICAL NEUROLOGY Q2 (data in 2025)

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

[9] **NOVAKOVA, Lubomira**, Martin GAJDOS, Jana MARKOVA, Alice MARTINKOVICOVA, Zuzana KOSUTZKA, Jana SVANTNEROVA, Peter VALKOVIC, Zsolt CSEFALVAY and Irena REKTOROVA. Language impairment in Parkinson's disease: fMRI study of sentence reading comprehension. Frontiers In Aging Neuroscience [online]. 2023, 15(1117473, Article 1117473). ISSN 1663-4365. Available at: doi:10.3389/fnagi.2023.1117473

Document Type: Article; IF = 4,100; median IF NEUROSCIENCES – 2,800; according to IF NEUROSCIENCES Q2; according to AIS NEUROSCIENCES Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
90	80	80	80

[10] **NOVAKOVA, Lubomira**, Martin GAJDOS, Daniel CARBOL and Irena REKTOROVA. Sentence comprehension in Lewy body diseases: a functional magnetic resonance imaging study. Brain Communications [online]. 2025, 7(6, Article fcaf423). ISSN 2632-1297. Available at: doi:10.1093/braincomms/fcaf423

Document Type: Article; IF = 4,500; median IF CLINICAL NEUROLOGY – 2,800; according to IF CLINICAL NEUROLOGY Q1; according to AIS CLINICAL NEUROLOGY Q1

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
80	80	80	80

[11] CARBOL, Daniel, **Lubomira NOVAKOVA**, Patricia KLOBUSIAKOVA and Irena REKTOROVA. Language network disruption in patients with Lewy body diseases. Journal Of Neural Transmission [online]. 2026. ISSN 1435-1463. Available at: doi:10.1007/s00702-026-03128-w

Document Type: Article; IF = 4,400; median IF CLINICAL NEUROLOGY – 2,800; according to IF CLINICAL NEUROLOGY Q1; according to AIS CLINICAL NEUROLOGY Q2 (data in 2025)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	80	30	80

[12] ELIASOVA, Ilona, **Lubomira ANDERKOVA**, Radek MARECEK and Irena REKTOROVA. Non-invasive brain stimulation of the right inferior frontal gyrus may improve attention in early Alzheimer's disease: A pilot study. Journal Of The Neurological Sciences [online]. 2014, 346(1), 318–322. ISSN 1878-5883. Available at: doi:10.1016/j.jns.2014.08.036
Document Type: Article; IF = 2,474; median IF CLINICAL NEUROLOGY – 2,289; according to IF CLINICAL NEUROLOGY Q2; according to AIS CLINICAL NEUROLOGY Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
50	20	30	40

[13] ANDERKOVA, Lubomira and Irena REKTOROVA. Cognitive effects of repetitive transcranial magnetic stimulation in patients with neurodegenerative diseases - Clinician's perspective. Journal Of The Neurological Sciences [online]. 2014, 339(1), 15–25. ISSN 1878-5883. Available at: doi:10.1016/j.jns.2014.01.037
Document Type: Review; IF = 2,474; median IF CLINICAL NEUROLOGY – 2,289; according to IF CLINICAL NEUROLOGY Q2; according to AIS CLINICAL NEUROLOGY Q2

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

[14] ANDERKOVA, Lubomira, Dominik PIZEM, Patricia KLOBUSIAKOVA, Martin GAJDOS, Eva KORITAKOVA and Irena REKTOROVA. Theta Burst Stimulation Enhances Connectivity of the Dorsal Attention Network in Young Healthy Subjects: An Exploratory Study. Neural Plasticity [online]. 2018, 2018(3106918, Article 3106918). ISSN 1687-5443. Available at: doi:10.1155/2018/3106918
Document Type: Article; IF = 3,591; median IF NEUROSCIENCES – 2,902; according to IF NEUROSCIENCES Q2; according to AIS NEUROSCIENCES Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	70	80	70

[15] NOVAKOVA, Lubomira, Martin GAJDOS and Irena REKTOROVA. Theta-burst transcranial magnetic stimulation induced cognitive task-related decrease in activity of default mode network: An exploratory study. Brain Stimulation [online]. 2020, 13(3), 597–599. ISSN 1876-4754. Available at: doi:10.1016/j.brs.2020.01.015
Document Type: Letter; IF = 8,955; median IF CLINICAL NEUROLOGY – 3,290; according to IF CLINICAL NEUROLOGY Q1; according to AIS CLINICAL NEUROLOGY Q1

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	70	80	70

[16] PIZEM, Dominik, **Lubomira NOVAKOVA *(corresponding author)*,** Martin GAJDOS and Irena REKTOROVA. Is the vertex a good control stimulation site? Theta burst stimulation in healthy controls. Journal Of Neural Transmission [online]. 2022, 129(3), 319–329.
ISSN 1435-1463. Available at: doi:10.1007/s00702-022-02466-9
Document Type: Article; IF = 3,300; median IF CLINICAL NEUROLOGY – 3,200; according to IF CLINICAL NEUROLOGY Q2; according to AIS CLINICAL NEUROLOGY Q2

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

[17] KROPACOVA, Sylvie, Kristina MITTEROVA, Patricia KLOBUSIAKOVA, Lubos BRABENEC, **Lubomira ANDERKOVA**, Nela NEMCOVA-ELFMARKOVA, Zuzana BALAZOVA, Ivan REKTOR, Roman GRMELA, Lenka SVOBODOVA, Pavlina VACULIKOVA and Irena REKTOROVA. Cognitive effects of dance-movement intervention in a mixed group of seniors are not dependent on hippocampal atrophy. Journal Of Neural Transmission [online]. 2019, 126(11), 1455–1463. ISSN 1435-1463. Available at: doi:10.1007/s00702-019- 02068-y
Document Type: Article; IF = 3,505; median IF CLINICAL NEUROLOGY – 2,611; according to IF CLINICAL NEUROLOGY Q2; according to AIS CLINICAL NEUROLOGY Q2

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

[18] MINSTEROVA, Alzbeta Sejnoha, Patricia KLOBUSIAKOVA, Sylvie KROPACOVA, **Lubomira NOVAKOVA**, Lubos BRABENEC, Zuzana BALAZOVA, Roman GRMELA, Alena SKOTAKOVA, Lenka SVOBODOVA and Irena REKTOROVA. Multishell Diffusion MRI Reflects Improved Physical Fitness Induced by Dance Intervention. Neural Plasticity [online]. 2020, 2020(8836925, Article 8836925). ISSN 1687-5443. Available at: doi:10.1155/2020/8836925
Document Type: Article; IF = 3,599; median IF NEUROSCIENCES – 3,627; according to IF NEUROSCIENCES Q3; according to AIS NEUROSCIENCES Q2

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

[19] BALAZOVA, Zuzana, Radek MARECEK, **Ľubomira NOVAKOVA**, Nela NEMCOVA-ELFMARKOVA, Sylvie KROPACOVA, Lubos BRABENEC, Roman GRMELA, Pavlina VACULIKOVA, Lenka SVOBODOVA and Irena REKTOROVA.

Dance Intervention Impact on Brain Plasticity: A Randomized 6-Month fMRI Study in Non-expert Older Adults. Frontiers In Aging Neuroscience [online]. 2021, 13(724064, Article 724064). ISSN 1663-4365. Available at: doi:10.3389/fnagi.2021.724064
Document Type: Article; IF = 5,702; median IF NEUROSCIENCES – 3,800; according to IF NEUROSCIENCES Q1; according to AIS NEUROSCIENCES Q2 GERONTOLOGY Q2

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

[20] KOVAC, Daniel, Lubomira NOVAKOVA, Jiri MEKYSKA, Krystof NOVOTNY, Lubos BRABENEC, Patricia KLOBUSIAKOVA and Irena REKTOROVA. Digital speech biomarkers for assessing cognitive decline across neurodegenerative conditions. Computers in Biology and Medicine [online]. 2025, 198. ISSN 0010-4825. Available at: doi:10.1016/j.compbiomed.2025.111251

Document Type: Article; Category: Health Informatics – SJR Q1

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