M U N I

COMMENTARY TO HABILITATION THESIS[1]

Characteristics of the Investigated Matter

The habilitation thesis presents the results of an investigation on the topic of subarachnoid hemorrhage (SAH), with a focus on two main issues: the partial pressure of oxygen in brain tissue ($PbtO_2$), which was an important subject of our previous research, and inflammation, which represents a main topic of our recent research. The compilation contains fifteen peer-reviewed original and review articles.

The main objectives of the thesis are:

• Characterization of partial pressure of oxygen in brain tissue ($PbtO_2$) with a respect to the pathophysiology of SAH.

• Description of inflammatory response early after SAH and its pathophysiological and clinical consequences.

Employed Methodologies

The research integrated both experimental and clinical studies exploring various parameters and laboratory markers in blood and brain/cerebrospinal fluid. $PbtO_2$ monitoring has been a major tool in studies investigating cerebral oxygen levels in patients with SAH. In studies focused on inflammation, we have predominantly used ELISA and RT-PCR methods to assess protein or mRNA expression and correlate them with key clinical characteristics.

Presented results

This thesis demonstrates that:

• Dynamics of $PbtO_2$ is significantly higher in patients without cerebral vasospasm when increasing the fraction of inspired oxygen to 100%, demonstrating the effect of cerebral vasospasm on blood supply to the brain.

• $PbtO_2$ correlates with those parameters of transcranial dopplermetry, which reflect conditions related to vessel resistance and microvasculature, suggesting the role of small vessels in the development of delayed cerebral ischemia.

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[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.

• There is a moderate negative correlation between $PbtO_2$ and IL-6 levels in cerebrospinal fluid of SAH patients, implying the role of inflammation in the pathophysiology of SAH.

• IL-6 is massively increased in CSF early after SAH, and the levels correlate with poor patient outcomes, but the variability of IL-6 levels is too high to establish a threshold for diagnostics.

• Inflammatory response is triggered early after experimentally induced SAH and is significantly pronounced in severe cases.

• Experimentally induced SAH is in severe cases associated with an inflammatory response in the whole brain, not only in areas affected by the hematoma, suggesting that SAH may have a global impact on the brain or that severe SAH may lead to deregulation of inflammatory response.

• Pharmacological stimulation of α7 nicotinic acetylcholine receptor reduces associated neuronal apoptosis in an experimental model of SAH, suggesting the role of cholinergic anti-inflammatory pathway (CHAIP) in the pathophysiology of SAH.

Applicant's Contribution

The author is the first or corresponding author of the publications presented in this habilitation thesis. His contributions cover the entire research process – from conceptualization and study design, through data collection and experimental work, to statistical analysis, interpretation, and manuscript writing.

[1][2] **ĎURIŠ, Kamil*(corresponding author)***, Martin SMRČKA, Pavel ŠEVČÍK, Roman GÁL, Vilém JURÁŇ, Eduard NEUMAN, Marek SOVA, Václav VYBÍHAL and Michal KÝR. Evaluation of changes in brain tissue oxygen levels (PbtO2) for detection of vasospasm in patients after subarachnoid haemorrhage. *Anesteziologie a intenzivni Medicina*. 2009, **20**(2), 102–106. ISSN 1214-2158.
Document Type: Article; Category: Anesthesiology and Pain Medicine – SJR Q4; Critical Care and Intensive Care Medicine – SJR Q4

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	50	70	60

[2] DURIS, K.*(corresponding author)*, E. NEUMAN, A. MRLIAN, V. VYBIHAL, V. JURAN, M. KYR and M. SMRCKA. Correlation between Brain Tissue Oxygen Monitoring Parameters and Transcranial Dopplerometry in Patients with Severe Subarachnoid Hemorrhage. *Ceska a slovenska neurologie a neurochirurgie*. 2014, **77**(2), 196–201. ISSN 1802-4041.
Document Type: Article; IF = 0,165; median IF SURGERY – 1,478; Quartile by IF SURGERY Q4; Quartile by AIS SURGERY Q4

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	50	70	60

[2] Bibliographic record of a published scientific result, which is part of the habilitation thesis.

[3] DURIS, Kamil, Anatol MANAENKO, Hidenori SUZUKI, William ROLLAND, Jiping TANG and John H. ZHANG. Sampling of CSF via the Cisterna Magna and Blood Collection via the Heart Affects Brain Water Content in a Rat SAH Model. *Translational Stroke Research* [online]. 2011, **2**(2), 232–237. ISSN 1868-4483. Available at: doi:10.1007/s12975-010-0063-z
Document Type: Article

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
90	70	90	90

[4] JELINEK, Matyas, Michal JURAJDA and **Kamil DURIS*(corresponding author)***. Oxidative Stress in the Brain: Basic Concepts and Treatment Strategies in Stroke. *Antioxidants* [online]. 2021, **10**(12, Article 1886). ISSN 2076-3921. Available at: doi:10.3390/antiox10121886
Document Type: Review; IF = 7,675; median IF CHEMISTRY, MEDICINAL – 3,727; Quartile by IF CHEMISTRY, MEDICINAL Q1; Quartile by AIS CHEMISTRY, MEDICINAL Q1

Literature research (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	50	20	50

[5] JELINEK, M., M. JURAJDA and **K. DURIS*(corresponding author)***. The Role of Oxidative Stress in Early Brain Injury after Subarachnoid Hemorrhage. *Oxidative Medicine and Cellular Longevity* [online]. 2020, **2020**(Article 8877116). ISSN 1942-0994. Available at: doi:10.1155/2020/8877116
Document Type: Review; IF = 6,543; median IF CELL BIOLOGY – 4,513; Quartile by IF CELL BIOLOGY Q2; Quartile by AIS CELL BIOLOGY Q2

Literature research (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	50	20	50

[6] DURIS, Kamil, Anatol MANAENKO, Hidenori SUZUKI, William B. ROLLAND, Paul R. KRAFFT and John H. ZHANG. α7 Nicotinic Acetylcholine Receptor Agonist PNU-282987 Attenuates Early Brain Injury in a Perforation Model of Subarachnoid Hemorrhage in Rats. *Stroke* [online]. 2011, **42**(12), 3530–3536. ISSN 1524-4628. Available at: doi:10.1161/Strokeaha.111.619965
Document Type: Article; IF = 5,729; median IF CLINICAL NEUROLOGY – 2,128; Quartile by IF CLINICAL NEUROLOGY Q1; Quartile by AIS CLINICAL NEUROLOGY Q1

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
90	70	90	90

[7] LIPKOVA, Jolana and **Kamil DURIS*(corresponding author)*.** The Role of microRNA in Ischemic and Hemorrhagic Stroke. *Current Drug Delivery* [online]. 2017, **14**(6), 816–831. ISSN 1875-5704. Available at: doi:10.2174/1567201813666160919142212

Document Type: Review; IF = 2,078; median IF PHARMACOLOGY & PHARMACY – 2,481; Quartile by IF PHARMACOLOGY & PHARMACY Q3; Quartile by AIS PHARMACOLOGY & PHARMACY Q4

Literature research (%)	Supervision (%)	Manuscript (%)	Research direction (%)
30	70	20	40

[8] DURIS, K., Z. SPLICHAL and M. JURAJDA. The Role of Inflammatory Response in Stroke Associated Programmed Cell Death. *Current Neuropharmacology* [online]. 2018, **16**(9), 1365–1374. ISSN 1875-6190. Available at: doi:10.2174/1570159X16666180222155833
Document Type: Review; IF = 4,568; median IF NEUROSCIENCES – 2,902; Quartile by IF NEUROSCIENCES Q1; Quartile by AIS NEUROSCIENCES Q2

Literature research (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	60	70	70

[9] DURIS, K., E. NEUMAN, V. VYBIHAL, V. JURAN, J. GOTTWALDOVA, M. KYR, A. VASKU and M. SMRCKA. IL-6 Levels in the Cerebrospinal Fluid and their Association with Brain Oxygen Partial Pressure and Cerebral Vasospasm Development in Patients with Aneurysmal Subarachnoid Haemorrhage. *Ceska a slovenska neurologie a neurochirurgie*. 2016, **79**(5), 573–578. ISSN 1802-4041.
Document Type: Article; IF = 0,368; median IF SURGERY – 1,701; Quartile by IF SURGERY Q4; Quartile by AIS SURGERY Q4

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	50	70	60

[10] DURIS, Kamil, Eduard NEUMAN, Vaclav VYBIHAL, Vilem JURAN, Jana GOTTWALDOVA, Michal KYR, Anna VASKU and Martin SMRCKA. Early Dynamics of Interleukin-6 in Cerebrospinal Fluid after Aneurysmal Subarachnoid Hemorrhage. *Journal of Neurological Surgery Part A-Central European Neurosurgery* [online]. 2018, **79**(2), 145–151. ISSN 2193-6323. Available at: doi:10.1055/s-0037-1604084
Document Type: Article; IF = 1,060; median IF SURGERY – 1,883; Quartile by IF SURGERY Q4; Quartile by AIS SURGERY Q4

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

[11] DURIS, K., J. LIPKOVA, Z. SPLICHAL, T. MADARASZOVA and M. JURAJDA. Early Inflammatory Response in the Brain and Anesthesia Recovery Time Evaluation After Experimental Subarachnoid Hemorrhage. *Translational Stroke Research* [online]. 2019, **10**(3), 308–318. ISSN 1868-601X. Available at: doi:10.1007/s12975-018-0641-z
Document Type: Article; IF = 5,780; median IF NEUROSCIENCES – 3,052; Quartile by IF NEUROSCIENCES Q1; Quartile by AIS NEUROSCIENCES Q2

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

[12] DURIS, K. and M. JURAJDA. Evolutionary concept of inflammatory response and stroke. *Journal of Neuroscience Research* [online]. 2020, **98**(1), 98–104. ISSN 1097-4547. Available at: doi:10.1002/jnr.24392
Document Type: Article; IF = 4,164; median IF NEUROSCIENCES – 3,627; Quartile by IF NEUROSCIENCES Q2; Quartile by AIS NEUROSCIENCES Q2

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

[13] JELINEK, Matyas and **Kamil DURIS*(corresponding author)*.** Inflammatory response in sepsis and hemorrhagic stroke. *Brain Hemorrhages* [online]. 2023, **4**(2), 96–107. ISSN 2589-238X. Available at: doi:10.1016/j.hest.2022.10.005
Document Type: Review; IF = 1,300; median IF CLINICAL NEUROLOGY – 2,400; Quartile by IF CLINICAL NEUROLOGY Q4; Quartile by AIS CLINICAL NEUROLOGY Q4

Literature research (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	50	20	50

[14] DURIS, Kamil, Jolana LIPKOVA and Michal JURAJDA. Cholinergic Anti-inflammatory Pathway and Stroke. *Current Drug Delivery* [online]. 2017, **14**(4), 449–457. ISSN 1875-5704. Available at: doi:10.2174/1567201814666170201150015
Document Type: Review; IF = 2,078; median IF PHARMACOLOGY & PHARMACY – 2,481; Quartile by IF PHARMACOLOGY & PHARMACY Q3; Quartile by AIS PHARMACOLOGY & PHARMACY Q4

Literature research (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70	60	70	70

[15] JELINEK, Matyas, Jolana LIPKOVA and **Kamil DURIS*(corresponding author)***. Vagus nerve stimulation as immunomodulatory therapy for stroke: A comprehensive review. *Experimental Neurology* [online]. 2024, **372**(Article 114628). ISSN 1090-2430. Available at: doi:10.1016/j.expneurol.2023.114628
Document Type: Review; IF = 4,200; median IF NEUROSCIENCES – 2,900; Quartile by IF NEUROSCIENCES Q1; Quartile by AIS NEUROSCIENCES Q2

Literature research (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	50	20	50