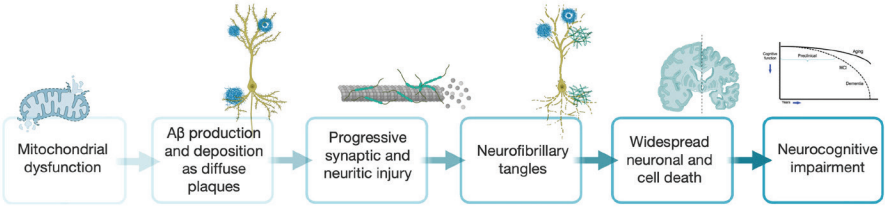
From mitophagy to neurocognitive impairment

Conference by the Department of Neurology,
Second Faculty of Medicine, Charles University
and Motol University Hospital
with the University in Oslo.



8:30—9:00 ► Meeting Check-in

9:00—9:15 ► **Opening ceremony** ► Martin Vyhnálek, Evandro F. Fang, Kateřina Veverová

Mitophagy in basic research

Chairing: Evandro F. Fang

9:15—10:00 ► Genetic dissection of mitophagic mechanisms in ageing and age-associated neurodegenerative disorders — Nektarios Tavernarakis

10:00—10:20 ► The application of multi-omics combined with wet lab techniques to explore novel mechanisms of AD — Sofie Lautrup

10:20—10:40 ► Novel mechanisms of neuronal loss in AD — Johannes Frank

10:40—11:00 ► Coffee break

Mitophagy and clinical point of view

Chairing: Nektarios Tavernarakis

11:00—11:30 ► Alteration of human CSF and serum-based mitophagy biomarkers in the continuum of Alzheimer's disease and frontotemporal lobar degeneration — Kateřina Veverová, Martin Vyhnálek

11:30—12:00 ► The '5As': ageing, Alzheimer's disease, autophagy, AI, and an 'A' molecule in brain health and longevity — Evandro F. Fang

12:00—12:30 ► Health benefits of the mitophagy activator Urolithin A — From preclinical models to clinical studies — Davide D'Amico

12:30—13:45 ► Lunch

13:45—13:50 ▶	Alzheimer's Foundation	Šárka Kovandová	

Blood-based biomarkers in AD

Chairing: Kateřina Veverová

13:50—14:20 ▶	Using brain organoids to model Alzheimer's disease in vitro	Dáša Bohačiaková	
14:20—15:00 ▶	Plasma biomarkers of Alzheimer's disease: state of the art and next steps toward clinical implementation	Giovanni Bellomo	
15:00—15:30 ▶	Coffee break		

Neurocognitive impairment in AD

Chairing: Martin Vyhnálek

15:30—15:50 ▶	Detecting early cognitive markers of Alzheimer's disease: from subjective experience to objective memory testing	Hana Horáková	
15:50—16:10 ▶	Spatial navigation in Alzheimer's disease	Jan Laczó	
16:10—16:30 ▶	Current and future treatment of Alzheimer's disease	Jakub Hort	
16:30—16:50 ▶	Mental and spiritual well being, the impact on brain maintenance	Kateřina Sheardová	
16:50—17:00 ▶	**Closing ceremony**	▶ Martin Vyhnálek, Evandro F. Fang, Kateřina Veverová	

Nektarios Tavernarakis

Nektarios Tavernarakis is Professor of Molecular Systems Biology at the Medical School of the University of Crete, in Heraklion, Greece. He is also the Chairman of the Board of Directors at the Foundation for Research and Technology-Hellas (FORTH), and Research Director at the Institute of Molecular Biology and Biotechnology (IMBB) of FORTH, where he is heading the Neurogenetics and Ageing laboratory. He is the Founder and first Director of the Graduate Program on BioInformatics at the University of Crete. He is Chairman of the *European Institute of Innovation and Technology (EIT)* Governing Board, and has served as Vice President of the *Scientific Council* of the *European Research Council (ERC)*, and Director of IMBB. He is a member of the *American Association for the Advancement of Science (AAAS)*, the *European Molecular Biology Organization (EMBO)*, the *German National Academy of Sciences (Leopoldina*), *Academia Europaea*, and the *Academy of Athens*. He earned his Ph.D. degree at the University of Crete, and trained as a postdoctoral researcher at Rutgers University in New Jersey, USA. His work focuses on the molecular mechanisms of necrotic cell death and neurodegeneration, the interplay between cellular metabolism and ageing, the mechanisms of sensory transduction and integration by the nervous system, and the development of novel genetic tools for biomedical research. He has published numerous scientific papers in top-tier, cross-discipline, international scientific journals, in addition to invited book chapters, and other publications, including editorials, commentaries, and science-popularizing articles. He has received several notable scientific prizes, including two *ERC Advanced Investigator Grants*, and an innovation-supporting *ERC Proof of Concept Grant*. He is also the recipient of the *EMBO Young Investigator* award, the Alexander von *Humboldt Foundation*, *Friedrich Wilhelm Bessel* research award, the *Helmholtz International Fellow Award*, the *Galien Scientific Research Award*, the *BioMedical Research Award* of the *Academy of Athens*, the *Bodossaki Foundation Scientific Prize for Medicine and Biology*, and the *Empeirikeion Foundation Academic Excellence Prize*.

Sofie Lautrup

Sofie Lautrup is a senior researcher in the group of Evandro F. Fang at Akershus University Hospital and University of Oslo. Dr Lautrup has studied the importance of NAD+ metabolism and mitophagy in both premature ageing diseases and Alzheimer's disease, and she is particularly interested in the changes occurring during both ageing and Alzheimer's disease in the brain. She is using a multi-OMICS approach to evaluate human post-mortem brain tissue combined with cellular and *C. elegans* models for mechanistic validations.

Johannes Frank

Johannes Frank embarked on his academic journey with a Bachelor's degree in Medical and Pharmaceutical Biotechnology from IMC University of Applied Sciences Krems, Austria, followed by a Master's degree in Molecular Biology with a specialization in Neuroscience. Throughout his early academic career, he has dedicated himself to ageing research, particularly focusing on its impact on the brain. Last year, he commenced his Ph.D. studies within the Fang Lab, a part of the NADIS consortium, which was established in 2022 and is funded by the European Union through the Marie Skłodowska-Curie Actions (MSCA) grant.

Evandro F. Fang

Dr. Evandro Fei Fang is a molecular gerontologist whose research focuses on understanding the molecular mechanisms of human ageing and age-related diseases. His team uses bench-top knowledge to guide the development of novel interventional strategies towards human ageing, with a final goal of improving the quality of life in all older people. After finishing his PhD at the Chinese Universtiy of Hong Kong, he completed a 6-year postdoc with Prof. Vilhelm Bohr on molecular gerontology and Prof. Mark Mattson on neuronal resilience in Alzheimer's disease at the National Institute on Ageing, Baltimore; he opened his lab in Oslo in the fall of 2017. He is the founding (co)coordinator of the Norwegian Centre on Healthy Ageing network (NO-Age, www.noage100.com), the Norwegian National anti-Alzheimer's disease Network (NO-AD, www.noad100.com), and the Hong Kong-Nordic Research Network.

Kateřina Veverová

Dr. Kateřina Veverová (Čechová) is a cognitive neuroscientist at the Second Faculty of Medicine, Charles University in Prague, and Motol University Hospital. She completed her PhD in 2021, focusing on BDNF as a marker for prediction, follow-up, and intervention in neurodegenerative diseases in the Czech Brain Aging Study (www.cbas.cz). She is currently a laboratory team leader within the Mit-AD grant, and assistant professor at the Department of Psychology (teaching neurophysiology and neuroscience), Charles University, and vice-chair of the Neuropsychology Section of the Czech-Moravian Psychological Society. Her main research interest is the interaction of biofluid and cognitive markers of Alzheimer's disease, with a special focus on mitophagy as a promising molecular mechanism underlying the pathogenesis of Alzheimer's disease.

Martin Vyhnálek

Associate Professor Martin Vyhnálek is a cognitive neurologist based at Motol University Hospital, Charles University in Prague, Czech Republic, and principal investigator of the Mit-AD EAA grant. After his medical studies, he completed a degree in clinical neuropsychology at Montpellier University in France. After returning to Prague, he co-founded the Czech Brain Aging Study, the only Czech longitudinal, observational study on aging and dementia. He is responsible for neuropsychological core and biobanking. His research focuses mainly on early cognitive and neuropsychiatric markers of neurodegeneration and the role of subjective cognitive complaints in early AD diagnostics.

Davide D'Amico

Davide D'Amico is a molecular and cellular biologist at the biotech company Amazentis, based in the Swiss Federal Institute of Technology (EPFL) Innovation Park, in Lausanne, Switzerland. He completed a doctoral degree in molecular oncology at the University La Sapienza in Rome, Italy. After a postdoc in the laboratory of Prof. Johan Auwerx, focused on the study of mitochondrial in health, aging and disease, he joined Amazentis. Here, he opened Amazentis reaserch laboratory and now oversees the company's preclinical and clinical biomarker projects to translate the benefits of mitophagy activators to human health. Davide helds a position of Visiting Professor in the Department of Molecular Medicine at the University La Sapienza of Rome.

Dáša Bohačiaková

Dr. Dasa Bohaciakova, an assistant professor at Masaryk University in Brno, Czech Republic, specializes in stem cell research. Her work encompasses studying pluripotency biology, exploring targeted differentiation mechanisms, and currently leading a team focused on disease modeling. They have recently developed a brain organoid model for in vitro replication of the Alzheimer's disease phenotype, concentrating their efforts on unraveling the mechanisms underlying early pathogenesis.

Giovanni Bellomo

Giovanni Bellomo is a postdoctoral researcher at the Laboratory of Clinical Neurochemistry, Section of Neurology, Department of Medicine and Surgery at the University of Perugia, Perugia, Italy and the responsible of Lab of Artificial Intelligence in the same University. He earned his bachelor's degree in physics from the University of Perugia. He then pursued his master's degree in physics, specializing in Biophysics and Medical Physics, at the University

of Bologna, Italy. Subsequently, he was awarded a fellowship for the International Doctorate in Structural Biology at the European Center for Magnetic Resonance (CERM) of the University of Florence. Dr. Bellomo obtained his Ph.D. with honors and embarked on a post-doctoral position at the Laboratory of Clinical Neurochemistry, University of Perugia, under the guidance of Prof. Lucilla Parnetti. His research concentrates on discovering novel fluid biomarkers and diagnostic/prognostic algorithms for Parkinson's and Alzheimer's diseases. This encompasses cerebrospinal fluid and blood biomarkers, as well as α-synuclein seed amplification assays, contributing to the advancement of understanding and diagnosis in neurodegenerative diseases.

Hana Horáková

Hana Horáková, M.A., Ph.D., is a clinical neuropsychologist and post-doctoral researcher at the Department of Neurology, Second Faculty of Medicine, Charles University and Motol University Hospital in Prague, Czech Republic. She is a member of the neuropsychological core of the Czech Brain Aging Study (CBAS), the only longitudinal, observational study on aging and dementia in the Czech Republic. At the Department of Neurology, she is responsible for supervising psychologists in clinical training, and specifically within the CBAS, she is responsible for coordinating and supervising clinical and experimental neuropsychological assessments. Her research focuses on subjective and objective cognitive markers of Alzheimer´s disease and related disorders and their role in the early diagnosis.

Jan Laczó

Professor Jan Laczó is a cognitive neurologist and neuroscientist working at Motol University Hospital and Charles University, Second Faculty of Medicine, Prague, Czech Republic. He is the head of the Spatial Cognition Laboratory, and his research focuses on early diagnosis of neurodegenerative diseases using cognitive markers, especially experimental tests of spatial navigation.

Jakub Hort

Dr. Hort is a professor of neurology at the Department of Neurology, Charles University, Second Faculty of Medicine and Motol Hospital, Prague, Czech Republic and PI of the Czech Brain Ageing Study (CBAS), conducted in collaboration with the International Clinical Research Centre in Brno, Czech Republic. The CBAS is a unique longitudinal prospective study launched in 2011 to investigate the early functional, metabolic and structural biomarkers of Alzheimer's disease and other dementias. (See: www.cbas.cz) Dr. Hort has been elected Chair of the Cognitive Neurology Section of the Czech

Neurological Society (2005—2018, 2023—current) and served as co-chair of the European Academy of Neurology (EAN) Panel of Scientists on Dementia and Cognitive Neurology (2015—2019). Dr. Hort is the author of European guidelines on Alzheimer's disease and contributed to EAN guidelines on non-Alzheimer's dementia and combination therapy in Alzheimer's disease. He is a member of the Expert Advisory Panel of Alzheimer Europe in 2023. Dr. Hort has recently been involved in numerous initiatives to integrate new artificial Intelligence (AI) technologies, machine learning, virtual reality, and blockchain into Alzheimer's research and clinical practice. He is co-founder of Telemedicine/Blockchain Project Terrapino/Alzheimerchain and NFT Non-Fungible Brain Project. Dr. Hort has been involved in numerous drug development projects as a consultant, SAB member (Alzheon, Eisai, Neuroscios, Schwabe), and Principal Investigator. In 2011, he founded the Czech Alzheimer Fund, which has supported many research projects and grants for young scientists.

Kateřina Sheardová

Dr. Sheardova is a medical director and co-founder of the Czech Brain Aging Study (www.cbas.cz), based at the International Clinical Research Centre at St. Anne's University Hospital in Brno. CBAS is a longitudinal, observational study on aging and dementia from two large centers (Brno, Prague) in the Czech Republic combining clinical care and clinical Research. Dr. Sheardova is also a member of advisory boards of several international scientific organizations (Alzheimer's Research and Prevention Foundation, Tucson, Arizona; International Neurodegenerative Disorders Research Center — a non-profit, global research institute applying AI and machine learning in the understanding of neurodegenerative disorders) and pharmaceutical companies involved in world leading Alzheimer disease research. As a neurologist, Dr. Sheardova works with patients who have a wide range of memory disorders. Her primary interest is the research of the risk-protective factors of dementia, focusing on preventive lifestyle measures, mindfulness techniques, and spiritual well-being.

Alzheimer's foundation

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Alzheimer nadační fond (the Alzheimer's Foundation) was founded in 2011 to support the research of Alzheimer's disease and other neurodegenerative and vascular brain disorders which lead to deficits in cognitive function and dementia. In addition to supporting researchers both in the Czech Republic and abroad, we aim to improve the quality and conditions of local patient care and broaden the scope of care provided. We regularly announce grants for young scientists, doctors and other professionals who research Alzheimer's disease and related dementias. › www.alzheimernf.cz

Genetic dissection of mitophagic mechanisms in ageing and age-associated neurodegenerative disorders

Nektarios Tavernarakis

- *Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology-Hellas*
- *Medical School, University of Crete, Heraklion, Crete, Greece*

Mitochondria, the indispensable and highly dynamic, energy-generating organelles in all eukaryotic cells, play essential roles in fundamental cellular processes. Aberrant accumulation of mitochondria in diverse cell types is a shared hallmark of many human pathologies and ageing. How mitochondrial biogenesis coordinates with the removal of damaged or superfluous mitochondria to maintain cellular homeostasis is not well understood. We found that mitophagy, a selective type of autophagy targeting mitochondria for degradation, interfaces with mitochondrial biogenesis to regulate mitochondrial content in *Caenorhabditis elegans*. Impairment of mitophagy compromises stress resistance and triggers mitochondrial retrograde signalling through a transcription program that regulates both mitochondrial biogenesis genes and mitophagy. These observations reveal a homeostatic feedback loop that integrates metabolic signals to coordinate the biogenesis and turnover of mitochondria. Uncoupling of these two processes during ageing contributes to overproliferation of damaged mitochondria and decline of cellular function. Our findings suggest that impaired removal of damaged mitochondria is a pivotal event in ageing and senescent decline, highlighting mitophagy as a potential target for therapeutic intervention against age-associated pathologies.

The application of multi-omics combined with wet lab techniques to explore novel mechanisms of Alzheimer's disease

Sofie Lautrup

- *Department of Clinical Molecular Biology, University of Oslo and Akershus University Hospital, 1478, Lørenskog, Norway*
- *The Norwegian Centre on Healthy Ageing (NO-Age), Oslo, Norway*

Sofie Lautrup will present her work on the role of the NAD+-mitophagy axis in Alzheimer's disease (AD). She is using a multi-OMICS approach to study human brain tissue and blood samples from AD patients. Moreover, Dr Lautrup is using human cell models and *C. elegans* models of AD to study the underlying mechanisms.

Novel mechanisms of neuronal loss in Alzheimer's disease

Johannes Frank

- *Department of Clinical Molecular Biology, University of Oslo and Akershus University Hospital, 1478, Lørenskog, Norway*
- *The Norwegian Centre on Healthy Ageing (NO-Age), Oslo, Norway*

Johannes Frank, a Ph.D. candidate of the Fang-lab at the University of Oslo, is deeply intrigued by the influence of ageing on cellular susceptibility to ferroptosis and its connection

to neuronal ageing. His research endeavors to investigate how NAD+ levels can modulate the redox potential of cells, actively controlling defense mechanisms against ferroptosis. By utilizing Caenorhabditis elegans, cell lines, induced pluripotent stem cells (iPSCs), and human tissue and blood samples, Johannes aims to understand the impact of ferroptosis on ageing in neurons. His interdisciplinary approach promises to unravel critical insights into the mechanisms underlying neurodegenerative diseases like Alzheimer's disease, offering potential therapeutic avenues for intervention.

Alteration of human CSF and serum-based mitophagy biomarkers in the continuum of Alzheimer's disease and frontotemporal lobar degeneration

Kateřina Veverová, Martin Vyhnálek

- *Memory Clinic, Department of Neurology, Second Faculty of Medicine, Charles University and Motol University Hospital, V Úvalu 84, Prague, 150 06, Czech Republic*

Defective mitophagy is consistently found in postmortem brain and iPSC-derived neurons from Alzheimer's disease (AD) patients. However, whether these changes are reflected in the biofluids of individuals with AD and non-AD pathologies and whether these changes are associated with AD-related phenotypes remains unknown. We quantified biomarkers of mitophagy/autophagy and lysosomal degradation (PINK1, BNIP3L and TFEB, respectively) in CSF and serum from 300 biomarker-defined individuals recruited from the Czech Brain Aging Study. These individuals covered MCI due to AD, dementia due to AD, MCI due to FTLD, and cognitively unimpaired individuals. Cognitive function and brain atrophy were also assessed. Our data show that serum and CSF PINK1 and serum BNIP3L were higher, and serum TFEB was lower in individuals with AD than in corresponding CU individuals. In FTLD there was a significant increase in CSF ULK1 and serum TFEB levels compared to AD. Additionally, the magnitude of mitophagy impairment correlated with the severity of clinical indicators. This study reveals mitophagy impairment reflected in biofluid biomarkers of individuals with AD and FTLD, suggesting a different role of mitophagy in the sub-type of neurocognitive disorders.

The '5As': ageing, Alzheimer's disease, autophagy, AI, and an 'A' molecule in brain health and longevity

Evandro F. Fang

- *Department of Clinical Molecular Biology, University of Oslo and Akershus University Hospital, 1478, Lørenskog, Norway*
- *The Norwegian Centre on Healthy Ageing (NO-Age), Oslo, Norway*

Increased lifespan enables people to live longer, but not necessarily healthier lives. Ageing is arguably the highest risk factor for numerous human diseases, including Alzheimer's disease (AD); thus understanding the molecular mechanisms of human aging holds the promise of developing interventional and therapeutic strategies for many diseases simultaneously, promoting healthy longevity. Accumulation of damaged mitochondria is a hallmark of aging and age-related AD. However, the molecular mechanisms of impaired mitochondrial homeostasis and their relationship to AD are still elusive. Mitochondrial autophagy (mitophagy) is the cellular self-clearing process that removes damaged and superfluous mi-

tochondria, and therefore plays a fundamental role in maintaining neuronal homeostasis and survival. We hypothesise that age-susceptible defective mitophagy causes accumulation of damaged mitochondria, which in combination with the two AD-defining pathologies, Aβ plaques and tau tangles, further exacerbates AD onset and progression. Restoration of mitophagy, through pharmaceutical (e.g., NAD+, passion fruit components, and urolithin A) and genetic approaches, forestalls pathology and cognitive decline in mouse models of AD and improves neuronal function in AD iPSC-derived neurons. Additionally, artificial intelligence (AI) is now being used to propel drug screening, as well as being used for drug design specifically targeting AD and ageing pathways. The Evandro Fang lab is now involved in several clinical trials looking into the use of NAD+ precursors to treat AD and premature ageing diseases, among others.

Health benefits of the mitophagy activator Urolithin A – From preclinical models to clinical studies

D. D'Amico[1], S. Liu[2], A.M. Fouassier[1], P.A. Andreux[1], Johan Auwerx[3], Chris Rinsch[1], D. Marcinek[2], A. Singh[1]

- *[1]Amazentis, Swiss Federal Institute of Technology (EPFL) Innovation Park, Switzerland*
- *[2] Department of Radiology, University of Washington, Seattle, WA, USA*
- *[3] Laboratory of Integrative Systems Physiology, Swiss Federal Institute of Technology (EPFL), Switzerland,*

Urolithin A (UA), a natural compound produced by the gut microbiome from ellagitannins found in pomegranates, berries, and nuts, has been shown to enhance mitophagy in pre-clinical models of aging and age-associated conditions, offering health benefits in tissues including skeletal muscle, heart, and brain. Our Phase I clinical study, the first of its kind in humans, confirmed UA's safety and its ability to enhance mitochondrial gene expression in human skeletal muscle. We further validated UA's benefits for muscle health through two randomized, placebo-controlled clinical trials in middle-aged, overweight adults (NCT03464500) and healthy elderly (NCT03283462). In the first study, UA administration at doses of 500 mg and 1000 mg for four months significantly improved leg muscle strength by 10%. Muscle proteomics analysis revealed elevated levels of proteins involved in mitophagy and oxidative phosphorylation, indicating improved mitochondrial quality and respiratory capacity. In the second study, supplementation with 1000 mg of UA led to significant enhancements in muscle endurance among healthy elderly participants. In both trials, UA reduced circulating levels of acylcarnitines, indicating higher mitochondrial efficiency, and markers of inflammation. These findings build on previous preclinical and clinical evidence with UA and provide evidence for its use as a nutritional intervention targeting mitochondria to support muscle health and promote healthy aging.

Using brain organoids to model Alzheimer's disease in vitro

Dáša Bohačiaková

- *Masaryk University Brno, Czech Republic*

The advancements in stem cell technology and the possibility of obtaining stem cells directly from patients represent a great promise for modeling Alzheimer's disease (AD) in

vitro. Our work aims to create such a model directly from patients' cells to study the development of AD pathogenesis. Using cell reprogramming, we successfully created induced pluripotent stem cells (iPSCs) from AD patients with familial AD mutations (PSEN1/PSEN2), created 3D cerebral organoids and tested the presence of AD-specific pathology. Our results show that AD organoids accumulate APP protein, increase secreted Aβ42/40 ratio, and P-Tau. Organoids also react to drug treatment by decreasing secreted Aβ42 and Aβ40 peptides. We also noticed significant developmental alterations in AD organoids confirmed by single-cell sequencing analysis. Our data thus suggest that developmental perturbations and altered neurogenesis could significantly contribute to the development of fAD. Studies are ongoing to elucidate molecular mechanisms and pathways that underlie this phenomenon.

Plasma biomarkers of Alzheimer's disease: state of the art and next steps toward clinical implementation

Giovanni Bellomo

- *Center for Memory Disturbances, Lab of Clinical Neurochemistry, Section of Neurology, Department of Medicine and Surgery, University of Perugia, Perugia, Italy*

The timely and precise diagnosis of neurodegenerative disorders is vital for the success of clinical trials and the effectiveness of disease-modifying therapies. Recently, there has been a transition from diagnosing using cerebrospinal fluid biomarkers to plasma-based ones. Adopting plasma biomarkers brings notable benefits, providing advanced molecular diagnostics accessibility for both healthcare providers and patients. Moreover, it allows for repeated sampling, crucial for disease course monitoring and therapy effectiveness evaluation. Alzheimer's has been a focal point for substantial plasma biomarker development. Recent studies indicate that plasma assays measuring β-amyloid, phosphorylated tau protein, β-synuclein, GFAP, and neurofilament light chain hold significant diagnostic and prognostic potential. Automated platforms may soon replace lumbar punctures in specific cases. However, interpreting biomarkers may be affected by systemic co-pathologies, and for disorders like Lewy body dementia and frontotemporal dementia, blood-based diagnosis remains intricate. Despite advancements, the immediate application of plasma biomarkers for these conditions remains uncertain.

Detecting early cognitive markers of Alzheimer's disease: from subjective experience to objective memory testing

Hana Horáková

- *Memory Clinic, Department of Neurology, Second Faculty of Medicine, Charles University and Motol University Hospital, V Úvalu 84, Prague, 150 06, Czech Republic*

As the population ages, concerns about cognitive decline associated with Alzheimer's disease (AD) are becoming an increasingly important issue and motivation for seeking medical care. The real clinical challenge is to reliably identify cognitive decline that precedes dementia since the emerging therapeutic interventions are likely to be effective only when performed in the earliest stages of the disease. Neuropsychological testing is a standard approach to identify those individuals in whom a more detailed and invasive examination

is necessary to reliably determine the aetiology of the difficulties they are experiencing. However, standard memory tests may not be sensitive to the earliest cognitive changes associated with AD. Novel neuropsychological approaches have been developed. Based on the results of the Czech Brain Aging Study, the potential of subjective cognitive complaints (SCCs) evaluation and challenging memory tests to contribute to the detection and monitoring of subtle cognitive decline will be presented.

Spatial navigation in Alzheimer's disease

Jan Laczó

- *Memory Clinic, Department of Neurology, Second Faculty of Medicine, Charles University and Motol University Hospital, V Úvalu 84, Prague, 150 06, Czech Republic*

Currently, there is an urgent need to identify individuals with preclinical and prodromal Alzheimer's disease (AD) who may benefit from potential prevention strategies and disease modifying therapies. Neuroimaging, cerebrospinal fluid and newly also blood-based biomarkers are used as diagnostic measures of AD pathophysiology. However, highly sensitive and specific cognitive markers to identify preclinical and prodromal AD individuals are also needed. The brain areas highly susceptible to and affected earliest by AD pathophysiology constitute the core network for spatial navigation. Therefore, spatial navigation deficits may reflect underlying AD pathophysiology in the earliest disease stages. In accordance with this theoretical model, recent studies have demonstrated that individuals with preclinical and prodromal AD show alteration of specific spatial navigation patterns even before any other cognitive symptom onset. Spatial navigation deficit is thus emerging as a potential cost-effective cognitive marker to detect early AD, which has important implications for future diagnostics and treatment approaches.

Current and future treatment of Alzheimer's disease

Jakub Hort

- *Memory Clinic, Department of Neurology, Second Faculty of Medicine, Charles University and Motol University Hospital, V Úvalu 84, Prague, 150 06, Czech Republic*

The currently available treatment for Alzheimer's disease is only symptomatic, i.e. it is one that alleviates symptoms but does not treat the causes of the disease. Drugs from the acetylcholinesterase inhibitor group and memantine can delay the most severe stages of the disease, prolong patients' self-sufficiency, improve cognitive function, and reduce the burden on caregivers. In recent years, there have been advances in the development of biological treatments. In the US, lecanemab (Leqembi) received full approval in the summer of 2023 and also received registration in Japan in September 2023. Positive results from a study with donenumab were also published in July 2023. These drugs are monoclonal antibodies administered by infusion. The administration of this biological therapy is conditional on the determination of metabolic biomarkers. Some patients may experience side effects — local brain edema or micro-hemorrhage. ALZ-801 is also in advanced development and is being tested in ApoE4 homozygotes.

Mental and spiritual well being, the impact on brain maintenance

Kateřina Sheardová

- *International Clinical Research Center, St. Anne's University Hospital, Brno, Czech Republic*

Lifestyle can significantly influence the brain's ability to resist ageing and pathological changes. Physical activity, a healthy diet and the prevention of vascular and metabolic diseases are known to be protective factors. Chronic stress and depression are also important risk factors for dementia. Techniques to influence stress and depression are very effective in protecting healthy brain ageing and preventing dementia, as scientific studies have shown. A combination of these measures has the greatest effect, as shown by the results of multi-domain interventions. In this presentation, we will review the different lifestyle components that have been studied in relation to healthy ageing. We discuss their potential effects in the context of brain maintenance and dementia prevention. We comment on the results of recent global non-pharmacological intervention trials, their advantages and shortcomings, and their potential contribution to clinical practice.

Acknowledgment

The **Validation of specific mitophagy biomarkers across Alzheimer's disease continuum** benefits from a € 1 404 000 grant from Iceland, Liechtenstein and Norway through the EEA Grants and the Technology Agency of the Czech Republic within the KAPPA Programme.

Iceland Liechtenstein Norway grants

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Podporujeme výzkum a vzdělávání odborníků v oblasti Alzheimerovy nemoci a dalších neurodegenerativních onemocnění mozku.

NAŠE PROJEKTY

- **Kurz metodologie výzkumu:** příprava a publikace článku, analýza dat, vědecká práce a kariérní postup. **Kurz se koná 6. a 7. 6. 2024**, **na 2. LF UK a FN Motol**, lektor: prof. Rostislav Anděl, Ph.D., Arizona State University, 2. LF UK, ICRC Brno.
- **Stipendium pro vědkyně – matky,** cílem projektu je zlepšit situaci a postavení matek v jejich profesním vědeckém životě a umožnit jim skloubit vědeckou kariéru s péčí o děti, která je v českém prostředí stále především záležitostí žen. Uzávěrka přihlášek 31. 5. 2024.
- **Soutěž o Cenu MUDr. Jana Bureše** za nejlepší odbornou publikaci mladých autorů, zaměřenou na problematiku Alzheimerovy choroby a demencí v oblasti neurologie, psychiatrie, geriatrie a neurověd. Uzávěrka přihlášek 31. 5. 2024.
- **Soutěž o Cenu manželů Elišky a Zdeňka Strmiskových** za význačný přínos k výzkumu a léčbě Alzheimerovy choroby a spřízněných neurodegenerativních onemocnění. Nominace přijímáme do 30. 11. 2024.
- **Projekt na podporu školitelů v geriatrii, Pilotní projekt na podporu geriatrických ambulancí, ve spolupráci s Českou gerontologickou a geriatrickou společností ČLS JEP.**
- **Cestovní granty na prestižní světové konference (AAIC, EAN, ADPD).**

JSME TU PRO VÁS

Chcete se aktivně zúčastnit odborné konference, zajímavého kurzu nebo máte nabídku stáže na zahraničním pracovišti? Přihlaste se do některého z našich projektů nebo podejte samostatnou žádost.

Více na www.alzheimernf.cz nebo FB, kontakt: sekretariat@alzheimernf.cz.

Notes:

mitophagyad.eu

Organizers: Martin Vyhnálek, Kateřina Veverová