Neurobiology Research Unit

Annual Report 2023

Department of Neurology, Neuroscience Centre
Copenhagen University Hospital, Rigshospitalet

www.nru.dk

Cover page: A fraction of the NRU staff photographed in May 2023.

REGION Rigshospitalet

KØBENHAVNS UNIVERSITET
DET SUNDHEDSVIDENSKABELIGE FAKULTET

Contents

Preface

It is a pleasure to present you with the 2023 annual report describing the activities of the Neurobiology Research Unit (NRU).

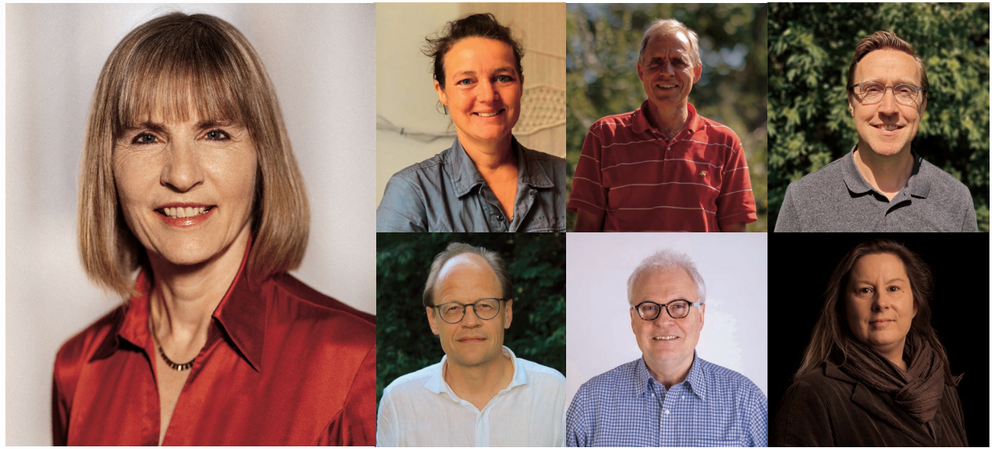
In the year 2023, we extended a warm welcome to a remarkable total of 62 new members and affiliates, marking the largest influx of fresh talent in NRU's history. Notably, we celebrated the appointment of two esteemed senior scientists, Vibe Frøkjær and Lars Pinborg, to professorial positions at the University of Copenhagen. Vibe now holds the prestigious title of professor in neuropsychiatry, a groundbreaking achievement at the University of Copenhagen, while Lars specializes in epilepsy research. Additionally, our ranks were enriched by the addition of 2 postdoctoral fellows, 2 research assistants, 10 technical-administrative staff members, 13 visiting scholars, and 35 pre-graduate students. As of December 2023, our NRU family encompassed 135 individuals representing 18 diverse nationalities, epitomizing the richness of our staff's diversity and the interdisciplinary ethos that underpins our research endeavours.

Funding from external sources is vital for us in advancing our mission. Throughout the year, 25 of our research grant proposals have been successful and in total they have secured more than 20 million DKK in external funding. Noteworthy, we became partners in two highly interesting Novo Nordisk Foundation Tandem Programme projects, the first of which is entitled "Neuroplastic effects of psychedelics" and is a collaboration with Professor Matthias Herth from Dept of Drug Design and Pharmacology, University of Copenhagen, and the second of which is entitled "Synaptogenesis and Neuroinflammation in Epilepsy" and is a collaboration between Professors Jens Mikkelsen and Lars Pinborg. Also, we joined as partners in the large EU infrastructure proposal "EBRAINS 2.0: A Research Infrastructure to Advance Neuroscience and Brain Health" which was funded by an impressive grant of around 38 million EUR.

NRU remained steadfast in its commitment to scholarly output in 2023. Three PhD students successfully defended their theses, marking significant milestones in their academic journeys. Many of our researchers showcased their pioneering work at international congresses, conferences, and meetings, culminating in the publication of 74 peer-reviewed scientific papers.

I extend heartfelt gratitude to all NRU staff for their unwavering dedication, as well as to our host institution, Rigshospitalet, and our invaluable national and international collaborators. Their steadfast support has been integral to ensuring another year of resounding success for NRU.

I invite you to delve into the pages of this 2023 annual report, and encourage all interested readers to stay abreast of our latest developments through our website, https://nru.dk.



In 2023 the NRU management group was composed of Gitte Moos Knudsen (photo credit to Royal Academy of Sciences and Letters) and (from left to right, top row first) Vibe G. Frøkjær, Claus Svarer, Patrick M. Fisher, Lars H. Pinborg, Jens H. Mikkelsen, and Dea S. Stenbæk.

On behalf of the NRU management group

Gitte Moos Knudsen
Professor, Head of Department

Our Mission & Activities

The mission of NRU is to conduct translational neuroscience research with the aim to promote preventive, diagnostic, and therapeutic advances.

We make use of neuropsychological and behavioural assessments combined with MRI, PET, SPECT and EEG in humans to investigate basic neurobiological mechanisms in the healthy brain and brain disorders, as well as neuropharmacological effects on the brain. Advanced image processing and statistical methods are applied to our data. We also use animal and cell models to bring pre-clinical discoveries into healthy volunteers and patients as early as possible.

The activities within NRU fall in ten different categories:

1) Basic neurobiological and translational neuroscience research
2) Development and validation of new *in vivo* imaging probes
3) Neuropharmacological research in e.g. psychedelics
4) Open science, AI, and advanced data analysis
5) Neuroimaging research
6) Diagnostic brain imaging of neurological patients
7) Neuropsychology research
8) Cohort studies of patients with epilepsy and major depressive disorder
9) Education and training
10) Dissemination of results

We see our role at Rigshospitalet and in the Capital Region of Denmark as a key unit to conduct innovative diagnostic, therapeutic and preventive neuropharmacological research. This takes place in close interaction with the hospital clinics, universities and industry, enabling immediate implementation of prevention strategies, diagnostics, innovative drugs, and non-pharmacological treatments of patients with brain disorders. NRU collaborates with many other national and international research institutes.

Education

NRU is a major training site for pre- and postgraduate students. In 2023, we supervised almost 30 bachelors- and master theses for University of Copenhagen and The Danish Technical University. We train national and international research staff at all levels; medical students, graduate students, PhD students and post docs. We organize pre- and post-graduate courses with prominent speakers and well-attended programs, including the Master's program in Neuroscience, and an international PhD course on pharmacokinetics. During the semester, we have a fixed meeting program with at least 5 weekly research presentations, journal clubs, etc. where the pre- and postgraduate students also are expected to present their work.

NRU faculty members are engaged in research-based teaching and education within their fields of expertise. Below are some of the major contributions to teaching programs.

The Master's program in Neuroscience in Copenhagen

Professor Jens H. Mikkelsen, PhD from NRU and Institute of Neuroscience, University of Copenhagen, is the study director of a two-year Master of Science program and education in neurosciences which was started in 2020. Courses are offered in cellular neuroscience, neural circuits, higher brain functions, and experimental neuroscience, as well as elective courses in animal models, drug discovery and computer science. Every year the university enroll about 30 bachelor students in the Master's program in Neuroscience. We receive every year a large interest from all over the world for this program. Many applicants come mostly from China, North America and throughout Europe. Unfortunately, we are not able to accept all qualified applicants. The NRU faculty provide teaching in neuropharmacology, homeostasis, cognition, drug discovery and imaging in the form of lectures, exercises, and journal clubs, and we have every year Neuroscience students to do their master thesis here.

Danish Institute of Study Abroad

Each semester, associate professor Patrick Fisher guest lectures for the following university-level courses at the Danish Institute of Study Abroad: "Neuroplasticity", "Neuroscience of Creativity", "Neuroscience of Fear", and "Neurological Disorders and Disease".

Basic Kinetic Modelling in PET and MR Imaging

From Feb 27th to Mar 3rd, 2023, we hosted our annual one-week PhD course on pharmacokinetics with participation by 11 national and international researchers. The course organizers are Gitte Moos Knudsen, Henrik Larsson, Claus Svarer and Dorthe Givard.

Facilities

NRU facilities cover more than 1,400 m^2 and are spread over several locations at Rigshospitalet (RH), but mainly located at fifth and sixth floors of the North Wing building, sections 8057 and 8067.

At fifth floor, we span 822 m^2, including 15 offices with space for 57 desks, a conference room with kitchen, a regular meeting/conversation room, a science lounge, two smaller quiet rooms for video calls, a laboratory for handling human specimens, a storage room, two sound-proof rooms with facilities for neuropsychological and -physiological testing, a calm sleep/intervention room, and an EEG-room equipped with high density EEG equipment as well as an adjacent observation room. Furthermore, a server room and two printer rooms which house all the equipment needed to run our own IT-infrastructure.

At sixth floor, the NRU experimental laboratory has 167 m^2 of well-equipped facilities for basic neuroscience *in vitro* studies. We have four GMO-1 approved laboratories, one of which is also approved as an isotope lab with an S1 permission, a storage room equipped with two -80 degrees freezers, a dedicated 4-degree room, i.e., a build-in room fridge, as well as a small office. Equipment in the laboratories include several lab benches with hoods and standard equipment, gamma- or beta-counters, a cell culture room, cell harvester, autoradiography, and much more.

At seventh floor, in the Neuromuscular Research Unit, we have access to a shared microscope room and in the basement, we share a large (62 m^2) freezer-core facility for biobank material together with our colleagues from the Danish Dementia Research Centre and the Memory and Neuromuscular clinics.

In building 93, RH section 9302, we have two dedicated laboratories for our *in vivo* studies, including small animal storage facilities and facilities for testing animal behaviour. These rooms cover 46 m^2 and both are approved as isotope labs with an S1 permission. Furthermore, we have access to a storage room equipped with three -80 degrees freezers, shared with the other research groups in the building.

NRU has a close collaboration with the PET and Cyclotron Unit at RH, which provides NRU with key access to radiochemistry production and to PET- and combined PET-MR scanner facilities. This collaboration is continuing with the new chair of Dept. Clinical Physiology, Malene Fischer, who in 2023 took over from professor Lotte Højgaard. Our MRI facilities include the NRU brain research dedicated 3 Tesla Siemens Prisma MR-scanner (MR001) which is located in 120 m^2 state-of-the-art facilities on the ground floor in the North Wing. In the basement of the North Wing, we have a Siemens mock-up MR scanner installed, mimicking our real scanner environment in MR001. The mock-up scanner can be used as a training facility to prepare persons, especially children or people with claustrophobia, for scanning in a real MR-scanner.

The SPECT laboratory of NRU is located on the ground floor in the North Wing. The facility is used both diagnostically and for research purposes. The laboratory consists of an office, a type B approved isotope laboratory, waiting room facilities for patients, and a scanner room equipped with a newer 3-headed dedicated brain SPECT/CT scanner (Mediso AnyScan) with unique multi-pinhole collimator. The SPECT laboratory also has a dedicated storage room in the basement and thereby occupy in total 130 m^2.

Worth mentioning is also the Cimbi database and the Cimbi biobank which represent unique and valuable research instruments for NRU. Over the last 20 years, we have systematically acquired high-resolution brain imaging data (PET, MRI, rsMRI, and fMRI) from thousands of carefully screened and well-characterized healthy individuals and patients with various neuropsychiatric disorders. These data have been collected along with a wide range of associated data including demographic, neuropsychological, biochemical, and genetic data. The wealth of acquired data is stored in the Cimbi Database in a highly structured and safe manner. The Cimbi biobank is the associated collection of biological specimens from the cohort, including saliva, blood, and in some instances, urine and hair samples, which allow for additional biochemical and genetic analyses. The biobank is stored safely in the dedicated freezer-core facility in the basement of the North Wing. The Cimbi database and biobank provide quality-controlled resources for future hypothesis-generating and hypothesis-driven studies, and from an international perspective, the comprehensive nature and the sample sizes are exceptional. In 2023, a total of 30 official Cimbi applications for data access were approved or extended and several papers based on data from the Cimbi database and biobank were published. Currently, there are 59 active projects using data from the database. The PET neuroimaging data are also an asset to the OpenNeuroPET project, you can read more about it on page 33.

Staff in 2023

NRU management group
Gitte Moos Knudsen, Head of NRU, professor, MD, DMSc
Claus Svarer, chief engineer, PhD
Dea S. Stenbæk, associate professor, PhD
Jens D. Mikkelsen, professor, MD, DMSc
Lars H. Pinborg, professor, MD, DMSc
Olaf B. Paulson, professor emeritus, MD, DMSc
Patrick M. Fisher, associate professor, PhD
Vibe G. Frøkjær, professor, MD, PhD

Chief technologist
Gerda Thomsen

Administration and research
Arafat Nasser (biobank manager)
Birgit Tang (HR)
Dorthe Givard (finances)
Peter S. Jensen (center manager)

Senior researchers
Anjali Sankar, PhD
Brice Ozenne, associate professor, PhD
Cyril Pernet, PhD
Hanne D. Hansen, instructor, PhD
Louise M. Jørgensen, associate professor, MD, PhD
Melanie Ganz-Benjaminsen, associate professor, PhD
Mikael Palner, associate professor, PhD
Pontus Plavén-Sigray, PhD
Vibeke Dam, PhD

Post docs
Annette Johansen, MD
Burcu Azak Pazarlar, PhD
Cassis Varlow, PhD
Cheng T. Ip, PhD
Friederike Holze, PhD
Jonas Svensson, PhD
Martin Korsbak Madsen, PhD
Sagar Sanjay Aripaka, PhD
Sofi da Cunha-Bang, MD, PhD
Sophia Armand, PhD
Vincent Beliveau, PhD

PhD students
Drummond McCulloch, pharmacology
Gjertrud L. Laurell, medical nuclide techniques
Kristian R. Jensen, MD
Kristian Larsen, neuroscience
Maja R. Marstrand-Jørgensen, MD
Miriam L. Navarro, pharmacy
Ruben Dörfel, biomedical engineering
Sara Marie Larsen, MD
Sidsel H. Andersen, psychology
Silvia E.P. Bruzzone, neuroscience
Stinne Høgh, midwifery
Søren V. Larsen, MD

Visiting professors
Todd Ogden, professor, Columbia University, USA

Visiting scientists
Alberte W. Breum, NAD fellow, Univ. Copenhagen
Anders S. Olsen, PhD-stud, Technical University of Denmark
Anastasia Tsopanidou, NAD fellow, Univ. Copenhagen
Barbara Nordhjem, post doc, Dept of Paediatrics and Adolescent Medicine, Righospitalet
Camilla Iavazzo, Erasmus-stud, Univ. Trieste, Italy
Camilla T. Vo, NAD fellow, Univ. Copenhagen
Christina K. Christensen, BSc-stud, Univ. Southern Denmark
Clara Rosenvinge, MSc-stud, Univ. Copenhagen
Dan Peters, PhD, DanPET, Sweden
Janus Magnussen, unenrolled PhD-stud, Aixial Group, UK
Kat F. Kiilerich, research assistant, Univ. Southern Denmark
Kathrine S. Madsen, senior researcher, Univ. College CPH
Lea Hallebye-Hansen, BSc-stud, Univ. Southern Denmark
Lourdes C. Arevalo, associate professor, Univ. Copenhagen
Lydia Arias Vázquez, MSc-stud, Univ. Copenhagen
Margot Morssinkhof, PhD-stud, Univ. Copenhagen
Marko Rosenholm, post doc, Univ. Copenhagen
Markus Hjorth, MD, Psychiatric Center Ballerup, Denmark
Martin Nørgaard, assistant professor, Univ. Copenhagen
Martin Schain, PhD, Antaros Medical, Sweden
Mathilde Cherouvrier, Erasmus-stud, Sorbonne Université, France
Mohamed El Fakiri, PhD-stud, Univ. Copenhagen
Nadia B. Pedersen, MSc-stud, Univ. Copenhagen
Natalie Beschorner, PhD, post doc, Univ. Copenhagen
Nicolaj Daugaard, PhD-stud, Univ. Southern Denmark
Nina Fultz, research assistant, Massachusetts General Hosp., USA

Oliver R. Hovmand, PhD-stud, Mental Health Services South
Silas Haahr Nielsen, MD, Dept of Neurosurgery, Rigshospitalet
Tobias Gustavsson, post doc, Univ. Copenhagen
Vladimir Shalgunov, PhD, Univ. Copenhagen
Willem van Strien, Visiting resident, Amsterdam UMC

Research assistants

Catharina Messell, music therapy
Clara Madsen, molecular biomedicine
David Reydellet, biomedical sciences
Martin Prener, MD
Mikkel Frederiksen, neuroscience

Technical staff

Ajla Sabitovic, MRI-student assistant
Arthur Diness, EEG-student assistant
Asta K. Vølund, MRI-student assistant
Astrid T. Mikkelsen, medicine
Astrid F. Vestereng, psychology
Astrid S.N. Nielsen, medicine
Caroline Lund, psychology
Cecilie R. Hvass, MRI-student assistant
Christina C. Schnohr, MRI-student assistant
Delal Yücel, psychology
Elisabeth Kolesnik, neuroscience
Emilia A. Steenstrup, MRI-student assistant
Emilie L. Henriksen, radiographer
Emma Balsby, psychology
Emma Højte, psychology
Helga Appel, medicine
Holger Lyng, EEG-student assistant
Ian Nørgaard McLeod, MRI-student assistant
Ida-Sofia B. Wehner, medicine
Julius L. Søgaard, EEG-student assistant
Kathrine S. Christensen, psychology
Kristian G. Lambertsen, MRI-student assistant
Kristoffer Brendstrup-Brix, MRI-student assistant
Lauge A. Rasmussen, IT-support
Laxmy Krishnapillai, EEG-student assistant
Lone I. Freyr, project nurse
Lærke V. Kristiansen, MRI-student assistant
Maja M. Tranholm, MRI-student assistant
Malthe T. Andersen, medicine
Marc Cummings, IT-support
Maria Grzywacz, psychology
Maria S. Christiansen, psychology
Marie Linneberg, psychology
Mille Rasmussen, HPLC-student assistant
Minna H. Litman, project nurse
Ofelia F. Godske, EEG-student assistant
Oliver Overgaard-Hansen, psychology
Paw P. Randrup, psychology
Robert D. Pedersen, EEG-student assistant
Robin de Nijs, Medical physicist
Sandra N. Madsen, HPLC-student assistant
Sarah Bargmeyer, HPLC-student assistant
Simon Sabroe, MRI-student assistant
Sofie Hvitved, medicine
Sofie Ølgod, psychology
Stine S. Olsen, psychology
Svitlana Olsen, medical technologist
Thilde K. Nielsen, psychology
Thomas W. Jørgensen, IT-support
Thurid W. Madsen, project nurse

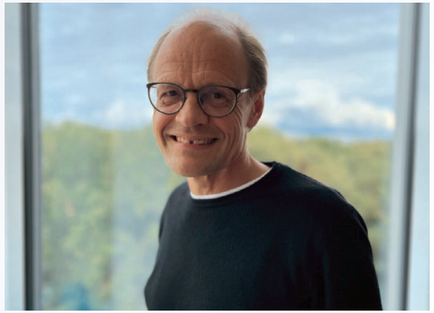
Pregraduate students

Adam Ujhelyi, neuroscience
Ahmad Al-Baka, pharmacy
Aitana Martínez Velasco, neuroscience
Aje Al-Awssi, medicine
Alexander R. Andersen, bioinformatics
Alexander T. Ysbæk-Nielsen, psychology
Alma Mouritzen, psychology
Anders Spanggaard, medicine
Andrea Juvik, medicine
Anna Kauffmann, medicine
Asmus T. Dalsgaard, biomedical engineering
Camilla M. C. Xu, medicine
Cheng Chen, bioinformatics
Christopher L. Porterfield, bioinformatics
Dilja Ketilsdottir, medicine
Emil Colliander, medicine
Emilie Mauritzon, medicine
Emna Daadouche, medical and molecular biology
Hannah W. Julsgart, biomedical engineering
Hector L. Mebenga, statistics
Helene Kaas, medicine
Jacob Lund, bioinformatics
Jayson Teruo Guo, neuroscience
Joanna Wilkosz, neuroscience
Johan B. Nielsen, psychology
Jonas Ingerslev, human physiology and psychology
Jonas Kendal, medicine
Jonathan Gelvan, psychology
Juliane C. Vestergaard, medicine
Kamilla M. Lindegaard, molecular biomedicine
Katarina Bubulovic, human biology
Kirstine H. Andersen, medicine
Lauren French, biophysics
Malene V. Sørensen, medicine
Marcus K. Riis-Vestergaard, psychology
Mathilde E. Brøgger-Jensen, medicine
Mette Hochheim, medicine
Nikita Morel, psychology
Noa Roumimper, psychobiology
Nora D. Falck, medicine
Peter M. Skov-Andersen, pharmaceutical sciences
Philip Fink-Jensen, medicine
Phoebe Linde-Atkins, molecular biomedicine
Puk Rising, physics
Rikke B. Bangsgaard, medicine
Sara V. Rehtmar, medicine
Sarah F. Akobe, medicine
Sif Olsen, psychology
Valdemar Kruse, psychology
Victor Neufeld, medicine
Victoria Garre, medicine
Yaron Lahav, bioinformatics
Younes Subhi, medicine
Zinet Ritschel, psychology

New Professors

Two NRU senior staff members were appointed as professors at the University of Copenhagen in 2023. This is a welcomed contribution to our senior scientist staff and will facilitate additional training and supervision of future pre- and postgraduate students.

Clinical professorship in neurology with special focus on epilepsy



As of Sep 1st, 2023, Lars H. Pinborg is appointed clinical professor in neurology with special focus on epilepsy at the Department of Clinical Medicine, University of Copenhagen. Lars has been affiliated with NRU for more than 20 years and as NRU senior researcher and chair of the Danish epilepsy surgery programme, he has a long track record of research within epilepsy and advanced imaging. His scientific focus area includes clinical epileptology, molecular and structural neuroimaging, drug resistance in epilepsy, and epilepsy surgery. On top of being a productive researcher, he is also a very active lecturer, teacher and research advisor. Furthermore, Lars is a work package leader for the BrainDrugs-Epilepsy (BDE) project in WP4 and member of the Executive Board.

His aim of the professorship is to contribute to a better understanding of the course of epilepsy for the individual patient because, according to him, this is where the key to a better treatment of epilepsy and prevention of side effects must be found. Lars says: "*We do not know enough about how epilepsy develops and why it is so different from person to person. We cannot say in advance which medicine works best and who is at greatest risk of developing which side effects of the epilepsy. We do not know enough about what factors such as education, personality traits and lifestyle factors mean for life with epilepsy. But thanks to advanced ways of analysing EEG and brain scans, we are now beginning to understand how epilepsy changes the brain's network both in the early and late stages of the disease*".

For Lars, it is important that his research goes hand in hand with and contributes to the clinic, and he is happy that with his professorship he can help set the direction for research, education and clinical practice within epilepsy. As the new professor says: "*The clinical work is our inspiration for the hypotheses that we test scientifically and when our results are translated into action in the clinic, it is all worth it!*".

Clinical professorship in neuropsychiatry

As of Dec 1st, 2023, NRU senior researcher Vibe G. Frøkjær is appointed clinical professor in neuropsychiatry at the Department of Clinical Medicine, University of Copenhagen. The interdisciplinary professorship has been established in collaboration between neurology and psychiatry, and focuses on research that utilizes imaging methods to uncover the function of the living human brain and map risk, robustness and treatment mechanisms for brain diseases with psychological manifestations and for comorbidity to promote brain health.

Vibe is not only a productive researcher but also an active public clinical science communicator. Furthermore, she participates in the BrainDrugs research alliance where she serves on the BrainDrugs Executive Board. She also is work package leader in WP3 and leverages Deep Phenotyping Data from Established Research Cohorts by bridging such data with National Health register read outs of later development of depressive episodes in participants who were included in healthy states or prognostic markers in patient groups.

Vibe has been affiliated with NRU since the mid 2000's and lately has been focusing her research on molecular imaging of serotonergic neurotransmission in the context of steroid hormone biology (stress and sex-hormones), and genetic and personality risk factors for neuropsychiatric disease. This particularly includes uncovering how particular biomarkers in the brain can explain why some people are more at risk - or particularly resistant - to developing mental disorders and can inform relevant risk stratification prevention and treatments strategies. In her work, Vibe incorporates imaging studies of the brain's structure, network organization, chemistry and function, and pharmacological risk models and naturally existing models, such as, e.g., hormonal fluctuations in connection with childbirth. Vibe also conducts randomized clinical trials in order to translate basic knowledge into better prevention and treatment of brain diseases with psychological manifestations, such as cognitive disturbances or depression.

In her cross-disciplinary professorship, Vibe will have shared appointments at NRU and the Psychiatric Center Copenhagen.

PhD Degrees in 2023

Sophia Armand - **Affective cognition and brain serotonin in healthy individuals - The role of brain serotonin in cognitive-affective biases and amygdala response to threat**

PhD school at the Department of Psychology, Univ. Copenhagen

This PhD project consisted of three studies with an overall aim to advance our understanding of the role of brain serotonin in regulating affective cognition. The project focused on cognitive-affective biases and threat-related amygdala reactivity because of their central involvement in normal brain function and the risk of developing affective disorders.

Sophia Armand completed her PhD under the main supervision of associate professor Dea S. Stenbæk from NRU and Dept of Psychology, Univ. Copenhagen, and co-supervised by professor Gitte Moos Knudsen from NRU and Dept of Clinical Medicine, Univ. Copenhagen, professor Barbara Sahakian, from Dept of Psychiatry, Univ. Cambridge, UK, and associate professor Patrick Fisher, from NRU and Dept of Drug Design and Pharmacology, Univ. Copenhagen.

Dr. Armand successfully defended her thesis on Jan 20th, 2023, with professor Kamilla Miskowiak from Dept of Psychology, Univ. Copenhagen, and Psychiatric Centre Copenhagen, as chair, and senior research fellow Susannah Murphy, Dept of Psychiatry, Oxford University, UK, and associate professor Kim Kuypers, Faculty of Psychology and Neuroscience, Maastricht University, Netherlands, as opponents.

Gjertrud Louise Laurell - **Development of Novel Methods for PET-Based Quantification of Drug Interactions in the Living Human Brain**

Graduate School of Health and Medical Sciences, Univ. Copenhagen

The overall aim of this thesis was to improve the utility of PET for quantification of drug interactions in the living human brain. This aim was reached by evaluating common assumptions concerning analytical methods and experimental design, and by developing new analytical methods, applicable for different types of tracers and study designs.

Gjertrud Laurell completed her PhD under the main supervision of professor Gitte Moos Knudsen from NRU and Dept of Clinical Medicine, Univ. Copenhagen. Co-supervisors were professor R. Todd Ogden from Dept of Biostatistics, Columbia University, USA, Dr. Martin Schain from Antaros Medical, Sweden, and Drs. Claus Svarer and Pontus Plavén-Sigray from NRU.

Dr. Laurell's successful defense took place on Mar 10th, 2023, with professor Henrik B.W. Larsson from Dept of Clinical Medicine, Univ. Copenhagen as chair, and professor Ronald Boellaard, Dept of Radiology and Nuclear Medicine, VU University Medical Center Amsterdam, The Netherlands, and Dr. Gaia Rizzo from Invicro, UK, as opponents.

Annette Johansen - **Molecular neuroimaging of synaptic plasticity in the human brain**

Graduate School of Health and Medical Sciences, Univ. Copenhagen

The overall aim of the thesis was to employ Synaptic Vesicle glycoprotein 2A (SV2A) PET neuroimaging to investigate synaptic plasticity in the human brain in relation to pharmacological modulation of the serotonin system. To this end, we first implemented and characterized the PET radiotracer [^{11}C]UCB-J in humans, and second, we conducted two intervention studies in healthy volunteers to evaluate the effects of serotonin transporter inhibition and serotonin 2A receptor stimulation, respectively, on cerebral SV2A density.

Annette Johansen's PhD work was done under the main supervision of professor Gitte Moos Knudsen from NRU and Dept of Clinical Medicine, Univ. Copenhagen. Co-supervisors were associate professor Patrick Fisher from NRU and Dept of Drug Design and Pharmacology, Univ. Copenhagen, and Dr. Pontus Plavén-Sigray from NRU.

Dr. Johansen successfully defended her thesis on Dec 8th, 2023, with professor Steen Hasselbalch, Dept of Clinical Medicine, Univ. Copenhagen, as chair and with Dr. Johan Lundberg, Dept of Clinical Neuroscience, Karolinska Institutet, Sweden, and professor Richard E. Carson, Yale PET Center, Yale University, USA, as opponents.

Positions of Trust

Professor Gitte Moos Knudsen
Past-president of European College of Neuropsychopharmacology (ECNP), chair of the ECNP Psychedelics Thematic Working Group, chair of the Scientific Advisory Board for The Human Brain Project, board member of the Neuroscience Academy Denmark, board member of the Elsass Foundation, and member of Scientia Fellows program assessment committee at the University of Oslo, Norway, and of the Hospital del Mar Medical Research Institute Foundation, Barcelona, Catalonia. Representing Professor for Neurology at Univ. Copenhagen. Scientific advisor for the Savværksejer Jeppe og hustru Ovita Juhls mindelegat. Adjunct professor at University of Vienna, Austria. Board member of The Danish Academy of Neuroscience. In 2023, PhD-examiner of Dr Angharad De Cates, Corpus Christi College, Oxford University and reviewer for a number of journals, including Nature Neuroscience, Nature, and Molecular Psychiatry.

Professor Emeritus Olaf B. Paulson
Member of the Research Ethical Committee for Science and Health at Univ. Copenhagen and of the Research Ethical Committee of the Capital Region of Denmark. Member of the International Advisory Board for the NeurInsight LLC project, a program led by professor Stefan Posse, Albuquerque, USA and supported by the NIH. Auditor for Danish Society for Neuroscience.

Professor Jens D. Mikkelsen
Deputy Chairman for external evaluations of medical educations in Denmark (Censorformandskabet for Lægeuddannelsen i Danmark). Reviewer for several journals including, PNAS and Translational Psychiatry

Professor Vibe G. Frøkjær
Appointed Danish representative in the management committee for the EU-based Riseup-Post Partum Depression (PPD) COST Action, and member of the Neuroimaging Network, the Psychedelics Thematic Working Group and the Meta network on depression of ECNP. Board member of Danish Society for Affective Disorders. Research advisory board member for "Sygeforsikring Danmark" donations and Independent Research Council Norway. PhD-assessor at Karolinska University, Sweden, Tübingen University, Germany, and Univ. Copenhagen, Denmark, and reviewer for several scientific journals including Nature Mental Health and Molecular Psychiatry.

Professor Lars Pinborg
Member of the board of the Danish Epilepsy Society, and chair of the Danish Epilepsy Surgery Programme.

Associate professor Patrick M. Fisher
Member of the ECNP Psychedelics Thematic Working Group. Member of the Lundbeck Foundation Investigator Network. Editorial Board member of the Psychedelic Medicine peer-review journal publication. Scientific Committee Member of psychedelicsEUROPE, a group advocating to the European Union for consideration of evidence-based medical applications of psychedelics. Auditor for the Danish Society for Neuroscience. Reviewer for several scientific journals.

Associate professor Dea S. Stenbæk
Member of the ECNP Psychedelics Thematic Working Group. Guest editor of research topic on psychotherapeutic framing of psychedelic drugs, Frontiers Psychology. Committee member of The Ethical Committee, Dept Psychology, Univ. Copenhagen.

Associate professor Melanie Ganz
Member of the Cross-Academy Collaboration sub-committee under the Danish Data Science Academy.

Associate professor Louise Møller Jørgensen
Committee member of The National Medical Ethical Committee (National Ethic Center). Chairman of the committee for spine surgery (DNKS). Member of 'Innovation Working Group' (SUND, Univ. Copenhagen), 'Strategic Partnerships' (DTU and Rigshospitalet) and 'New National Research Network for Spine Surgery' (DRKS). Course co-leader of "Innovation" (SUND, Univ. Copenhagen). Reviewer for scientific journals (Acta Neurochirurgica, Brain Sciences).

Senior Research Software Developer Cyril Pernet
Co-chair of the Organization for Human Brain Mapping (OHBM) Best Practice Committee. Steering group member of the Brain Imaging Data Structure (BIDS) working group. Member of the International Neuroinformatic Coordinating Facility (INCF) Council for Training, Science and Infrastructure. Member of the Ethic and Society committee for EBRAINS, the EU neuroscience infrastructure. Editorial board member for Scientific Data, Scientific Reports and Brain Topography. Reviewer for several scientific journals. In 2023, PhD examiner of Dr Lucas La Fisca, Univ. Mons, Belgium.

Strategic Collaborations

Strong collaborations are fundamental for excellent brain research to happen. We have for many years worked closely together with colleagues within Dept of Neurology and with many different partners within Denmark and internationally. Listed below are some of our major strategic collaborations, which are particularly key for us.

PET and Cyclotron Unit, Rigshospitalet

We highly appreciate our long-lasting and outstanding collaboration with professor Malene Fischer and her dedicated staff at the PET and Cyclotron Unit at Dept of Clinical Physiology, Nuclear Medicine & PET. The collaboration covers research and developmental activities and provides NRU with excellent expertise and infrastructure for radiochemistry, and PET-, and MR-PET scanner facilities. We highly appreciate this crucial collaboration and look forward to continuing the joint research activities.

Dept of Radiology, Rigshospitalet

Over the last decade, we have had a well-established collaboration with the Dept of Radiology. In 2023, we have in particular worked closely together with Dr. Vibeke Andrée Larsen, professor Adam Espe Hansen, chief radiographer Susanne Stampe and radiographers Kevin Robert Brow and Rasmus Nagstrup Jensen. The Dept of Radiology uses our Siemens Prisma 3T MR scanner for clinical neuro-examinations 50% of the weekly working hours.

Dept of Obstetrics and Gynaecology, Rigshospitalet, Herlev, Hvidovre and Hillerød

NRU collaborate in translational clinical trials with senior consultants Kristina Renault, Eleonora Cvetanovska, Ellen Løkkegaard and Anette Kjærbye-Thygesen at Obstetrics Depts in the Capital Region of Denmark in projects aiming at evaluating preventive strategies for perinatal depression in high-risk groups. Also, we collaborate with professor Øjvind Lidegaard in epidemiological studies on the brain and mental health consequences of oral contraceptive use.

Dept of Growth and Reproduction, Rigshospitalet

We collaborate with professor Anders Juul at Dept of Growth and Reproduction on determination of sex steroids in large clinical populations related to brain signatures of hormonal rhythms.

University of Copenhagen

Since the establishment of Cimbi in 2006, we have had a close collaboration on PET radioligand development with Dept of Drug Design and Pharmacology (Dr. Herth, professors Kristensen and Jensen). Likewise, we also appreciate our long-standing collaboration on biostatistics with Section of Biostatistics, Faculty of Public Health, with whom we share a biostatistical associate professor (Dr. Ozenne) and a biostatistical PhD-student (Dr. Ziersen) through the *BrainDrugs* project, The Center for Translational Neuromedicine (professor Nedergaard), and with the Dept of Psychology with whom we share an associate professor (Dr. Stenbæk). Finally, we also highly appreciate our strategic collaboration with Dept of Computer Science, facilitated by a joint associate professor (Dr. Ganz) as well as cooperation in the *BrainDrugs* project. Last but not least, professor Jens H. Mikkelsen heads the Master's program in Neuroscience.

Copenhagen Business School

Together with professor Toke Reichstein, we are conducting a study of cognition, risk-related decision making and brain function in entrepreneurs.

Mental Health Services in the Capital Region of Denmark

NRU has close collaborations with Mental Health Services in the Capital Region of Denmark, including with professors Martin Balslev Jørgensen and Lars Vedel Kessing who are both directly involved in *BrainDrugs*, with professor Kamilla Miskowiak and her Neurocognition and Emotion in Affective Disorders (NEAD) group through *BrainDrugs* and some NEAD projects, as well as with professors Anders Fink Jensen and Birte Glenthøj. Through *BrainDrugs*, the collaborative network has been expanded to also include professor Poul Videbech and Klaus Martiny.

For our *BrainDrugs* project, we benefit greatly from our close collaboration with Allan Lohmann-Olsen and Eva Hundrup from CVD ('Center for Visitation og Diagnostik'), a unique central referral site for 'treatment packages', e.g., for patients with depression or obsessive-compulsive disorder who can be treated in outpatient settings.

University of Cambridge, UK

We are collaborating with professors Trevor Robbins and Barbara Sahakian from University of Cambridge on two joint research projects funded by the Lundbeck Foundation; the collaboration includes bilateral secondments. The data acquisition for the project with Sahakian was completed in 2021 and has so far led to two joint publications and one book chapter [B1], whereas the data acquisition for the Robbins project is still ongoing and expected to be completed during Spring 2024.

Stanford University, National Institutes of Health, and Martinos Center, US

The OpenNeuroPET project, funded through the BRAIN initiative and the Novo Nordisk foundation has been going on since 2019. You can read more about the project on page 33.

Martinos Center, Massachusetts General Hospital, US

We have since 2011 had a fruitful collaboration with the Athinoula A. Martinos Center for Biomedical Imaging in Boston, US, which has pioneered brain imaging with MRI. The collaboration has so far included retreat meetings, the successful achievement of a joint 2-year NIH grant, the NRU-anchored *NeuroPharm* Center grant (2015-22) from the Innovation Fund Denmark, and funding from Lundbeck Foundation for instructor at Harvard University, Dr. Hansen, as well as bilateral exchange of scientists. Joint research areas include PET-MR of animals, PET data modelling and motion correction. The collaboration has so far resulted in more than 20 publications.

The Serotonin and Beyond European Training Network (ETN)

We have been a partner in the consortium behind the Serotonin and Beyond ETN (https://www.serotonin-and-beyond-project.eu/) since its establishment in 2021. NRU PhD student Silvia EP Bruzzone is funded through this ETN which aims to train the next generation of serotonin researchers and deliver new fundamental insights in how early life changes in serotonin caused by genetic or environmental factors alter brain development and thereby contribute to the cause of serotonergic psychiatric disorders.

Preclinical Neurobiology

Experimental neurobiological research is conducted at NRU where several researchers are working on research projects to study mechanisms *in vitro* and *in vivo*.

We have in rodents investigated the effects of low, repeated doses of psilocybin, so-called microdoses, and found that they affect stress resilience and compulsive behaviours while also inducing changes (**Figure 1**) in serotonergic receptors and neuroplastic effects in the para-ventricular thalamic nucleus [32]. The paper was well received with many news outlets reporting on the findings.

Jens H. Mikkelsen
Professor

Synapse loss in ageing and in Alzheimer's disease

Synaptic alterations in certain brain structures are related to cognitive decline in neurodegeneration and in aging. We tested the (pre)synaptic vesicular glycoprotein 2A (SV2A) PET ligand [^{18}F]SynVesT-1 as a proxy for presynaptic density at different ages in healthy mice [74]. PET scans revealed that [^{18}F]SynVesT-1 brain retention was lower in the oldest group of mice, indicating a decrease in synaptic density in this age group, but no gradual age- dependent decrease in synaptic density at a region-specific level was observed. Immunostaining indicated that SV2A expression and neuron numbers were similar across all three age groups. In general, these data obtained in healthy aging mice are consistent with previous findings in humans where synaptic density appeared stable during aging up to a certain age, after which a small decrease is observed.

Previous data have demonstrated neurodegenerative changes in the cerebral cortex in patients with AD and it has been suggested that this represents a loss of synapses. PET imaging of SV2A has demonstrated a reduction in synapse density in AD in the hippocampus, but not consistently in the neocortex. We have used the same tools *ex vivo* and have examined the level of [^{3}H]UCB-J binding in postmortem cortical tissue from patients with AD and matched healthy controls using autoradiography. In AD brains, SV2A density was significantly lower in the middle frontal gyrus only while we saw in the parietal, temporal, or occipital cortex. The binding levels in the frontal cortex in the AD cohort displayed large variability among subjects. These results add further evidence for SV2A being be an important biomarker in AD patients for synapse loss [49].

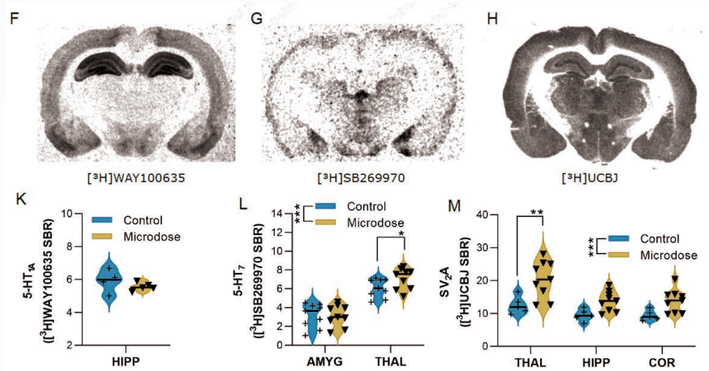


*Figure 1: Receptor levels and synaptic density in the para-ventricular thalamic (PVT) nucleus of the rat following microdoses of psilocybin. The upper panel shows autoradiography slices of the rat brain displaying the (**F**) 5-HT$_{1A}$ and (**G**) 5-HT$_{7}$ receptor distributions, and the (**H**) SV2A distribution, a proxy of synaptic density. The lower panel shows the corresponding post-mortem levels of (**K**) 5-HT$_{1A}$ in the hippocampus (HIPP), (**L**) 5-HT$_{7}$ in the amygdala (AMYG) and thalamus (THAL), and (**M**) SV2A in THAL, HIPP and the cortex (COR). Compared to control rats, psilocybin-treated animals have increased post-mortem levels of 5-HT$_{7}$ in THAL and of SV2A in PVT. Modified from [32], Copyright © 2023, the Author(s).*

Development of novel ligands for neuroinflammation

Radioligands targeting microglia cells have been developed to identify and determine neuroinflammation in the living brain. One recently discovered ligand is JNJ-64413739 that binds selectively to the purinergic receptor P2X7R. Expression of P2X7R is increased under inflammation, hence the ligand is considered useful in detection of neuroinflammation in the brain. However, until now only healthy subjects have been studied and the radiotracer remains to be validated *in vitro* in human brain tissues and in larger cohorts. We have studied a total of 48 temporal cortical samples resected under neurosurgical operations for intractable temporal lobe epilepsy, and processed these tissues for autoradiography to define the binding characteristics of [^{3}H]JNJ-64413739. Binding was detected in both cortical grey and subcortical white matter. Whereas affinity was similar in both tissue types, B_{max} was larger in white than in the grey matter. The between-patient variability in binding was 38% in both compartments, but not explained by age, sex, or the duration of the disease. [^{3}H]JNJ-64413739 has a different spatial binding pattern than the translocator protein (TSPO). These data suggest JNJ-64413739 is an interesting radioligand for glial cells targeting a novel site and a different type of mechanism than reflected by TSPO [48].

The NRU Neuroimaging Laboratory

3T MRI scanner

Emilie Henriksen
Radiographer

Magnetic resonance imaging (MRI) is central to many of our research projects. We also facilitate collaborative, high-quality clinical brain imaging research studies at Rigshospitalet. We acquire MRI data primarily at MR001, NRU's own Siemens 3T Prisma scanner in the North Wing building. Dept of Radiology has access to MR001 for clinical scanning 50% of working hours with the remaining time available for NRU research. We have trained MR-assistants that can help with research studies during working hours as well as evenings and weekends.

We continue to enjoy a great collaboration with Siemens, including the invaluable support from Karen Kettless, Siemens MRI Applications Specialist. This collaboration shortens the time from new ideas to implementation on the scanner.

Below is a brief overview of on-going MRI-based studies in 2023:

- In collaboration with professors Trevor Robbins and Barbara Sahakian from Cambridge University (UK) we are evaluating SSRI effects on cognitive processing in healthy individuals and individuals with OCD.
- The ALTIBRAIN, CAVIR and TRANSCIN studies rooted in the NEAD group led by professor Kamilla Miskowiak from Psychiatric Center Copenhagen acquires structural and functional MRI (fMRI) to evaluate brain imaging markers associated with mood disorders, associated treatments, alterations in cognition, and neuroplasticity.
- The REFORM project with professor Messoud Ashina from the Danish Headache Center at Rigshospitalet-Glostrup continues a large data collection endeavor to evaluate structural and functional brain markers of an antibody treatment for migraine.
- The BrainDrugs initiative collects MRI data in cohorts with depression and epilepsy.
- BIND (Brain Involvement in Dystrophinopathies) is a multi-site clinical research study with professor John Vissing from the Dept of Neurology at Rigshospitalet with an arm that will acquire structural and functional imaging in Becker Muscular Dystrophy patients.
- OLF fMRI with professor Christian von Buchwald from Ear-Nose-Throat Surgery at Rigshospitalet aims to evaluate brain imaging measures of sense of smell in patients with impairment following Covid-19.
- The EU-funded R-Link project with professor Lars Kessing from Psychiatric Center Copenhagen aims to optimize response to Lithium treatment through personalized evaluation of individuals with bipolar I disorder.
- The ECAC project with professor Tiit Mathiesen from the Dept of Neurosurgery at Rigshospitalet aims to investigate correlations between arachnoid cysts and cognitive dysfunction, to elucidate the eventual role played by inflammation and glymphatic flow dysfunction and to identify the impacted functional networks.
- Associate professor Melanie Ganz from NRU is continuing the application of real-time motion correction to assist with clinical brain imaging of small children, mitigating the need for general anesthesia.
- The UFMR project with NRU PhD student Sara Marie Larsen applies an ultra-fast and non-invasive MRI tool for measuring brain pulsations to aid diagnosing patients with increased intracranial pressure.
- The Pill Project led by professor Vibe Frøkjær at NRU, is a longitudinal study evaluating effects of oral contraceptives on cognition and the brain in healthy women.
- The MAMA project with professor Vibe Frøkjær examines the effect of breast-feeding and oxytocin on brain structure and function.
- The Stroke Project led by professor Gitte Moos Knudsen from NRU applies MRI to evaluate structural and functional brain changes following stroke.
- The ADHD project led by Sofi da Cunha at NRU uses fMRI and spectroscopy to evaluate brain activation during reward, response inhibition, and working memory in individuals with ADHD.
- The Neuromelanin project led by NRU chief technologist Gerda Thomsen aims to compare methods for estimating DAT levels in the brain with PET and MRI.
- The COG-iEEG project with Drs. Pascal Stevens and Ron Kupers aims to compare responses to sensory, cognitive, social, and affective stimuli measured with sEEG with functional MRI responses to the same type of stimuli in epilepsy patients.
- The QUANTUM Trip Trial with professor Anders Fink Jensen from Psychiatric Center of Copenhagen is a randomized trial that aims to compare placebo vs. psilocybin treatment in alcohol abuse disorder.
- The SEMALCO study with professor Anders Fink Jensen investigates GLP-1 receptor agonist treatment for reducing alcohol intake in patients with alcohol use disorder and comorbid obesity, it applies fMRI and MRS Spectroscopy (MRS) to evaluate brain effects.
- The RESETTLE project led by professor Signe Sørensen Torekov acquires structural and functional MRI data to characterize brain effects of lifestyle-intervention treatment of obesity in young adults.
- The BHB project led by professor Nadia Micali from Center for Eating and feeding Disorders research applies fMRI and MRS to evaluate tolerance of a ketone-based nutritional supplement in refeeding in patients with anorexia nervosa.
- The MECT study with associated professor Anders Jørgensen from Psychiatric Center Copenhagen aims to examine brain morphology and focus on cognition and brain age in relation to ECT treatment.

SPECT-CT system

The SPECT laboratory of NRU is located next to the Dept of Radiology on the ground floor in the North Wing of Rigshospitalet. The facility is used both diagnostically and for research purposes. Our 3rd generation high-resolution AnyScan SPECT-CT Mediso scanner provides very good images, and we continue to develop new methodologies in collaboration with Mediso.

Gerda Thomsen
Chief technologist

Research projects

In a retrospective study we have investigated the predictive value of SISCOM for successful epilepsy surgery [58]. We found that precise definition of a well-executed ictal SPECT scan with respect to seizure duration after injection of above 30 seconds enhances the positive predictive value and odds ratio for successful surgical outcome, surpassing previous findings, whether the focus is in the resected lobe or neighboring. SPECT imaging with the tracer 99mTc-HMPAO visualizes cerebral hyperperfusion during epileptic seizures to localize the epileptogenic zone. In a second retrospective study we investigated the added value of visualizing areas of hypoperfusion alongside hyperperfusion, termed reversed SISCOM, in 56 epilepsy surgery patients. We found that reversed SISCOM improved prediction of surgical outcomes, especially in cases with longer seizure durations.

Furthermore, we have enrolled and scanned patients referred for dopaminergic investigation as part of an ongoing study which is a 'head-to-head' comparison of the [^{123}I]FP-CIT SPECT-CT and [^{18}F]FE-PE2I PET-CT modalities as well as an evaluation of the usefulness of adding MR-based neuromelanin measurements. Data collection for this study ended December 2023 and data analysis is ongoing.

Clinical work

Patients with neurological disorders are referred to the NRU SPECT-laboratory for diagnostic SPECT investigations from Dept of Neurology, Rigshospitalet, the epilepsy hospital in Dianalund, and other hospitals in Denmark. The diagnostic investigations include:

Regional cerebral blood flow (CBF) with the SPECT ligand [^{99m}Tc]HMPAO

This examination is mostly used as a technique for localizing the epileptic focus in patients with drug-resistant epilepsy that are candidates for epilepsy surgery. We are the only laboratory in Denmark to conduct ictal-interictal SPECT imaging with co-registration to MRI (SISCOM) This requires personnel specifically trained to inject as soon as the epileptic activity commences.

Striatal dopamine transporter (DAT) imaging with the SPECT ligand [^{123}I]FP-CIT

This is a robust technique for early detection of dopaminergic deficits and is used diagnostically in patients with movements disorder and/or dementias of uncertain origin. The diagnostic report comes with a reference to a healthy age-matched population and is evaluated by a neurologist specialized in reading DAT-SPECT scan data. We are currently completing the acquisition of a new diagnostic reference material for FP-CIT.

Together with the NRU data analysis group automatic methods for evaluating these clinical scans have been developed and refined. For the method used for evaluation of clinical DAT scans, in 2023 a new set of 20 healthy control scans with an age span of 20-80 years has been acquired. The program used for evaluation of patient DAT scans has been optimized to take full advantage of this new database and the higher resolution of the scanner. The clinical specificity of the database and the program will be evaluated in different patient groups in the year to come, but has already proven its usability.

Data Analysis

The NRU data analysis group optimizes methods and algorithms for analysis of data acquired in research projects that NRU take part in. In particular, we work to make more robust methods that also can handle smaller samples sizes and noisy data. Our data sources include SPECT, PET- and MR-imaging data, EEG, and different neuropsychology and other state or trait markers sampled from project participants. NRU is also taking the lead in data sharing initiatives, as described below.

The “biological age” of the human brain is traditionally assessed based on structural MR brain images. The difference between a person’s chronological age and the estimated brain age may reflect deviations from a normal aging trajectory, indicating a slower or accelerated biological aging process. Based on MRI scans from 372 healthy volunteers, we have evaluated the outcome of six publicly available pre-trained software packages with respect to (1) predictive accuracy, (2) test–retest reliability, and (3) the ability to track age progression over time [14]. When assessing the accuracy and test–retest reliability, we found good correlations between predicted brain age and chronological age (**Figure 2**), and we found that ‘pyment’ and ‘brainageR’ performed best.

Claus Svarer
Chief engineer

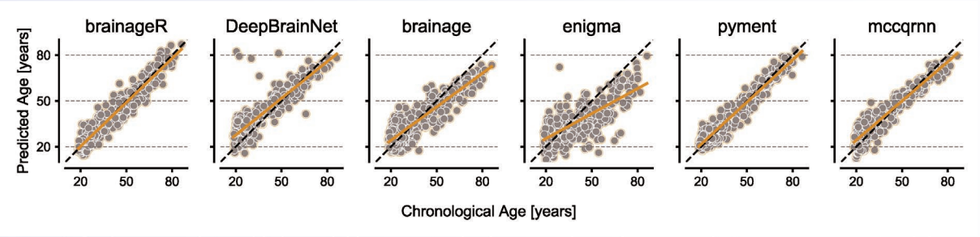


Figure 2: Performance of six publicly available pre-trained software packages for age-prediction on a cross-sectional dataset based on 372 T1-weighted structural MR scans of healthy controls. The identity line is in dashed black, and the model regression line is colored. From [14], Copyright © 2023, The author(s).

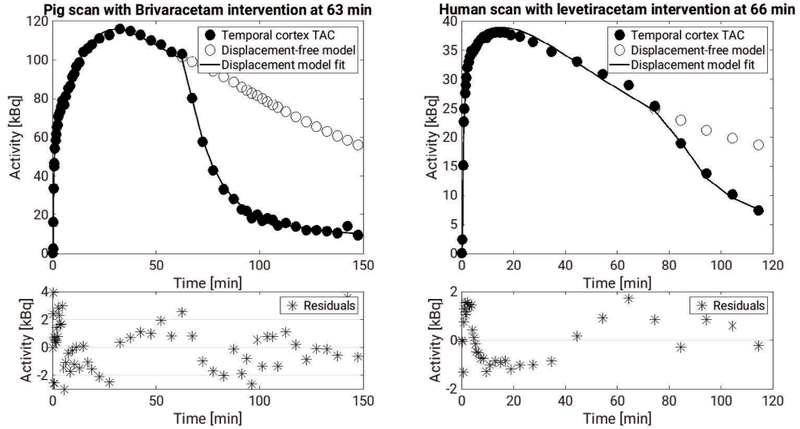


Figure 3: Kinetic modeling of data from a [^{11}C]UCB-J PET displacement study with (left) a pig scan where the tracer was displaced by Brivaracetam, and (right) a human scan where the tracer was displaced by Levetiracetam. Upper panel shows the time-activity curve (TAC) for the temporal cortex together with outcome from the kinetic model, and the lower panel illustrates that there is no systematic difference between measured data and model outcome. Figure courtesy: Gjertrud L. Laurell.

Quantification of the interaction of drug and target can be done by PET receptor occupancy studies and traditionally, these target engagement studies require two separate PET scans for each participant; one before and one after administration of the drug. We have developed a new blood-based pharmacokinetic model that enables analysis of data from a PET displacement experiment, where the competing drug is administered during an ongoing PET scan (**Figure 3**) [40]. This reduces the number of required scans, thus reducing both costs and radiation exposure. We are currently validating the approach in clinical studies and have promising outcomes.

In continued efforts to establish a PET tracer detecting α-synuclein pathology we took part in the evaluation of the novel PET ligand, [^{18}F]ACI-12589 [65]. Using autoradiography and in vivo PET imaging, we showed that the tracer has high in vitro affinity and specificity for pathological α-synuclein in tissues from patients with different α-synuclein-related disorders including Parkinson’s disease and Multiple-System Atrophy (**Figure 4**). [^{18}F]ACI-12589 PET imaging is found useful for diagnosis of the latter, and could potentially be used for in vivo assessment of novel α-synuclein targeting therapies.

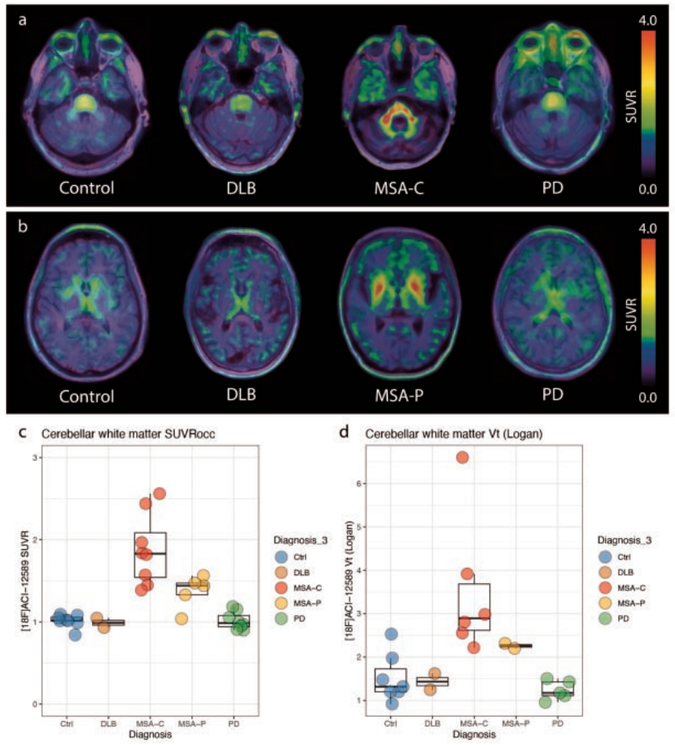


*Figure 4: [18F]ACI-12589 PET in participants with a-synucleinopathies. **a)** Transversal images at the level of the middle cerebellar peduncles in a control participant, and patients with DLB, MSA-C and PD. **b)** Transversal images at the level of the basal ganglia in a control participant, and patients with DLB, MSA-P and PD. SUVR images for (**a**, **b**) have been created using occipital cortex as a reference region. **c)** SUVR values in the cerebellar whitematter in the different disease groups (Control: n=8, DLB: n=2, MSA-C: n=8, MSA-P: n = 5, PD: n=8). **d)** VT values derived from Logan graphical analysis modeling in the cerebellar white matter in the different disease groups with available blood and dynamic PET data. Boxplots show median, IQR (box) and whiskers (Q1 − 1.5*IQR/Q3 + 1.5*IQR or minimum/maximum value, outliers not included) (Control: n =7, DLB: n =2,MSA-C: n=6, MSA-P: n =2, PD: n= 5). DLB = dementia with Lewy bodies, MSA-C = multiple system atrophy with a cerebellar phenotype, MSA-P = multiple system atrophy with a parkinsonian phenotype, occ = occipital cortex reference region, PD = Parkinson's disease, SUVR = standardized uptake value ratio, VT = volume of distribution. From [65], Copyright © 2023, The author(s).*

OpenNeuroPET

Cyril Pernet
Senior Research Software Developer

The NovoNordisk Foundation funded OpenNeuroPET initiative is done in collaboration with NIHM and aims to enable PET data sharing to, e.g., increase sample sizes and thereby improve the statistical power and validity of research findings. Expensive PET neuroimaging data must be shared in a FAIR way (Findable, Accessible, Interoperable, and Reusable). Firstly, by extending the Brain Imaging Data Structure (BIDS) to cover PET data, we have made molecular imaging datasets more interoperable and reusable. This year, we have released a companion software; PET2BIDS (https://github.com/openneuropet/PET2BIDS) to convert raw PET data to the BIDS format. Many new open datasets have been made available on OpenNeuro with the help of the OpenNeuroPET team (https://openneuro.org/search/modality/pet). We have also described the evolution of the history of the BIDS initiative from 2014 [P1] and experiences gained [21], which we are leveraging to develop PET BIDS derivatives, i.e., the sharing of processed data. To this end, we hosted an international workshop with all BIDS parties, defining the derivatives standard (https://github.com/openneuropet/outreach/tree/main/BIDS_derivatives2023). This work has been presented by NRU senior researcher Melanie Ganz-Benjaminsen at the OpenKMI Workshop at IEEE Medical Imaging Conference 2023 (https://www.openkmi.org/workshop/openkmi_mic2023). We have also described how to make shared data available and the associated costs with huge cloud-based databases [54]. First, data must be curated and then processed for storing the data on a media that can be accessed without too much manual intervention. Data curation includes preservation, storage and disposal of data that are not usable or used. Data storage has to be optimized for minimizing financial but also ecological cost, by analyzing data access and providing "hot storage", i.e., on-line storage with short re▫

Neuropsychology

Vibeke Dam
Senior researcher

2023 was a busy year for the Cognitive Neuropsychology Group. Sophia Armand successfully defended her PhD thesis and we welcomed six new students into the group, expanding our research capacity. Altogether, our hardworking team of neuropsychological testers (12 psychology and 8 medical students) collected more than 360 cognitive datasets in both healthy individuals and patient cohorts across 12 active NRU studies.

A central focus of our research in 2023 revolved around cognition in mood disorders. Notably, we showed a positive association between serotonin 4 receptor levels and memory performance in patients with depression [37], shedding light on a new potential therapeutic target. Additionally, we were able to report that poor verbal memory is linked to an increased risk of psychiatric hospitalization among individuals with mood disorders [63] while data from a collaborative study with Prof Barbara Sahakian from the Cambridge Cognition Group yielded new insight into the effect of escitalopram on reinforcement sensitivity in healthy individuals [38]. Our collaboration with the Cambridge group was further strengthened through a co-written chapter on the EMOTICOM battery in the SAGE Handbook of Neuropsychology [B1].

As a new and expanding research interest, we are also focusing more and more on somatic disorders [71,72] and are very pleased to have finalized data collection on the ALLSTAR and MyBrain projects in collaboration with the Paediatric Oncology Research Laboratory who are investing long-term cognitive effects of cancer treatment in children. In addition, we completed a large survey in neurological patients focusing on patient experience during clinical MR-scans, further bridging the gap between research and clinical practice.

Psychedelics

Dea S. Stenbæk &
Patrick Fisher
Senior researchers

Interest in psychedelic drugs has exploded over the past 10 years as potential therapeutics for hard-to-treat brain disorders. At NRU, we started human psychedelic research studies as part of our Center for Experimental Medicine Neuropharmacology (NeuroPharm, 2015-2022, https://np.nru.dk/) and we continue to pursue research questions about psychedelics and the brain.

The Copenhagen University Clinic for Psychedelic Research (NOESIS, https://psy.ku.dk/noesis/) was established by associate professor Dea S. Stenbæk; this extends our facilities and capacity for conducting psychedelic, and a curriculum for two novel master level courses in psilocybin-assisted therapy have been established at the Dept of Psychology, University of Copenhagen.

The perspective of psychedelic therapy has been burgeoning world-wide. In that context, NRU has been collaborating with colleagues from the European Medicines Agency to define some of the challenges with the therapeutic potential of psychedelics, seen from a European regulatory perspective [9] and also discussed the concept of psychotherapeutic framing of psychedelic drug administration [7].

In collaboration with colleagues at University of Copenhagen, we have highlighted the potential for psychedelic therapy to treat eating disorders [17]. We have also reviewed the unique concept of how single doses of classical psychedelics can generate beneficial sustained effects in humans [B2, 36].

Clinical Neuropsychiatry

By identifying biomarkers that indicate both risk and resilience for brain disorders with psychological and cognitive symptoms, we can better understand the underlying mechanisms of these disorders and develop more targeted prevention and treatment strategies. This approach can help us tailor treatments to individual patients, which is the essence of precision medicine. This is pursued through our many cross-disciplinary collaborations with Depts of Neurology, Psychiatry, and Psychology, with computer science, molecular genetics, and through participation in international data sharing consortia [20, 21, 22, 27, 34, 45, 50, 56, 57]. We hold a special expertise in molecular brain imaging of neurotransmitter systems [8, 11, 12] and synaptic density involved in neuropsychiatric disorders and their treatments. For example, we have for the first time mapped the temporal evolution of brain plasticity in response to selective serotonin-reuptake inhibitors by in vivo imaging of a marker for synaptic density (**Figure 5**) [30]. Also, we have pointed to potential serotonergic signatures of maladaptation to stress in MDD [69].

Vibe G. Frøkjær
Professor

Major depressive disorder (MDD)

Together with our collaborators at Dept of Psychiatry, University of Copenhagen, and building on existing data acquired in our Center for Experimental Medicine Neuropharmacology (NeuroPharm, 2015-2022, https://np.nru.dk/) we study plausible treatment mechanisms and work to identify relevant biomarkers to define subtypes of MDD that respond differently to treatment. This includes, e.g., EEG-based markers [25,28], mechanisms by which ECT may exert antidepressant effects [4], and structural and functional prognostic markers of affective disorders [18, 31, 43, 44, 63, 73]. In a study collaboration with Imperial College London where we take advantage of a PET tracer developed at NRU, we show that serotonin release capacity is reduced in depressed patients [16]. We have also shown that serotonin 4 receptor brain binding is markedly reduced in unmedicated patients with moderate to severe MDD relative to healthy controls. Intriguingly, this reduction of serotonin 4 receptor levels in MDD patients is associated with memory performance [37], stress hormone dynamics [69], and emotion processing [64], and in women appears to be linked to anhedonia which is a core symptom of depression [61]. Importantly, this work highlights stimulation of the serotonin 4 receptor as a promising treatment target in MDD including cognitive symptoms of the disorder [19]. Together, our work firmly establishes a role for serotonergic changes in the depressed brain and also serves as a guidance for future studies of novel treatments for MDD.

Sex-steroid hormones and reproductive mental health

The dynamic interplay between brain biology and sex-steroid hormone systems represents a potent driver of risk and resilience for neuropsychiatric disorders. We have proposed that maladaptation to hormone transitions may play a role in distinct “hormone sensitive” subgroups within MDD, while others adapt well [52]. This hormone sensitivity hypothesis is supported by national health register-based work suggesting that women who develop depressive episodes when exposed to hormonal shift by hormonal contraceptive use also face a higher risk of perinatal depression [39].

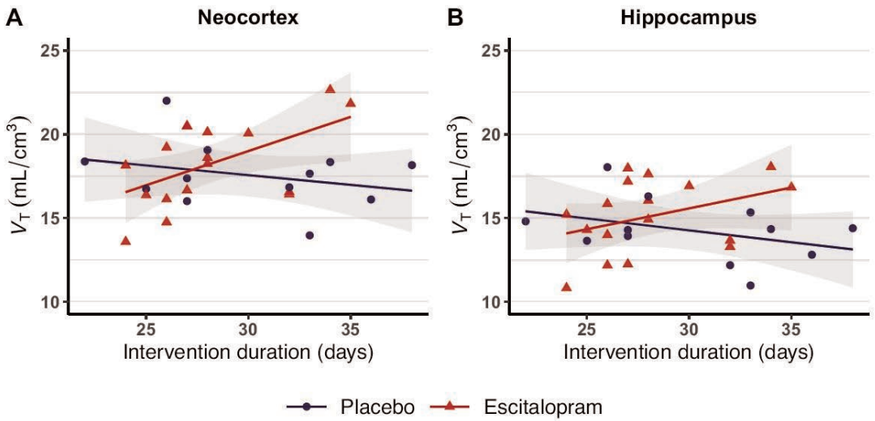


*Figure 5: Time-dependent effects of escitalopram on SV2A density. Relationship between [^{11}C]UCB-J binding (V_T) and the duration of the intervention for the placebo group (n = 12) and the escitalopram group (n = 17) in (**A**) the neocortex and (**B**) the hippocampus. The shaded grey area represents the 95% CI. From [30], Copyright © 2023, The author(s).*

Epilepsy

Lars Pinborg
Professor

NRU works closely together with the Epilepsy Clinic at Rigshospitalet and the Univ. of Copenhagen to improve diagnosis, prevention, and treatment of future patients with epilepsy. Much of this work takes place within the framework of the strategic research alliance BrainDrugs which is described in detail on the following pages.

We are very focused on making the enormous amount of information about epilepsy stored in the last 15 years' electronic health records accessible for clinical research. This is done, among other things, through the use of AI such as text-mining [70]. We are also intensely working on creating smaller but very deeply phenotyped prospective cohorts of newly diagnosed patients and patients with their first epileptic seizure [46] (**Figure 6**). Finally, we are working with the existing deeply phenotyped cohort of patients with drug-resistant focal epilepsy being assessed for epilepsy surgery. We have published articles on the use of SISCOM-SPECT [58, 59], and MRC and FreeSurfer [35] to identify the specific area in the brain where the epileptic seizure starts. When it is possible to identify this area and remove it during surgery, we can afterwards use the removed tissue to identify new potential targets for drugs against epilepsy [33] and to evaluate new ligands of importance for understanding the pathogenesis of brain diseases including epilepsy [48].

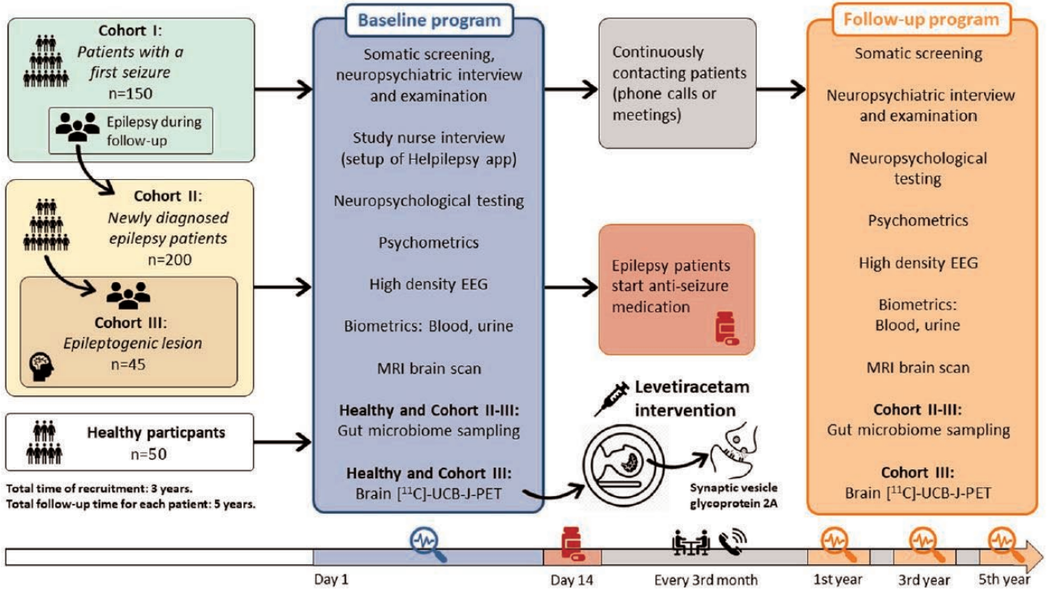


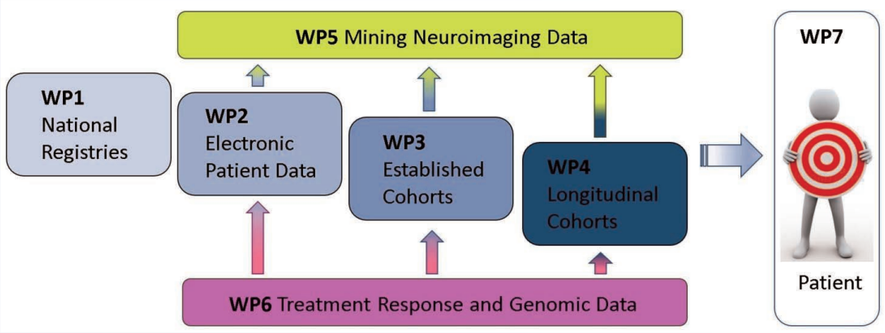
Figure 6: Workflow of The BrainDrugs-Epilepsy Study Cohort I-III and healthy controls. EEG: Electroencephalography. MRI: Magnetic resonance imaging. PET: Positron emission tomography. From [46], Copyright © 2023, Published by Elsevier B.V. on behalf of European College of Neuropsychopharmacology.

BrainDrugs

Center director
Gitte Moos Knudsen

The strategic research alliance *BrainDrugs* (2019-26) is our large-scale precision medicine project in epilepsy and major depressive disorder (MDD) (https://braindrugs.nru.dk). The alliance which is funded by 40 mio DKK from the Lundbeck Foundation establishes key features predictive of drug response in patients with epilepsy or MDD.

The alliance builds on strong cross-disciplinary research environments within universities and hospitals in Denmark and by affiliated partners from Lausanne University Hospital, Switzerland and VU University Medical Center in Amsterdam, the Netherlands. The involved Danish institutions span several different departments at Copenhagen University Hospital, Rigshospitalet, Univ. Copenhagen, Aarhus University Hospital, and Aarhus University, as well as the Filadelfia Epilepsy Hospital and the three mental health centers: Psychiatric Center Copenhagen, Psychiatric Center Glostrup, and Mental Health Center Sct. Hans. The project consists of seven coherent work packages, as depicted in the diagram below; the progress of WP1-WP5 is listed below.



The overall project is well underway and to ensure maximal and timely synergy between the work packages and campuses, early career scientists gather every third week online in the BrainDrugs Early Career Forum (ECF) meetings and we have quarterly Work Package Leader meetings. In June we hosted the fourth *BrainDrugs* annual meeting at Comwell Borupgaard (see photo above) with 45 participants. The meeting included 17 oral presentations followed by many productive scientific discussions, and the evening of the first meeting day was reserved for dinner and informal social gathering for all participants.

WP1-leader: Professor
Lars V. Kessing

WP1: National registries

Danish registries represent a unique opportunity to explore enormous data amounts with respect to health data, e.g., registries of prescriptions combined with morbidity data and other patient record data with phenotypic information. Within this WP, we focus on both patient groups' drug intake to identify comorbidity, potential side effects, and drug response. We also use Danish population-based registries to validate the outcome of various pharmacological interventions. The national registries also play an increasing role in WP3 and WP5.

Over the last 12 months, WP1 has published a paper in which we identified a bi-directional relationship between depression and epilepsy: The risk of depression was highest in the few years preceding and after an epilepsy diagnosis, and vice versa, but remained elevated. Getting a diagnosis of

depression after an epilepsy diagnosis is associated with a 1.20-fold hazard ratio of acute hospital admission with seizures (doi: 10.1212/wnl.0000000000201542). In 2023, WP1 PhD student Eva Bølling-Ladegaard handed in and successfully defended her PhD thesis, thereby becoming the first PhD out of the *BrainDrugs* alliance.

WP2-leaders: Professors Søren Brunak & Anders Søgaard

WP2: Electronic patient data: Text mining and machine learning

WP2 uses text mining methods to extract detailed, phenotypic features from free text in Electronic Patient Records which come from either the Capital Region of Demark and Region Zealand from 2009-2018 or from the specialized national epilepsy hospital, Filadelfia.

In 2023, we have published two papers, the first of which is a central WP2 paper on how to electronically subgroup epilepsy cases into focal and generalized subcategories [70]. We here demonstrate how text-mining can be used to overcome the limited diagnostic precision of epilepsy diagnoses as listed in the National Patient Registry by letting text-mining drive the epilepsy subtype classification into focal, generalized, or unclassifiable epilepsy types. This improves the use of the register for our in-depth studies in *BrainDrugs* and we will employ the resulting subgroupings going forward when examining adverse drug reactions based on the Electronic Patient Records, and for pharmacogenomics work when genotypes are available. In a second paper we have published examples of different types of plots and tools useful for the overviewing and analysing of large longitudinal health datasets (doi: 10.3389/fbinf.2023.1112113).

WP2 capitalizes greatly from the epilepsy expertise available in WP1 and WP4, and at the same time also contributes directly to the other work packages by enabling broader access to the WP2 developed tools.

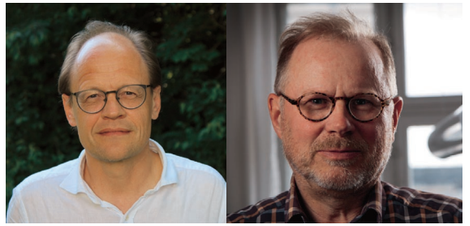
WP3. Deep phenotyping data from established research cohorts

By exploiting existing data from the NRU-anchored Lundbeck Foundation Center Cimbi database and from the Neurocognition and Emotion in Affective Disorders (NEAD) Group database, WP3 aims to identify biomarkers that are predictive of symptom resilience or vulnerability, or treatment outcome; e.g., certain genetic, epigenetic, cognitive, molecular and functional neuroimaging features. These existing cohorts are particularly important because they also contain deep phenotyping data from a large number of healthy controls which serve as an important reference for our patient studies. They also uniquely enable us to conduct register-based follow-up studies to establish which features in clinically healthy individuals can predict later development of depressive episodes; information which can be extracted from the national registries.

WP3-leaders: Professors Vibe Frøkjær & Kamilla Miskowiak

In 2023, we have continued working with our “deep phenotyping” data from the Cimbi Database and the NEAD database in combination with data from the National Health Register and the drug prescription register, and this has resulted in a total of eight publications [37], most of which are discussed in other sections of this annual report.

WP4. Deep phenotyping data from new research cohorts



WP4-leaders: Professors Lars Pinborg & Martin B. Jørgensen

WP4 establishes two new cohorts of patients with MDD and epilepsy, respectively. Patients are deep phenotyped and followed longitudinally. With the experience gained from the other work packages, we use these cohorts to address new research questions and when relevant, to replicate previous findings.

As for the MDD cohort, we work in close collaboration with the Mental Health services in the Capital Region, where patients are recruited through the central visitation and six clinics. So far, we have included 280 patients, accounting for approximately 10% of the Region’s annual patient flow. We acquire either basic or expanded clinical, cognitive, psychometric, and biological data, and for a subset of patients, we also collect MRI and EEG data, and in another subset PET imaging data with the [^{11}C]-UCB-J tracer of synaptic density is also done. The study protocol is described in detail in [28]. A preliminary analysis finds that patients that undergo neuroimaging do not differ from those who do not; depression severity and several other metrics are similar reassuring that there is limited selection bias.

Patients with epilepsy are recruited from the Copenhagen area with assistance from dedicated neurologists from Rigshospitalet, Bispebjerg Hospital, and Herlev Hospital. At Rigshospitalet, 6 specialist doctors, 1 neuropsychologist, and a project nurse are directly involved in the project on a daily basis. All workflows have been optimized so patients are promptly seen in the epilepsy clinic and undergo an extensive examination program in close collaboration with NRU, Dept of Diagnostic Radiology, and Dept of Clinical Physiology & Nuclear Medicine. Over the past year, more than 100 patients have been enrolled and they are followed in the epilepsy clinic with frequent check-ups, distribution of questionnaires, and through self-reporting via a smartphone app developed for the project. We are constantly working on implementing the project experiences into the clinical routine, including utilizing the capabilities of the electronic patient journal system. The study protocol is described in detail in [46].

WP5. Mining neuroimaging data

WP5 focuses on establishing models to identify structural abnormalities relevant to epilepsy in structural MR images in order to assist clinicians in their diagnosis. To train these models, we leverage existing MR data available from the PACS medical imaging archival system of the Capital Region of Denmark. We aim to create language models able to process the associated radiology reports and provide corresponding labels characterizing the pathologies described.

WP5-leaders: Associate professor Melanie Ganz-Benjaminsen & professor Gitte Moos Knudsen

In 2023, we have pushed forward the data extraction from the data archival system of Rigshospitalet. We retrieved the MR images and corresponding radiology reports from our first cohort of 4,500 epilepsy patients. Furthermore, another ~1.6 million radiology reports were extracted and these will allow us to create large language models specialized for Danish medical text. We also obtained a data extraction from Sundhedsplatformen with detailed data from 42,000 epilepsy patients, including clinical notes, demographics and diagnostic history. This new invaluable source of information will be used to drive our analyses and also be essential for identifying patients missing from the initial cohort and significantly enlarge our dataset.

By using data from the first cohort of epilepsy patients we have established end-to-end workflows for labelling abnormalities identified in radiology reports and identifying these features in the corresponding MR images. Extensive work was first accomplished to manually label some of the radiology reports for training language models to label unseen reports. We identified an efficient strategy to compensate for the lack of Danish language models by using an approach combining knowledge distillation and a few-samples training. By using this approach, our language models achieved an accuracy ranging from 85 to 90% in a limited sample. We also trained deep learning classifiers to use the labels associated to the radiology reports and identify abnormalities in MR images. In a preliminary investigation, our model was able to identify the presence or absence of abnormalities in MR images with an accuracy of 85%. Future work will concentrate on improving the language and image classification models as well as extend them to specific types of brain abnormalities specific to epilepsy.

Based on data from the Cimbi Database, we have investigated the association between the EEG-based loudness dependence of auditory evoked potential (LDAEP), serotonergic neurotransmission and treatment outcome in patients with MDD [25]. Our results support that both the LDAEP and the cerebral serotonin 4 receptor are indices of cerebral serotonin levels in healthy individuals while this association is disrupted in MDD. We conclude that the combination of the two biomarkers may be useful for stratifying patients with MDD in terms of how they can benefit from serotonin reuptake inhibitor drug treatment.

ecnp Neuroscience applied

For the science and treatment of disorders of the brain

The European College of Neuropsychopharmacology (ECNP) is an independent scientific association dedicated to the science and treatment of disorders of the brain. It is the largest non-institutional supporter of applied and translational neuroscience research and education in Europe.

As president of ECNP from 2019-22, professor Gitte Moos Knudsen is now board member as ECNP past-president, from 2022-25.

The ECNP Thematic Working Group (TWG) on Psychedelics, chaired by Gitte Moos Knudsen, organized the ECNP New Frontiers Meeting in Nice in March. The meeting was very well attended by both academia, European Medicines Agency, and the industry within the field of psychedelics and the TWG subsequently together wrote two status papers on knowledge gaps (https://doi.org/10.1016/j.nsa.2023.103929 and https://doi.org/10.1016/j.nsa.2024.103938).

Every year, NRU receives interns through the ECNP visiting scientists' program. NRU is involved in several of the ECNP Networks and in 2023, more than 15 NRU scientists were represented at the annual congress in Barcelona (see photo to the right).

Dissemination in 2023

Since the beginning of 2023, NRU has published a total of 3 PhD dissertations, 19 Master's or Bachelor theses and reports, and 74 scientific peer-reviewed papers, and 1 preprint. All papers that have either been printed or are online ahead of print during 2023 are included.

PhD dissertations

- Annette Johansen. Molecular neuroimaging of synaptic plasticity in the human brain. University of Copenhagen, Faculty of Health and Medical Sciences. Defended Dec 08, 2023
- Gjertrud Louise Laurell. Development of Novel Methods for PET-Based Quantification of Drug Interactions in the Living Human Brain. University of Copenhagen, Faculty of Health and Medical Sciences. Defended Mar 10, 2023
- Sophia Armand. Affective cognition and brain serotonin in healthy individuals - The role of brain serotonin in cognitive-affective biases and amygdala response to threat. University of Copenhagen, Faculty of Social Sciences. Defended Jan 10, 2023.

Master's and Bachelor theses and reports

The following list of NRU-affiliated students have successfully defended their theses or research year reports during 2023:

- Anna Kauffmann - *The role of combined oral contraceptive use on serotonin 2A receptor brain architecture in healthy women*. Master's thesis in medicine, University of Copenhagen. Primary supervisor: Vibe G. Frøkjær.
- Camilla Mingzi Cao Xu - *Resting state functional magnetic resonance imaging as a non-invasive tool for epilepsy surgery and prediction of outcome*. Master's thesis in medicine, University of Copenhagen. Primary supervisor: Lars H. Pinborg
- Cheng Chen - *Myelin in MDD*. Master's thesis in bioinformatics, University of Copenhagen. Primary supervisor: Melanie Ganz-Benjaminsen.
- Emil Colliander - *Synaptic density and intelligence in healthy individuals: A [11C]UCB-J PET study.* Master's thesis in medicine, University of Copenhagen. Primary supervisor: Gitte Moos Knudsen.
- Emilie Frederikke Boye Mauritzon - *The association between neuroticism and cognitive flexibility: A CIMBI database study of healthy controls. Three instruments applicable in future studies of patients with chronic pain.* Master's thesis in medicine, University of Copenhagen. Primary supervisor: Louise Møller Jørgensen.
- Fatema Alseelawi - *Treatment response of lumbar fusion in patients with underlying depression and/or anxiety compared to patients without these comorbidities*. Bachelor's thesis in medicine, University of Copenhagen. Primary supervisor: Louise Møller Jørgensen.
- Hannah Juelsgart - *Investigating the Microstructure of Frontotemporal Grey and White Matter in Major Depressive Disorder Using Neurite Orientation Dispersion and Density Imaging*. Bachelor thesis in biomedical engineering, Technical University of Denmark and University of Copenhagen. Primary supervisors: Kristian Reveles Jensen & Cyril Pernet.
- Jacob Lund & Yaron Lahav - *Reproducibility and functional connectivity within eyes-closed resting state electroencephalography*. Bachelor thesis in machine learning and data science, University of Copenhagen. Primary supervisors: Melanie Ganz-Benjaminsen & Cyril Pernet.
- Joanna Wilkosz - *Neural processing of risk taking in entrepreneurs*. Master's thesis in neuroscience, University of Copenhagen. Primary supervisor: Gitte Moos Knudsen.
- Juliane Conradi Vestergaard - *Is serotonin transporter availability associated with the cortisol awakening response? An independent nonreplication*. Master's thesis in medicine, University of Copenhagen. Primary supervisor: Vibe G. Frøkjær.
- Kathrine Søndergaard Christensen - *MR-skanning af børn i alderen 4-10 år uden brug af generel anæstesi eller sedation*. Master's thesis in psychology, University of Copenhagen. Primary supervisor: Kamilla Woznica Miskowiak.
- Kristoffer Brendstrup-Brix - *Diffusion along the perivascular space and brain microstructural measures are associated with circadian time and self-reported sleep quality*. Master's thesis in medicine, University of Copenhagen. Primary supervisor: Gitte Moos Knudsen.
- Nina Elise Fultz - *Psilocybin modulates cortical and cerebrospinal fluid dynamics in healthy controls and headache-disordered patients*. Master's thesis in neuroscience, University of Copenhagen. Primary supervisors: Gitte Moos Knudsen & Hanne D. Hansen.
- Nora Falck - *Persisting effects of psilocybin on functional brain-network modularity in healthy volunteers*. Master's thesis in medicine, University of Copenhagen. Primary supervisor: Patrick M. Fisher.
- Ofelia Fischer Godske - *The effect of SSRI on patients with depression and childhood trauma compared to patients with depression and without childhood trauma*. Master's thesis in medicine, University of Copenhagen. Primary supervisor: Kristian Reveles Jensen.
- Robert Dunker Pedersen - *Exploring Neural Reactivity through Loudness Dependent Auditory Evoked Potentials: A Novel Analysis Method*. Master's thesis in biomedical engineering, Technical University of Denmark and University of Copenhagen. Primary supervisors: Kristian Reveles Jensen & Cyril Pernet.

- Thilde Koefeod Nielsen - *Association between the inflammation marker hsCRP and cognitive functioning in depression*. Master's thesis in psychology, University of Copenhagen. Primary supervisor: Signe Vangkilde.
- Victor Neufeld - *Persisting effects of psilocybin on functional brain activity during focused attention*. Master's thesis in medicine, University of Copenhagen. Primary supervisor: Patrick M. Fisher.
- Victoria Frederikke Stenderup Garre - *A Scoping Review of Functional Genomics in Perinatal Depression*. Master's thesis in medicine, University of Copenhagen. Primary supervisor: Vibe G. Frøkjær.

Books and book chapters

B1. Dam VH, Langley C, Stenbæk DS, Sahakian BJ. (2023) EMOTICOM Test Battery. In: The SAGE Handbook of Clinical Neuropsychology: Clinical Neuropsychological Assessment and Diagnosis. https://doi.org/10.4135/9781529789539

B2. Knudsen GM. Om hvordan én dosis af et klassisk psykedelisk stof kan have langvarige virkninger. In: Kevin Mikkelsen (ed). Et psykedelisk Danmark. København, 2023:50-60. ISBN: 9788793716988

B3. Messell C. Musikkens terapeutiske potentiale i forbindelse til udvidet bevidsthed. In: Kevin Mikkelsen (ed). Et psykedelisk Danmark. København, 2023:186-196. ISBN: 9788793716988

Papers in peer-reviewed journals

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2. Amiri M, Raimondo F, Fisher PM, Cacic Hribljan M, Sidaros A, Othman MH, Zibrandtsen I, Bergdal O, Fabritius ML, Hansen AE, Hassager C, Højgaard JLS, Jensen HR, Knudsen NV, Laursen EL, Møller JE, Nersesjan V, Nicolic M, Sigurdsson ST, Sitt JD, Sølling C, Welling KL, Willumsen LM, Hauerberg J, Larsen VA, Fabricius ME, Knudsen GM, Kjærgaard J, Møller K, Kondziella D. Multimodal Prediction of 3- and 12-Month Outcomes in ICU Patients with Acute Disorders of Consciousness. Neurocrit Care. 2023 Sep 11. doi: 10.1007/s12028-023-01816-z. *Epub ahead of print*
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Conference papers, preprints and proceedings

P1. Poldrack RA, Markiewicz CJ, Appelhoff S, Ashar YK, Auer T, Baillet S, Bansal S, Beltrachini L, Benar CG, Bertazzoli G, Bhogawar S, Blair RW, Bortoletto M, Boudreau M, Brooks TL, Calhoun VD, Castelli FM, Clement P, Cohen AL, Cohen-Adad J, D'Ambrosio S, de Hollander G, de la Iglesia-Vayá M, de la Vega A, Delorme A, Devinsky O, Draschkow D, Duff EP, DuPre E, Earl E, Esteban O, Feingold FW, Flandin G, Galassi A, Gallitto G, Ganz M, Gau R, Gholam J, Ghosh SS, Giacomel A, Gillman AG, Gleeson P, Gramfort A, Guay S, Guidali G, Halchenko YO, Handwerker DA, Hardcastle N, Herholz P, Hermes D, Honey CJ, Innis RB, Ioanas HI, Jahn A, Karakuzu A, Keator DB, Kiar G, Kincses B, Laird AR, Lau JC, Lazari A, Legarreta JH, Li A, Li X, Love BC, Lu H, Maumet C, Mazzamuto G, Meisler SL, Mikkelsen M, Mutsaerts H, Nichols TE, Nikolaidis A, Nilsonne G, Niso G, Norgaard M, Okell TW, Oostenveld R, Ort E, Park PJ, Pawlik M, Pernet CR, Pestilli F, Petr J, Phillips C, Poline JB, Pollonini L, Raamana PR, Ritter P, Rizzo G, Robbins KA, Rockhill AP, Rogers C, Rokem A, Rorden C, Routier A, Saborit-Torres JM, Salo T, Schirner M, Smith RE, Spisak T, Sprenger J, Swann NC, Szinte M, Takerkart S, Thirion B, Thomas AG, Torabian S, Varoquaux G, Voytek B, Welzel J, Wilson M, Yarkoni T, Gorgolewski KJ. The Past, Present, and Future of the Brain Imaging Data Structure (BIDS). ArXiv [Preprint]. 2023 Sep 11:arXiv:2309.05768v1

Media attention

Feb 02: Louise Møller Jørgensen was interviewed to an article "Hospital innovation to ensure more human contact through tech" published by Copenhagen Science City: https://copenhagensciencecity.dk/hospital-innovation-to-ensure-more-human-contact/ and on social media https://www.linkedin.com/company/copenhagen-science-city

Feb 6: Gitte Moos Knudsen was interviewed in a Human Brain Project podcast on her work exploring the impact of drugs on the brain, her involvement in the Human Brain Project, and the advice she'd give her younger self. YouTube: https://lnkd.in/eCax8mh9

Feb 11, 2023: PhD-student Kristian R. Jensen in the article "Med denne diagnose risikerer kvinder igen igen at blive set som uligevægtige og ustabile" in Jyllandsposten.

Feb 16: Gitte Moos Knudsen in the RH news article "Ny viden om dårlig hukommelse hos deprimerede": https://www.rigshospitalet.dk/presse-og-nyt/nyheder/nyheder/Sider/2023/februar/ny-viden-om-daarlig-hukommelse-hos-deprimerede.aspx

Mar 17: Gitte Moos Knudsen in the article "På vej til behandling af depression, angst og PTSD PSYKEDELISKE LÆGEMIDLER STÅR PÅ SPRING:" in Dagens Medicin:
https://dagensmedicin.dk/psykedeliske-laegemidler-staar-paa-spring-paa-vej-til-behandling-af-depression-angst-og-ptsd/

Mar 23: Des S. Stenbæk in the article "Danske forskere udvikler musikprogram til psykedelisk behandling" in Neurologisk Tidsskrift:
https://neurologisktidsskrift.dk/nyheder/448-danske-forskere-udvikler-musikprogram-til-psykedelisk-behandling.html

Apr 4: Gitte Moos Knudsen in the newspaper article "Nogle føler nemmere glæde end andre, men der er meget, du selv kan gøre for at få et lykkeligt liv" in Berlingske:
https://www.berlingske.dk/eksistens/nogle-foeler-nemmere-glaede-end-andre-men-der-er-meget-du-selv-kan-goere

Apr 7: Gitte Moos Knudsen in the newspaper article "PENGE GØR OS IKKE GLADE. DET GØR DE ANDRE" in Berlingske.

Apr 19: Gitte Moos Knudsen in the article "Depression giver dårligere hukommelse" in Medicinsk Tidsskrift:
https://www.medicinsktidsskrift.dk/behandlinger/psykiatri/4484-depression-giver-darligere-hukommelse.html

Apr 21: Mikael Palner wrote the article "Kan man aflære angst?" to videnskab.dk:
https://videnskab.dk/krop-sundhed/angst-gemmer-sig-i-din-hjerne-kan-du-aflaere-den-igen/

Apr 27: Gitte Moos Knudsen in the article "Depression giver dårligere hukommelse" in Sundhedspolitisk Tidsskrift:
https://sundhedspolitisktidsskrift.dk/nyheder/sygdom/7639-forskere-depression-giver-darligere-hukommelse.html

May 8: Vibe G. Frøkjær was interviewed as a guest on ABC radio about "Hormonal contraception as postpartum depression risk indicator":
https://www.abc.net.au/radionational/programs/healthreport/hormonal-contraception-as-postpartum-depression-risk-indicator/102317002

May 9: Mikael Palner in the newspaper article "Den tripfri version af lsd, tak" in Weekendavisen:
https://www.weekendavisen.dk/2023-19/ideer/den-tripfri-version-af-lsd-tak

May 11: Gitte Moos Knudsen in the Human Brain Project Podcast series in "Episode 2 - Psychedelics and Neuropharmacology: A Conversation with Gitte Moos Knudsen":
https://www.humanbrainproject.eu/en/follow-hbp/news/2023/05/11/listen-entire-human-brain-project-podcast-series/

May 17: Mikael Palner in the article "Opløser din virkelighed: Hjerneforskere bruger det psykedeliske stof DMT til at gå på opdagelse i bevidstheden" in videnskab.dk:
https://videnskab.dk/krop-sundhed/oploeser-din-virkelighed-hjerneforskere-bruger-det-psykedeliske-stof-dmt-til-at-gaa-paa-opdagelse-i-bevidstheden/

May 31: Louise Møller Jørgensen was interviewed to a newspaper article: *"Innovation bliver obligatorisk på Medicin: Det er*

supervigtigt, at læger fremover ved, hvad det kræver at realisere en god idé" published in Uniavisen: https://uniavisen.dk/innovation-bliver-obligatorisk-paa-medicindet-er-supervigtigt-at-laeger-fremover-ved-hvad-det-kraever-at-realisere-en-god-ide/

Jun 20: Mikael Palner was interviewed to the DR radio program "Op af kaninhullet" as part of the episode "Er DMT nøglen til en anden dimension?": https://www.dr.dk/lyd/special-radio/op-af-kaninhullet/op-af-kaninhullet-2023/op-af-kaninhullet-er-dmt-noeglen-til-en-anden-dimension-16122393121

Sep 13, 2023: PhD-student Kristian R. Jensen in "Kristian behandler "dræber-PMS". De her gener går igen hos kvinderne" in Femina.

Oct 9: Vibe G. Frøkjær in a podcast episode on "Hormoner som forskningsmæssig kampplads" as part of the podcast series '24 spørgsmål til professoren' with science journalist Lone Frank: https://www.weekendavisen.dk/24spoergsmaal/hormoner-som-forskningsmaessig-kampplads

Oct 12: Mikael Palner was interviewed to the Mind & Matter podcast as part of the episode "Psychedelics, Microdosing Psilocybin, Stress Resilience, Anxiety & OCD": https://www.youtube.com/watch?v=AU_uQ-XOW2s

Oct 12: More than 200 different media attentions related to our recent Molecular Psychiatry paper [30], Almetric Score 332, including a press release from the ECNP: Is this how antidepressants work, and why they take weeks to kick-in?

Oct 23: Gitte Moos Knudsen quoted in the article https://ucscsciencenotes.com/feature/depression-treatment-with-mushrooming-potential/s

Oct 26: Melanie Ganz in the article "*Eksperter bag nyt forskningsprojekt kalder på forsigtig udrulning af AI-modeller i det offentlige*" in Altinget about AI in the public sector: https://www.altinget.dk/digital/artikel/eksperter-bag-nyt-forskningsprojekt-kalder-paa-forsigtig-udrulning-af-ai-modeller-i-det-offentlige

Oct 29: Mikael Palner was interviewed to the Radio4 podcast "Notesbogen" as part of the episode "Line Knutzon: Er jeg en svamp?": https://radio4.dk/podcasts/notesbogen/line-knutzon-er-jeg-en-svamp

Nov 9: Article with Gitte Moos Knudsen about our recent Molecular Psychiatry paper (Johansen et. al) and article with Vibe G. Frøkjær about anhedonia and depression.

Nov 29: PhD-student Kristian Larsen was interviewed in Go' Morgen Danmark on TV2 about the LSD project in which the first participant had the first intervention later the same day: https://play.tv2.dk/serie/go-morgen-danmark-tv2/nye-danske-lsd-forsoeg-mod-depression-46e89020-4544-4f83-a655-d544f0e09579 (from 4:19 to 12:43)

Dec 27: Gitte Moos Knudsen in the article "Ny bog om medicinsk brug af psykedelika skiller skidt fra kanel" in Sundhedskultur: https://sundhedskultur.dk/boger/670-ny-bog-om-medicinsk-brug-af-psykedelika-skiller-skidt-fra-kanel.html

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